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Phytochemical study of plants used traditionally for cosmetics and medicine in the island of Mayotte.

Matthew Saive

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Saive Matthew, (2021). Phytochemical study of plants used traditionally for cosmetics and medicine in the island of Mayotte. (PhD thesis). University of Liège – Gembloux Agro-Bio Tech. 213p., 23 fig., 9 table

Summary: The Indian ocean is one of the biggest source of botanical diversity in the world, 25% of the world's flora can be found in those islands. In addition, people living in that area, have been using what nature has to offer to treat themselves for centuries. In this work we focused on the Comoros archipelago and more precisely on the island of Mayotte. The socio-economic situation of the area has been precarious since the end of the Ylang-ylang (*Cananga odorata* (Lam.) Hook.f. & Thomson) industry. The aim of this thesis is to provide the inhabitants with an analysis of plant species with the potential for the development of local cosmetic products. Through the analysis of the traditional knowledge we were hoping to find the ideal species for this project. First, a preliminary study was conducted leading to the identification of more than 200 different species which could be useful. Following this first work, an infield ethnobotanical study was conducted allowing for the identification of 69 species which were interesting. By cross referencing the previously gathered information 21 different species were identified for collection and the analysis so as to validate their real biological activity: the lipoxygenase inhibition potential, the tyrosinase inhibition potential and the DPPH (2,2-diphenyl-1-picrylhydrazyl) reduction potential. The most active species then underwent a selection process based on current knowledge-to-date and availability. Following this selection, we focused on the roots of the litchi plant (*Litchi chinensis* Sonn.). The last step of this work consisted of the identification of the compound responsible for the observed activities. This was achieved by submitting the crude extract of *L. chinensis* to a bio-guided fractionation until only a single compound remained. The purified compound then went through the following molecular identification process: UV, IR, MS, RMN and colorimetric analysis. Finally, these process allowed us to identify a compound from the polyphenol family: cinnamtannin D2 (CAS number : 97233-47-1).

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Résumé: L'océan Indien est une des plus grande source de variété botanique du monde, 25% de la flore mondiale peut être trouvée dans les îles qui s'y trouvent. De plus les peuples qui habitent ces régions utilisent ce que la nature a à leur offrir pour se soigner depuis des centaines d'années. Dans ce travail nous nous somme focalisés sur l'archipel des Comores et plus précisément, l'île de Mayotte. Cette région est en situation socio-économique précaire depuis le déclin de l'industrie de l'Ylang-ylang (*Cananga odorata* (Lam.) Hook.f. & Thomson). Cette thèse a pour but de fournir aux habitants une analyse des espèces végétales potentiellement valorisables pour le développement de produits cosmétiques. En analysant les savoirs traditionnels, nous avions l'espoir de trouver l'espèce idéale pour ce projet. Dans un premier temps, une étude préliminaire a été réalisée, à la suite de laquelle plus de 200 espèces différentes ont été identifiées. Ce premier travail fut suivi d'une étude de terrain, à l'issue de laquelle 69 espèces intéressantes ont pu être identifiées. En croisant les informations obtenues lors des 2 premières étapes de ce travail, un total de 21 espèces ont été collectées afin d'être analysées pour cibler les échantillons présentant des activités biologiques réelles. Celles-ci étaient les suivantes : l'évaluation du pouvoir d'inhibition de la lipoxygénase, l'évaluation du pouvoir d'inhibition de la tyrosinase et l'évaluation du pouvoir de réduction du DPPH (2,2-diphenyl-1-picrylhydrazyl). Les espèces présentant les meilleures activités ont fait l'objet d'une sélection basée sur l'état des connaissances les concernant et leur disponibilité. A l'issue de cette sélection, nous avons décidé de nous focaliser sur les racines de Litchi (*Litchi chinensis* Sonn.). La dernière étape de ce travail a consisté en l'identification d'un composé responsable des activités observées. Pour se faire l'extrait brut de racine de *L. chinensis* a été soumis à un fractionnement bio-guidé jusqu'à l'obtention d'un composé unique. Celui-ci a ensuite été soumis aux tests d'identification moléculaire suivants : UV, IR, MS, RMN et colorimétrique. Le résultat de ces analyses nous a permis d'identifier un composé issu de la famille des polyphénols, le cinnamtannin D2 (numéro CAS : 97233-47-1).

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“It does not matter how slowly you go so long as you do not stop.”

Confucius

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1

GENERAL INTRODUCTION

1. Global context of the study

This work is part of a European operation that started in 2014. The objective behind this project was to contribute to developing Mayotte's economy, through the valorization of locally available resources. Due to its location as the most southern Island of the Comoros archipelago, Mayotte is home to more than 1300 vascular species (O Pascal, 2002). In addition to this wide biodiversity, the Mahoran (inhabitants of Mayotte) women, are known for the traditional cosmetics they wear proudly day in and day out. Thus, biodiversity and tradition led to the idea of exploring the floral potency of the island through the development of cosmetics. The expected outputs from such undertaking were, the recognition and recording of valuable knowledge, the identification of potential cosmetics crops, medicinal crops or both so as to implement a new economic sector.

2. Economic situation of the study area

Up until the 19th century, the local population lived from self-sufficient subsistence production. Starting in 1805, the sugar cane industry started to flourish and considerably enriched the inhabitants of the island. This lucrative commerce lasted until 1885, then declined until the last sugar company close its doors in 1955. As this first industry diminished, local growers started diversifying their production, progressively replacing sugar cane by cloves, coffee, cocoa, copra, sisal and especially vanilla. This diversification, however, was not as flourishing as the sugar cane industry and started marked the end of the colonial cash crop model. By the end of the second world war that economic models were barely sufficient. Due to low sales, a lack of organization for the vanilla industry, and the appearance of synthetic fibers which replaced the sisal industry cash crop could no longer provide enough revenue. Therefore, a new industry was developed. Barks, flowers, roots, leaves, seeds from all sorts of plants were transformed into essential oils, through hydro-distillation or vapo-distillation. Lemon grass (*Cimbopogon nadrus*), palmarosa (*Cymbopogon martini*), jasmin (*Jasminum bojeri*), basil (*Ocimum* sp.), vetiver (*Vetivera* sp) and ylang-ylang (*Cananga odorata*) were the most used. That is when the Island got its honorary surname "Île au Parfum" meaning the Perfume Island. The fragrance business fluctuated between 1955 and 1970, even with the diversification of essential oil production to include other species such as cloves (*Syzygium aromaticum*), cinnamon, (*Cinnamomum* sp.) orange blossom (*Citrus* sp.). The additional products yield the expected results and only the production of ylang-ylang essential oil subsisted after 1970 and until 1999. This was thanks to the creation of the perfume "*Maora*" by Jean-Paul Guerlain. Since then, Mayotte has disappeared from the maps from an economic point of view (Nace, 2008). Ever since, the local population has returned to its old habits and the locals mostly live on subsistence crops (Mayet et al., 2014).

3. Political and social status of the study area

These successive industrial phases took place on an island that was also undergoing changes from a political viewpoint. In 1843 Mayotte was given to France by the Sultan Andriantsouli. In contrast to the other islands in the archipelago, it became a French Colony. Then in 1946, the whole archipelago officially became a French outer sea territory (Territoire d'outre mer).The question of the independence of the archipelago arose in 1974, leading to a separation between Mayotte and the three other islands. As more than 60% of the population wanted to stay under French protection, Mayotte obtained the title of Territorial Collectivity of the Republic. In 2001, Mayotte officially became a departmental collectivity and in 2011 it became the 101st French department. The last political change Mayotte went through results from a request France made to the European Union, asking for Mayotte to become a European ultra-peripheric region (RUP). This request was accepted in 2012 and officially signed in 2014 (Ali Charif et al., 2016). These latest changes led to the development of a "catch-up policy" based on public transfers (budgetary allocations, increase in social minima, new services, indexation of public wages) and an increase in expenses. This campaign created fast-economic growth and an increase in the average quality of life for most of the population. However, it maintained the territorial and wage disparities. With the accession to RUP status, Mayotte became entitled to ask for European structural funds. This was a historic opportunity for Mayotte to finish what had been started with the accession to French departmental privileges.

The massive investment in Mayotte led to some issues with the surrounding islands. The Comoros Union composed of Anjouan Moheli and Grande-Comore is poor and the distance between Mayotte and the closest Island of the Comoros (Anjouan) is only 70km. This led to the tempting option of migrating to the Island in hopes of a better life. The crossing is not without risk for the inhabitants of the Comoros. The boats (also known as "*Kwasa kwasa*" (meaning coffin) used by the smugglers are usually small fishing boats destined for 8 to 12 persons, but most of the time more than double that number is on board. That and the fact that this part of the ocean can be capricious renders the trip very dangerous. The people on board these boats risk their lives. Moreover, if by chance they do reach the Mahoran coasts, their situation is still very precarious. They will most probably end up in slums and be subject to abuse as their illegal immigrant status prevents any form of control. They could also be sent back to where they came from, rendering the dangerous crossing futile. For example, in 2005, 7655 illegal immigrants were sent back. Due to the number of immigrants arriving, up to 16000 per year (in 2015) (Wu-Tiu-Yen, 2015), and due to the island's small size (374km^2), the immigration issue has caused tension between the migrant population and the Mahoran population (Chaussy et al., 2019; Wu-Tiu-Yen, 2015).

In addition to this high immigration rate, Mayotte is also the French department with the highest birth rate of 5 children per woman (INSEE, 2019). Such massive demographic growth calls for investments so as to feed, house and educate the population, requiring increasingly greater assistance from the European Union.

Why is Mayotte so dependent on external aid? In 2016 the island produced 65% of the goods required to sustain its population, meaning that 35% of the goods available

on the Island had to be imported (DAAF, 2017). In addition, due to its geographical and geological conformation Mayotte is not designed to produce cash crops.

The first issue resides in its size. Mayotte is a tiny Island (374 km³). The second issue is linked to its volcanic origin, causing a very hilly landscape which is difficult to cultivate. 63% of the island is covered by 15% or more slopes (Mayet et al., 2014). Even if 42% of the island is covered by agricultural crops, they must be shared between 80% of the inhabitants who depend on these for subsistence. With an average surface per household of 1/2 hectare, manioc and banana are the main cultivated crops (Ministere de l'agriculture et de l'alimentation, 2016). A few ylang-ylang and vanilla plantations are still running, but not so much for production as for agrotourism.

Developing new cash crops is in line with the objectives set by the EU between 2014 and 2020, whose main points as mentioned in the "Programme Opérationnel FEDER-FSE Mayotte 2014 - 2020" are as follows:

- Promote entrepreneurship and the creation of SMEs (small and medium-sized enterprises), including micro-enterprises
- Increase access to employment for unemployed and inactive people, including the long-term unemployed and those furthest from the labor market
- Improve the competitiveness of SMEs
- Preserve biodiversity

The cash crop would have to valorize readily available knowledge in order to be rapidly implementable and therefore should take into account the history of the island and the cultural habits of the inhabitants. One of these cultural habits is the wearing of the traditional masks by the local women during the day. These beauty masks are called "*Mzindzano*" (Fig. 1) and are composed of all sorts of species of plants and herbs for many different purposes. The composition of the masks impacts the color and has benefits for the skin. When cross referencing such information with the historical background of the island, especially the Ylang-ylang era and what is left of Jean-Paul Guerlain's perfume, the cosmetics industry was the ideal target. Not only was it in line with what the island had to offer, it could also lead to high added value products, compensating for the lack of cultivatable surface.

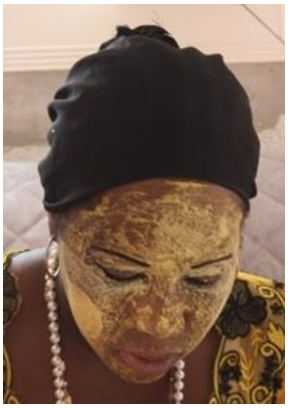

Figure 1: Traditional beauty mask (Mzindzano). Credit Matthew Saive.

4. Geography of the study area

As mentioned above, Mayotte is the southernmost and oldest (around 8 000 000 years) island of the Comoros archipelago, with a land area of 374 km², located north of the Mozambique Channel between Madagascar (295 km) and the African continent (500 km) (Fabien Barthelat & Viscardi, 2012). It is composed of two main islands (Grande-Terre and Petite Terre) and around 30 other small islets. This group of islands is surrounded by a double coral reef 160 km long which encloses one of the biggest lagoons in the world (more than 1110 km²). The main island was shaped by 6 eroded mountains. The highest summit of the island reaches 660 m (mount Benara). This geological conformation earned it the name of Seahorse island (Fig. 2) (Ali Charif et al., 2016).

The whole archipelago is of volcanic origin; the islands are volcanic peaks. Outside the coral reef, the sea bottom can reach a depth of 3400 m in some places (Lacquement et al., 2013). This volcanic origin also causes a very specific type of soil. The main island (Grande-Terre) has a soil composed of basaltic rock, ashes, and calcic debris deposited while it was emerged, and which had the time to react with the atmosphere over millennia and become ferralitic. Whereas the small island (Petite-Terre) is relatively young (1 000 000 years old) and therefore has a substrate composed mainly of calcic materials with very little ferrallitization (Fabien Barthelat & Viscardi, 2012).

Figure 2: Map of Mayotte's location, relief and main agglomerations. The 6 mountains composing the shape of the seahorse are Mount Bénara (660 m), Mount Choungui (594 m), Mount Mtsapéré (572 m), Mount Combani (481 m), Mount Dziani Bolé (439 m) and the peak Ngoujou (292 m) (geoportail.gouv.fr, 2016).

5. Climate of the study area

The climate of the island is tropical maritime; there are two seasons, a warm and rainy season, and a dry and colder season. The austral summer corresponding to the rainy season occurs between October and March when the temperatures range between 29°C and 34°C, the relative humidity is high (around 85%) and most of the

yearly rainfall occurs. Mayotte can be subject to tropical storms but they generally decline in magnitude when crossing Madagascar. The Austral winter corresponds to the dry season and lasts from April to September. During that time, the temperature range is between 22°C and 25°C.

During the dry season, there is a strong variation in the amount of precipitation between the southern part of the island and the northern part of the island as illustrated in figure 3. The northern part of the island can have receive up to 2300 mm whereas in the southern part the amount of rainfalls rarely exceeds 1200 mm (Fabien Barthelat & Viscardi, 2012). This can be explained by the presence of a north wind that brings moist air to the island during the austral summer. This air is retained by the mountains, producing a rain shadow on the other side known as the orographic effect (Météo France, 2020).

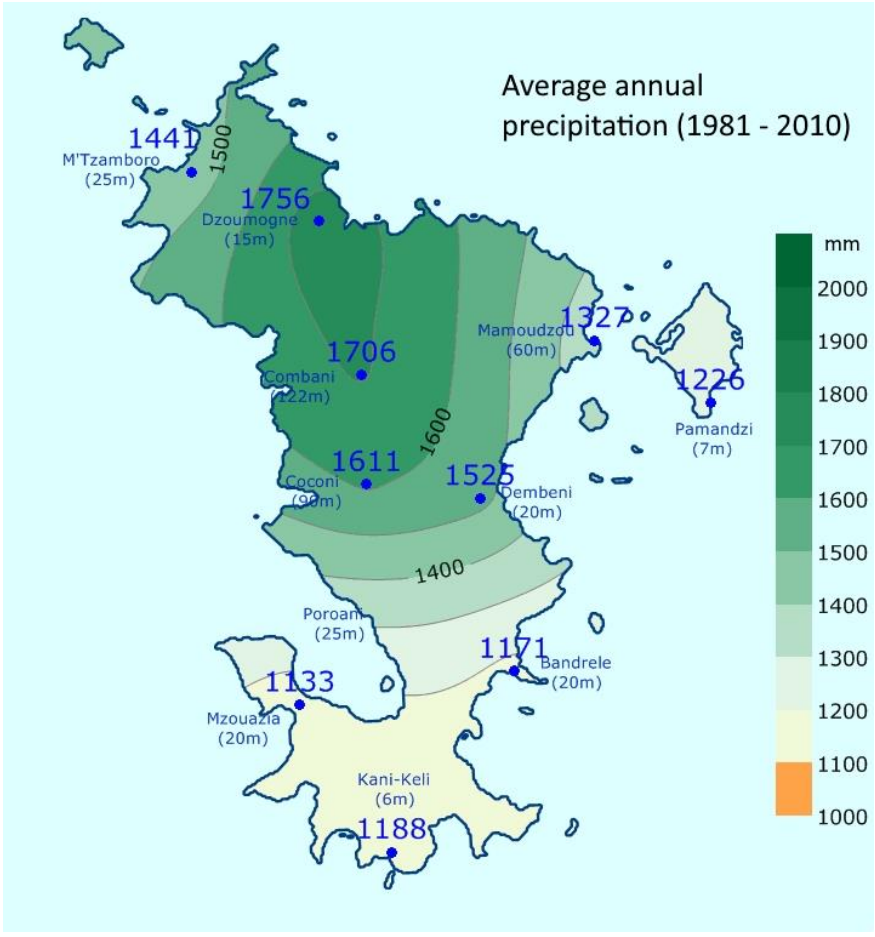

Figure 3: Average annual precipitation observed between 1981 and 2010 based on at least 16 years of data (Météo France, 2020).

6. Flora of the study area

The climatic, geopedological, geographic, and geologic characteristics of Mayotte produce a variety of environments. Due to the island's configuration, a phytogeographic classification can be made as shown in figure 4. Plants linked to coastal environments are found at sea level; as the terrain rises, the following environments can be found and are classified thusly: ad coastal, sub humid, meso humid, humid and submontane. On the one hand, the amount of precipitation is impacted by the altitude and is also strongly impacted by the orientation. On the other hand the temperature is only impacted by the altitude of the different regions. Such versatility of conditions is ideal for the development of many different species. This might be why, regardless of its small size, Mayotte is home to more than 1300 vascular species (Fabien Barthelat, 2019). Among those species, 49 are strictly endemic to Mayotte, 70 are endemic to the Comoros Archipelago and 145 are endemic to the western region of the Indian Ocean. 399 species are indigenous to Mayotte. The other species are exotic (Fig. 5).

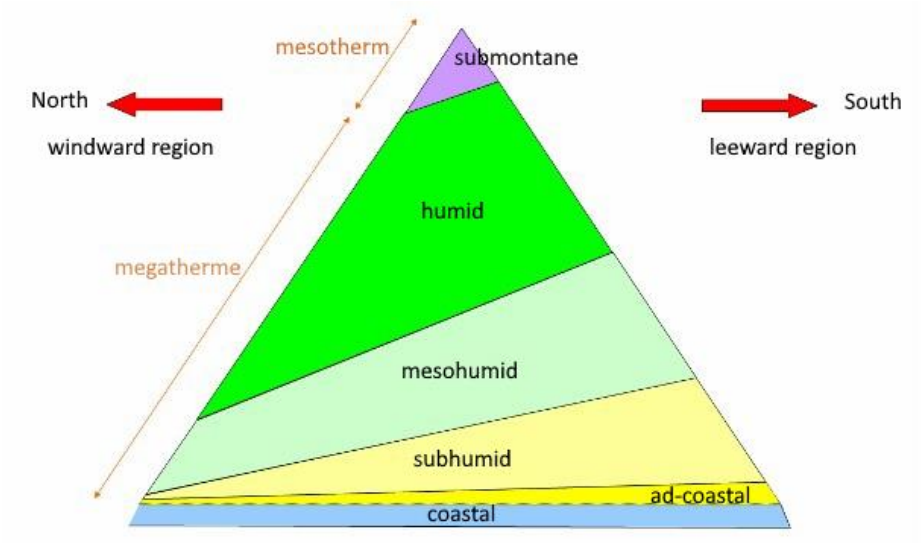

Figure 4: Summary of the main types of habitat observed on Mayotte based on orientation, temperature and altitude (Boullet, 2016).

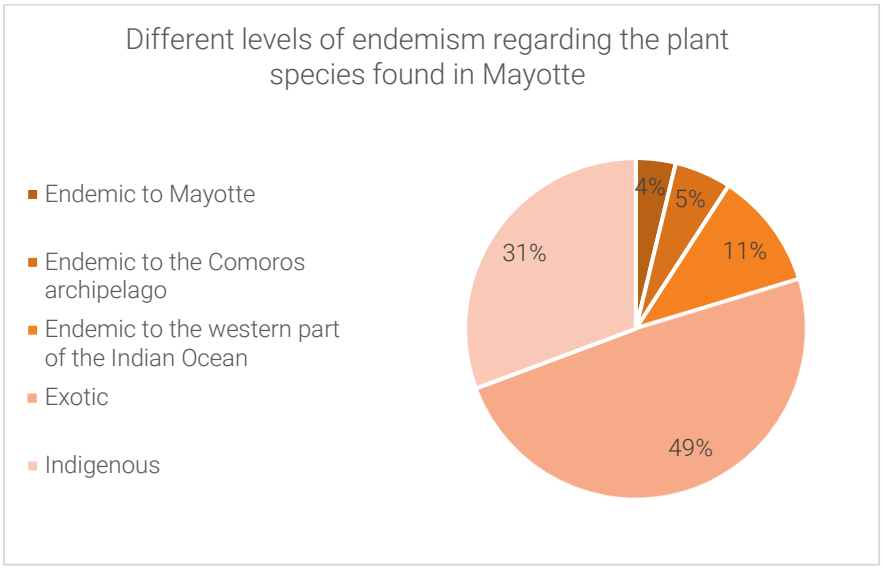

Figure 5: Repartition percentage of endemism of the species found in Mayotte based on the work of (Fabien Barthelat & Viscardi, 2012).

7. Key concepts

7.1. Ethnobotany, ethnopharmacology and phytochemistry

Ethnobotany can be defined as "*The study of the classification, use and management of plants by people.*" (Martin, 1995). It covers a wide diversity of disciplines such as botany, anthropology, ecology, economics, and linguistics. Through these disciplines, ethnobotany aims to identify and understand the relationship between humans and plants by using specific tools and techniques (Heinrich, 2015). Trotter and Logan have played an important role in the developpement of these tools and techniques. In their work entitled:" *Informant Consensus: A New approach for Identifying Potential Effective Medicinal Plants*", they have identified certain working conditions destined to enhance the quality of the collected data. These conditions are: a sufficiently large data base, a defined scope for the interviews, and a clear identification of the mentioned species. Once the raw data has been gathered, they also worked on the development of tools destined to evaluate the significance of the information collected as well as the potential real effectiveness of the species (Trotter & Logan, 1986). This approach is directly linked to what would become known later as ethnopharmacology. This discipline can be defined as a "*multidisciplinary area of research concerned with the observation, description, and experimental investigation of indigenous drugs and their biological activity*" (Rivier & Bruhn, 1979). It purposes to study certain species based on their traditional uses to evaluate their biological activities. This discipline is strongly linked to the discovery of many important drugs still in use today. However, to identify the compound(s) responsible for the different biological activities(s), the targeted species must undergo a phytochemical analysis which focuses on the composition of plants. Through analytical techniques, the chemical composition of crude extracts originating from plant species chosen based on ethnobotanical work and ethnopharmacological studies can be determined. The combination of all the above disciplines has led to the discovery of many important compounds such as, opiates from *Papaver somniferum* L. (Marciano et al., 2018), quinine from *Cinchona sp.* (Frosch et al., 2007), vinblastine and vincristine from *Catharanthus roseus* (S. N. Pandey et al., 2020) or cocaine from *Erythroxylum coca* L. (Beyer, 2013; Weniger & Bourdy, 2008).

8. Thesis organization

8.1. Objective of the first article – what is known

As the type of industry had been targeted and the subject matter had been identified, the first requirement for this work was some in-depth research on the species used traditionally as skin care products by the inhabitants of Mayotte. This task was covered through the realization of a bibliographic review on the traditional uses of plants in the Comoros Archipelago and it allowed for a better understanding of what to expect when doing the infield research. However, when the available information was cross referenced with that found in the literature, a feeble percentage of uses were only for cosmetics. This observation meant that the infield work would have to include

traditional medicinal practices linked to skin care in order to broaden the spectrum of species of interest for the following steps of this work.

8.2. Objective of the second article – let's ask the ones who know

The aim of the second part of this work resided in gathering as much information as possible on the traditional uses of plants for cosmetics and skin care in Mayotte. This was achieved by looking for the keepers of the knowledge, also known as "*Foundi*" in Mayotte and by applying the ethnobotanical principle developed by (Trotter & Logan, 1986). The information was gathered through the realization of interviews oriented towards the uses of plants for cosmetics and skin care applications. As the search for information was oriented, the people interviewed were composed of traditional doctors as well as estheticians and masseuses, in addition to some other women who were willing to speak about the "*Mzindzano*". Surprisingly enough, when it came to the composition of the mask, not all women wanted to share their secrets.

8.3. Objective of the third article – evaluation of the activities

This section aimed to validate the real effectiveness of the available species from either the review work or the ethnobotanical study. This task was achieved following an infield sampling mission. The sample collection was made at sunrise and regardless of the traditional way the species were used, all available parts of the plant at the time of the mission were collected. The plant parts were then conditioned and submitted to assays destined to establish their potency as reactive oxygen species reducing properties, lipoxygenase inhibitory properties and tyrosinase inhibitory properties. These properties were chosen as they would be of interest in the creation of a cosmetic related new source of revenue. In addition to allowing for focus on species showing measurable biological activity it also gave insight into the reliability of results from the previous ethnobotanical studies.

8.4. Objective of the fourth article – molecular identification

Based on the results of the third article, we decided to focus on a single organ from a single species. Therefore, the purpose of this part of the work was to identify the compound responsible for the measured biological activity. This was achieved through a bio-guided fractionation using chromatographic techniques. Each new intermediate fraction was submitted to the targeted biological assays, thus tracking the activity as we moved towards obtaining a purified compound. The final step of this work was the molecular identification of the compound of interest using colorimetric assay, ultra-violet, infrared, nuclear magnetic resonance, and liquid chromatography coupled with mass spectrometry. The identified compound was then compared with the literature based on the observed biological activities and phytochemical analysis performed on other organs of the selected species.

2

BIBLIOGRAPHIC REVIEW

Saive, M., Frederich, M. and Fauconnier, M.-L. (2020) 'Plants used in traditional medicine in the Comoros archipelago: a review', Biotechnologie, Agronomie, Société et Environnement. Presses Agronomiques de Gembloux, 24(2), pp. 117–141.

In this primary approach to the traditional uses of plant, we were looking for information that would allow us to have clear understanding of what traditional medicine and cosmetics meant and what was already available in the literature regarding the area of interest. We found some valuable information including some database used by ethnobotanists as well as books written in collaboration with the local inhabitants. We also needed to obtain an overview of the huge amount of knowledge the local population had gathered from ancestral practices. As the information was written down, it entered into a process of safekeeping as well as of making it available for others. Through this first step we identified species of interest to be used in medicine and cosmetics.

From a methodological point of view, the selection of the data was obtained by extensive bibliographical research. A systematic approach was chosen to conduct this review. The data was obtained by analyzing the worldwide accepted scientific database and the ethnobotanical database "PRELUDE". The research was conducted using the following key words: "Comoros archipelago ethnobotany", "Comoros archipelago ethnopharmacology", "Comoros archipelago traditional medicine", "Comoros archipelago traditional cosmetics". As the PRELUDE data base had already gathered information regarding traditional uses, the search was conducted using only the location of interest, in this case "Comoros". Once the list of plants was established, each

species was integrated into an additional systematic search. The key words were “X Reunion island traditional medicine”, “X Mauritius traditional medicine”, “X Seychelles traditional medicine”, “X Madagascar traditional medicine”, where X stood for the Latin name of each species. The aim of this work was to create a non-exhaustive list; however, some bias might be found as the search was conducted only through English.

Plants used in traditional medicine in the Comoros archipelago: a review

Les plantes utilisées en médecine traditionnelle dans l'archipel des Comores: une revue

*Matthew Saive[1], Michel Frederich[2] & Marie-Laure Fauconnier[1]

[1]University of Liège, Gembloux Agro-Bio Tech, Laboratory of Chemistry of Natural Molecules, Passage des Déportés 2, 5030 Gembloux, Belgium: msaive@student.uliege.be

[2]Department of Pharmacognosy, University of Liège, Liège, Belgium

Résumé

Introduction : Dans l'archipel des Comores, comme dans de nombreuses régions d'Afrique, le premier réflexe adopté par les populations quand il s'agit de se soigner est la médecine traditionnelle. Ce travail illustre la diversité des remèdes à base de plantes que l'on retrouve dans cette région du monde. C'est à l'aide de travaux similaires à celui-ci que des espèces potentiellement intéressantes pour le monde pharmaceutique et cosmétiques peuvent être identifiées. De plus, ce type d'étude contribue à la préservation d'un savoir ancestral en voie de disparition.

Littérature : Les informations mentionnées dans ce travail sont issues de bases de données construites par des ethnobotanistes ainsi que d'articles scientifiques validés par les pairs. Une partie des données proviennent aussi de travaux réalisés par des locaux en collaboration avec des organismes reconnus.

Conclusion : La littérature scientifique concernant la pharmacopée traditionnelle de l'archipel des Comores cite 207 espèces différentes. Parmi ces espèces, 9 sont endémiques de l'archipel. La totalité des espèces a été comparée aux autres iles de l'Océan Indien ainsi qu'aux régions avoisinantes du point de vue des usages respectifs. A l'issue de ce travail, il s'avère que seulement 3% de ces espèces sont utilisées de manières similaires dans ces différentes régions.

Mots clefs: Médicament traditionnel, ethnobotanique, Océan Indien, Comores.

Abstract

Introduction: In the Comoros archipelago, as in many places in Africa, traditional medicine is the first reflex people have when it comes to finding a cure. This work illustrates the diversity of remedies found in this group of islands. The plant species potentially effective from a pharmaceutical point of view can be targeted through the comparison of different databases. The present study also illustrates the importance of preventing the loss of traditional knowledge based on hundreds of years of observations.

Literature: The information in this paper originates from databases built by ethnobotanists as well as peer reviewed scientific articles. In addition, some information also comes from work done by locals working with recognized organisms.

Conclusion: The scientific literature cites 207 different species that are used for traditional practices in the Comoros Archipelago, among which 9 are endemic. These species were compared to the pharmacopoeias of other islands and surroundings from

the Indian Ocean in terms of similarities and differences between targeted ailments. Only 3% of the cited species present similarities in use among the islands of the Indian Ocean and surroundings.

Keywords: Traditional medicines, ethnobotany, Indian Ocean, Comoros.

1. Introduction

As long as humankind can remember, plants have been part of Human's development. In addition to the management of the carbon equilibrium, they can be a source of food, medicine, cosmetics, fabric, energy, as well as of construction materials (Bouloc, 2006; Cartier, 1994; Hoffman et al., 2007; Rakotoniaina et al., 2018; Said Hassane Soidrou et al., 2013). The earliest records of plant use for medicine, among other habits and beliefs, were found in ancient Egypt and are estimated to date from 2500 BCE (Kelly, 2009). Even though the way plants are used has been changing, their use is still a common practice nowadays. In the 19th century, as science and medicine progressed, traditional uses of plants in medicine provided an ever-growing source of inspiration for the development of new drugs and treatments (Norman R. Farnsworth, 1966; Heitzman et al., 2005; Katiyar et al., 2012), starting with the isolation of morphine from *Papaver somniferum* Linn., by Friedrich Sertüner, in 1806 (Brownstein, 1993).

These discoveries were the early stages of what would become the birth of ethnopharmacology in 1967 (Heinrich, 2015). This field of study is defined as "the interdisciplinary scientific exploration of biologically active agents traditionally employed or observed by man, putting in relation plants, fungi, animals, microorganisms, minerals, the way people use them and the biological and pharmacological effects of those ingredients. It is a discipline tightly linked to ethnobotany and phytochemistry" (Holmstedt, 1991). The ethnobotanical part of this discipline led to the gathering of huge amounts of data. In order to simplify the access to that immense source of knowledge, ethnobotanists have been creating many very complete data bases such as: NAPRALERT (United States of America); PHARMEL (Belgium); PRELUDE (Belgium); PROTA (Netherlands); Kew MPNS (Great Britain); MNHN (France). These data bases contain information that can prove very interesting for laboratory scientists in order to target the species on which detailed analyses should be implemented (N R Farnsworth, 1994).

Ethnobotany has proven to be effective for the discovery of important medicine: e.g. in Madagascar, *Catharanthus roseus* (L.) G. Don has been used traditionally to treat many pathologies, such as pancreatic pain, colitis, chest pain, heartburn and gastritis (Randriamiharisoa et al., 2015; Razafindraibe et al., 2013). Phytochemical studies were conducted on this species and led to the discovery of many alkaloids such as vindoline I, vindolidine II, vindolicine III, vindolinine IV as well as vinblastine and vincristine. Among these alkaloids some are used nowadays as anti-cancer drugs in modern medicine (Dugé de Bernonville et al., 2015; Tiong et al., 2013). Other plants, originating from different places have been subject to similar investigations and led to the discovery of interesting new compounds. As an example, in the Reunion Island, *Centella asiatica* (L.) Urb. is used traditionally to treat many benign and malignant ailments (e.g. aspergillosis, scabies, fungal infections). After a phytochemical study was undertaken, compounds such as asiaticoside, brahmoside, brahminoside or kaempferol were identified (Hashim et al., 2011). Thus, *Centella asiatica* (L.) Urb. was proven to be useful against serious immune disorder diseases. Even though not all compounds and mechanisms have been investigated and studied in depth, this species is currently used as an ingredient in patented phytomedicines (Rangel, 2009).

The two species mentioned above come from places known for their wide biodiversity, which are called biodiversity hotspots. The Indian Ocean is home to many biodiversity hot spots as 25% of the world's biodiversity can be found there, as well as in sub-Saharan Africa (Gurib Fakim, 2011).

Among the large number of different species found in the western part of the Indian Ocean, many are endemic. Mauritius, Réunion, Rodrigues, Seychelles, the Comoros archipelago and Madagascar together are home to 11 endemic plant families, including at least 310 endemic genera, leading to a total of around 10 000 endemic species (Rasoanaivo, 2011).

While several studies on Madagascar, Reunion Island, Mauritius and Rodrigues review current knowledge in ethnobotany in these areas, it's surprising to note that despite the incredible potential of the Comoros archipelago, no study has been devoted to them.

People from the Comoros archipelago live in rural areas. Poverty and difficult access to a modern health care system have led them to develop their own health system based on natural products. The cultural background of these people, being a mix of African Bantu and Arab-Muslim (Liszkowski, 2000), gave to this region of the world a diversified and rich knowledge when it comes to traditional medicine. The conservation of this knowledge is based on an oral transmission from one generation to the next (Kaou et al., 2008; Said Hassane Soidrou et al., 2013).

We thus focused on this part of the world in this work for the previously mentioned reasons, that is: it's known as a biodiversity hotspot and the birthplace for many different species (Tatayah, 2011).; due to its location, it has had the cultural influences of many ethnicities (Kaou et al., 2008; Said Hassane Soidrou et al., 2013).; lastly, only very little data compilation has been done on the botanicals used in traditional medicine in this part of the world.

Mainly peer reviewed documents were taken into account and most of the ethnobotanical information can be linked to one or several vouchers stored in herbaria. As some work was done by locals, in collaboration with a recognized botanic conservatory (CBNM – Concervatoire botanique national de Mascarin), these data were also taken into account.

In the end, this work has led to the creation of an exhaustive list of plant species and their traditional uses, based on all available and significant literature. The perspective of development, risks and limitations linked to the use of plants from the Comoros archipelago in traditional medicine are also discussed.

To find the information mentioned in this article, systematic bibliographic research was conducted in the PRELUDE database as well as in Google Scholar. As the first database already targets ethnobotanical information the key word used was *Comores*. The key words used to do the research in Google Scholar were the following: *Comoros archipelago, Moheli, Mwali, Mayotte, Maore, Anjouan, Ndzuwani, Grande Comore, Nagzidja* linked *to ethnobotany, traditional practices, traditional medicine, cosmetics.* This process led to the identification of 102 bibliographic references.

1.1.Context and study area

In a context where exports equal a tenth of the imports (13,8 M $ *versus* 129,6 M $) in 2007 (UNCTAD, 2011), it's crucial to find new ways to finance the region. One way to reach that goal is to seek high added values in available goods. In this case, the rich and diverse flora of the archipelago has been targeted. As mentioned by El Hilaly et al, and Mhame, P. P. in 2004 folk medicine can be an asset helping the financial status of a region(El-Hilaly et al., 2003; Mhame, 2004). Through the discovery of valuable plant species for the pharmaceutical and cosmetic business, the import and export balance could be influenced towards a healthier situation. It's vital for the exploitation of these goods to be carried out in a sustainable manner or else this type of work cannot guarantee solid change in the long term (Abdurazag et al., 2003).

1.2.Geography and climate

The Comoros archipelago lies in the Northern region of the Mozambique Channel. It is composed of four main islands, respectively Grandes Comores (950 km²), Anjouan (378 km²), Mayotte (370 km²) and Mohéli (216 km²). In addition, around 60 islets are found in the surrounding seas, especially south of Mohéli and in the Mahoran lagoon. The archipelago is the result of the separation of the Malagasy and African plates, between the Miocene and the late Pleistocene, which led to the creation of this volcanic pack of islands (Nougier et al., 1986). Due to their volcanic origin, these islands present a hilly landscape with summits reaching 2361 m (Mount Karthala) for Grande Comore, 1595 m (Mount Ntringui) for Anjouan, 790 m (Mzé Koukoulé) for Moheli and 660 m (Mount Benara) for Mayotte (Quod et al., 2000). The climate is tropical, with a hot and rainy season from December to April, during which the monsoon prevails and is characterized by an average temperature reaching 27°C during the day. The dry season starts in May and ends in November, with an average temperature reaching 23°C during the day. The pluviometry of the different islands is strongly influenced by their relief as clouds tend to form and stay in places with high altitudes. On mount Karthala, rainfall can reach up to 5000 mm per year, whereas the average yearly pluviometry of Moroni (located west of Anjouan Island, near the sea) only reaches 2700 mm per year. The average pluviometry of Moheli, Grande Comore and Mayotte reach respectively 2100 mm, 2300 mm and 1250 mm per year (OMM, 2018). Differences in pluviometry can also vary within the islands: e.g. in Mayotte, the south of the island measures rainfall below 1300mm per year and the north of the island regularly records rainfall reaching more than 2000 mm per year (Boullet, 2016). All these characteristics within the archipelago and within the different islands are some of the reasons for the wide biodiversity (Rasoanaivo, 2011).

1.3.Flora

The flora of the Comoros archipelago has not been studied in depth, in opposition to other islands in the Indian Ocean (Morat & Lowry, 1997; O Pascal, 2002; Olivier Pascal et al., 2001). Floristic studies of the Comoros archipelago began in the first part of the 20th century, when Voeltskow, published "Flora und Fauna der Komoren. Reise in Ostafrika in den Jahren 1902–1905" (Vos, 2003) in which he identified 935 vascular plant species, including 416 endemic species. His work was completed by a more

recent project aiming to identify the flora of the Comoros archipelago. The main studies made in Comoros were carried out by Moinjoin in 1981, Adjanohoun in 1982 and the PLARM (Study of the characteristics and composition of Aromatique and Medicinal Plants) project (Adjanohoun et al., 1982; Gurib Fakim & Guého, 1999). More recently, studies of Kaou et al. and Soidrou et al. were added to this list (Kaou et al., 2008; Said Hassane Soidrou et al., 2013). The latest botanical studies for the Comoros archipelago estimate the number of species as being over 2000 (indigenous and introduced) (Adjanohoun et al., 1982; F Barthelat & Boullet, 2005; Fabien Barthelat & Viscardi, 2012; O Pascal, 2002).

2. Methods

Targeting significant literature to provide valuable data for those who will use it afterwards is of paramount importance. Likewise, we must highlight that within the identified posology mentioned in the literature, some remedies are more strongly linked to rites than to biological material, which calls for a cautious review on how the species are used. The ideal criteria in the ethnobotanical literature are, according to (Trotter & Logan, 1986), as follows: the database should be significant, the scope should be comparable and complete, the plant specimens must be properly identified, vouchers need to be stored for further verification and, if possible, activity tests in the field should have been carried out so as to prove the potency of the concerned remedy. Considering how little ethnobotanical work has been done in the Comoros archipelago, only a few articles meet the criteria mentioned above. Therefore, the selected data originates from peer reviewed articles or from work done by recognized organisations such as the “Conservatoire Botanique du Mascarin” (CBNM) in collaboration with local inhabitants.

In fine, the data collected consists of the family name, the scientific name, the endemism of the plant as well as the targeted ailment and the part of plant used when available. The collected data were then studied so as to identify any type of consensus on the way the species were used in the Comoros and in the surrounding islands.

Based on the work carried out on the collected information, it was observed that in the Comoros archipelago, as well as in the other Islands of the Indian Ocean, the number of uses per species varies widely. As this phenomenon was observed worldwide by many ethnobotanists, several data reduction tools have been developed to enhance the significance of the work. First to develop these tools were Trotter and Logan in 1986, then (Prance et al., 1987) mentioned the concept of quantitative ethnobotany. Following on from this, many researchers have used different approaches towards developing the significance of the data they have collected. Most indicators require information such as the number of informants, number of ailments per species, number of mentions for each species or treatment; this type of information is found when doing infield observations. As this work is a review, only the body system impacted and the number of health issues targeted per species were available, leading to the selection of the indicators as follows.

Considering these elements, the RII (Relative Importance Index) was established for each species using the work of (Bennett & Prance, 2000), This indicator reflects

the versatility of a species based on the normalized number of pharmacological properties and the normalized number of body (BS) systems it affects, using the following formula:

$$\frac{BS_S}{BS_T} + \frac{HI_S}{HI_M} \times 50$$

Where:

- BS_T = total number of body system as mentioned in the literature (12) (Bennett & Prance, 2000)
- BS_S = body system specifically targeted by the concerned species
- HI_S = number of health issues claimed to be managed by a specific species
- HI_M = maximal number of health issues claimed to be managed by a specific species within this data set.

This indicator gives a good idea of the versatility a plant can have. In 2003 as explained by Pardo-de-Santayana developed a new indicator also called Relative Importance Index (RI) (Pardo-De-Santayana, 2003; Tardío & Pardo-De-Santayana, 2008). Similar to the RII mentioned previously, it's based on the relative number of use-categories (RNU); however, it doesn't take the body systems into account, rather it integrates the relative frequency of citation (RFC). In this present work, it's not possible to determine the RFC as there is no survey linked to the data in table 1 (Tardío & Pardo-De-Santayana, 2008). On its own, the RNU can be considered as an indicator of the type of ailment that is more of a concern for the inhabitants of the archipelago. All the ailments mentioned in table 1 were sorted into 89 uses (data not shown); then the following formula was applied to the data set:

$$RNU = \frac{NU_S}{NU_{MAX}} \times 100$$

Where:

- NU_s = number of mentions of a specific use
- NU_{max} = maximum number of specific uses mentioned within the whole data set

3. Data collection

All the collected data has been gathered in Table 1. A total of 207 different species from 80 different families have been mentioned in the literature, when it comes to the traditional use of plants of the Comoros archipelago. Among these families, the most

frequently found are *Fabaceae* (9%), *Asteraceae* (7%), *Euphorbiaceae* (5%), and *Malvaceae* (5%) (Table 1).

Table 1: List of plants mentioned in the literature linked to traditional practices. The different species were verified using the MPNS database (Kew, 2019) and the INPN database (MNHN, 2019). (End) The species is endemic to one or several islands of the archipelago. ***Different uses in different regions of the Indian Ocean and surroundings **Same use in different regions of the Indian Ocean and surroundings *used only in the Comoros. Plant parts abbreviations: (L) leaves, (B) bark, (FB) flower buds, (F) fruits, (WP) whole plant, (S) stem, (Sd) seed, (Fl) flower, (Re) resin, (Rz) rhizome (Li) liana, (Co) cotyledon, (Pp) pulp, (La) latex, (Tu) tuber, (Sa) sap, (Fu) fungi, (St) styles, (Sg) stigmas, (ND) no data.

Family	Species	Use/symptoms (Plant parts)	RII	Ref.
Acanthaceae	*Asystasia gangetica* (Linn) T. Anderson ***	Colitis (L), abdominal syndrome (L), haemorrhoids (B) (L), pregnancy disorder (ND), menstrual flow disorder (ND)	21,43	(Adjanohoun, 1989; Mchangama & Salaün, 2012)
Alangiaceae	*Alangium salviifolium* (Lf.) Wangerin ***	Fatigue (ND), purgative (ND), female fertility (ND), boils (WP) and asthma (L), menstruation disorder (F)	31,55	(Mchangama & Salaün, 2012; Panara et al., 2016; Saive et al., 2018; Singh Tanwer & Vijayvergia, 2014)
Amaranthaceae	*Aerva lanata* (L.) Juss. ex Schult. ***	Stomach pain (L), diuretic(L), kidney stones (ND), liver disease (ND), gonorrhoea (L), pregnancy follow-up (B)	23,21	(Mchangama & Salaün, 2012)
Amaryllidaceae	*Allium cepa* Linn ***	Sexual incapacity (Bl), sexual asthenia (Bl), erectile dysfunction (Bl), impotency (Bl)	15,48	(Adjanohoun, 1989)
Anacardiaceae	*Anacardium occidentale* Linn. ***	internal parasitism (oxiure, ascaris, tenia) (ND), amoebiasis (ND), colibacillus (ND), Cysticercose (ND), cococsidiosis (ND), maggot (ND), giardiase (ND), gingivitis (ND), odontalgia (ND), toothaches (ND), tooth decay (ND)	27,98	(Adjanohoun, 1989)

Annonaceae	*Annona muricata* Linn. ***	Benign positional vertigo (L), deworming (ND), febrifuge (ND), astringent (ND), diarrhoea (ND), dysentery (ND), lice (ND), sedative (ND), antispasmodic (ND), hypotensive (L), epilepsy (ND), cardiac pain (ND)	38,10	(Adjanohoun, 1989; Mchangama & Salaün, 2012; Sussman, 1980)
	Annona reticulata Linn. ***	Contusion (ND), bruise (ND), sprain (ND), swelling (ND), lumbago (ND), sciatica (ND), epilepsy (ND) cardiac pain (ND)	25,00	(Adjanohoun, 1989; Gurib Fakim & Brendler, 2004)
	Annona senegalensis Pers. ***	Lumbago (R), redness (L)	11,90	(Mchangama & Salaün, 2012; Saive et al., 2018)
	Annona squamosa Linn. ***	Vertigo (ND), dizziness (B), syncope (ND), malaria (L)	23,81	(Adjanohoun, 1989; Gurib Fakim & Brendler, 2004; Jain & Srivastava, 2005; Kaou et al., 2008)
	Monanthotaxis glaucocarpa (Baill.) Verdc. *	Bad luck (L), impotence (R), rheumatism (R), orchitis (ND)	19,64	(Mchangama & Salaün, 2012)
	Cananga odorata (Lam.) Hook. F. & Thomson***	Cosmetic (Fl)	1,79	(Saive et al., 2018)
Aphloiaceae	*Aphloia theiformis* (Vahl.) Benn. ***	Dizziness (L), leucorrhoea (L), stomach pain (L) (S), diarrhoea (L), malaria (L), diabetes (L), intestinal parasites (L), stomach pain (L)	37,50	(Gurib Fakim & Brendler, 2004; Jonville et al., 2008; Kaou et al., 2008; Poullain et al., 2004; Saive et al., 2018)
Apiaceae	*Coriandrum sativum* Linn. ***	Stomach pain (Sd)	5,95	(Saive et al., 2018)

Apocynaceae	*Carissa edulis* (Forssk.) Vahl. ***	Fever (W), chest pain (ND), heart pounding (ND), stomach pain (B), headache (ND), headache (W), acne (W)	29,17	(Daruty, 2018; Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012; Saive et al., 2018)
	Carissa spinarum Linn. ***	Headache (W), acne (W), cosmetic (W)	13,69	(Saive et al., 2018)
	Leptadenia madagascariensis Decne. ***	Fever (S), malaria (L) (W) (S), convulsion (ND), rheumatism (ND), colic (S), diabetes (ND), help expel the placenta after child-birth (ND)	41,67	(Adjanohoun et al., 1982; Godara et al., 2015; Gurib Fakim & Brendler, 2004; Kaou et al., 2008)
	Petchia erythrocarpa (Vatke) Leeuwenb. ***	Redness (L) (W), stomach pain (L) (W)	11,90	(Saive et al., 2018)
	Plumeria rubra Linn. ***	Cosmetics (Fl)	1,79	(Saive et al., 2018)
	Secamone astephana Choux *	Tonic (W) (L), purgative (W) (L)	11,90	(Saive et al., 2018)
	Tylophora sp. ***	Colitis (L), abdominal syndrome (L)	7,74	(Mchangama & Salaün, 2012)
Araceae	*Pothos scandens* Linn. *	Arthritis (R), low back pain (R), orchitis (ND), localized pain (R)	19,64	(Mchangama & Salaün, 2012)
Arecaceae	*Areca catechu* Linn. ***	Aphrodisiac (Sd), anthelminthic (F)	11,90	(Gurib Fakim & Brendler, 2004)
	Cocos nucifera Linn. ***	Fresh cut (L), fever (R), menstrual disorders (ND), diarrhoea (L), vomiting (S), dandruff, dysentery (L) , boils (F), asthma (L)	36,90	(Mchangama & Salaün, 2012; Panara et al., 2016; Rakotoarivelo et al., 2015; Singh Tanwer & Vijayvergia, 2014)
	Hyphaene coriacea Gaertn. ***	Cervicalgia (L)	5,95	(Mchangama & Salaün, 2012)

Asphodelaceae	*Aloe* sp.***	Blepharitis (L), blindness (L), eye disease (L), trachoma (L), abscess (L), cyst (L), furuncle (L), pimple (L), skin lesion (L), skin diseases (L), lupus (L), abdominal pain (R), stomach pain (R), colic (R), gastritis (R), heartburn (R), gastralgia (R), arthritis (L), articular pain (L), cramps (L), kidney pain (R), myalgia (L), sciatica (L).	70,24	(Adjanohoun, 1989; Gurib Fakim, 2002, 2003; Rabearivony et al., 2015; Samoisy & Mahomoodally, 2015)
	Aloe mayottensis A. Berger* (End)	Arthritis (L), joint pain (L), rheumatism(L), sciatica(L), redness (L), stomach pain (L)	27,38	(Mchangama & Salaün, 2012; Saive et al., 2018)
Asteraceae	*Acmella oleracea* (L.) R. K. Jansen ***	Joint pain (FB)	5,95	(Mchangama & Salaün, 2012)
	Ageratum conyzoides Linn. ***	Ague (ND), fever, malaria (L), dizziness (ND), rheumatism (L), diarrhoea (L), Skin (l, St), wounds (l), anthrax (l), eye (R), eczema (R), diarrhoea (l), amoebic disease (WP), dysentery (l), malaria (WP), typhoid (WP)	60,12	(Adjanohoun et al., 1982; Gurib Fakim, 1990; Jain & Srivastava, 2005; Kaou et al., 2008; Sussman, 1980)
	Ayapana triplinervis (Vahl.) R.M. King & H. Robinson ***	Diearrhoea (L), headache (L), hypertension (ND), epigastric pain (L), nausea (L), vomiting (L), stimulant (ND), astringent (ND), scurvy (ND), sudorific (ND), skin infections (ND)	40,48	(Adjanohoun et al., 1982; Daruty, 2018; Gurib Fakim & Brendler, 2004; Pourchez, 2014)

	Bidens pilosa Linn. ***	Cuts (L), worms (WP), headache (ND), sore throat (L) (WP), water retention (WP), irritation (ND), poisoning (WP), dysentery (WP), jaundice (L) (WP), pharyngitis (WP), diabetes (WP), hypertension (WP), toothache (ND), urinary tract infections (ND), stomach pain (L), febrifuge (WP), nervous system problems (ND), haemorrhoids (ND), insect bites (ND), conjunctivitis (L) (WP), malaria (WP), dysmenorrhea (WP), convulsions (ND), parturition (ND) , cough (WP), nosebleed (WP) (L), intestinal illness (WP), diarrhoea (St) (L) (Fl)	100,00	(Adjanohoun, 1989; Bartolome et al., 2013; Gurib Fakim & Brendler, 2004; Kaou et al., 2008; Mchangama & Salaün, 2012)
	Crassocephalum bojeri (DC.) Robyns*	Antalgic (R), migraine (children) (R)	11,90	(Adjanohoun et al., 1982)
	Elephantopus mollis Kunth ***	Diabetes (L)	5,95	(Mchangama & Salaün, 2012)
	Helichrysum fulvescens DC. * (not in INPN and MPNS)	Diarrhoea (WP)	5,95	(Kaou et al., 2008)
	Microglossa pyrifolia (Lam.) O. Kuntze. ***	Dysmenorrhoea (L), hypermenorrhoea (L), sterility (S) (L), infertility (S) (L), impotence (S) (L), bleeding (L), nosebleed (L)	20,83	(Adjanohoun et al., 1982)

	Crassocephalum bojeri (DC.) Robyns	Child severe headache (R)	5,95	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004)
	Solanecio angulatus (Vahl) C. Jeffrey *	Headache (R)	5,95	(Kaou et al., 2008)
	Sphagneticola trilobata (L.) Pruski *	Dermal reaction linked to allergies and mycosis (Li)	5,95	(Mchangama & Salaün, 2012)
	Struchium sparganophorum (L.) Kuntze ***	Cosmetics (Fl)	1,79	(Saive et al., 2018)
	Tithonia diversifolia (Hemsl.) A. Gray ***	Diabetes (L)	5,95	(Mchangama & Salaün, 2012)
	Vernonia colorata subsp. *grandis* (DC.) C.Jeffrey *	Diarrhoea (WP)	5,95	(Kaou et al., 2008)
Balsaminaceae	*Impatiens auricoma* Baill.* (End)	Haemorrhoids (L)	5,95	(Mchangama & Salaün, 2012)
Boraginaceae	*Cordia myxa* var. *ixiocarpa* (F.Muell.) Domin *	Skin smoothing (B), cosmetics (B)	7,74	(Saive et al., 2018)
	Cordia subcordata Lam.*	Allergy (L) (S), dermal reaction (L) (S), mycoses (L) (S)	13,69	(Mchangama & Salaün, 2012; Saive et al., 2018)
	Trichodesma zeylanicum (Burm.) R. Br. ***	Wound healing (L), analgesic (L)	11,90	(Adjanohoun et al., 1982; Maregesi et al., 2013)
Burseraceae	*Commiphora arafy* H. Perrier *	Sadness (L)	5,95	(Mchangama & Salaün, 2012)
Calophyllaceae	*Calophyllum inophyllum* Linn. ***	Fresh cut (L), abscess (R) , facial neuralgia (ND), ulcers (R), eye infections (L) (R), orchitis,	38,69	(Abe & Ohtani, 2013; Gurib Fakim & Brendler, 2004; Jain & Srivastava, 2005;

		rheumatism (Re), psoriasis (Re), skin infection (Re), boils (Re)		Mchangama & Salaün, 2012)
Cannabaceae	*Trema orientale* (L.), Blume ***	Oxytocic (L) (B)	5,95	(Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012)
Caricaceae	*Carica papaya* Linn. ***	Internal parasitism (F), malaria (L)	11,90	(Adjanohoun et al., 1982; Gurib Fakim, 1990; Kaou et al., 2008)
Caryophyllaceae	*Drymaria cordata* (L.) Willd. ex Schult.. **	Haemorrhoids (L) (B), psychomotor disability (children) (L), urogenital infection (S) (L), gingivitis (WP), dental pain (WP)	21,43	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012)
Celastraceae	*Mystroxylon aethiopicum* (Thunb.) Loes. ***	Chronic fatigue (ND), neuralgia (ND), tonic (ND)	9,52	(Gurib Fakim et al., 1997; Gurib Fakim & Brendler, 2004)
Combretaceae	*Combretum coccineum* Lam.***	Intestinal parasites (F), swollen spleen (Fl) (R)	11,90	(Gurib Fakim & Brendler, 2004; Nicolas, 2012)
	Terminalia catappa Linn. ***	Fever (ND), epilepsy (ND)	11,90	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004)
Commelinaceae	*Commelina africana* Linn. ***	Anaemia (L), asthenia (L), Oxytocic (L)	13,69	(Adjanohoun et al., 1982)
Convolvulaceae	*Ipomoea batatas* (L.) Lam. ***	Wound healing agent (ND), anti-septic (ND), disinfectant (ND), cicatrizing (ND), vulnerary (ND), burns (Pp), diffuse pain (ND), sores (ND)	26,79	(Adjanohoun et al., 1982)

	Ipomoea obscura (L.) Ker Gawl. *	Fever (Li), work overload (S), sinusitis (L), nasal congestion (L), gonorrhoea (L), asthma (WP)	27,38	(Kaou et al., 2008; Mchangama & Salaün, 2012)
	Ipomoea pes-caprae (L.) R. Br. ***	Muscular pain (L), rheumatism (L), malaria (L), psychomotor disability (children) (L), malaria (WP)	25,60	(Kaou et al., 2008; Mchangama & Salaün, 2012)
	Jacquemontia tamnifolia Griseb. *	Headache (L), fever (L)	11,90	(Saive et al., 2018)
	Merremia peltata Merr. ***	Postpartum treatment (L), fatigue during pregnancy (Li), vomiting (Li), vaginal infection (L) (Li), soreness (Sa), acne (Sa)	31,55	(Mchangama & Salaün, 2012; Saive et al., 2018)
Crassulaceae	*Kalanchoe pinnata* (Lam.) Pers. ***	Earaches (L), sprains (L), fever (ND), headache (ND), heartburn (L), urinary inflammation (L), fungal infections (ND), inflammations (ND), bronchitis (ND), eye irritation (ND), abdominal irritation (L), cholera (ND), indigestion (L), flatulence (L), rheumatism (ND) , muscle pain (L), varicose ulcer (ND), evolved diabetes (ND), psychomotor disability (children) (L), swollen feet (ND), wounds (ND), fractures (L), fatigue (L)	82,74	(Adjanohoun, 1983; Gurib Fakim, 1990; Gurib Fakim & Brendler, 2004; Lartigau Roussin, 2002; Mchangama & Salaün, 2012; Saive et al., 2018)
Cucurbitaceae	*Kedrostis* sp. *	Scabies (Tu)	5,95	(Mchangama & Salaün, 2012)

	Momordica charantia Linn. ***	Malformation (WP), diarrhoea (S) (L), lower back pain (WP), orchitis (WP), colitis (ND), fever (L), redness (L), allergy (L)	35,12	(Adjanohoun et al., 1982; Kaou et al., 2008; Mchangama & Salaün, 2012; Saive et al., 2018)
Dioscoraceae	*Dioscorea bulbifera* Linn. **	Foot fleas (WP) and burns (R)	7,74	(Gurib Fakim & Brendler, 2004)
Ebenaceae	*Euclea mayottensis* H. Perr. * (End)	Cosmetics (traditional tinctures) (ND) gonorrhoea (ND)	7,74	(Gurib Fakim & Brendler, 2004)
Erythroxylaceae	*Erythroxylum lanceum* Bojer * (End)	Pain (L), soreness (L)	7,74	(Saive et al., 2018)
Euphorbiaceae	*Acalypha lyallii* Baker **	Rheumatism (L)	5,95	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Seebaluck et al., 2015)
	Aleurites moluccanus Willd.***	Orchitis (F)	5,95	(Mchangama & Salaün, 2012)
	Argomuellera trewioides (Baill.) Pax & K. Hoffm *	Inflammation (L)	5,95	(Saive et al., 2018)
	Euphorbia hirta Linn. ***	Laxative (WP), diarrhoea (WP) urogenital infection (WP), abdominal pain (WP), gonorrhoea (WP)	21,43	(Adjanohoun et al., 1982; Ekoumou, 2003; Gurib Fakim & Brendler, 2004; Kaou et al., 2008; Soule et al., 2014)
	Euphorbia prostrata Aiton ***	Spinal curvature (WP), back pain (WP)	11,90	(Adjanohoun et al., 1982)
	Flueggea virosa subsp. *virosa* G.L.Webster ***	Malaria (S) (L) (W)	5,95	(Kaou et al., 2008)

	Jatropha curcas Linn. ***	Fresh cut (La), muscle pain (F), gingivitis (La), abscesses (F), boils (F), vomiting (L), malaria (L), haemostatic (La), fractures (F), swelling (F), influenza (ND), acne (Sa)	42,26	(Adjanohoun et al., 1982; Kaou et al., 2008; Lartigau Roussin, 2002; Mchangama & Salaün, 2012; Saive et al., 2018; Soule et al., 2014)
	Manihot esculenta Crantz. ***	Inflammation (L), abscess (L)	11,90	(Saive et al., 2018)
	Ricinus communis Linn. ***	Laxative (O), purgative (O), constipation (O), haemorrhoids (L), local analgesic (ND), malaria (WP)	19,05	(Adjanohoun et al., 1982; Kaou et al., 2008)
	Securinega virosa (Roxb. ex Willd.) Baill. *	Headache (R), migraine (R), antispasmodic (ND), hiccup (ND), abdominal pain (R), stomach-ache (R), gastric ulcer (R)	25,00	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004)
	Tragia furialis Bojer ***	Redness (L)	5,95	(Saive et al., 2018)
Fabaceae	*Abrus precatorius* Linn. ***	Sadness (L), cough (B), Bronchitis (ND), dysentery (ND), lupus (ND), tuberculosis (ND) gonorrhoea (ND), syphilis (ND), ulcers (ND), conjunctivitis (ND)	38,69	(Gurib Fakim et al., 2011; Mchangama & Salaün, 2012; Rabearivony et al., 2015; Saive et al., 2018)
	Caesalpinia bonduc (L.) Roxb.***	Orchitis (B), malaria (L), diarrhoea (S) (L)	17,86	(Kaou et al., 2008; Mchangama & Salaün, 2012)

	Cajanus cajan (L.) Millsp. ***	Anaemia (Sd), oral inflammation (L), scabies (ND), tensions (ND), influenza (L), inflammation blepharitis (L), blindness (L), cataract (L), conjunctivitis (L), glaucoma (L), trachoma (L), malaria (L), abscess (Sd)	44,05	(Adjanohoun et al., 1982; Kaou et al., 2008; Mchangama & Salaün, 2012; Terrac, 1947)
	Cassia alata Linn. ***	Blisters (L), brucellosis (Fl), depurative (ND), dermatomycosis (L), eczema (L), erysipelas (L), herpes (Sd) (L), impetigo (Sd) (L), itch (Sd) (L), mange (Sd) (L), nettlerash (Sd) (L), pelada (Sd) (L), purpura (Sd) (L), tinea capitis (Sd) (L), vitiligo (Sd) (L), whitlow (Sd) (L), dandruff (ND), hypertension (L)	44,64	(Adjanohoun et al., 1982; Fortin et al., 2002; Gurib Fakim, 1990)
	Cassia occidentalis Linn. ***	Depurative (L), diuretic (L), oxytocic (L), dystocia (L), antispasmodic (ND), hiccup (ND), diarrhoea (L), stomach aches (L), constipation (L) (R), headache (ND), malaria (WP) , inflammation (ND), diabetes (ND), fever (L) (Sd), bleeding (L) (W), allergy (L) (W), acne (L) (W), rheumatism (R), gonorrhoea (R), asthma (R), conjunctivitis (WP)	70,83	(Adjanohoun et al., 1982; Kaou et al., 2008; Saive et al., 2018; Soule et al., 2014; Terrac, 1947)

	Cassia singueana Delile ***	Dermatomycosis (L), eczema (L), herpes (L), impetigo (L), itch (L), mange (L), purpura (L), tinea capitis (L), vitiligo (L), whitlow (L), dandruff (L), paronychia (L), diarrhoea (WP), back pain (L)	37,50	(Adjanohoun et al., 1982; Kaou et al., 2008)
	Cassia tora Linn. ***	Eye diseases (L), pain (ND), Hyperactivity (children) (Fl)	9,52	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012)
	Dalbergia arbutifolia Baker *	Rheumatism (R), orchitis (ND), localized pain (R)	17,86	(Mchangama & Salaün, 2012)
	Desmodium ramosissimum G. Don *	Impotence (Li)	5,95	(Mchangama & Salaün, 2012)
	Entada rheedei Spreng ***	Orchitis (Co) (Sd)	5,95	(Mchangama & Salaün, 2012)
	Hymenaea verrucosa Gaertn. **	Allergy (R) (S) (L), dermal reaction (R) (S), mycoses (R) (S)	13,69	(Mchangama & Salaün, 2012; Saive et al., 2018)
	Lonchocarpus madagascariensis (Vatke) Dunn ex Polhill *	Pain of the limbs inside the bone (arms and shins) (L)	5,95	(Mchangama & Salaün, 2012)
	Pterocarpus indicus Willd. *	Acne (W)	5,95	(Saive et al., 2018)
	Rhynchosia viscosa DC. *	Stomach pain (L)	5,95	(Saive et al., 2018)
	Senna singueana (Delile) Lock*	Bleeding (L) (W), ache (L) (W), allergies (L) (W), Acne (L) (W), Diarrhoea (WP)	23,21	(Kaou et al., 2008; Saive et al., 2018)

	Tamarindus indica Linn. ***	Blisters (F), cough (B) (L), tooth-ache (B), fracture (R), contusions (L), loss of appetite (Sd), back-ache (R), redness (B) (L) (W), acne (B) (L) (W)	32,74	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012; Saive et al., 2018)
	Tephrosia vogelii Hook. f. ***	Toothache (L)	5,95	(Adjanohoun et al., 1982)
	Vigna adenantha (G. Mey.) Maréchal, Mascherpa & Stainier *	Abscess or furuncle (Sd), Panaris (Sd)	7,74	(Mchangama & Salaün, 2012)
Flacourtiaceae	*Flacourtia indica* (Burn. F.) Merr. ***	Malaria (S) (L)	5,95	(Kaou et al., 2008)
Flagellariaceae	*Flagellaria indica* Linn. ***	Infected throat (S), pharyngitis (S)	7,74	(Mchangama & Salaün, 2012)
Icacinaceae	*Apodytes dimidiata* E. Mey. ex Arn. *	Redness (L)	5,95	(Saive et al., 2018)
Lamiaceae	*Leucas grandis* Vatke *	Rhinorrhoea (L), rhinitis (allergic) (L)	11,90	(Mchangama & Salaün, 2012)
	Ocimum americanum Linn. ***	Parturition (L), diarrhoea (WP), vaginal infection (L), malaria (S), dismenorrhoea (WP), leucorrhoea (WP)	23,21	(Kaou et al., 2008; Mchangama & Salaün, 2012)

	Ocimum canum Sims. ***	abdominal pain (WP), stomach pain (WP), gastric ulcer (WP), stomach ulcer (WP), colic (WP), antispasmodic (ND), migraine (WP), fever (WP), malaria (WP), shortness of breath (WP), body aches (WP), ear washings (WP), mumps (WP), angina (WP), stomach cramps (WP), diarrhoea (WP), dysmenorrhea (WP), insomnia (WP), anxiety (WP)	63,10	(Adjanohoun et al., 1982; Hassane et al., 2011)
	Ocimum gratissimum Linn. ***	Gingivitis (L), aphthous stomatitis (L), diarrhoea (L), epilepsy (ND), cough (WP), whooping cough (ND), hypertension (ND), nose bleeding (ND), headache (ND), vaginal infection (L), malaria (S), fever (L), haemorrhoids (L), dysmenorrhoea (WP), leucorrhoea (WP), abortive (WP)	61,90	(Gurib Fakim et al., 1997; Kaou et al., 2008; Mchangama & Salaün, 2012)
	Ocimum suave Willd. ***	Vaginal prolapsed (L), uterine prolapses (L), uterus disease (L), vertigo (L), dizziness (L), faint (L), syncope (L), giddiness (L), fever (S) (L), malaria (S) (L), abdominal pain (ND), stomach pain (ND), pelvic pain (L), antispasmodic (ND)	45,83	(Adjanohoun et al., 1982)

	Plectranthus amboinicus (Lour.) Spreng. ***	Cough (L) colic (ND), flatulence (ND), rheumatism (ND), furuncle (ND), sprain (ND), painful swelling (ND), constipation (ND), vaginal infection (ND), malaria (R) , influenza (ND) stomach aches (WP), diarrhoea (ND), intestinal worms (ND), vaginal infection (L), abdominal gripes (WP), dysuria (WP), laxative (WP), hiccup (ND)	65,48	(Gurib Fakim & Brendler, 2004; Hassani et al., 2012; Kaou et al., 2008; Lartigau Roussin, 2002; Mchangama & Salaün, 2012; Soule et al., 2014)
	Plectranthus madagascariensis Benth. ***	Redness (L), stomach pain (L), headache (L)	17,86	(Saive et al., 2018)
	Premna serratifolia Linn. ***	Furuncle (ND), injuries (ND), insomnia (L), cough (ND), influenza (ND)	25,60	(Gurib Fakim et al., 1997; Mchangama & Salaün, 2012)
	Vitex trifolia Linn. ***	Insomnia (L), nightmares (L)	7,74	(Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012)
Lauraceae	*Cassytha filiformis* Linn. ***	Dermatomycosis (L), eczema (L), herpes (L), impetigo (L), itch (L), mange (L), purpura (L), tinea capitis (L), vitiligo (L), whitlow (L), dandruff (L), paronychia (L)	29,76	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Said H. Soidrou et al., 2014)
	Cinnamomum zeylanicum Blume . ***	Malaria (L)	5,95	(Kaou et al., 2008)
	Laurus nobilis Linn. *	Urogenital infection (L)	5,95	(Adjanohoun et al., 1982)

	Litsea glutinosa (Lour.) C.B. Rob. ***	Varicose ulcer (W), skin disease (W), antiseptic (B), painful menstruation (F), diarrhoea (B), emollient for sprains (B), diabetes (W), redness (Sa)	39,29	(Mchangama & Salaün, 2012; Saive et al., 2018; Vos, 2003)
	Ocotea comoriensis Kosterm. * (End)	Child's eczema (W), headache (ND), urinary disorder (ND), stomach disease (ND)	23,81	(Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012)
	Persea americana Mill. ***	Acne (Sd)	5,95	(Saive et al., 2018)
Lecythidaceae	*Barringtonia asiatica* Kurz ***	Epigastric (B), rheumatism (WP) (L)	11,90	(Abe & Ohtani, 2013; Gurib Fakim & Brendler, 2004; Jain & Srivastava, 2005; Mchangama & Salaün, 2012)
	Barringtonia racemosa (L.) Spreng. ***	Sciatica (B)	5,95	(Mchangama & Salaün, 2012)
Liliaceae	*Lomatophyllum purpureum* T. Durand & Schinz ***	Conjunctivitis (ND), wounds and burns (ND), weaning (Sa)	17,86	(Gurib Fakim et al., 1997; Lartigau Roussin, 2002)
Loganiaceae	*Strychnos spinosa* Lam. ***	Scabies (R), fever (ND), beauty mask (ND)	13,69	(Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012)
Lythraceae	*Ammannia multiflora* Roxb.*	Psychomotor development delay (L)	5,95	(Mchangama & Salaün, 2012)

	Lawsonia inermis Linn. ***	Panaris (L), paronychia (L), dys-menorrhoea (L), hypermenorrhoea (L), anxiety (ND), stress (ND), nervous disorder (ND), abortive (ND), headache (L) (Fl)	32,74	(Adjanohoun et al., 1982; Durasnel et al., 2014; Mchangama & Salaün, 2012; Saive et al., 2018)
	Woodfordia fruticosa Kurz***	Impotence (R), constipation (R), diarrhoea (WP)	13,69	(Kaou et al., 2008; Mchangama & Salaün, 2012)
Malvaceae	*Adansonia digitata* Linn. ***	Fever (F), cough, diarrhoea(F), renal inflammation (ND), cystitis (ND), depurative (ND), asthma (ND), malaria (ND), dysentery (B), wounds (ND), urinary problems (ND), herpes (ND), fatigue (ND), diffuse pains (ND), eye disease (ND), mumps (ND), deworming (F), redness (F), skin infection (F)	71,43	(Gurib Fakim & Brendler, 2004; Jain & Srivastava, 2005; Mchangama & Salaün, 2012; Saive et al., 2018)
	Carpodiptera Africana Mast. *	Cosmetics (W)	1,79	(Saive et al., 2018)
	Grewia cuneifolia Juss. *	Allergy (L)	5,95	(Saive et al., 2018)
	Heritiera littoralis Aiton ***	Painful periods (B), heavy periods (B), stomach pain (B) (L)	13,69	(Mchangama & Salaün, 2012; Saive et al., 2018)
	Hibiscus surattensis Linn. *	Throat illness (WP), urinary tract infection (WP)	11,90	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012)
	Hibiscus tiliaceus Linn. ***	Allergy (R) (S), dermal reaction (R) (S), mycoses (R) (S), acne (L)	15,48	(Mchangama & Salaün, 2012; Saive et al., 2018)

	Sida rhombifolia Linn. ***	Abscess (L), boils (L), furuncle (L), herpes (L), skin lesion (L), skin disease (L), lupus (L), erysipelas (L), arthritis (ND), articular pain (ND), muscular inflammation (ND), spinal curvature (ND), backache (ND), redness (Fl)	41,67	(Adjanohoun et al., 1982; DaSilva et al., 2009; Saive et al., 2018)
	Sida stipulata Cav. ***	Panaris (L) (R)	5,95	(Mchangama & Salaün, 2012)
	Sida urens Linn. *	Redness (L)	5,95	(Saive et al., 2018)
	Thespesia populneoides (Roxb.) Kostel ***	Dermal reaction linked to allergies and mycosis (S) (Fl)	5,95	(Mchangama & Salaün, 2012)
	Triumfetta rhomboidea Jacq. ***	Abscess (R)	5,95	(Mchangama & Salaün, 2012)
Melastomataceae	*Clidemia hirta* (L.) D. Don. ***	Rheumatism (ND), abdominal pain (L), hypotensive (ND), depurative (ND)	23,81	(Gurib Fakim & Brendler, 2004)
	Tristemma mauritianum J.F. Gmel. ***	Wounds (ND), cough (ND), premenstrual tension (ND)	17,86	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004)
Meliaceae	*Turraea sericea* Sm. ***	Haemorrhoids (ND), vertigo (L), orchitis (B), hydrocele (B)	19,64	(Mchangama & Salaün, 2012)
	Xylocarpus moluccensis M. Roem. *	Orchitis (Sd)	5,95	(Mchangama & Salaün, 2012)
Menispermaceae	*Cissampelos pareira* Linn. ***	Sadness (L), heartburn (W) childhood eczema (R)	17,86	(Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012)

	Triclisia capitata Diels * (End)	Impotence (R), orchitis (ND), pain in the lower body (R)	13,69	(Mchangama & Salaün, 2012)
Mimosaceae	*Acacia farnesiana* (L) Willd.***	Cosmetic (Fl)	1,79	(Saive et al., 2018)
Molluginaceae	*Mollugo nudicaulis* Lam. ***	Cough (WP)	5,95	(Kaou et al., 2008)
Monimiaceae	*Tambourissa leptophylla* A. DC. ***	Aborting agent (L), dermatitis (L), antifungal (F), antimicrobial (F), healing wounds (F), malaria (F), diarrhoea (F)	29,17	(Adjanohoun et al., 1982; Gallori et al., 2001; Gurib Fakim & Brendler, 2004; Kaou et al., 2008)
Moraceae	*Ficus cocculifolia* Baker. ***	Warts (ND), skin infection (ND)	7,74	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004)
	Ficus hispida L.f.***	Abortive (ND), abdominal pain (ND)	11,90	(Gurib Fakim & Brendler, 2004)
	Trophis montana (Leandri) C.C. Berg. *	Fever (L)	5,95	(Saive et al., 2018)
Moringaceae	*Moringa oleifera* Lam. ***	Sting of centipede (Sd), better lactation (ND), deworming (ND), constipation (ND), wounds (ND), ulcers (ND), stress (ND), bruising (ND), arthritis (ND), asthma (ND), hiccups (ND), nodes (ND), fresh cut (ND), choleretic (ND), liver disease (L), antispasmodic (ND), eye disease (Sa), redness (L)	61,31	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Lartigau Roussin, 2002; Mchangama & Salaün, 2012; Pernet, 1957; Saive et al., 2018)
Musaceae	*Musa* sp. ***	Orchitis (L), stomach ulcer (ND), stomach pain (ND), bloody diarrhoea (ND), dysentery (ND),	41,07	(Adjanohoun et al., 1982; Kaou et al., 2008;

		fresh cut (ND), fortifying (ND), malformation (ND), malaria (L)		Mchangama & Salaün, 2012)
Myristicaceae	*Myristica fragrans* Houtt. ***	Redness (F), headache (F), stomach pain (F), malaria (F)	19,64	(Kaou et al., 2008; Saive et al., 2018)
Myrtaceae	*Eucalyptus* sp. ***	Headache (L), women sterility (L), diffuse pain (L)	13,69	(Adjanohoun et al., 1982; Blanchy et al., 1993)
	Psidium guajava Linn. ***	Digestive (L), antispasmodic (ND), antiseptic (L), astringent (ND), diarrhoea (L), stomach disorders (L), dizziness (ND), colitis (L), diabetes (ND), dysmenorrhoea (ND), toothache (B), gingivitis (B), infected wound (ND), malaria (ND), intestinal worm (L), inflammation (ND), cholera (ND)	55,36	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012; Soule et al., 2014)
	Syzygium aromaticum (L.) Merr. & L.M. Perry ***	Articular pain in the lower part of the body (FB), fatigue (L), articular pain (R), cough (F) (FB), purgative (Fl), redness (Fl), headache (Fl), toothache (F)	30,95	(Kaou et al., 2008; Mchangama & Salaün, 2012; Saive et al., 2018)
Nyctaginaceae	*Boerhavia diffusa* Linn.*	Pelvic pain (L)	5,95	(Adjanohoun, 1989)
	Mirabilis jalapa Linn. ***	Furuncle (L), abscess (L), loss of appetite (Li), purgative (Li)	15,48	(Mchangama & Salaün, 2012)
Oleaceae	*Jasminum nummularifolium* Baker *	Acne (Fl)	5,95	(Saive et al., 2018)
	Noronhia comorensis S. Moore * (End)	Tonic (L)	5,95	(Saive et al., 2018)

Ophioglossaceae	*Ophioglossum reticulatum* Linn. ***	Astringent (ND), childhood eczema (ND)	7,74	(Gurib Fakim et al., 1997)
Orchidaceae	*Vanilla planifolia* Andrews ***	Haemostatic (L)	5,95	(Kaou et al., 2008)
Oxalidaceae	*Averrhoa bilimbi* Linn. **	Febrifuge (L), scurvy (F), caterpillar sting (F)	17,86	(Abe & Ohtani, 2013; Daruty, 2018; Mchangama & Salaün, 2012)
	Oxalis corniculata Linn. ***	Diarrhoea (WP), caterpillar sting (L), diarrhoea (WP), dysmenorrhoea (WP), cough (L), urogenital infection (ND), haemorrhoids (L)	27,38	(Adjanohoun et al., 1982; Kaou et al., 2008; Mchangama & Salaün, 2012)
Pandanaceae	*Pandanus mayotteensis* H. St. John * (End)	Impotence (R)	5,95	(Mchangama & Salaün, 2012; Olivier Pascal et al., 2001; Saive et al., 2018)
Pedaliaceae	*Sesamum indicum* Linn. *	Redness (S), acne (S)	7,74	(Saive et al., 2018)
Phyllanthaceae	*Phyllanthus amarus* Schumach. & Thonn. ***	Antiemetic (ND), stomach pain (ND), gastric ulcer (ND), stomach ulcer (ND), colitis (ND), gastritis (ND), heartburn (ND),	20,83	(Adjanohoun et al., 1982)
	Phyllanthus casticum P. Willemet. ***	Abcesses (ND), furuncles (ND)	7,74	(Gurib Fakim & Brendler, 2004; Pernet, 1957)
	Phyllanthus nummulariifolius Poir. ***	Blisters (WP), oedema (WP), brucellosis (WP), hypertension (WP)	19,64	(Adjanohoun et al., 1982)
	Phyllanthus tenellus Roxb. *	Diarrhoea (L) (S) (W), cough (L) (S) (W)	11,90	(Kaou et al., 2008)

Piperaceae	*Piper* sp. ***	Impotence (R), malaria (L), diarrhoea (L) (S) (W), malaria (ND), gynaecological diseases (ND), diabetes (L), hypertension (L), intestinal parasites (L), tooth diseases (S), influenza (ND), redness (L)	34,52	(Kaou et al., 2008; Mchangama & Salaün, 2012; Saive et al., 2018; Said H. Soidrou et al., 2014; Soule et al., 2014)
Plantaginaceae	*Scoparia dulcis* Linn. ***	Allergy (W)	5,95	(Saive et al., 2018)
Poaceae	*Chrysopogon zizanioides* (L.) Roberty***	Cosmetics (R)	1,79	(Saive et al., 2018)
	Cynodon dactylon (L.) Pers. ***	Injury (S) (L), cut (S) (L), wound (S) (L), chap (S) (L), scars (S) (L), bleeding (S) (L), epistaxis (S) (L), nosebleed (S) (L)	22,62	(Adjanohoun et al., 1982)
	Eleusine indica Gaertn. ***	Allergy (L), dermal reaction (L), mycoses (L)	13,69	(Mchangama & Salaün, 2012)
	Zea mays Linn. ***	Bleeding (ND) umbilical wound (F), liver disease (St) (Sg), gonor-rhoea (Sg)	19,64	(Adjanohoun et al., 1982; Kaou et al., 2008; Mchangama & Salaün, 2012)
Polypodiaceae	*Phymatosorus scolopendria* (Burm. f.) Pic. Serm. ***	Oxytocic (ND), prevent miscarriage (ND),	11,90	(Mchangama & Salaün, 2012)
Portulacaceae	*Portulaca oleracea* Linn. ***	Urinary infection (ND), night incontinence (L), tonic (L)	13,69	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012)
	Portulaca quadrifida Linn. ***	Migraine (WP), headache (WP)	7,74	(Adjanohoun et al., 1982)

Ranunculaceae	*Clematis simensis* Fresen. *	Antalgic (S), migraine (S), anxiety (ND), stress (ND), nervous disorder (ND)	17,26	(Adjanohoun et al., 1982)
Rhizophoraceae	*Bruguiera gymnorrhiza* (L.) Lamk.***	Haemorrhages (ND)	5,95	(Gurib Fakim & Brendler, 2004)
Rosaceae	*Rosa chinensis* Jacq. *	Fever (Fl) (L)	5,95	(Saive et al., 2018)
Rubiaceae	*Canthium bibracteatum* Hiern *	Fortifying gum and teeth (ND), colic (ND), constipation (ND), painful periods (ND)	15,48	(Gurib Fakim & Brendler, 2004)
	Guettarda speciosa Linn. ***	Allergy (R) (S), dermal reaction (R) (S), mycoses (R) (S), acne (W) (Fl) (L), malaria (Fl)	21,43	(Kaou et al., 2008; Mchangama & Salaün, 2012; Saive et al., 2018)
	Paederia foetida Linn. ***	Bladder problem (ND), gastric pains (ND)	11,90	(Gurib Fakim et al., 1997; Gurib Fakim & Brendler, 2004)
	Pentas lanceolata (Forssk.) Deflers ***	Oxytocic (R), sterility (S) (L), impotence (S) (L), diffuse pain (S) (L)	19,64	(Adjanohoun et al., 1982)
	Vangueria madagascariensis J.F. Gmel ***	Skin infection (ND), abscesses (ND)	7,74	(Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004)
Rutaceae	*Citrus aurantium* Linn. ***	Sexual asthenia (ND), impotency (ND) Fever (L), fatigue (L), backache (L), haemorrhoids (L)	31,55	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012)

	Citrus aurantiifolia (Christm.) Swingle ***	Inflammatory fever (L), jaundice (F), typhoid fever (L), Panaris (F), asthma (F), indigestion (L), hiccups (L), chronic constipation (L), cephalalgia (L), stomach ache (L), nosebleed (ND), poisons (ND), colitis (L) diarrhoea (L), malaria (L), influenza (L), dysmenorrhoea (F), hypermenorrhoea (F)	57,14	(Adjanohoun et al., 1982; Gurib Fakim & Guého, 1994; Kaou et al., 2008; Mchangama & Salaün, 2012; Pernet, 1957; Soule et al., 2014)
	Citrus medica Linn. ***	Vaginal infection (L)	5,95	(Mchangama & Salaün, 2012)
	Citrus nobilis Lour. *	Malaria (L)	5,95	(Kaou et al., 2008)
	Vepris boiviniana (Baill.) Mziray ***	Redness (L) (W)	5,95	(Saive et al., 2018)
Santalaceae	*Santalum album* Linn. *	Acne (W)	5,95	(Saive et al., 2018)
Sapindaceae	*Cardiospermum halicacabum* Linn. ***	Hyperactivity in children (Fl), child fever (L) (Sd) (R), upset stomach (L), painful ear (L), skin infection (L), deworming (children) (L) (R),oxytocic (WP), arthritis (L) (R) (Sd), cramp (R) (Sd), muscular inflammation (WP), myalgia (WP), sciatic (WP), sprained joint (WP), aching joints (WP)	54,17	(Abe & Ohtani, 2013; Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Jain & Srivastava, 2005; Mchangama & Salaün, 2012; Sreekeesoon & Mahomoodally, 2014; Sussman, 1980)
	Dodonaea viscosa Jacq. ***	Vertigo (L), headache (ND)	11,90	(Gurib Fakim & Brendler, 2004; Jain & Srivastava, 2005)

	Litchi chinensis Sonn.***	Redness (W) (R), skin smoothing (W) (R)	11,90	(Saive et al., 2018)
	Paullinia pinnata Linn. ***	Arthritis (ND), rheumatism (ND), back pain (R), tonic (Li), diffuse pain (R), orchitis (ND), loss of appetite (Li), stomach pain (F), redness (F)	32,74	(Mchangama & Salaün, 2012; Saive et al., 2018)
	Sapindus saponaria Linn. *	Mycoses (F), irritations due to continuous rubbing (F)	7,74	(Mchangama & Salaün, 2012)
Sapotaceae	*Mimusops comorensis* Engl. * (End)	Haemorrhoids (B), hydrocele (B), orchitis (B), localized pain (B).	19,64	(Mchangama & Salaün, 2012)
Simaroubaceae	*Quassia indica* (Gaertn.) Noot. *	Prevents miscarriage (B)	5,95	(Mchangama & Salaün, 2012)
Smilacaceae	*Smilax anceps* Willd. ***	Lower back pain (R)	5,95	(Mchangama & Salaün, 2012)
Solanaceae	*Cestrum nocturnum* Linn.*	Cosmetics (FL)	1,79	(Saive et al., 2018)
	Datura metel Linn. ***	Ear pain (F), suppurative otitis (F), cough (Fl) (L), asthma (Fl) (L), respiratory disease (Fl) (L), emphysema (Fl) (L), phlegm (Fl) (L), diarrhoea (WP), gonorrhoea (WP), urethral flow (WP)	38,69	(Adjanohoun et al., 1982; Kaou et al., 2008; Mchangama & Salaün, 2012)
	Solanum mauritianum Scop. ***	Children's oral mycoses (L)	5,95	(Adjanohoun et al., 1982)

	Solanum nigrum Linn. ***	Abdominal pain (L), stomach ache (L), gastric ulcer (L), stomach ulcer (L), colitis (L), arthritis (ND), articular pain (ND), rheumatism (ND), muscular inflammation (ND), sciatic (ND), joint pain (ND), antispasmodic (ND), diarrhoea (WP), cough (WP)	45,83	(Adjanohoun et al., 1982; Kaou et al., 2008)
Strelitziaceae	*Ravenala madagascariensis* Sonn. ***	joint pain linked to childbirth (FB)	5,95	(Mchangama & Salaün, 2012)
Verbenaceae	*Lantana camara* Linn. ***	Hypermenorrhoea (R), fatigue (L), stomach-ache (L), postpartum pain (L), blisters (L), oedema (L), depurative (ND), diuretic (ND), hypertension (L)	41,07	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012; Saive et al., 2018)
	Lantana trifolia Linn. *	Vaginal infection (L)	5,95	(Mchangama & Salaün, 2012)
	Stachytarpheta jamaicensis (L.)Vahl ***	Redness (Fl)	5,95	(Saive et al., 2018)
Vitaceae	*Cissus quadrangularis* Linn. ***	Malformations (S)	5,95	(Adjanohoun et al., 1982)
	Leea guineensis G. Don. ***	Acne (W), allergy (W)	11,90	(Saive et al., 2018)
	Leea spinea Desc. *	Allergy (R) (S), dermal reaction (R) (S), mycoses (R) (S)	13,69	(Mchangama & Salaün, 2012)
	Rhoicissus revoilii Planch. *	Vulvar pruritus (L), leucorrhea (L)	7,74	(Adjanohoun et al., 1982)
Zingiberaceae	*Curcuma longa* Linn. ***	Injuries (Rz), dermatosis (ND), bruising (Rz), cough (L), paronychia (Rz)	21,43	(Mchangama & Salaün, 2012; Saive et al., 2018)

	Zingiber officinale Roscoe ***	Constipation (Rz), fever (Rz), backache (Rz), pharyngitis (Rz), abscess (L), boils (L), furuncle (L), pustules (L), skin disease (L), snake bites (Rz), vaginal prolapsed (Rz), uterine prolapses (Rz), uterus diseases (Rz), urogenital infection (ND), choleretic (ND), pelvic pain (Rz)	53,57	(Adjanohoun et al., 1982; Mchangama & Salaün, 2012)
	Zingiber zerumbet (L.) Sm. ***	Redness (L)	5,95	(Saive et al., 2018)

When applying the two different indicators on the data in table 1, the following information stands out. *Leptadenia madagascariensis* Decne. and *Ocimum canum* Sims. both affect 7 body systems, however, *L madagascariensis* is claimed to treat 7 health issues, giving a RII of 41,67 where *O. canum* is claimed to treat 19 different health issues, leading to a RII of 63,10. Ergo the latter is more versatile and could be studied in many different contexts. When it comes to the RNU, it seems that the main concern of the inhabitants of the Comoros Archipelago are ailments linked with the following symptoms: Abdominal syndrome (RNU = 71,9), skin disorder (RNU = 69,7), inflammation (RNU = 42,7), diarrhoea (RNU = 40,4) and urogenital issues (RNU = 33,7). This information is interesting for further research in ethnopharmacology when focusing on diseases linked to these symptoms.

4. Tendencies and cultural consensus

Based on table 1, information on the consensus was also collated, leading to the following noteworthy points:

- 56 species with one or more specific uses are known to be used only in the Comoros archipelago. Among these the one most mentioned is: *Pandanus mayotteensis* H. St. John. The dried roots of this species are ground together with the roots of *Woodia fruticose* (L.) Kurz, *Desmodium ramosissimum* G. Don., *Triclisia capitate* Baillon and *Monanthotaxis glaucocarpa* (Baill.) Verdc. The powder obtained is used as a decoction and drunk two times a day for seven days. This preparation is used to treat impotence (Mchangama & Salaün, 2012; Olivier Pascal et al., 2001; Saive et al., 2018).
- Only 6 species are used for the same purpose in several islands of the Indian Ocean, thus showing an agreement on use between traditional healers. Among these the ones most mentioned are: *Averrhoa bilimbi* Linn. and *Acalypha lyallii* Baker. In the Comoros archipelago, the fruit of *Averrhoa bilimbi* Linn. are used to treat itching; they are crushed with water and ashes to make a paste that is applied to the affected area (Abe & Ohtani, 2013; Daruty, 2018; Mchangama & Salaün, 2012). *Acalypha lyallii* Baker is used as a leaf decoction to massage the body to treat rheumatism (Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Seebaluck et al., 2015).
- 145 species are used widely in the Indian Ocean and surroundings, including the Comoros archipelago islands, for many different ailments. Among these the one most mentioned is: *Cardiospermum halicacabum* Linn. Leaf decoctions are used to treat eczema, anasarca, ear diseases and wounds. Roots are used to treat dizziness, eye diseases, rheumatism and stiffness. Stems are used to manage fever in India. In the islands of the Indian Ocean, stems and roots are used as laxative and emetic as well as to treat cysts, bladder catharsis and gonorrhoea. The leaves are used to treat boils, rheumatisms, eczema and impetigo (Abe & Ohtani, 2013; Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Jain & Srivastava, 2005; Mchangama & Salaün, 2012; Sreekeesoon & Mahomoodally, 2014; Sussman, 1980).

Throughout the classification in table 1, these 145 species are found the most frequently. Even though *Cardiospermum halicacabum* Linn. is the most often mentioned (7 sources), it doesn't have the widest variety of uses (RII = 54.17), ergo there is a certain consensus for the specific uses of this plant.

On the other hand, *Plectranthus amboinicus* (Lour.) Spreng. has fewer sources (6) but has many different uses (RII = 65.48), therefore pointing towards a higher versatility. e.g. A total of 21 traditional uses for this plant have been mentioned in the literature. In the Comoros archipelago, it is used as a cure for ailments ranging from a simple cough to colitis and flatulence, as well as rheumatism, malaria and furuncles. In Madagascar, leaves are added in meals as a food complement and are also used in decoctions or in fumigation to treat colds (Nicolas, 2012). In the Réunion Island, leaves of *Plectranthus amboinicus* (Lour.) Spreng are used in baths, infusions and for massage, to treat the symptoms caused by the chikungunya virus (fever, sore muscles and articulations) (Minker, 2007).

When it comes to similarities between different regions, the species *Moringa oleifera* Lam. (RII = 61,31), is used in the Comoros archipelago to treat asthma, hiccups and spasms among other uses (Cf. Table 1) (Adjanohoun et al., 1982; Gurib Fakim & Brendler, 2004; Mchangama & Salaün, 2012; Saive et al., 2018). In Mauritius and Seychelles, this species is linked to the treatment of throat related infections. For the anti-spasmodic effect of *Moringa oleifera* Lam., people from Madagascar, Mauritius, Seychelles, as well as peoples from the Comoros archipelago tend to agree. As for the other uses mentioned in the Comoros archipelago, other places have their own use versatility: only inhabitants of Rodrigues and Seychelles use this species to treat high blood pressure, coughs and as an abortifacient, whereas in Madagascar, Mauritius and Rodrigues it's used to treat helminthiasis, in Mauritius, this plant is also used to treat nervous disorder ear infections and fever and in Seychelles, this species is consumed as a refreshing drink (Adjanohoun, 1983; Gurib Fakim & Brendler, 2004; Pernet, 1957).

In some cases, some plants are used in other islands of the Indian Ocean and surroundings and are part of the flora of the Comoros Archipelago, but are not known to be part of the Comorian pharmacopoeia. Therefore, these species are not mentioned in Table 1:

e.g.: *Cabucala erythrocarpa* (Vatke) Leeuwenb. is endemic to Madagascar and the Comoros archipelago. In Madagascar, a bark decoction is drunk to treat viral hepatitis, malaria, stomach pain and diarrhoea. The bark is also used as a bitter ingredient in some alcoholic beverages, which are considered as strongly aphrodisiac. Leaves are used to treat skin infections and are consumed as decoctions to treat hypertension (Schmelzer & Gurib-Fakim, 2008). In the Reunion Island, an infusion of *Hypercum lanceolatum* Lam. yellow flowers is considered as refreshing, meaning that it helps manage fever as well as heartburn caused by the ingestion of hot and spicy food. This infusion is also considered helpful against urinary tract inflammation and will often be used as a depurative and to regulate menstruations (Lavergne & Vera, 1989). These plants are found in the Comoros archipelago; however, no use reports are mentioned there.

As expected, plants with fewer mentioned medicinal uses are more likely to be used the same way in different places, in comparison to plants with multiple medicinal uses. *Acalypha lyallii* Baker is only used for rheumatism in the Indian Ocean, whereas *Bidens pilosa Linn.* is known for many uses in the Comoros archipelago but has even more uses in the surrounding islands. Out of the 207 different species mentioned in the present work, only 27% are used exclusively in the Comoros Archipelago for a variety of purposes, 3% are used in the Comoros Archipelago and in several islands and surroundings of the Indian Ocean for the same purposes and 70% are used in the Comoros archipelago and in other islands and surroundings of the Indian Ocean for comparable or different purposes. For the latter category, its size can be explained by the fact that many non-endemic species have been transported through the years and have diverse origins. Therefore, they might be used very differently in the different areas of the world where they are found.

When looking at different ethnobotanical studies carried out in the Maurice archipelago, Mauritius Island and Rodrigues Island are studied separately. On the other hand, most of the studies that were performed in the Comoros archipelago did not separate the different islands; in the present work however, separating the islands is important as some species are endemic to only one or two islands of the archipelago: e.g.: *Syzygium humblotii* (h. Perrier) labat & Schatz and *Eugenia choungiensis* Byng & N. Snow have been reported to be endemic to Mayotte. *Syzygium tringiense* Byng & N. Snow is known to be endemic to the island of Anjouan (Byng et al., 2016) and *Gyrostipula comorensis* Homolle ex J.-F. Leroy was only endemic to Grande Comores and Mohéli but its endemicity has been widened to include Anjouan (Mouly, 2009). As these species are not found in all the Comorian islands, the archipelago should therefore not be studied as a whole but rather be investigated in its separate parts. When a clear separation between the geographic regions is made, the collected data have a higher impact when integrated into ethnobotanical indicators such as the informant agreement ratio.

Identification of species of interest for modern medicine is not the only reason to study the relationship the local people have with the flora that surrounds them. Other factors such as biodiversity management and protection (Nazarea, 1999), as well as the preservation of ancestral knowledge are two important objectives for ethnobotany studies, especially as traditional knowledge is mostly shared through oral tradition. Due to the growing access to modern medicine, the interest for traditional medicine tends to disappear; therefore, the number of traditional healers and their knowledge plummets. Ethnobotanists store plant specimens in herbaria, gather information on the uses of species and thereby preserve ancestral knowledge from extinction (Kaido et al., 1997).

The fact that plants have been used for centuries as medicines does not mean they are harmless. Their presumed innocuousness is based on hundreds of years of empirical observations (Fennell et al., 2004). Just as for modern medicines, there can be some deleterious effects. Due to the way traditional knowledge is transmitted, adverse effects are not always fully understood and serious poisoning due to traditional medicines is not uncommon. In South Africa, the estimated mortality due to traditional medicines ranges between 10.000 and 20.000 cases per year. This huge variability is

due to a lack of precise data. Indeed, many cases of poisoning which are not recorded could possibly be linked to traditional medicine (Popat et al., 2001; Thomson, 2000).

As mentioned previously, some species are traditionally used for numerous diseases, which means that these species are under a strong anthropic pressure due to their biological value (Adjanohoun, 1983; Gurib Fakim, 1990; Gurib Fakim & Brendler, 2004; Lartigau Roussin, 2002; Mchangama & Salaün, 2012). If there is no management of these plants, there are chances that they will become extinct (Rasoanaivo, 2011).

When focusing on the case of the Comoros Archipelago, it's important to remember that it came to exist through volcanic activity and therefore it has a very hilly landscape (Nougier et al., 1986), which is not ideal for crop production, even though the soil is rich and fertile (Clement et al., 2016). The discovery of medicinal values in plants in such places is an important opportunity to promote the development of these regions through the sustainable exploitation interesting species. The high added value compensates for the lack of infrastructure for more traditional crops. Needless to say, the knowledge gathered from the traditional healers should be returned in one way or another to the population from which it originated (McManis, 2003; Rasoanaivo, 2011).

5. Conclusions

This review is an attempt to gather and examine numerous species used in the traditional Pharmacopoeia of the Comoros Islands. Since the 19th century, ethnobotany and ethnopharmacology have been an important part of the drug and cosmetic industry. Based on that affirmation, the study of biodiversity hotspots, especially the ones found on islands seems essential as they present a high concentration of different species in a defined area. In addition, the ethnobotanical work done in these places on Earth will allow us to maintain the knowledge developed by the people who have been working with these species for centuries and who have had the time to test the effectiveness of the remedies empirically. In the present work, 207 species were identified as part of the traditional pharmacopoeia of the Comoros archipelago. Some species are already known worldwide for their properties. However, many are still to be studied in order to validate their biological activities.

The specific uses for the different species mentioned herein can be compared to other databases and then using the previously mentioned tools, species that are more likely to be really effective and interesting for medicinal and cosmetic purposes can be identified and integrated into more hands-on studies. These differences and similarities will probably be of interest when this database is compared to data from around the world, giving more clues as to which species are likely to produce new cures.

6. Acknowledgment

The authors are grateful to the University of Liège (Belgium) for allowing us to gain access to all the information required for an exhaustive study of the subject.

7. Complementary discussion

Not in the published paper.

Various tendencies could be observed based on the gathered data. Based on the RNU, obtained using the data in table 1 and the ailment classification observed in appendix 1 it was established that the most requested medical assistance was linked to gastrointestinal syndromes, skin issues, urogenital infections, diarrhea, nervous issues, malaria, bleeding, respiratory diseases, headaches and fever. These tendencies are partially in line with the information given by the World Health Organization (WHO). The leading cause of death in 2020 in the low income countries were Neonatal conditions, lower respiratory tract infections, ischaemic heart disease, stroke, diarrhoeal diseases, malaria, road injuries; tuberculosis, HIV/AIDS and cirrhosis (WHO, 2020). The clear common ground between this work and that of the WHO are diarrhoea, malaria and respiratory disease. Some conditions mentioned in the study are however very generic. For example, conditions such as tuberculosis can be linked to respiratory disease and fever. Bleeding is a very generic reason for medicinal assistance but can be linked to road injuries. As for the nervous issues, some may be remnants of a stroke (Abdullahi et al., 2020). Meaning that out of the top ten health issued mentioned in this review, 6 are aligned with worldwide tendencies.

When comparing the identified species from this first article with the Mahoran flora, 15 species are not reported as being part of that flora. This means that 93% of the species mentioned in this work could potentially enter the following steps.

The WHO made an attempt to identify all the medicinal plants worldwide and the outcome of this work led to the conclusion that between 14% to 28% of the plants on earth have been used for traditional medicine at least once. Based on the conservative agreement that there are 250.000 higher plant species on earth, this suggests that between 35.000 and 70.000 species have been used worldwide. When applying such an observation to this case study, where the number of vascular species in the Comoros archipelago has been estimated to be around 1500 (Vos, 2003), the number to be studied should be between 210 and 420 species. *Ergo*, this work might underestimate the number of species used traditionally in the archipelago.

3

ETHNOBOTANICAL STUDY

Saive, M., Frederich, M. and Fauconnier, M.-L. (2018) 'Plants used in traditional medicine and cosmetics in Mayotte Island (France): An ethnobotanical study', Indian Journal of Traditional Knowledge, 17 (4).

Following this primary approach aiming at identifying the species used in the Comoros Archipelago for traditional medicine and cosmetics, it is remarkable that for some species the sources agree on the link between species and the targeted ailment, whereas for others, there is a strong variation between the sources. Eg: *Averrhoa bilimbi* L. has been linked to similar uses in the Comoros and even in other islands of the Indian ocean. On another hand it seems that the information concerning *Cardiospermum halicacabum* L. diverges.

Among other notion, gathered through this preliminary investigation, the mention of the disappearance of traditional knowledge due to a loss of interest by the new generation seems to be a frequently used argument to promote the execution of ethnobotanical work around the world. Another point of interest is linked to the value of that knowledge. In places where infrastructures are not available for the development of financial sustainability. Adding value to available plants through a simple use for medicines or cosmetics has proven to be beneficial for the country's economy as long as the benefits originating from the uses of that traditional knowledge is redistributed in a fair manner. In addition, the fact that most of the previously mentioned species can be found in Mayotte strengthened our belief that an ethnobotanical study would be of interest on the island. The logical step forward was the execution of such a study.

A first mission took place, during which contacts were made and primary information was gathered. Throughout that mission we were able to meet some of the informants and establish a field laboratory, with the hopes of gathering extracts from

fresh plant samples. The second mission was focused on meeting as many significant informants as well as gathering as much vegetable material as possible. What made an informant significant was the recognition he /she had around the island and the surrounding villages. One informant stood out regarding the uses of plants for cosmetics as she was known even off the island and as she received an honorific title from the Order of the Arts and Letters by the French Minister of Culture and Communication in 2011. Another informant stood out as he was already working in collaboration with the CBNM (Conservatoire Botanic National du Mascarin) and had contributed to the publication of the work "Recueil d'une pharmacopée à Mayotte". This source was of major interest for the writing of the review study.

On meeting an informant, the information was collected by filling in an interview record card as found in appendix 2. However, as the original aim of the work was oriented towards the finding of plants used for cosmetics, a strong bias was generated as the informant only spoke of cures and treatment used for superficial skin conditions. Finally all the data was analyzed using the informant agreement ratio and the use value developed by Trotter and Logan (Trotter & Logan, 1986) and Phillips and Gentry (Phillips & Gentry, 1993). The use value gives insight into the relative importance of species known locally whereas the informant agreement ratio gives insight into the significance of the informant's affirmations on specific uses of plants. Ethnobotanical data are of interest to minimize the screening process linked to the identification of species with actual biological activity.

Plants used in traditional medicine and cosmetics in Mayotte Island (France): An ethnobotanical study

Matthew Saive[1]*, Michel Frederich[2] & Marie-Laure Fauconnier[1]

[1]Departement of Organic and General Chemistry, Gembloux Agro-Bio Tech, University of Liège, Gembloux, Belgium

[2]Departement of Pharmacognosie, University of Liège, Liège, Belgium;

*Gembloux Agro-Bio Tech, University of Liège, Passage des déportés 2, 5030 Gembloux, Belgium

E-mail: msaive@ulg.ac.be

Abstract

Mayotte is a small island located in the Mozambique canal and due to this location it has long been an important cultural and botanical crossroad. Species from Madagascar, China, India and the African continent, as well as some endemic species are found on this small island. Semi structured interviews were carried out throughout the island with 29 informants known for their knowledge of the traditional uses of plants. We based our work on the hypothesis that the more a plant was mentioned by the interviewees, the higher the chances would be to find an effective biological activity. In the end 69 species of interest were identified through the interviews. Flowers of *Jasminum nummularifolium* Baker, wood of *Carissa spinarum* L., roots of *Curcuma longa* L., leaves of *Lawsonia inermis* L., and wood of *Santalum album* L. tend to be the most known and the most used in Mayotte for traditional medicine and cosmetics. In the end those plants are used for medicine or for cosmetics, however, when it comes to medicinal uses, the traditional doctors are not looking for the cause of the disease and will orient their treatment towards the curing of the symptoms. On another hand, it is clear that the locals have a strong cultural bond with the use of traditional cosmetics in addition to traditional medicine.

Keywords: Traditional medicine, Traditional cosmetics, Mayotte, Use value, Informant agreement ratio

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SAIVE *et al.*: PLANTS USED IN TRADITIONAL MEDICINE AND COSMETICS IN MAYOTTE ISLAND, FRANCE

*Corresponding author

1. Introduction

As long as human kind can remember, plants have always been used as medicine (Petrovska, 2012). Over the years, traditional practices have had many influences and are the sum of much empirical testing. Even though some practices have been proven to be inefficient, some traditional knowledge has had a very important role in the development of modern medicine (Gurib-Fakim, 2011; Heitzman et al., 2005; Katiyar et al., 2012).

The African continent is home to between 40,000 to 60,000 plant species, out of which around 35,000 are endemic, with 70 % growing in only few regions, known as biodiversity hotspots (Serageldin, 2014). Anthropic pressure (most often linked to environmental degradation) on these hotspots has never been as strong as at present and might lead to a significant loss of biodiversity.

Ethnobotanical studies can contribute positively in the management of biodiversity, as it consists of recording the habits of local populations towards both plants and biodiversity. The results of such studies can also be used as indicator of the value of some species. Indeed, the WHO has estimated that the international market for herbal medicine products is worth US $ 62 billion, which is expected to increase to US $ 5 trillion by the year 2050 (Nunkoo & Mahomoodally, 2012). When it comes to cosmetics (cosmetics, toiletries and fragrances), in 2001 the world market was estimated at US $ 124 billion and just for the skincare products, US $ 31,3 billion (Sameer Kumar, 2005).

In addition to the economic value of cosmetics, several trends are currently being observed, the environmental impact, the ethics of production, as well as a growing interest in cosmetics intended for ageing populations and ethnic groups are important aspects for the industry (Sameer Kumar, 2005).

The study reported herein was carried out on the island of Mayotte in the Indian Ocean for three reasons: firstly, it is known as a hotspot for its important biodiversity (Rasoanaivo, 2011); secondly, the women in this area of the globe are known for their traditional masks (*M'sindzano*) made out of plants harvested in the neighborhood and thirdly, as in many regions from this part of the world, the population first relies on traditional medicine for cultural or financial reasons (Rakotoarivelo et al., 2015). At the end of this work, we were able to identify some of the plant species used in traditional remedies and cosmetics, especially the ones used in the realization of the traditional masks.

2. Methodology

2.1. Study area

Mayotte is a French department located north of the Mozambican canal in the Comoros archipelago. It is constituted of two separate main islands of volcanic origin called "Grande Terre" and "Petite Terre". In addition to those two main land, 30 islets are spread in the 1100 km² lagoon. 63 % of "Grande Terre" is covered with slopes with a 15 % gradient or more. Mayotte has a maritime tropical climate. During the wet season, the temperatures can reach 34 °C, the air is very moist with up to 85 %

humidity and up to 85 % of the rainfall takes place. During the dry season, the temperatures drops to around 25 °C and the rainfall tends to be scarcer. Mayotte also has a strong climatic gradient between the North and the South of the island. The annual rainfall can vary from 1000 mm in the south to 6000 mm 40 km farther to the North (Ali Charif et al., 2016; Vos, 2003).

2.2. Botany

Due to its location, climate, relief, soil characteristics, distance from other islands and continents, Mayotte's flora is one of the richest per square kilometer in the world (Fabien Barthelat & Viscardi, 2012).

To date, more than 1300 vascular species and 93 mosses and allied plants have been identified. Among these species, 48 % are exotic, 34 % are indigenous, 10 % are endemic from Madagascar and the Comoros archipelago, 5 % are endemic from the Comoros archipelago and 4 % are strictly endemic. 95 % of the territory has been modified by humans; these areas contain only 48 % of the total flora of Mayotte. The 52 % of the flora which is indigenous or endemic is found in 5 % of the untouched territory. Within this very rich flora, 613 species are considered to be directly useful for humankind. Those plants are mainly used for food, but some of them are used for fuel, construction, medicine, cosmetics or ornamental purposes. Most of them are exotic and grown intentionally on the islands; others are indigenous or even endemic (Amann et al., 2011).

2.3. Culture

Within this extensive biodiversity, many plants are used traditionally by the indigenous populations for many different practices. For medicine, religion, cosmetics, but also as building and heating material. In Mayotte the keepers of the knowledge are called "*Fundi*"; their knowledge usually originates from an oral tradition. The people who collect and use plants are known as "*Fundi mpuamizi*" (literally, the master who collects roots). In addition to using the plants, traditional remedies are often taken following certain rituals destined to enhance the efficiency of the treatments. The most common ways to dispense the treatments are: in decoctions, as balms (grated vegetal material with sandalwood and water to form a past) or as poultice and by inhalation. Mahoran traditional medicine is linked not only to what plant remedies are required but also to what food is forbidden so that the treatment will be effective (Mchangama & Salaün, 2012).

In addition to the use of plants by the "*Fundi*", they are also used by many women all over the island for cosmetic, hygienic and toiletry preparations. For instance, when preparing their "*M'sindzano*".

A previous study was carried out by (Mchangama & Salaün, 2012). Based on that work, 135 plant species were mentioned by a single traditional doctor. Within those 135 species, 8 were rare or endemic, leading to questions on how to allow the local people to use them for healing and at the same time to manage the risk of an eventual over exploitation of these species. This previous work was entirely based on the knowledge of one very specialized traditional practitioner. Therefore, in a sense it cannot be considered a proper ethnobotanical study as only one informant was

involved. The present study, on the other hand, has included the interventions of many informants, living in various areas around the island.

2.4.Data collection

When it comes to targeting plants that are likely to have a scientifically established effect, several approaches exist. Firstly, "*the historic depth*" which is based on: "*the assumption that if a given species was employed in the past for a specific disorder, and people today employ the same species for the same purpose, then the plant is likely to be effective"*(Trotter & Logan, 1986). A second approach is called the "*Cross Cultural comparison*" and relies on the fact that plants used in a similar manner in two or more populations of different areas and cultural background are likely to be effective (Trotter & Logan, 1986).

Both approaches assume that in order to establish the potency of plants used traditionally, there must be some sort of consistency between the answers given by the concerned populations (Moerman, 2007; Weller, 2007). In this work, we have focused on the historic depth principle. In order to be valid, several conditions had to be established and respected within the study(Giday et al., 2009; Trotter & Logan, 1986).

2.4.1. **Condition 1: Size of the database**

The target number of informants was obtained based on works by Karangawa, Lusakibanza & Frederich, Martin, Nunkoo & Mahomoodally (Karangwa, 2006; Lusakibanza Manzo & Frederich, 2012; Martin, 1995; Nunkoo & Mahomoodally, 2012). The two main criteria for the estimation of the target number of people to interview were the island's population density, as well as the time available for research on the island. Based on the relationship between traditional knowledge and the "keeper's" knowledge (Maffi, 2005), it seemed interesting to focus the interviews on the known "keeper's" around the island (Kayabaşı et al., 2018).

2.4.2. **Condition 2: Interviews**

The interviews were carried out in French when possible; if the informant only spoke a local language (Shibushi or Shimaore) help of an interpreter was taken. The interviews were realized using a semi-structured guide (Zambrana, 2017).

2.4.3. **Condition 3: Taxonomic identification**

The vegetal material mentioned throughout the interview had to be identified accurately. To do so, two pathways have been suggested in the literature (Trotter & Logan, 1986): The first is the collection of plant material in collaboration with professional botanists; the second is the linkage of the common name to its scientific name based on other ethnobotanical studies. In this work, plant identification was done as follows: As Moerman (Moerman, 2007) suggested, plants that could not be identified with enough certainty were not supposed to enter into the ethnobotanical study. The botanical identification was carried out with the help of the "Conservatoire Botanique National du Mascarin" (CBNM) in Mayotte. During the interviews, data with different level of certainty were obtained. In order to identify the species mentioned by the informants, several approaches were used. The plant names were given in French, in Shibushi or in Shimaore. The names were translated to their botanical names with the

help of the CBNM, their herbarium and database known as the "Flore vasculaire de Mayotte"(Boullet, 2016). When available during the interview, the vegetal material was collected in order to be stored in the CBNM's herbarium (MAO numbers in Table 2)[1]. However, sometimes, the plant material given by the traditional practitioner did not allow for the creation of a herbarium specimen (small pieces of wood, dried seeds). When it occurred, the botanical name was established by using the previous botanical work done by the botanists from the CBNM in order to target one or several probable botanical names. Those names were then used to find plant pictures and herbarium specimen from the MNHN (Museum national d'histoire naturelle) database (P numbers in Table 2). Those pictures were then shown to the informant in order to validate the species[2]. In some case, the pictures could not be found and we based our data only on the expertise of the botanists working at the CBNM and the available ethnobotanical data[3].

2.4.4. **Condition 4: Data analysis**

When it comes to treating the different answers given by the informants, estimating what might be biologically effective out of all the beliefs and other placebo effects linked to the use of specific species is a challenge (Moerman, 2007). As an ethnobotanical study, this work has several purposes, one of which is to target species that might have relevant biological activities. In order to target the plants with the highest potential, the use value (UV), and the informant agreement ratio (IAR) were used.

Search for keepers of knowledge was carried out by visiting the different villages and asking the people in the streets about who their reference within the area was, when it came to the use of plants for cosmetics and health. By doing so, the number of interviewed informants was efficiently limited. Some areas, where no informants were interviewed, were ruled out due to a massive emigration of Europeans, rendering the search for keepers of knowledge irrelevant.

2.5.Interviews

The questionnaire had close and open-ended questions. The closed questions were of a demographic order asking the informants on their age, gender, level of education, occupation and religion. The open ended part asked for plants used traditionally in medicine and cosmetics, the name of the plants, the parts used, the preparations as well as what they were used for (Nunkoo & Mahomoodally, 2012). Before each interview the project was explained thoroughly so that the informant would know to whom and for what they were giving the information.

The average age of the interviewees was 48 yrs old, with a strong majority of women (Table 3). Among the informants a few "*Fundi*" (keepers of the knowledge) could

[1]This data is considered as very strong and is marked by * in Table 1

[2]This data is considered less strong and needs to be confirmed by the creation of herbarium material. It is marked by ** in Table 1

[3]This data is considered as an attempt to identify the plant material and needs to be confirmed by the creation of herbarium material. It is marked by *** in Table 1

mention 15 or more different remedies; however, the average amount of remedies mentioned per informant was close to 7. The interviews were conducted all over the island. Most informants were known for their knowledge of plants. That knowledge had been passed onto them by their parents. Most of them did not go to high school. Some of them had begun secondary education but didn't complete. Three informants had graduated from higher education (Table 3).

2.6. Data analysis

2.6.1. **Use value**

In order to determine the relative importance of any one species, the sum of the use report of that particular plant was divided by the total number of informants based on the following formula (Arı et al., 2018):

$$UV = \frac{\sum Ui}{n}$$

Where, *Ui*: number of use-reports cited the informants for a given species.

n: total number of informants.

The closer the answer is to 0, the smaller the number of use-reports. It is important to point out that the use value does not distinguish if a plant is used for a specific purpose or for many purposes (Nunkoo & Mahomoodally, 2012; Srithi et al., 2009).

2.6.2. **Informant agreement ratio (IAR)**

The aim of this technique is to determine the variability ratio in the answers given by the informants (Moerman, 2007). This degree of agreement is known as the IAR (Trotter & Logan, 1986).

$$IAR = \frac{(Totalcases\ for\ ailment) - (Number\ of\ remedies\ for\ ailment)}{(Totalcases\ for\ ailment) - 1}$$

The result obtained is between 0 and 1; the closer the answer is to 1, the greater the assumed consensus on a given use, whereas an answer close to 0 suggests that the plants are chosen randomly, thereby revoking the hypothesis of exchange of information among the informants (Moerman, 2007; Nunkoo & Mahomoodally, 2012; Srithi et al., 2009; Trotter & Logan, 1986).

3. Results and discussion

Twenty-nine informants answered the semi-structured interviews and 249 answers were obtained. These answers were given in French, Shimaore or Shibushi, therefore, translating the vernacular names into botanical names was necessary. To do so, three techniques were used depending on the quality of the information and vegetal material obtained during the interviews. Using several botanical databases and with the help of the botanists from the "Conservatoire Botanique National du Mascarin", most of the vernacular names could be translated: 69 different taxa were identified.

Sixteen species were identified based on the collection and storage of plant material in the CBNM herbarium. Thirty-four species were identified using pictures from the MNHN database. Nineteen species could not be identified using the herbarium vouchers nor pictures from the MNHN originating from the Mahoran collection, their identification is an attempt based on the CBNM database.

The species were issued from 44 different families, of which the *Fabaceae* and the *Malvaceae* are the most represented with 6 species each (worth 8,7% of the different species). The next most used family is the *Apocynaceae* with 4 species (5,8%) (Table 2).

The fact that this work is oriented towards understanding of the traditional cosmetics in addition to traditional medicine might have influenced the answers given by the informants, leading to classification of the treatments into 4 categories; as suggested in the work of Inta *et al*. (Inta et al., 2013). The different uses were classified into several main activities. The following answers: pain, soreness, redness, stomachache, headache, acne, allergies, fever were grouped under inflammation (Holliman, 1992; Iwalewa et al., 2007). This work resulted in 76 citations linked to a supposed anti-inflammatory activity where 47 plants were used in these treatments. The number of citations and number of plants used for the whitening activity were 49 citations for 15 species. For the smoothing effect, 57 citations made use of 18 different species. As we also took into account uses for perfume, it was mentioned 47 times with 16 different species. These numbers led to the following Informant agreement ratio (IAR):

- Anti-inflammatory : 0,38
- Whitening : 0,71
- Smoothing : 0,69
- Perfume : 0,67

The very low number obtained for the anti-inflammatory activities lies in the fact that many ailments linked to an internal or an external pain, to fever, or to any kind of soreness can be linked to inflammation (Holliman, 1992; Iwalewa et al., 2007) and can be explained by the fact that the traditional practitioner tend to heal the symptoms prior to the disease. The informants tended to agree more on the plants to use for skin whitening, skin smoothing and as perfume; this can be explained by the fact that these treatments are more specific and therefore, the plants used will be more specific.

The use value gives us an idea of the favored species used in Mahoran traditional cosmetics and medicine. As these plants are used more, we can assume that, from an empirical point of view, they have more chances of being really effective. However, as this indicator doesn't take specific uses into account it cannot be used alone. In this study, many species have a very low use value as they were mentioned for one or two specific uses by only one informant out of 29. The plants with the highest use value were *Jasminum nummulariaefolium* Baker (0.58) *Lawsonia inermis* L. (0,51) and *Carissa spinarum* L. (0,28). Interestingly enough, *Carissa spinarum* L. was mentioned only 8 times but as most informants agreed on the several uses of this plant, it raised the UV higher than species that were mentioned more times but with fewer different uses (e.g. *Curcuma longa* L.) (Samoisy & Mahomoodally, 2015).

4. Conclusion

Plants have been used for thousands of years for all sorts of activities, such as medicine and cosmetics. These uses have had a very important role throughout the years in the development of modern medicine.

The 29 interviewed informants selected based on their reputation, gave us a total 249 plant names, however, through the process of translation and botanical name identification, this number was reduced to 69 different plant species. Those answers were analyzed using the IAR and the UV in order to evaluate their potential for medicine and cosmetics. The different treatment could be categorized in 3 main classes; anti-inflammatory, skin whitening and skin smoothing. However, as some plants might be interesting for the creation of cosmetics, the use of plants as perfume was also recorded. On one hand, the more specific uses, the informants tended to agree on what plant to use as skin smoothing or skin lightening as well as for perfume (respectively IAR: 0,69 , 0,71 and 0,67). On another hand, the IAR for anti-inflammatory activity is below 0,50. This can be explained by the fact that many ailments can be linked to inflammatory processes (pain, soreness, allergies, etc.). The most favoured species for use were *Jasminum nummulariaefolium* Baker (flowers) (UV: 0,58) *Lawsonia inermis* L. (leaves) (UV: 0,51) and *Carissa spinarum* L. (wood) (UV : 0,28). The ones mentioned several times and for which the informants agreed on their specific use were jasmine (*Jasminum nummulariaefolium* Baker) (flowers), henna (*Lawsonia inermis* L.) (leaves), curcuma (*Curcuma longa* L.) (rhizome) and sandal wood (*Santalum album* L.) (wood). The results obtained from this ethnobotanical work illustrate the strong cultural bond the inhabitants from Mayotte have with the traditional uses of plants. It also shows a great lack of consistency in the potential uses from an ailment point of view as well as what plant should be used. This work also illustrates the fact that informants will work toward healing the symptom first with only a little consideration to the cause of the diseases. When comparing this work, with previous work done on this island, many species are similar, however, the specific uses linked to those species tend to vary except for *Aloe mayottensis* A. Berger, *Curcuma longa* L., *Guettarda speciosa* L., and *Lawsonia inermis* L. The results originating from following studies are destined to be returned to the Mahoran population in order to help them valorize the island's flora.

5. Acknowledgment

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6. Tables

Table 2: List of identified species mentioned during the interviews. Cit.; amount of times the specific species was mentioned by the informants. Parts used: plant organ used to create the remedy. Use: targeted ailment. Status in Mayotte: ecological interest. UV: use value. Herbarium reference: vouchers reference code, P numbers are attached to the MNHN, MAO numbers are attached to the CBNM. (* very strong identification based on the deposition of a herbarium voucher. ** good identification, based on the vernacular names and the comparisons of specimen pictures originating from the MNHN herbarium *** attempted identification based on the vernacular names and the plant database from the CBNM.)

Botanical name(Vernacular name, language)	**Cit.**	**Parts used**	**Uses**	**Status in Mayotte [13]**	**UV**	**Herbarium reference**
Abrus precatorius L. subsp. *africanus* (Vatke) Verdc. (Masonaombigara, Schibushi)	1	Leaves	Stomach ache	Indigenous	0, 03	P00078910 **
Acacia farnesiana (L.) Willd. (Mugum'tsinzano, Shimaore)	3	Flowers	Perfume	Exotic, invasive	0,10	P00229214 **
Adansonia digitata L. (Mbuiu, Shimaore)	4	Fruits	Lightening, redness, acne, smoothing	Indigenous	0,14	MAO00046 *
Alangium salviifolium (L. f.) Wangerin (Mlijiliji, Shibushi)	1	Leaves	Redness	Indigenous	0,03	***
Aloe mayottensis A. Berger (Chiziamlili, Shibushi)	4	Leaves, mucilage	Redness, stomach-ache, smoothing	Indigenous, endemic	0,14	MAO00055 *
Annona senegalensis Pers. (Porpetraka, Shibushi)	1	Branches, bark	Redness	Exotic	0,03	***
Aphloia theiformis (Vahl) Benn. (Mfandrabo, Shimaore)	1	Leaves	Stomach ache	Indigenous	0,03	P00290489 **
Apodytes dimidiata E. Mey. ex Arn. (Mourimourou, Shimaore)	1	Leaves	Redness	Indigenous	0,03	P00273057**

Argomuellera trewioides (Baill.) Pax & K. Hoffm. (Sari kafe, Shibushi)	1	Leaves	Inflammation	Indigenous	0,03	P00273078 **
Calophyllum inophyllum L. (Mtondro, Shimaore)	1	Sap	Hair removal	Indigenous	0,03	P00229128 **
Cananga odorata (Lam.) Hook. f. & Thomson (Ilangilang, Shimaore)	4	Flowers	Perfume	Cultivated	0,14	MAO00054 *
Carissa spinarum L. (Mdjanfari, Shimaore)	8	Wood	Headache, acne, lightening, smoothing	Indigenous	0,28	P00273138 **
Carpodiptera africana Mast. (Mouhouvé, Shimaore)	1	Wood	Lightening	Indigenous	0,03	P00248732 **
Cassytha filiformis L. (Chiroungakangue-tandri, Shimaore)	1	Wood	Lightening	Indigenous	0,03	P00290360 **
Cestrum nocturnum L. (Jasmin de nuit, French)	2	Flowers	Perfume	Cultivated	0,06	***
Chrysopogon zizanioides (L.) Roberty (Vetier, French)	3	Roots	Perfume	Cultivated	0,10	***
Cocos nucifera L. (Coco, French)	7	Fruits	Smoothing, lightening	Exotic	0,24	***
Cordia myxa L. (Mrovu, Shimaore)	3	Bark	Fertility	Exotic	0,10	***
Cordia subcordata Lam. (Bouaroulahi; Shimaore)	1	Roots	Allergies	Indigenous	0,03	***
Coriandrum sativum L. (Coriandre, French)	1	Seeds	Stomach ache	Cultivated	0,03	***

Curcuma longa L. (Mtsindzano, Shimaore)	10	Roots	Redness, smoothing, lightening	Cultivated	0,34	P00273084 **
Erythroxylum lanceum Bojer (Loangati mena vavi, Shibushi)	1	Leaves	Pain, soreness	Endemic	0,03	MAO00045 *
Grewia cuneifolia Juss. (Ampalikeli, Shi-bushi)	1	Leaves	Allergies	Indigenous	0,03	P00229512 **
Guettarda speciosa L. (Fu mstanga, Shimaore)	5	Wood, flowers, leaves	Acne, allergies, perfume	Indigenous	0,17	P00248826 **
Heritiera littoralis Aiton (Moromoni, Shibushi)	2	Bark, leaves	Stomach ache, fertility	Indigenous	0,03	P00209700 **
Hibiscus tiliaceus L. (Hibiscus, French)	1	Leaves	Acne, allergies	Indigenous	0,03	***
Hymenaea verrucosa Gaertn. (Lembuku, Shibushi)	1	Leaves	Allergies	Cultivated	0,03	P00290421 **
Jacquemontia tamnifolia (L.) Griseb. (Sari kovehanimroutoutou, Shimaore)	1	Leaves	Head ache, fever	Indigenous	0,03	P00229351 **
Jasminum nummularifolium Baker (Enfu, Shimaore)	17	Flowers	Perfume, smoothing, lightening, acne	Indigenous	0,58	P00290466 **
Jatropha curcas L. (Pignon d'inde, French)	2	Sap	Lightening, acne, inflammations	Cultivated	0,06	***
Kalanchoe pinnata (Lam.) Pers. (Meawani, Shimaore)	3	Leaves	Inflammations	Cultivated	0,10	MAO00044 *
Lantana camara L. (Wavu n'kalaga, Shibushi)	2	Leaves	Stomach ache	Exotic	0,06	MAO00057 *

Lawsonia inermis L. (Mwinavavi, Shibushi)	15	Leaves, flowers	Redness, lightening, smoothing, headache, perfume	Cultivated	0,51	MAO00042 *
Leea guineensis G. Don. f. *Comoriensis* Desc (Sadrakidrakilahi, Shibushi)	1	Wood	Acne, allergies	Indigenous	0,03	MAO00047 *
Litchi chinensis Sonn. (Litchi, French)	6	Wood, roots	Lightening, smoothing	Cultivated	0,21	MAO00051 *
Litsea glutinosa (Lour.) C. Rob. (Mzavocamaro, Shimaore)	3	Sap	Redness	Exotic, invasive	0,10	MAO00052 *
Manihot esculenta Crantz. (Manioc, French)	2	Leaves	Inflammation, abscess	Cultivated	0, 06	P00248848 **
Merremia peltata (L.) Merr. (Vahi be, Shibushi)	1	Sap	Soreness, acne	Indigenous	0,03	P00209748 **
Momordica charantia L. (Antsaskatarondro, Shibushi)	1	Leaves	Redness, fever, allergies	Exotic	0,03	P00437820 **
Moringa oleifera Lam. (Mvunge, Shibushi)	1	Leaves	Redness	Cultivated	0,03	***
Myristica fragrans Houtt. (Koukou manga, Shimaore)	4	Fruits, seeds	Redness, headache, stomach ache	Cultivated	0,14	MAO00136 *
Noronhia comorensis S. Moore (Tsiletrikeli, Shibushi)	2	Leaves	Energizer	Indigenous	0,06	P00273167 **
Ocimum canum Sims (Hinsa, Shimaore)	3	Leaves	Perfume	Cryptogenic	0,10	***
Pandanus mayotteensis Martelli (Sari mluamasera, Shimaore)	7	Leaves, flowers	Perfume, smoothing, lightening, fertility	Indigenous	0,24	MAO00043 *

Paullinia pinnata L. (Vahimariranha, Shibushi)	2	Fruits	Redness, stomach ache	Indigenous	0,10	MAO00056 *
Persea americana Mill. (M'zavoca, Shimaore)	5	Core	Lightening, smoothing, acne	Cultivated	0,17	MAO00050 *
Petchia erythrocarpa (Vatke) Leeuvenb. (Mrimatratamotamo, Shibushi)	1	Leaves, wood	Redness, stomach ache	Indigenous	0,03	P00229384 **
Piper sarmentosum Roxb. (M'dawafilifili, Shimaore)	2	Leaves	Redness	Cultivated	0,06	***
Plectranthus madagascariensis (Pers.) Benth. (Paraovintiti, Shimaore)	4	Leaves	Redness, stomach ache, headache	Cultivated	0,24	P00437867 **
Plumeria rubra L. (Frangipanier, French)	2	Flowers	Perfume	Cultivated	0,06	P00646745 **
Pterocarpus indicus Willd. (Msandragon, Shimaore)	2	Wood	Smoothing, Lightening, acne	Cultivated	0,14	***
Rhynchosia viscosa (Roth) DC. (Antaka-mena, Shimaore)	1	Leaves	Stomach ache	Indigenous	0,03	P00229495 **
Rosa chinensis Jacq. (Sari kafémafeiki-mawa, Shibushi)	2	Flowers, leaves	Perfume, eyeliner, fever	Cultivated	0,06	***
Santalum album L. (Santal, Shimaore)	9	Wood	Smoothing, lightening , acne, pro-tection	N/A	0,31	***
Scoparia dulcis L. (Famafamavazaha)	1	Wood	Allergies	Cryptogenic	0,03	P00273130 **
Secamone astephana Choux (Tendri, Shi-bushi)	1	Wood, leaves	Energizer, purgative	Indigenous	0,03	P00248814 **

Senna singueana (Delile) Lock (Mrimbuzi, Shimaore)	3	Leaves, wood	Bleeding, ache, allergies acne	Indigenous	0,10	P00290372 **
Sesamum indicum L. (Sésame, French)	3	Seeds	Redness, acne, lightening, smooth-ing	Cultivated	0,10	P00290347 **
Sida rhombifolia L. (Sanda ouri, Shimaore)	1	Leaves	Redness	Cryptogenic	0,03	***
Sida urens L. (Sari ampissi, Shibushi)	1	Leaves	Redness	Cryptogenic	0,03	P00290435 **
Stachytarpheta jamaicensis (L.)Vahl (Jakwemavo, Shimare)	1	Flowers	Redness	Exotic	0,03	***
Struchium sparganophorum (L.) Kuntze (M'lalihapana, Shimare)	1	Flowers	Perfume	Exotic	0,03	P00273049 **
Syzygium aromaticum (L.) Merr. & L.M. Perry (Karafou, Shimaore)	4	Flowers	Redness, perfume, purgative, head-ache	Cultivated	0,14	MAO00053 *
Tamarindus indica L. (Tamarin, French)	5	Bark, Leaves, Wood	Lightening, Redness, acne, smoothing, protection	Indigenous	0,17	MAO00041 *
Terminalia catappa L. (Antafa, Shimaore)	1	Wood	Perfume, smoothing, protection	Indigenous	0,03	***
Tragia furialis Bojer ex Prain (Ampisi, Shibushi)	1	Leaves	Redness	Indigenous	0,03	P00229157 **
Trophis montana (Leandri) C.C. Berg (Voamami, Shibushi)	1	Leaves	Fever	indigenous	0,03	P00273161 **
Vepris boiviniana (Baill.) Mziray (Mani-mararu, Shibushi)	1	Leaves, wood	Redness	Indigenous	0,03	P00229139 **

Zingiber zerumbet (L.) Sm. (Tsingizoma-sera, Shimaore)	4	Roots	Redness, smoothing	Exotic	0,14	P00248730 **

Table 3: Informant data (n=29).

Location	Number of informants	Female proportion of informants	High school education
North	10	80%	20%
Centre	12	83%	25%
South	7	100%	28,5%

7. Complementary discussion

Not in the published paper

From a botanical point of view, out of the 1300 + species found on Mayotte, 69 were identified following the interview, 2 are strictly endemic to Mayotte, 31 are indigenous, 4 are cryptogenic, 8 are exotic, 2 are both exotic and invasive, and 21 are both exotic and cultivated for: food crops (e.g. *Litchi chinensis*) , as ornaments (e.g. *Cestrum nocturnum*) , as spices (e.g. *Myristica fragrans*), as aromatic herbs (e.g. *Coriandrum sativum*), as cosmetics (e.g. *Lawsonia inermis*) or for medicine (e.g. *Kalanchoe pinnata*). Their status gives us an idea of whether the species are easily available. All the cultivated ones are by nature easily available and are of interest in the perspective of crop use diversification, as the means for their cultivation are already known. The indigenous are either not referenced (17 species) or are tagged as "Least Concern" (13 species) in the IUCN list only *Apodytes dimidiata* E. Mey. ex Arn. has endangered status which might be an issue regarding its use in this project. Regarding the exotic species, 5 species are not referenced, 1 specie is referenced but as "Data deficient" meaning that not enough data has been gathered to give it a proper status and 2 species are tagged as "Least Concern". The Invasive ones are all tagged as "Least Concern" and are by nature easily available. However, they will present some issues if targeted for the development of a new product, as invasive species require some management to avoid the appearance of an ecological imbalance. The cryptogenic are not referenced in the IUCN list nor are the endemic ones. From such information, apart from the endangered, the invasive and the endemic species, all the others do not seem to present any issues if targeted for the development of a new business. Whichever the targeted species might be, an ecological incidence study will have to be performed.

Among the species mentioned numerous times, one particular species, sandalwood (*Santalum album*) is not part of the Mahoran flora. The informant using this species would buy it at the market; therefore the identification process was only based on the available data given by the CBNM. When considering the status of this species, it is listed as vulnerable on the IUCN list (A. N. A. Kumar et al., 2012) therefore, chances are that even if they called it sandalwood it could have been another species with a similar vernacular appellation (e.g. *Santalum. spicatum* (Autralian sandalwood) or *Tarenna madagascariensis*). This species is often sold as sandalwood from Madagascar.

When looking at the genus of the selected species Mayotte has 703 recorded genera (data from the MNHN herberium). Throughout this work only 10% of those genera are concerned, wherefore, it can be affirmed that the ethnobotanical work allowed us to target the species prone to showing valuable properties.

4

BIOLOGICAL EVALUATION

Matthew Saive, Manon Genva, Chloé Maes and Marie-Laure Fauconnier (Submitted). Study of the cosmetic potential uses of plants from Mayotte as skin care agents through the screening of their biological activities. Cosmetics (MDPI).

This chapter was the result of a collaboration between several researchers.

The data collection was made by Chloe Maes and Matthew Saive using protocols established by Matthew Saive. The redaction as well as the data analysis was a shared work between Matthew Saive and Manon Genva. This work was done under the supervision of Marie-Laure Fauconnier.

The species analyzed in the following chapter were chosen based on the data collection from the two previous works, as well as their availability during the sampling mission. The selected activities were chosen as they were within the scope of the cosmetic orientation of this work. Admittedly, cosmetics are linked to aesthetic; however, they are also strongly linked to wellbeing (Silva et al., 2019). Along with the well-known habit of actively changing ones' appearance in order to enhance the perception one has of oneself (Cash, 1988), cosmetics can have a more long term and profound effect linked to a direct feeling of well-being. Through the application of antioxidants, skin can feel regenerated as the application of anti-inflammatory lotions can reduce redness and swelling (Aburjai & Natsheh, 2003). Another biological activity targeted in this work is linked to a habit observed among people with a darker skin (types 4 to 6 Fitzpatrick types) (Dadzie & Petit, 2009) and people with skin pigmentation conditions (melasma, freckles, ephelide, senile lentigines) (Seo et al., 2003). Through the use of melanin synthesis regulating agents, skin color can be altered (Costin & Hearing, 2007). This specific biological activity however requires a cautious approach as such changes can have severely deleterious effects (Dadzie & Petit, 2009). Concerning the evaluation of the aforementioned activities, many types of test are available.

For the antioxidant activity, the most frequently used test is the DPPH test. Even though this method implies some bias as DPPH has limited similarities with peroxyl radicals, it is still commonly used to evaluate the content of antioxidant compounds in plant material. This test presents the advantage of being easy to implement and can

be used with varied solvent systems including ethanol, aqueous acetone, methanol, aqueous alcohol, and benzene (Cheng et al., 2006). Other methods exist but will be discussed in the following article.

When it comes to evaluating the anti-inflammatory potential of the plant species, we focused on the inhibition of isoform 1 of lipoxygenase (LOX) from *Glycin max* . In the human body, the 5-LOX is involved in the synthesis of immune inflammatory mediators known as leukotrienes. This specific enzyme, along with the cyclooxygenase (COX), are important actors in the complex arachidonic acid (AA) metabolism which is strongly involved in inflammatory reactions (Martel-Pelletier et al., 2003). Since the discovery of the implication of prostaglandins in the inflammatory reaction (Moncada et al., 1973), anti-inflammatory properties have been investigated using the COX inhibition method and more specifically COX-2 (second isoform from cyclooxygenase). This test like all *in vitro* tests gives an idea of the anti-inflammatory potency in a specific compound. Such observations have to be confirmed through *in vivo* analysis (Meade et al., 1993). The LOX and COX found in the human body share the same substrate, that is Arachidonic acid whereas LOX found in plants tend to use 18-carbon fatty acids (linoleate or linolenate); the common factor between these substrates being the presence of *cis*-double bonds (1,4 pentadiene) (Brash, 1999; Pergola & Werz, 2010). Even if all these enzymes have diverse structures, it has been observed that they share common features on their binding sites (Reddy et al., 2015). Considering the amount and diversity of the samples to analyze. We decided to work using a test targeting the inhibition of lipoxygenase from Soybean. This test has the advantage of being fast and easy to implement, and has been used as a model in previous work for the human lipoxygenase inhibition evaluation (Akula & Odhav, 2008; Ribeiro et al., 2014) therefore it was ideal in a primary screening context.

The third activity of interest is the evaluation of skin tone modification capacity. To do so the most widely used protocol in the cosmetic industry, developed by Pomerantz in 1966, is based on the inhibition of tyrosinase activity (Couteau & Coiffard, 2016; Pomerantz, 1966). Tyrosinase is produced only by melanocyte cells and is one of the most important enzymes in the synthesis of both types of melanin (Pillaiyar et al., 2017; Tief et al., 1996). Interference with the activity of this enzyme will lead to a visible result colorwise.

Study of the cosmetic potential uses of plants from Mayotte as skin care agents through the screening of their biological activities

Matthew Saive [1], Manon Genva [1,*], Chloé Maes [1] and Marie-Laure Fauconnier [1]

[1] Laboratory of Chemistry of Natural Molecules, Gembloux Agro-Bio Tech, University of Liège, Gembloux, Belgium; msaive@student.uliege.be; m.genva@uliege.be; Chloe.Maes@uliege.be; marie-laure.fauconnier@uliege.be

***** Correspondence: m.genva@uliege.be

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Abstract

The island of Mayotte, located in the Indian Ocean, possesses a remarkable biodiversity. A previous ethnobotanical study was already performed, allowing us to highlight 69 different plant species used in traditional medicine. Among those, 21 were traditionally employ for skincare by the local populations. The present study aimed at better understand the traditional use of those plants by investigating their *in-vitro* biological activities, and more specifically their antioxidant, anti-lipoxygenase and anti-tyrosinase properties. Results revealed high biological activities for several plant species, some of them displaying one strong single activity while others had at the same time anti-lipoxygenase, antioxidant and anti-tyrosinase effects. Those *in-vitro* biological activities were in agreement with the traditional use of those plant by the local population. It also highlights the high potential of those species from Mayotte in the development of new cosmetic ingredients for the treatment of many skin affections such as eczema.

Keywords: Mayotte, cosmetics, skin care agents, traditional uses, anti-inflammatory, anti-tyrosinase, antioxidant

1. Introduction

1.1.Context of the study

The island of Mayotte is part of the Comoros archipelago itself located in the Indian Ocean. One of the particularities of this island is its localization in a geographical area where the climate is appropriate for an exceptional biodiversity. Indeed, it has been reported that 25% of the earth biodiversity is present in the Indian Ocean area (Gurib-Fakim, 2011). It's around 1820 that tropical islands started to create a real interest from a botanical point of view, as De Candolle (O Pascal, 2002) suggested,"…'*Islands' flora is worth studying due to the peculiar characteristics shown by their vegetation or to the fact that the study areas are clearly defined, thus the studies can be done thoroughly…"*. This affirmation has been proven many times in many insular areas of the world, but Mayotte was not one of them as very little research has been done about this small Island (O Pascal, 2002).

On the other hand, the history of the island with the successive settlement of people from African Bantu and Arab-Muslim origins (Liszkowski, 2000) explains that the use of traditional medicine is still very common and deeply ingrained in the habits of the inhabitants of Mayotte (Conco, 1972; Majeed, 2005; Saive et al., 2020). In addition, those people have a strong bond to their cultural heritage, which explains that traditional cosmetic practices are still used nowadays. The conservation of this knowledge is based on an oral transmission which passes from one generation to another (Kaou et al., 2008; Said Hassane Soidrou et al., 2013). Mayotte has much to offer when it comes to ethnobotanical studies (Boullet, 2016).

During a previous ethnobotanical field study, we were able to identify on the Island of Mayotte 69 plants used in traditional medicine for many different conditions. Among these plants, we noted a large number of uses related to skin care, whether to treat a skin problem or for cosmetic purposes (Saive et al., 2018). Skin is the first protective layer of the human body. It withstands all types of stress, either endogenous, such as the effect of aging, or exogenous such as sun exposition. Those stresses are responsible for many skin imperfections and afflictions (Rogers et al., 1996). It did not take long for humanity to understand that these deleterious effects could be thwarted using what nature had to offer. Therefore, plants have been used to heal but also for aesthetic uses through makeup and perfume for as long as humanity can remember, these practices are deeply linked to man's evolution (Edwards et al., 2005; Weller, 2007).

In the present work, we decided to focus more particularly on 21 plants traditionally used for skincare on the basis of our previous ethnobotanical study and to investigate their potential for use as an ingredient in cosmetics through the study of three targeted biological activities that are outlined below (anti-lipoxygenase, anti-oxidant, pigmentation issue). Indeed, pharmaceutical industries are continuously searching for new bioactive molecules. For each targeted biological activity, the test used to evaluate it is described.

1.2. Biological activities

1.2.1. Inflammation

The inflammatory triggers can be divided into: infection, tissue injuries, as well as tissue stress and malfunction (Fig. 6). In this work we will focus mainly on the second and third types of infection since the anti-inflammatory properties are meant to be paired with cosmetic practices.

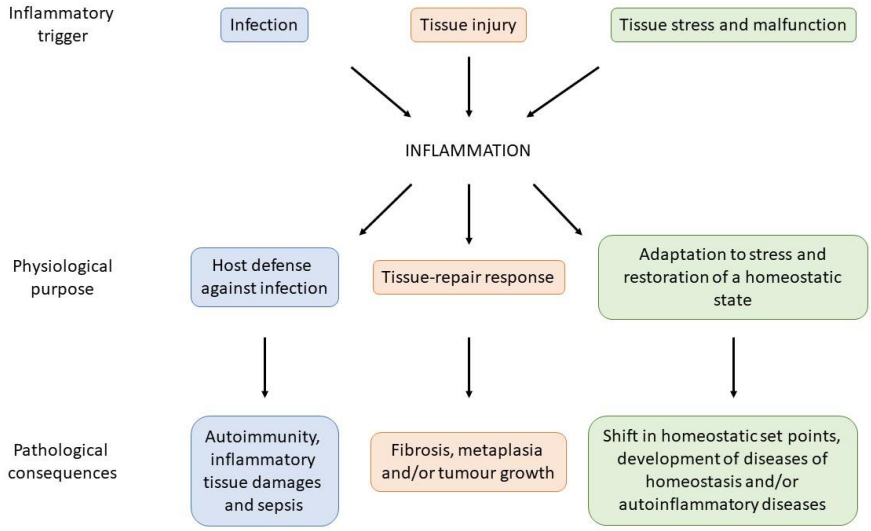

Figure 6: Scheme showing the main inflammatory trigger, the purpose of the inflammation reaction and the pathological consequences (Medzhitov, 2008).

The search for anti-inflammatory compounds in this work will mainly target the acute stages of inflammation, which can be characterized by physiologic reactions as explained hereafter. At local level, there is a transient vasoconstriction of the arterioles, followed by a vasodilatation of the arterioles and the nonfunctioning capillaries. Simultaneously, the vessels become abnormally permeable, allowing the plasma fluid to escape and to provoke swelling. The migration of fluids causes a change in the concentration of cellular elements. This phenomenon is known as hemoconcentration (Wells, 1973). Along with this reaction there is margination, where the red blood cells tend to concentrate at the center of the vessel while the white blood cells line the endothelial surface (Colditz, 1985). Another reaction is called adhesion and is characterized by a sticky comportment developed by the cells located in the margin part of the vessel. From a larger perspective, motile leukocytes arrive at the site of the inflammation. This phenomenon is called emigration and is the result of chemotaxis (Walzog & Gaehtgens, 2000). Once released from the blood vessel, the neutrophils will follow a chemical substance along a concentration gradient. Many chemotactic agents have been identified. They can be among others: lymphokines, platelet-derived growth factors, arachidonic metabolites, etc. Among the chemical compounds involved in the inflammatory reaction, there are also the degranulation of storage

vesicles and the formation of free radicals within the leucocyte. The last two steps are aggregation, where the cells will migrate towards the inflammatory site in a certain order based on the cause of inflammation and the chemotactic compounds, and phagocytosis, where the intruder is recognized by the neutrophils and macrophages, which then fix themselves to the target and begin engulfing it. Once fully englobed, the defense mechanism will cause the death of the unwanted element by the production of free radicals and the H_2O_2 myeloperoxidase-halide system of the neutrophils among other mechanisms (Holliman, 1992).

Among the different pathways linked to the appearance of inflammatory reactions, the arachidonic pathway plays an important role in permeability changes, vasoconstriction, and vasodilatation. It also plays a role in the development of pain and fever. This specific pathway involves cyclooxygenase (COX) and lipoxygenase (LOX). COX is mainly responsible for the synthesis of prostaglandins (PGE_2 and PGI_2) and thromboxane, which are vasodilators, and LOX is responsible for the synthesis of leukotriene B_4, C_4, D_4, and E_4. Leukotriene B_4 is a potent chemotactic involved in the emigration process and the three others are responsible for vasoconstriction and an increase of the vascular permeability (Holliman, 1992; Medzhitov, 2008). As observed in figure 7, some NSAID (nonsteroidal anti-inflammatory drugs) tend to interact with both COX and some are COX-2 specific. The main issue with non-selective NSAID is the way they affect the prostaglandin physiological balance leading to the appearance of adverse effects such as gastrointestinal hemorrhage, kidney failure and ulceration. As the cause for this unbalance is linked to the inhibition of 1-COX, many studies have been trying to identify COX-2 specific inhibitors (Ali et al., 2015; Charlier & Michaux, 2003; Sostres et al., 2010). Those compounds are known as "Coxibs", among those compounds, Celecoxib has been commercialized. However, this drug also presents some serious increase of cardiovascular risks. *Ergo* the current lead towards anti-inflammatory compound relies in the simultaneous inhibition of 5-LOX and COX-2 (Manju et al., 2018), drugs that work on multiple targets may produce better therapeutic profile. So far, several compounds (Tert-butyl phenols, acrylic acids, indoles, pyridines, pyrazoles, pyrazolines, thiazoles, triazoles derivatives as well as some plant derived compound), have shown 5-LOX/COX-2 inhibition properties (Altavilla et al., 2009; Manju et al., 2018).

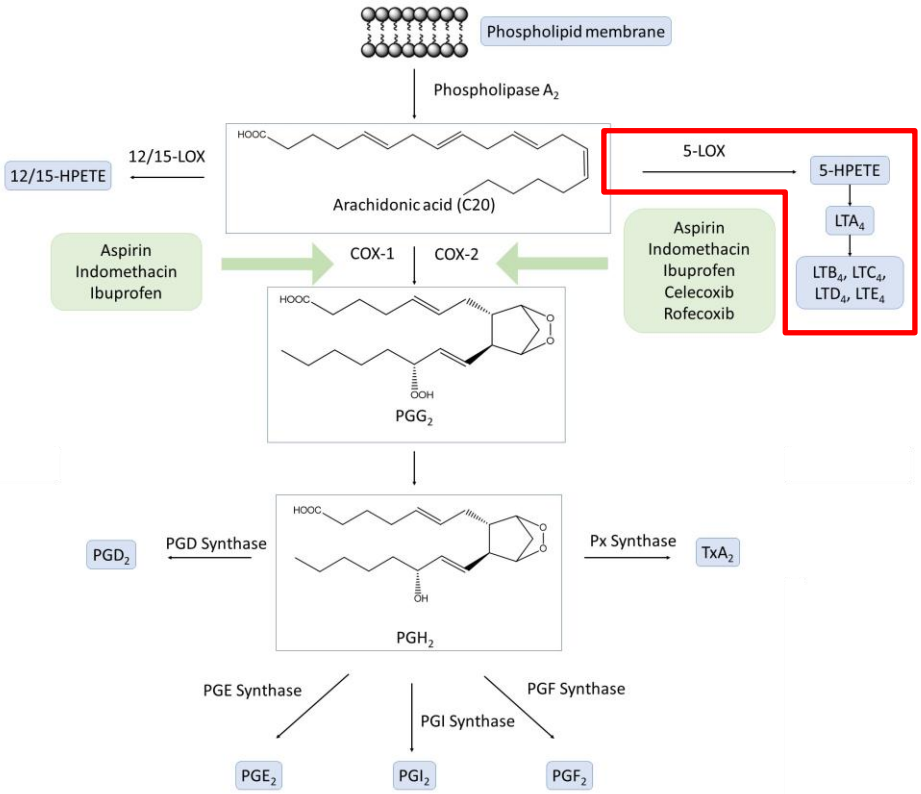

Figure 7: Representative biosynthetic pathway of prostaglandin (PG) biosynthesis from arachidonic acid (AA) via COX-1/COX-2 isoform catalysis. The nonsteroidal anti-inflammatory drugs (NSAID) aspirin, indomethacin and ibuprofen are non-selective inhibitors of COX isoforms whereas, celecoxib and rofecoxib are selective to COX-2. From AA, 12/15-HPETE and 5-HPETE are produced under the action of 12/15-LOX and 5-LOX respectively. From the 5-HPETE Leukotriene A is synthetized and from there, other leukotriene forms can be declined. (LTB to TLE) (Rao & Knaus, 2008).

As observed by (Srivastava et al., 2016) some compounds have shown some activity against 5-LOX as well as COX-2. In this work however, we focused on the lipoxygenase inhibition potency of the samples originating from the previous studies. LOX are part of a super family of enzymes with different origins and activities (Brash, 1999). These enzymes are found in the animal and plant kingdoms and are long single chain proteins with molecular masses of up to 103 kDa which have been classified based on their optimal pH activity, their sub-cellular location or the fatty acid oxygenation location specificity (Andreou & Feussner, 2009). Independently of these characteristics, LOX are iron-containing enzymes, requiring oxygen as co substrate (Prigge et al., 1997).

Among the six different LOX expressed by the human body, the 5-LOX has been identified as part of one of the biosynthesis pathways leading to the inflammatory reaction. This specific enzyme intervenes in two steps of leukotriene synthesis (Fig. 7

and 8). Firstly, 5-LOX allows the insertion of molecular available oxygen through what is known as the dioxygenase activity, which results in the synthesis of 5-HPETE (hydroxyperoxyeicosatetraenoïc acid) due to an homolytic cleavage and abstraction of the hydrogen on the 7th carbon, and the rearrangement and insertion of oxygen on the 5th carbon (Rådmark et al., 2015). The second action of lipoxygenase, also known as LTA_4 synthase activity, causes the abstraction of hydrogen on the 10th carbon of 5-HPETE, causing the migration of a radical on the 6th carbon and a double bond rearrangement that ends in the synthesis of an unstable epoxide, the leukotriene A_4 (LTA_4) (Fig. 8).

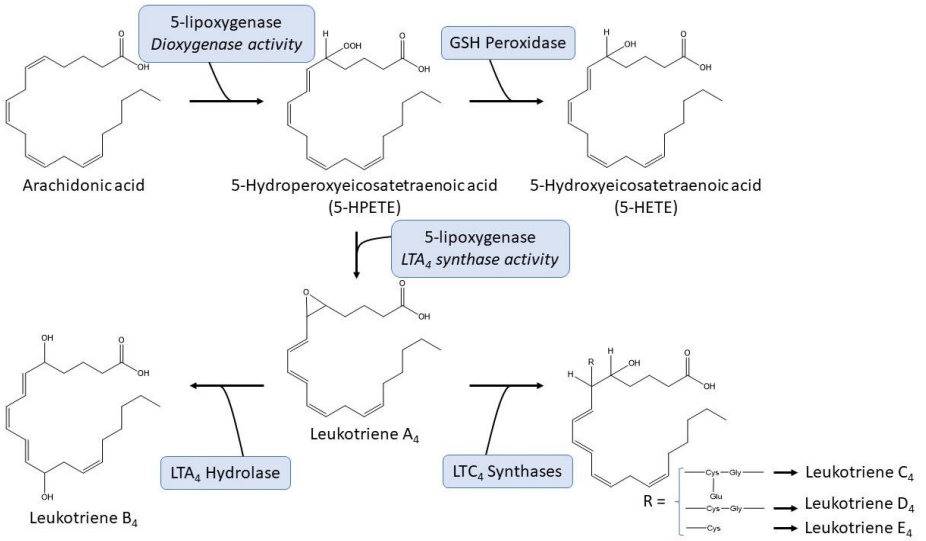

Figure 8: Summary of leukotriene synthesis from arachidonic acid (Rådmark et al., 2015).

The 5-LOX activity linked to the inflammatory process has been studied by focusing on the first activity (dioxygenase activity) that is also observable with 1-LOX from *Glycine max*. Due to the substrate specificity and inhibition characteristics similarities between 1-LOX and 5-LOX, 1-LOX has been used as a model in different studies (Mahesha et al., 2007). Hence it is expected that samples responsible for the inhibition 1-LOX should present comparable activities when in contact with 5-LOX as observed in the work of (Srivastava et al., 2016). 1-LOX inhibition test has also been used by (Ribeiro et al., 2014) while aiming to understand the structure activity relationship in 5-LOX. Another observation pointing towards the validity of 1-LOX as a model for 5-LOX studies resides in the fact that has been observed that 1-LOX and 5-LOX have 8 common features on their binding site (Reddy et al., 2015). In comparison, COX-2 and LOX-5 have 15 common features on their binding sites and these two enzymes have many common inhibitors (Leval et al., 2002; Manju et al., 2018). In order to observe the 1-LOX activity, arachidonic acid has to be replaced by linoleic acid. The use of one substrate instead of the other however does not impact the test as the targeted structure ((1*Z*,4*Z*)-pentadiene) is present in both substrates (Fauconnier & Marlier, 1996) (Fig. 9).

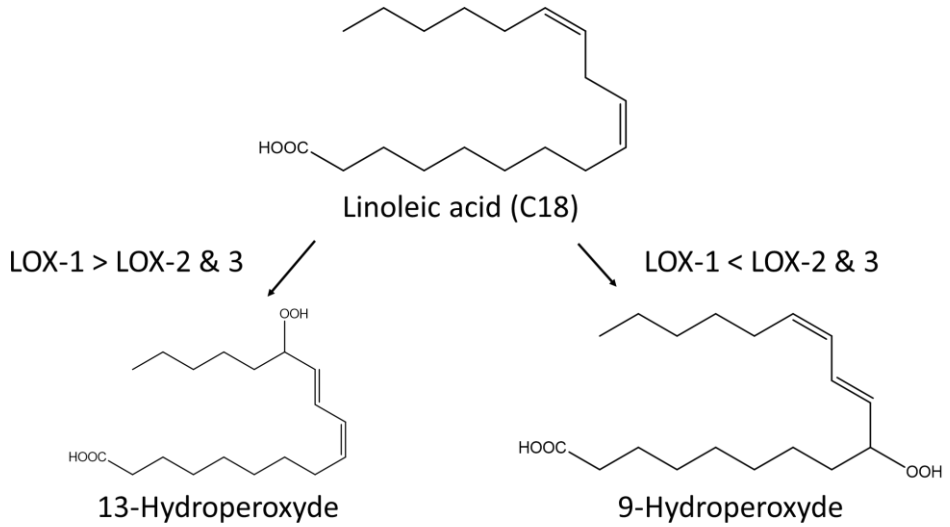

Figure 9: Different Hydroperoxyde synthetized from linoleic acid based on the LOX isozymes. LOX-1 tend to produce more 13-hydroperoxydes then LOX-2 & 3 when in optimal pH conditions (pH 9.5) *(Fauconnier & Marlier, 1996)*.

1.2.2. Oxidative stress

When it comes to preventing oxidative stress in the human body, many antioxidants are naturally synthetized and available. The occurrence of oxidative stress due to normal body functions is managed by these naturally occurring compounds which effect a permanent balance between pro-oxidant and antioxidant molecules. Sometimes, this balance is disturbed, leading to a series of reactions that can damage DNA, proteins and lipids, eventually causing cell death or damage (Hernández-Ruiz et al., 2019; Jones, 2008). This phenomenon has been identified as one of the causes of skin ageing, among other ailments such as cancer and cardiovascular disease (Molyneux, 2004). In such situations, the external input of antioxidants is suspected to be helpful (Subhasree et al., 2009).

Free radicals are atoms or molecules that have an unpaired electron in one of their atomic orbitals. Most of these are unstable and very reactive. Through oxidative reactions, they are the cause of all sorts of damages in the human body. The oxidative process can be divided into three main steps: initiation, propagation and termination. During the initiation step, the free radical rips off an electron from a surrounding molecule. Due to this electron loss, the molecule then also becomes a free radical seeking to reach a stable state. This is the beginning of the propagation step. This step lasts as long as free radicals are being generated. The termination step occurs when all the free radicals have reached a stable state. In most cases these steps are linked with the synthesis of undesired compounds (Bondet et al., 1997).

In the human body, one of the main reasons for the appearance of oxidative compounds is linked with basic biological requirements such as cellular breathing. During this process, molecular dioxygen is transformed into superoxides which are unstable

reactive oxygen species (ROS) that cause free radical oxidative reactions. Lipids are also sensitive to oxidative reaction leading to the synthesis of hydroperoxides (Bondet et al., 1997).

For the antioxidant activity, *in vitro*, *in vivo* and *ex vivo* evaluations have been developed and are still used nowadays. The main *In vitro* methods can be categorized as electron transfer reactions and hydrogen atom transfer reactions. Among the first category, the most commonly used test is the DPPH (2,2-diphenyl-1-picrylhydrazyl) proposed by Blois (Blois, 1958). However, other methods have been developed with different inconveniences and advantages. These are: FRAP (Ferric Reduction Antioxidant Power) which allows for the evaluation of antioxidant properties of hydrophilic substances; ABTS (2,2′-azino-di-(3-etylobenzotizoline-6-sulfonate)) which has the advantage of working with maximum absorbance at several wavelengths (417, 645, 734 and 815 nm) and can be used for both hydrophilic and lipophilic samples; CRA (Copper Reducing Activity) method has is of interest in the search for cosmetics due to its ability to reduce copper (II)[4]. So much so that it has been modified into the CUPRAC method (Cupric Reducing Antioxidant Capacity) which works be highlighting the reduction of CU II into CU I. This method is also usable in both hydrophilic and hydrophobic solvents and works at similar pH to the physiological pH (Apak et al., 2004). The second category aims to observe the kinetics of competing reactions occurring between the antioxidant contained in the sample and the molecular probe when in presence of peroxide radicals. These methods are more adapted for lipophilic antioxidant, which can be of interest when studying cosmetics, food and specific biological systems. A known HAT method is the ORAC (Oxygen Radical Absorbance Capacity) method. By measuring the decrease in fluorescence of molecular probes reacting with thermally generated free hydroperoxyl radicals. This method can be conducted in living cell cultures (Fočo et al., 2005) *in* (Ratz-Lyko et al., 2012).

In this work we focused on the reaction involving DPPH (2,2-Diphenyl-1-picrylhydrazyl), that has previously been described as a good indicator of the anti-oxidative power of the samples (Bondet et al., 1997). This specific test assay detects the scavenging potency of free radicals through the scavenging activity of the stable DPPH free radical. Using principles of Beer Lambert law, it is possible to observe the disappearance of free DPPH radicals at 517 nm by using a spectrophotometer as the reaction occurs (Fig. 10).

[4] copper is involved in the synthesis and stabilization of extracellular matrix skin proteins and angiogenesis (Borkow, 2014)

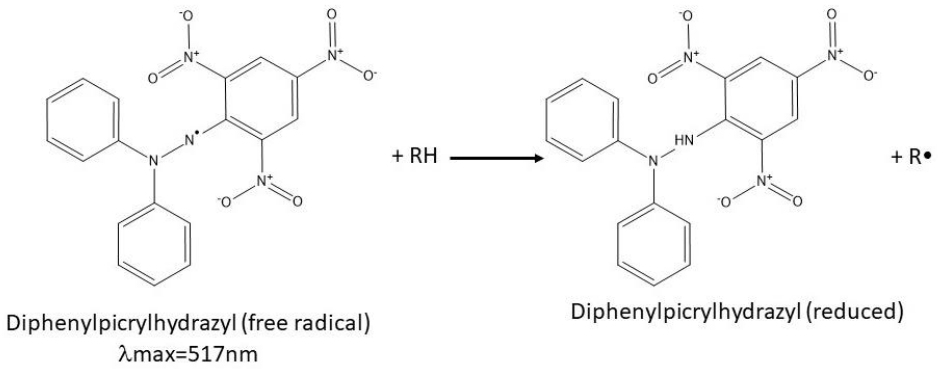

Figure 10: Reducing effect of hydrogen donors on DPPH *(Molyneux, 2004)*.

1.2.3. Pigmentation issues

As the first protective layer of the human body (Fisher et al., 2002; Raschke & Elsner, 2010), the skin is constantly exposed to external stresses, among which UV radiations coming directly from the sun. Melanin produced by melanocytes absorbs the UV sunlight and manages the amount of pro oxidative compounds linked to UV exposure (Costin & Hearing, 2007; Kim & Uyama, 2005). However, the types, amounts, and locations of melanin in the body allow an individual to be exposed to a certain amount of UV radiations before encountering harmful consequences (Mapunya et al., 2012). Consequently, people with lighter skin tend to be more sensitive to such radiations compared to people with darker skin. Melanin is responsible for the skin pigmentation, as well as for the phenomena known as hyperpigmentation and hypopigmentation, often visible in the form of darker or lighter spots, zones or body parts. In addition to the esthetic issue linked to those conditions, there is also a risk of the appearance of melanoma (Smit et al., 2009). The key enzyme in the biosynthesis of melanin being tyrosinase (Nerya et al., 2003), the search for compounds with inhibitory or promoting properties towards this specific enzyme is crucial in the development of cosmetics.

In the melanogenesis pathway, the tyrosinase enzyme works along with two other proteins known as TRP1 and TRP2 (tyrosinase related proteins) (Ando et al., 2007). These three enzymes allow for the synthesis of two different melanins; eumelanin, which is responsible for a more black or brown pigmentation, and pheomelanin, responsible for a more reddish or yellowish hue (Kim & Uyama, 2005).

The first (or proximal) biosynthesis step is common for both melanin types, and begins with the hydroxylation of tyrosine leading to the generation of L-DOPA (monophenolase activity of tyrosinase), followed by its oxidation into dopaquinone (diphenolase activity of tyrosinase) (Korner & Pawelek, 1982; Parvez et al., 2007). Oxygen is required for this reaction as it is a co-substrate (Garcia-Carmona et al., 1982).

Next, the synthesis of eumelanin implies a 1,4 intramolecular addition on the benzene cycle, causing the cyclisation of the DOPAquinone into leukoDOPAchrome. In the presence of excessive DOPAquinone, the leukoDOPAchrome is quickly oxidized

into DOPAchrome. This reaction also causes the DOPAquinone to reduce back into L-DOPA. The DOPAchrome then undergoes two potential transformations at a distal level, either by losing its carboxylic acid group and becoming DHI (5,6-dihydroxyindole) or by undergoing a new hydroxylation with the help of TRP2 (also known as DOPAchrome tautomerase EC 5.3.3.12), leading to the synthesis of DHICA (5,6-dihydroxyindole-2-carboxilic acid). This compound is then oxidized into indole-5,6-quinone-2-carboxylic acid by another TRP1 (also known as DHICA oxidase). In presence of tyrosinase, DHI is oxidized into indole-5,6-quinone. Whether it's indole-5,6-quinone, DHICA or indole-5,6-quinone-2-carboxilic acid, all are precursors/building blocks of eumelanin (Fig. 11).

Starting with dopaquinone, pheomelanogenesis requires the presence of thiols (cysteine or glutathione) to generate cysteinilDOPA. The series of cyclization and polymerization that follow have not been fully characterized. However, the resulting compound is 1,4-benzothiozinylalanine, which is the building bloc of pheomelanin (Fig. 11) (Kim & Uyama, 2005; T Kobayashi et al., 1994; Takeshi Kobayashi et al., 1995; Prota, 1988).

In this study, the tyrosinase inhibition capacity of plant extracts was used to evaluate their potential to treat skin pigmentation issues.

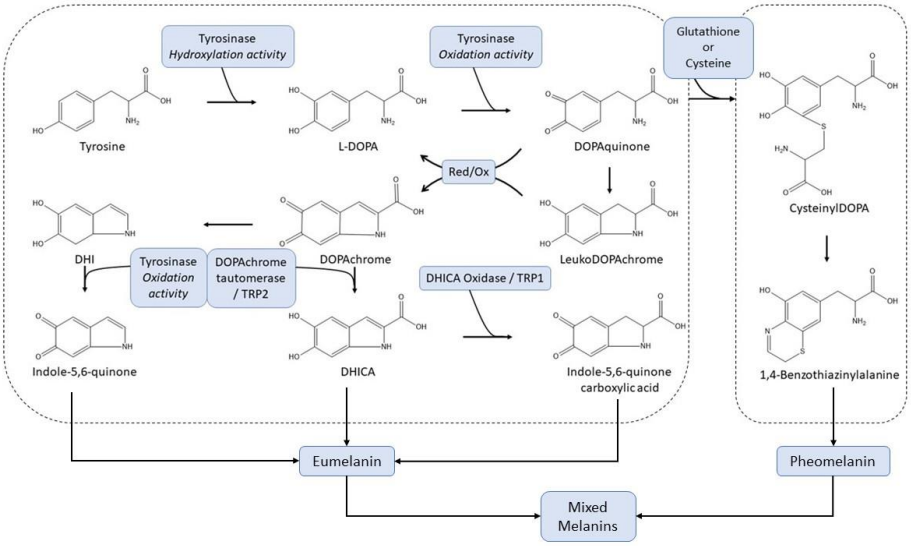

Figure 11: Biosynthesis of eumalanin and pheomelanin (Kim & Uyama, 2005; Takeshi Kobayashi et al., 1995; Prota, 1988).

2. Materials and Methods

2.1. Reagents

Acetone (≥99%, technical), Methanol (≥98.5%, technical), K_2HPO_4, KH_2PO_4, pure ethanol, NaOH, H_3BO_3 were purchased from VWR chemicals (Leuven, Belgium). DPPH (2,2-Diphenyl-1-picrylhydrazyl), mushroom tyrosinase (EC 1.14.18.1), kojic acid, TROLOX ((±)-6-Hydroxy-2,5,7,8-tetramethylchromane-2-carboxylic acid), linoleic acid, tween 80, L-DOPA (3,4-dihydroxiphenilalanine) and *Glycine max* lipoxygenase (EC 1.13.11.12) were purchased from Sigma-Aldrich (Darmstadt, Germany)

2.2. Plant extracts preparation

Based on the results of the previous ethnobotanical survey conducted by M. Saive in 2014 on the island of Mayotte, 21 different plant species were collected and a specimen was stored for each sample at the CBNM herbarium in Mayotte (Saive et al., 2018). All available organs at the time of the harvest were collected, leading to a total of 89 samples (See tables S1 to S8).

All samples were dried at 40±1°C in a drying oven for 48h. When the vegetal material allowed it, the samples were powdered using an analytical grinder IKA A11 (Staufen, Germany). The global size of the ligneous parts of the vegetal material was reduced using shears. Once the size allowed it, the samples were then ground using a laboratory hammermill mounted with a 6 mm mesh. The ground samples were kept vacuum-packed at -22±1°C until extracted. The extraction process was carried out using a Soxhlet apparatus. 2 g of dried and ground samples were weighed and poured into the extraction chamber. 30 mL of acetone was used (Eloff, 1998) and the extraction lasted for 6h. Once the extraction was completed, the crude extract was evaporated using a rotary evaporator (Heidolph, Laborota 4003, Schwabach, Germany). The dried crude extracts were kept at -22±1°C until used.

2.3. Lipoxygenase inhibition evaluation

Lipoxygenase is sensitive to heat; therefore, all the following experimental steps were performed on an ice-bath. A 0.1 mg/mL lipoxygenase solution (≥50000 U/mg) was prepared using distilled water. The 1 mM linoleic acid substrate solution was prepared as follows: 140 mg of linoleic acid, 18 mg of tween 80, and 100 µL of NaOH 5 mM were mixed and adjusted to 50 mL with distillate water. The enzyme solution as well as the substrate were divided into 1 mL aliquots and stored at -22±1°C until used, with only one thaw-out allowed.

As the expected product for the reaction was 13-HPOD, the optimal pH of the reaction matrix was obtained using a 0.1 M sodium borate buffer corrected to pH 9.5 using 5 M NaOH. To avoid false-positive results due to enzyme inactivation caused by acetone, pure ethyl alcohol was used for sample preparation. 5 mL of pure ethanol was added to the dry extracts which were then submitted to sonication and subsequently filtered using 0.45 µm PTFE syringe filters (Whatman, Puradisc™ 13, Maidstone, United kingdom). As the color of the crude extracts was an issue, all samples were diluted in the borate buffer from factor 10^{-1} to factor 10^{-4}. As oxygen is a co-substrate

for the reaction, the borate solution was oxygenated for 30 minutes at room temperature prior to the reaction. The control was realized using 0.1 M borate buffer, leading to a non-inhibited reaction, which can be expressed as 0% of inhibition and the blank was obtained by carrying out the experiment without the enzyme, which causes the absence of 13-HPOD synthesis and can be considered as 100% of inhibition.

The enzymatic reaction was performed by mixing 100 µL of plant sample with 35 µL of lipoxygenase and 800 µL of oxygenated buffer. For the control 900 µl of oxygenated buffer was used. For the blank, 900 µl of oxygenated buffer was used but no enzyme was added prior to the incubation. The mixtures were left to incubate for 15 minutes at room temperature and then added into quartz absorption cells along with 35 µL of the substrate solution. The synthesis of linoleic acid hydroperoxide was observed in real time as absorbance was measured every 20 seconds for 5 minutes at 234 nm. Each sample/control was done in triplicate (technical repetitions). The blank was systematically performed to assess the potential auto-oxidation of the substrate due to the oxygen present in the buffer. This was done to ensure that the linoleic acid used in assay was not oxidized non enzymatically (quality control of the substrate). If any auto-oxidation was detected, the substrate was discarded and new substrate was prepared. The relative activity was obtained by putting the slopes of the samples against the slopes of the control. As observed in the following formula:

Relative inhibition activity:

$$\%\ inhibition\ activity = \frac{Control\ Slope\ -\ Sample\ Slope}{Control\ Slope} \times 100$$

Where:

- Control Slope = slope of the control (0% inhibition) at the linear part of the reaction
- Sample Slope = slope of the samples at the linear part of the reaction

2.4. DPPH reducing potency evaluation

A 2.10^{-4} M DPPH solution was prepared using technical grade methanol. Once prepared, this solution was kept at 4±1°C in the dark and was used within the following 7 days.

The positive control for this test was a 2.10^{-3} M TROLOX solution prepared with methanol. The blank was likewise performed with methanol. For the sample analysis, 5 mL of methanol was added to the dry extracts. The crude extract was retrieved by sonication, the solution was then filtered using 0.45 µm PTFE syringe filter (Whatman, Puradisc™ 13, Maidstone, United Kingdom) and submitted to successive dilutions going from factor 10^{-1} to factor 10^{-4} in methanol. The analysis went as follows. A 1:1 DPPH:Sample/blank/TROLOX mix was performed and left to incubate at room temperature for 10 minutes. Then the absorbance of the reaction mix was observed using a UV/Vis spectrophometer ultrospec 9000 from Biochrom (Cambridge, United Kingdom) at 517 nm. Each sample was measured in triplicate (technical repetitions). The samples' relative activity was established by comparing the final absorbance with the absorbance obtained with the Blank and with the Trolox as seen in the following formula.

$$Corrected\ value = Final\ abs - Sample\ abs$$

Where:

- Final abs = absorbance of the reaction mix after 10 minutes
- Sample abs = absorbance of the sample at the studied concentration

Relative reduction activity:

$$\%\ reduction\ activity = \left(1 - \frac{Abs\ TROLOX - Corrected\ value}{Abs\ TROLOX - Abs\ BLANK}\right) \times 100$$

Where:

- Abs TROLOX = Activity of the positive control (100% of activity)
- Abs BLANK = Activity of the negative control (0% of activity)

2.5. Anti-tyrosinase activity evaluation

When working with tyrosinase, all reagents and solutions were kept on an ice-bath to avoid any loss of activity due to temperature-linked enzyme degradation. A 625 U/mL tyrosinase solution was obtained by adding 4 mL of K_3PO_4 0.05 M pH 6.5

buffer directly into the commercial vial containing the enzyme (25.000 U) and by vortexing it for 10 seconds. 1 mL was retrieved and diluted in the same buffer to reach the required concentration. The total solution was divided into 1 mL aliquots stored at -22±1°C until used. The aliquots were thawed only once. A 1 mM L-DOPA solution was prepared using distilled water. For this analysis, the inhibition control was a 1 mM kojic acid solution in distilled water and the blank was pure K_3PO_4 0,05 M pH 6.5 buffer. As for the lipoxygenase evaluation, pure ethyl alcohol was used for the sample preparation. Five mL of pure ethyl alcohol was added to the dry extracts and submitted to sonication. the solution was then filtered using 0.45 µm PTFE syringe filter (Whatman, Puradisc™ 13, Maidstone, United Kingdom) and submitted to successive dilutions going from factor 10^{-1} to factor 10^{-5} in K_3PO_4 0,05 M pH 6.5 buffer. As oxygen is a co-substrate for the reaction the buffer was oxygenated for 30 minutes at room temperature prior to the reaction observation.

The enzymatic reaction was performed by mixing 100 µL of sample/blank/control with 50 µL of tyrosinase and 250 µL of the oxygenated buffer. The mixture was left to incubate for 15 minutes at room temperature and then added into a quartz absorption cell along with 400 µL of the substrate solution. The synthesis of dopachrome was observed in real time and absorbance was measured every 15 seconds for 5 minutes at 475 nm. Each sample/control/blank was carried out in triplicate (technical repetitions). The relative activity was obtained by putting the slopes of the samples against the slopes of the blank. As observed in the following formula:

Relative inhibition activity:

$$\%\ inhibition\ activity = \frac{Blank\ Slope\ -\ Sample\ Slope}{Blank\ Slope} \times 100$$

Where:

- Blank Slope = slope of the blank (0% inhibition) at the linear part of the reaction
- Sample Slope = slope of the samples at the linear part of the reaction

2.6.Statistical analysis

For enzymatic inhibition assays, the relative activity was determined using the absorbance slope at its maximum intensity. For the DPPH reducing potency evaluation assay, the relative activity was based on the absorbance variation after a 10-minute reaction period at room temperature. In that case, the relative activity was obtained when comparing the control/blank with the sample results. Each assay was carried out in triplicate. For each activity and dilution, all the samples were compared two by two, using Tukey's grouping test (Statistical software Minitab 19 Minitab, Inc., Pennsylvania, USA) with the following parameters : the null hypothesis was that all averages are equal, the significance limit was α=0.05,the confidence interval was bilateral, and the error rate for the comparison was 5. This allowed for the isolation of the samples or group of samples showing significantly higher relative activities in comparison to the sample batch.

3. Results and discussion

3.1.Anti-lipoxygenase activity evaluation

78 out of the 89 collected plant samples were tested for their ability to inhibit the lipoxygenase activity at different dilutions. The remaining samples were not included in this assay as they showed a strong absorbance at 234 nm, which did not allow for an accurate measurement.

Using the % RSD (% relative standard deviation) on the values of the control immediately after the reagents were thawed, we established the lower limit of quantification (LLOQ). The observed limit %RSD on the replicates was 10%; this value is in concordance with standard procedures (National Association of Testing Authorities, 2012, 2013 *in* Sengul, 2015).

Out of 78 samples, 17 samples absorbed too much at the first dilution but entered the evaluation process starting at the second dilution. 27 were above LLOQ (lower limit of quantification) at dilution 10^{-1}. Out of those 27 + 17 samples, 9 were still above LLOQ at dilution 10^{-2}. Out of those 9 samples, 3 were still above LLOQ at dilution 10^{-3}. Only 1 sample remained above LLOQ at dilution 10^{-4}.

In addition to determining which species presents the highest relative activity in this specific configuration; this method also allows us to identify which species contains the highest available amount of active compound. As the same amount of sample was used for the initial extraction, species showing above LLOQ results up to the fourth dilution are expected to contain a higher diversity of compound in their crude extracts or compound with a higher efficiency.

Results for plants whose extracts displayed the highest anti-lipoxygenase relative activities are presented on figure 12. The relative activity was taken into account until the LLOQ was reached and the results from all the valid dilutions were then compared, two by two, and grouped using Tukey's test.

Results of the anti-lipoxygenase activity of the plant extracts' first dilution highlighted the presence of 15 different groups among the 27 samples (Appendix from chapter 4 - Table S1), some of them displaying strong anti-lipoxygenase activities up to 99.05%. Two species stand out as being only in group A: *Acalypha hispida* dried flower (99,05% ± 4.22) and *Erythroxylum corymbosum* dried leaf (98.83% ± 2.91). When looking at the results, the samples with activities ranging from 90.65% up to 99.05% are in the group letter A, even if there is some crossing over up to group D (activity ranging between 82.82% and 90.65%). These samples can be considered as the most effective ones (Appendix from chapter 4 - Table S1). For the second dilution (Appendix from chapter 4 - Table S2), there is a drop in activity implying a dose-dependent response. Out of the 9 samples, 5 groups were observed. The first group (group A) contained two samples with the following activities 68.73% ± 3.18 (*Zingiber zerumbet* Dried leaf) and 62.84% ± 1.26 (*Zingiber zerumbet* Dried flower). The later is also in group B (ranging from activities between 55.73% to 62.64%. Group A and B are significantly more active than the 3 other ones. Interestingly enough, the samples from these two groups only come from one species; *Zingiber zerumbet* (the added samples from the B group are *Zingiber zerumbet* Stem and *Zingiber zerumbet*

Fresh rhizome). When looking at the third dilution (Appendix from chapter 4 - Table S3), only 3 samples remained. They were divided into 2 groups, A and B. At this level of dilution, the only sample in group A was *zingiber zerumbet* Fresh rhizome with still 32.03% ± 2.57 of relative activity. Among the samples from the third dilution, one that was not considered in the most effective category in the two first dilutions still shows an activity and still is over LLOQ: *Acalypha hispida* Dried leaf. In the fourth dilution, only *Acalypha hispida* dried leaf remained above LLOQ.

Through the different dilutions, as long as the LLOQ was not reached, a dose-response change can be observed (fig. 12) in the relative activity except for *Acalypha hispida* dried leaves. This specific sample is among the most active ones in the first dilution, then loses more than 50% of relative activity at the second dilution. It then stays at that level of activity as if the inhibition was caused by several compounds. One losing activity as the dilution increases and the other one not being impacted by the dilution. Indeed, the relative activity stayed around 30% for the second, third and fourth dilutions. There is no simple explanation for these results. The study of enzyme inhibition potency of crude plant extract containing many different molecules, is not an easy process. The molecules have many interaction options throughout the whole analysis process. They can react with one another; they can also react with the substrate or with the enzyme. In the case of an enzyme interaction, several inhibition processes exist (competitive inhibition, noncompetitive inhibition, uncompetitive inhibition and mixt inhibition). Depending on the type of inhibition; the maximal speed of the reaction, the affinity between the enzyme and its substrate or both can be affected. As the inhibition evaluation was done through kinetic observations, the inhibition phenomenon can also be affected by the incubation time. In addition, other regulation mode can be in action and not be specifically linked to the enzyme inhibition process. All these phenomena render the study of the inhibition arduous. Even more so when using an inhibition media as complex as a plant crude extract. This can lead to unexpected observations such as the one observed for *Acalypha hispida* where the dilution does not seem to affect the results. Only an in-depth study of the different inhibition mechanisms occurring for this specific sample could help understand such phenomenon. It is primordial to limit the uses of these results as a primary indication in a screening context.

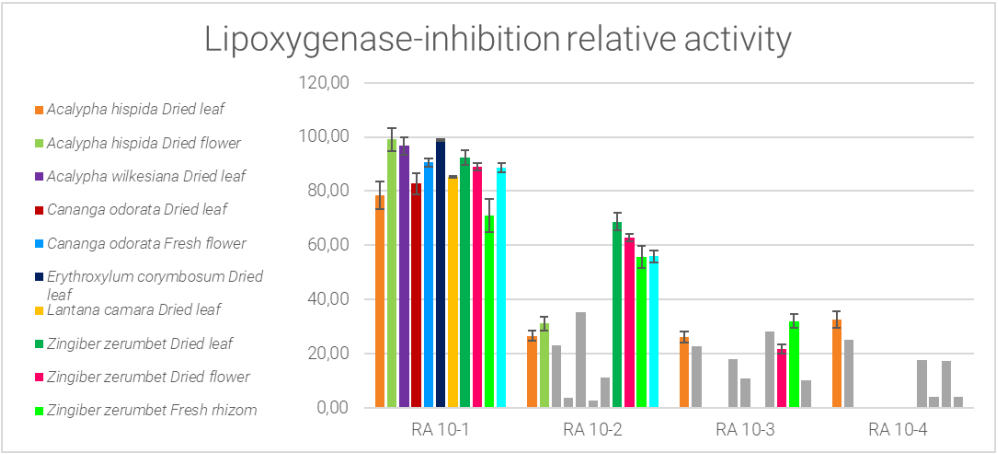

Figure 12: Evolution of the relative activity of the most potent sample's relative lipoxygenase inhibition activities through 4 different dilutions. The greyed results are below LLOQ hence not statistically valid, however, they are aligned with the theory of a dose-depend activity. RA 10-1 = Relative activity for dilution 10-1 / RA 10-2 = Relative activity for dilution 10-2 / RA 10-3 = Relative activity for dilution 10- 3 / RA 10-4 = Relative activity for dilution 10-4.

3.2. DPPH reducing activity evaluation

The antioxidant properties of the collected plant samples were evaluated through the DPPH test (Appendix 4). The average values were compared two by two and grouped using Tukey's test. The observed limit %RSD to establish the validity of the results was based on standard procedures; this limit being an %RSD of 10 (National Association of Testing Authorities, 2012, 2013) *in* (Sengul, 2015).

For the first dilution, out of the 89 samples, 77 were above LLOQ. One could not be analyzed at this specific concentration as it impeded with the detector at the given wavelength (517 nm); the latter was re-integrated in the measurements for the following dilutions. These sample were divided into 25 different groups. The group with the highest activity (Group A) (Appendix from chapter 4 - Table S4) showed activities ranging from 93.99% to 99.97%. In this group (group A) only one sample was just in group A: *Erythroxylum corymbosum* dried leaf (99.97% ± 0.06). The other samples in group A presented some crossing over up to group L with activities ranging from 88.91% to 99.96%. Together these groups count for a total of 52 samples, rendering it hard to significantly isolate the samples. This can be explained by the presence of polyphenols, compounds with known antioxidant properties, in many plants. The second and third dilutions allowed for a better separation.

Out of the initial samples and with the addition of the one removed from the first dilution, 56 remained above LLOQ after the second dilution. These samples were divided into 23 groups. The group with the highest activity (Group A) (Appendix from chapter 4 - Table S5) showed activities ranging from 92.58% to 98.76%. In this group (group A) only one sample was just in group A: *Acalypha hispida* fresh leaf (98.76% ± 1.08). The other samples in group A present some crossing over up to group G

(activities ranging from 86.63% up to 92.95%). A total of 28 samples were gathered among those high relative activity groups.

When looking at the third dilution, 21 samples remain above LLOQ. Their relative activity are divided into 9 groups. The group with the highest activities (Group A) (Appendix from chapter 4 - Table S6) contains 4 samples, of which 2 are just in group A: *Leea guineensis* dried leaf (45.91% ± 3.89) and *Litchi chinensis* dried leaf (43.10% ± 2.25) The other sample in group A presented some crossing over up to group B (activities ranging from 37.80% to 42.39%). A total of 5 samples were gathered among those high relative activity groups: *Lawsonia inermis* dried leaf, *Acalypha wilkesiana* fresh leaf, *Litchi chinensis* dried root, *Litchi chinensis* dried leaf and *Leea guineensis* dried leaf (Fig. 13). The fourth dilution did not leave any samples above LLOQ

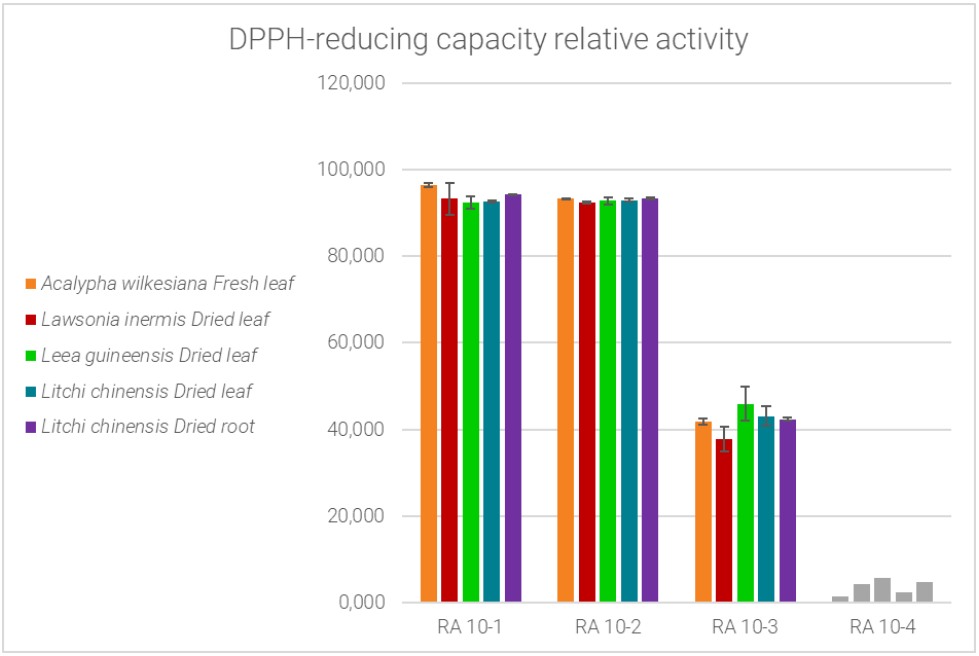

Figure 13: Evolution of the relative activity of the most potent sample's DPPH-reducing capacity relative activity through 4 different dilutions. The greyed results are below LLOQ, hence not statistically valid. However, they are aligned with the theory of a dose-dependent activity. RA 10-1 = Relative activity for dilution 10^{-1} / RA 10-2 = Relative activity for dilution 10^{-2} / RA 10-3 = Relative activity for dilution 10^{-3} / RA 10-4 = Relative activity for dilution 10^{-4}.

3.3.Anti-tyrosinase activity evaluation

The anti-tyrosinase activity of the collected plant samples was evaluated through the observation of tyrosinase inhibition. The activity averages were compared two by two and grouped using Tukey's test. The observed limit %RSD to establish the validity of the results was based in concordance with standard procedures; this being an %RSD of 10 (National Association of Testing Authorities, 2012, 2013) *in* (Sengul,

2015). Out of the 89 samples tested at four different dilutions, 6 samples could not be tested using the anti-tyrosinase protocol, as even when strongly diluted, they strongly absorbed at 475 nm, impeding an accurate reading.

For the first dilution, Tukey's test highlighted 22 different groups among the 52 samples above LLOQ. The group with the best activity (Group A) (Appendix from chapter 4 - Table S7) showed activities ranging from 89.74% to 98.57%. In this group (group A) only one sample was just in group A: *Litchi chinensis* dried leaf (98.57% ± 7.09). The other samples in group A presented some crossing over up to group D with activities ranging from 75.61% to 89.82%. Together those groups counted for a total of 11 samples.

After the second dilution, 7 samples remained above LLOQ. These samples were divided into 4 groups. The group with the best activity (Group A) (Appendix from chapter 4 - Table S8) had only one sample: *Litchi chinensis* dried leaf (51.36% ± 3.00). In this grouping process, no crossing over was observed. Group B contained *Leea guineensis* dried fruit (45.45% ± 2.08) and *Litchi chinensis* dried root (42.29% ± 3.11). Group C and D had activities ranging from 16.26% to 27.49%. The following dilution did not allow for any significant observations. The evolution of the activity of the most active sample is shown in figure 14.

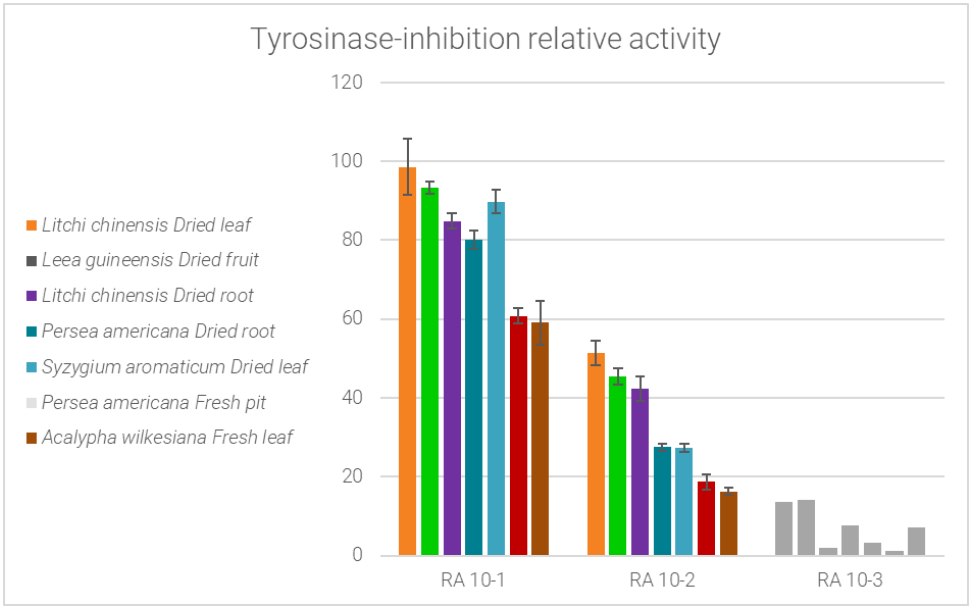

Figure 14: Evolution of the relative activity of the most potent samples' relative tyrosinase inhibition activities through 3 different dilutions. The greyed results are below LLOQ, hence not statistically valid. However, they are aligned with the theory of a dose-dependent activity. RA 10-1 = Relative activity for dilution 10^{-1} / RA 10-2 = Relative activity for dilution 10^{-2} / RA 10-3 = Relative activity for dilution 10^{-3}.

3.4.Comparison of the different activities

In the present work, different organs of plants collected in Mayotte were tested for their *in-vitro* Anti-lipoxygenase activity, DPPH reducing agent and anti-tyrosinase properties. The results presented below (Table 4) highlighted which plant samples were concerned for more than one interesting activity. Such observation may help in the selection of species for further works. Based on the limit of the analytical methods, the samples showing best potency for a specific activity were compared with the two other activities. To maximize the chances of observing differences, the dilutions used were closest to the LLOQ, meaning that the information in the DPPH reducing agent column is based on the observed activity at the third level of dilution and for the column anti-tyrosinase activity and anti-lipoxygenase activity, the evaluation is based on the second dilution.

Table 4: Comparison table of results for samples with significant activities for the multiple tests:+ means a weak activity (<15% relative activity), ++ median activity (>15%), +++ Strong activity (Most significantly active sample from the specific tests).

Sample	DPPH reducing agent	Anti-tyrosinase activity	Anti-lipoxygenase activity
Acalypha hispida Dried flower	++	N/A	+++
Acalypha hispida Dried leaf	++	N/A	+++
Acalypha wilkesiana Dried leaf	++	N/A	+++
Acalypha wilkesiana Fresh leaf	+++	+++	N/A
Cananga odorata Dried leaf	+	N/A	+++
Cananga odorata Fresh flower	N/A	N/A	+++
Erythroxylum corymbosum Dried leaf	++	N/A	+++
Lantana camara Dried leaf	+	N/A	+++
Lawsonia inermis Dried leaf	+++	N/A	N/A
Leea guineensis Dried fruit	++	+++	N/A
Leea guineensis Dried leaf	+++	N/A	N/A
Litchi chinensis Dried leaf	+++	+++	+
Litchi chinensis Dried root	+++	+++	N/A
Persea americana Dried root	N/A	+++	N/A
Persea americana Fresh pit	N/A	+++	N/A
Syzygium aromaticum Dried leaf	++	+++	N/A
Zingiber zerumbet Dried flower	N/A	N/A	+++
Zingiber zerumbet Dried leaf	N/A	N/A	+++
Zingiber zerumbet Dried stem	N/A	N/A	+++
Zingiber zerumbet Fresh rhizome	N/A	N/A	+++

4. Conclusions

On the basis of a previous ethnobotanical research in Mayotte, 21 different plants were selected for their potential as skin care agents. Different organs of these were collected and tested *in-vitro* for their capacity to reduce the stable free radical molecule DPPH, to inhibit the activity of Tyrosinase and/or lipoxygenase, in order to understand better why these plants are used in traditional medicine and to discover new biological sources of natural skin care agents.

When looking at the perspectives for future research, two interesting facts stood out. Firstly, 11 promising species were identified on the basis of their *in-vitro* biological activity for skin care. Among these species, some showed yet unknown biological activities. These specific species could enter future research targeting activities such as topical anti-inflammatory. Such plants would be of interest in the development of treatments against dermatitis/eczema and could possibly help to replace the common use of corticosteroids. Secondly, some other species did not show an outstanding specific activity but an average potency for several activities, leading to more generalist applications such as anti-ageing, pigmentation issues or for a relieving balm. When looking at these two points of view, both are of interest: a strong unique activity or a mild intensity but for multiple activities.

In conclusion, this study highlighted the interesting potential of many plants from Mayotte for their incorporation in cosmetic formulations. Further studies are now needed, including *in-vivo* tests, in order to confirm the activities showed here *in-vitro*. Additionally, toxicological test also should be conducted in order to ensure their innocuity. Moreover, if some of these plants begin to be used extensively for their properties, it would also be necessary to set up conservation measures in order to avoid their disappearance.

5

MOLECULAR IDENTIFICATION

Saive, M., Genva, M., Istasse, T., Frederich, M., Maes, C., and Fauconnier, M. L. (2020). Identification of a Proanthocyanidin from *Litchi Chinensis* Sonn. Root with Anti-Tyrosinase and Antioxidant Activity. Biomolecules, 10(9), 1347.

The previous part of this document is the last part of the funnel we have been going through since the beginning of this project. We started with 1300 different species. Then, progressively the number got smaller and smaller, allowing us to learn from our observations along the way, *e.g.* consensus of informants regarding the uses of plants is an interesting source of information, but can never be used alone to establish the real potency of species for specific uses. Considering all the information gathered, we decided to focus our attention on *Litchi chinensis* Sonn.'s root. This species has been mentioned many times throughout all the previous works due to its generally good results. *Litchi chinensis* has been widely used in many places and cultures in the world for treatments ranging from coughs to flatulence, diabetes, obesity, testicular swelling, epigastric conditions and many more (Ibrahim & Mohamed, 2015). The fact that there is some undeniable agreement concerning its uses and the fact that at the end of our selection process, it was still part of the most effective species for the activities targeted in this work explains why most organs from this species have undergone phytochemical studies. As yet, the roots of this plant, however, have not been studied. The specific sample studied in this work had a significant activity for both DPPH reducing capacities and tyrosinase inhibition. Around the world, the roots are used in decoction to treat fever and to treat throat related diseases (R. M. Pandey & Sharma, 1989; Perry & Metzger, 1980) *in* (Ibrahim & Mohamed, 2015). Another advantage of this specific species is its availability. It is widely distributed between 23°N and 23°S latitudes. (Fig. 15) In 2018, 57 Ha were dedicated for the cultivation of litchi in Mayotte (DAAF, 2018). Being a cultivated crop, its propagation means, agricultural requirements, cultivars, disorders and diseases have been studied (Menzel et al., 2005).

The last part of this work is a bio-guided fractionation of the crude extract of roots of *L. chinensis* followed by a classical molecular identification, to determine which compound(s) is/are responsible for the observed biological activities. In the previous work, the crude extract used for the samples' evaluation were obtained using acetone. This solvent has the advantage of being capable of extracting polar and semi polar content (Delaunay et al., 2002; Musarurwa & Tavengwa, 2020). However, acetone also has the tendency to absorb at the wavelength used for the compounds' detection (Victor et al., 2021). To prevent the presence of acetone remains in the crude extract, the extraction was carried out using HPLC grade methanol and HPLC grade dichloromethane, which were chosen in the hope of extracting as many compounds as if acetone had been used. In addition, as the crude extracts were destined to be fractionated, a higher volume of plant material was used. Following the Soxhlet extraction, the crude extracts were treated according to the protocol described in the chapter "Study of the cosmetic potential uses of plants from Mayotte as skin care agents through the screening of their biological activities".

Figure 15: Longan and Litchi main growing areas around the world.1 = China, 2 = Vietnam, 3 = Thailand, 4 = Nepal and Bangladesh, 5 = India, 6 = Israel, 7 = Spain, 8 = South Africa, 9 = Madagascar, 10 = Mauritius and Réunion, 11 = Australia, 12 = Indonesia, 13 = Philippines, 14 = Florida, 15 = Mexico and Costa rica, 16 = Brazil.*(Menzel et al., 2005)*

Identification of a Proanthocyanidin from *Litchi Chinensis* Sonn. Root with Anti-Tyrosinase and Antioxidant Activity

Matthew Saive [1,*,†], Manon Genva [1,*,†], Thibaut Istasse [2], Michel Frederich [3], Chloé Maes [1] and Marie-Laure Fauconnier [1]

[1] Laboratory of Chemistry of Natural Molecules, Gembloux Agro-Bio Tech, University of Liège, 4000 Liège, Belgium; m.genva@uliege.be (M.G.); Chloe.Maes@uliege.be (C.M.); marie-laure.fauconnier@uliege.be (M.-L.F.)

[2] Biomass and Green Technologies, Gembloux Agro-Bio Tech, University of Liège, 4000 Liège, Belgium; thibaut.istasse@uliege.be

[3] Laboratory of Pharmacognosy, Center for Interdisciplinary Research on Medicines (CIRM), University of Liège, 4000 Liège, Belgium; m.frederich@uliege.be

***** Correspondence: msaive@student.ulg.ac.be; Tel.: +32-498-67-87-16

† Contributed equally to the work.

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Abstract

This work follows an ethnobotanical study that took place in the island of Mayotte (France), which pointed out the potential properties of *Litchi chinensis* Sonn. roots when used to enhance skin health and appearance. Through *in vitro* testing of a crude methanolic extract, high anti-tyrosinase (skin whitening effect) and antioxidant activities (skin soothing effect) could be measured. HPLC successive bio-guided fractionation steps allowed the purification of one of the compounds responsible for the biological activities. The isolated compound was characterized by UV, IR, MS and 2D-NMR, revealing, for the first time in *Litchi chinensis* Sonn. roots, an A-type proanthocyanidin and thus revealing a consensus among the traditional use shown by the ethnobotanical study, *in vitro* biological activities and chemical characterization.

Keywords: proanthocyanidins; *Litchi chinensis*; anti-tyrosinase activity; DPPH; molecular identification

1. Introduction

1.1.Context

An ethnobotanical study which took place in the island of Mayotte (Saive et al., 2018) led to the conclusion that many plants are used traditionally among inhabitants of the island to promote health and for use in dermatological applications. Using indicators such as the Informant Agreement Ratio developed by Trotter & Logan, 1986 (Trotter & Logan, 1986), species of interest were selected for further studies. *In vitro* biological activities measurements realized on several crude extracts of the selected plants revealed that *Litchi chinensis* Sonn. roots, traditionally used for skin whitening and soothing, have high anti-tyrosinase and antioxidant activities.

1.2.Litchi chinensis

The species *Litchi chinensis* Sonn. which belongs to the *Sapindaceae* family (M. Kumar, Kumar, Bhalla-Sarin, et al., 2017; Menzel et al., 2005) mainly originates from southeast Asia but is now a cultivated economic crop in the countries around the world with appropriate climate for its culture (Bourgaud et al., 2001; Liu et al., 2013). The *Litchi* Sonn. genus only contains one identified species composed of three subspecies: *L. chinensis* subsp. *chinensis* Forest & Kim Starr, *L. chinensis* subsp. *phippinensis* Radlk, and *L. chinensis* subsp. *javensis* Leenh. (Diczbalis, 2011; Fan et al., 2011). The first one is mainly found in China (Menzel et al., 2005), the second subspecies is native from the Philippines, New Guinea, Malay Peninsula, and Indonesia and the last one is endemic from Java. Due to their commercial interest, *L. chinensis* subsp. *chinensis* Forest & Kim Starr and *L. chinensis* subsp. *phippinensis* Radlk are found all around the Indian ocean (M. Kumar, Kumar, Prasad, et al., 2017). In Mayotte, only the subspecies *chinensis* is encountered (Boullet, 2016).

L. chinensis is an evergreen, medium sized round-topped tree. Its leaves are leathery, pinnate or lanceolate, acuminate and glabrous. Its inflorescence is a branched panicle. The flowers are small going from white to pale yellow, with a tetramerous calyx without a corolla. They are functionally male and female. The litchi fruits are heart shaped to round covered by a rough rind of pericarp going from light pink to red. The root system is strongly influenced by the soil as well as the propagation technique used. Even if some specimens present a tap root, most of the *Litchi* trees found nowadays have fibrous roots (Fig. 16) found at depth between 0 and 60 cm (Menzel et al., 1990, 2005; Nacif et al., 2001).

Figure 16: Picture of Litchi chinensis roots. (Credit Matthew Saive).

In addition to its use as food, many work have pointed out the biological, including medicinal, properties of *L. chinensis* . Therefore phytochemical work have already been undertaken, highlighting the compounds found in many organ of this species (Table 5) (Bhat & Al-daihan, 2014).

Table 5: Main compounds and compound class found in *L. chinensis* with their location and identified biological activities (Ibrahim & Mohamed, 2015).

Compound Class/Subclass	Compound	Plant Part	Biological Activity
Polyphenols		Leaves Seeds Pulp Pericarp	Cytotoxic Anti-viral Antioxidant Antimicrobial Lipid peroxidation inhibitory activities α-glucosidase inhibitory activities
Tannin	Coumarin Litchtocotrienol A-G Macrolitchtocotrienol A Cyclolitchtocotrienol A	Seeds Antioxidant Leaves Cytotoxic	
Lignan	Schizandriside Isolariciresinol	Leaves Pericarp	Antioxidant Antioxidant
Sesquiterpenes	Litchioside A and B Pumilaside A Funingensin A Pterodontriol-D-6-O-β-D-glucopyranoside	Seeds	Cytotoxic
Triterpenes		Aerial parts Seeds Pericarp	Antiviral
Sterols		Aerial parts Seeds Pericarp	Antiviral
Others	Litchiol A and B Secoisolariciresinol-9′-O-β-D-xyloside 4,7,7′,8′,9,9′-hexahydroxy-3,3′-dimethoxy-8,4′-oxyneolignan Ehletianol C Sesquipinsapol B, Sesquimarocanol B Ethyl shikimate, Methylshikimate Benzyl alcohol 5-(hydroxymethyl)furfural Hydrobenzoin	Leaves Pericarp Fruits	Antioxidant Cytotoxic

1.3.Anti-Tyrosinase Activity

Skin pigmentation is due to melanogenesis, a biochemical phenomenon that takes place in the basal layer of the epidermis. The melanins are produced there and provide the skin with natural protection against harmful effects of UV rays. Melanogenesis can be disturbed due to external aggressions like UV, hormonal disturbances or aging and may result in the appearance of hyperpigmentation spots. The cosmetics sector is actively looking for compounds capable of inhibiting tyrosinase activity with a view to develop ethnic or anti-spot/anti-aging cosmetics (Kamagaju et al., 2013).

Ethnobotanical study and preliminary anti-tyrosinase and antioxidant *in vitro* activity measurements incited us to further study *Litchi chinensis* root extracts by purifying and characterizing a compound involved within the observed biological activities.

2. Materials and Methods

DMAC (4-dimethylamincinnamaldehyde), L-DOPA (3,4-dihydroxy-L-phenylalanine), kojic acid, formic acid (FA), K_3PO_4, TROLOX (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid), DPPH (2,2-diphenyl-1-picrylhydrazyl), tyrosinase (E.C. 1.14.18.1) from mushroom, ammonium formate were purchased from Sigma Aldrich (Darmstadt, Germany). NaH_2PO_4 was purchased from Merck (Darmstadt, Germany) and Na_2HPO_4 from UCB (Bruxelles, Belgium). All HPLC grade and technical solvents as well as absolute ethanol used in this work were purchased from VWR (Leuven, Belgium).

2.1.Plant Material

During the ethnobotanical study, *Litchi chinensis* roots were collected around the village of Coconi, (Mayotte Island, 12°50'03.3"S 45°08'24.2"E) and a specimen was stored into the CBNM's herbaria for proofing reasons (referenced as MAO00051). A total of three independent collects occurred between 2014 and 2017 on trees of similar size in the same area. The *L. chinensis*' roots were dried for 48 h at 40 ± 1 °C using a drying oven, they were then powdered, vacuum packed and stored at -22 ± 1 °C until being used. Extractions and purifications were therefore carried out on three completely independent biological samples.

2.2.Sample Preparation

Twenty grams of *L. chinensis* roots were precisely weighted and extracted with 400 mL of solvent in a Soxhlet apparatus. Extractions were made using either HPLC grade methanol or HPLC grade dichloromethane, and this led to the collection of a polar and a less-polar extract. The extracts were then evaporated at 40 ± 1 °C using a rotating evaporator (Sigma Aldrich, Darmstadt, Germany). The dried extracts were kept at -22 ± 1 °C until use. The polar samples were solubilized in a small amount of pure ethyl alcohol and the non-polar extracts were solubilized in HPLC grade dimethyl sulfoxide. The solvents were added gradually under ultrasonic bath until complete solubilization.

2.3. DPPH Antioxidant Activity

In order to determine the antioxidant potency of the plant samples, a protocol based on the DPPH method and adapted from M. S. Blois 1965 (Blois, 1958) was used. A 2.10^{-4} M DPPH solution was prepared using methanol and was then added to different dilution of the plant extracts. The solution was left to react for 30 min and then observed at 517 nm by UV/VIS spectrophotometer (Ultrospec 7000 from Biochrom, Cambridge, UK). The polar plant extract was diluted using HPLC grade methanol and the non-polar extract was diluted using HPLC grade ethyl acetate. The 10^{-2} and 10^{-3} dilutions were applied to the plant extracts. A 1:1 (v/v) ratio was applied with the reagent and the plant samples. The positive control for both kind of samples was TROLOX (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) 2.10^{-3} M in methanol and blank was 100% methanol.

2.4. Tyrosinase Inhibition

Tyrosinase (EC 1.14.18.1) is a key enzyme in the melanogenesis pathway. In this work, the polyphenol oxidase activity was exploited based on the adaptation of the work of Rangkadilok et al. (Rangkadilok et al., 2007). Through the consumption of L-DOPA, it produces dopachromes that are detected/measured at 475 nm. In order to evaluate the impact of the plant extract on the synthesis of these dopachromes, inhibitions were compared with the inhibitory action of 1 mM kojic acid in phosphate buffer (0.05 M–pH 6.5). Dilution factors of 10^{-1}, 10^{-2} and 10^{-3} were applied to the samples using the same phosphate buffer. The substrate solution was made of a 1 mM solution of L-DOPA in distilled H_2O and the enzymatic suspension was made at a 625 U/mL concentration in phosphate buffer. As oxygen is also part of the enzymatic reaction as a co-substrate, the phosphate buffer used in the reactive mix was saturated with pure oxygen for 30 min at room temperature prior to the analysis.

The enzymatic reaction was performed by mixing 100 µL of sample with 50 µL of tyrosinase and 250 µL of oxygenated phosphate buffer. This mixture was left to incubate for 15 min, and then added in a quartz absorption cell along with 400 µL of the substrate solution. The synthesis of dopachromes was observed in real time, and the absorbance was measured every 15 s for 5 min at 475 nm.

2.5. Bio-Guided Fractionation

Throughout the purification process, the anti-tyrosinase inhibition test and the antioxidant test were conducted for all fractions. Based on preliminary observation, the chromatograms were systematically recorded at 280 nm as it gave the best contrast; however, in order to control potential left out compounds, other wavelengths were also registered (254 nm, 310 nm and 360 nm) with the cut-off for eluants being at 190 nm.

2.5.1. **Preparative HPLC**

A first preparative HPLC step was conducted as follows: the column was a 150 × 21.2 mm–5 µm RP C8 column (Strategy, Interchrom, Interchim, Montluçon, France). Two mL solution (100 mg/mL) of the samples was injected at a 20 mL/min flow. The mobile phase was composed of solvent A: acetonitrile (ACN)–0.1% formic acid and

solvent B: H_2O–0.1% formic acid, and the optimized gradient was from 100% B to 20% (A)–80% (B) in 50 min, and then a final hold for 5 min. The mobile phase reached 60% (A)–40% (B) at 65:00 min and was then reset to 100% (B) in 10 min. From this first cycle, 17 fractions were collected and tested for the two biological activities. The most potent fraction went through a second preparative HPLC purification process.

The second preparative HPLC was conducted on this fraction with the same apparatus; the detector was set at 280 nm; 2 mL of sample at a 100 mg/mL were injected at a 16 mL/min flow rate. The instrument was fitted with a 250 × 22 mm–10 µm RP C4 column (Protein from Vydac, Hicrom, Lutterworth, UK). The same solvents were used for this fractionation. The gradient started with a steady step with 0% (A)–100% (B) between the 00:00 min mark and the 05:00 min mark. At the 10:00 min mark, it had reached 5% (A)–95% (B). At the 55:00 min mark, it had gone down to 30% (A)–70% (B); from that point it went back up to 0% (A)–100% (B) at the 57:00 min mark. From this second cycle, 5 fractions were collected and tested for the two biological activities. The most potent fraction was once again fractionated using an analytical HPLC setup mounted with a fraction collector.

2.5.2. **Purification through Analytical HPLC**

A Hewlett-Packard Agilent 1200 HPLC (Santa Clara, CA, USA) with a Multi Wave detector set at 280 nm was used, and the following parameters where applied. Ten microliter of 10 mg/mL sample was injected at a 0.5 mL/min flow rate. The solvent used were the same as the one used for the preparative HPLC. The instrument was equipped with a 250 × 4.6 mm–5 µm RP C8 column (Strategy from Uptisphere, Interchim, Montluçon, France). The gradient starts at 0% (A)–100% (B) for 10 min; then from the 10:00 min mark to the 55:00 min mark, it goes down to 20% (A)–80% (B); this is followed by a drop reaching 60% (A)–40% (B) at the 57:00 min mark. It finishes at the 59:00 min mark with a 0% (A)–100% (B) mobile phase. From this fractionation 5 fractions were collected and tested for the two biological activities. Once the purification process was complete, the compound was kept at 7 ± 1 °C in a dark container for a maximum 48 h before undergoing the analytical steps.

2.6. Molecular Characterization

The molecular characterization of the target compound was realized by combining IR, UV, 2D-NMR and MS techniques.

2.6.1. **IR**

The dry sample was analyzed using a Shimazu IR Affinity-1S FTIR (Nakagyo, Japan) spectrophotometer in transmission mode. The purified powder was placed directly on the diamond in order to establish its IR spectrum. The FT-IR spectrum of the sample was scanned between 4000 and 400 cm^{-1}.

2.6.2. **UV**

The UV spectra was obtained with a Ultrospec 7000 (Biochrom, Holliston, MA, USA) spectrophotometer. The sample was diluted at a 0.3 mg/mL in the MeOH and the absorbance was recorded in the UV/VIS range between 200 to 600 nm.

2.6.3. **MS**

The purified fraction of interest was solubilized in HPLC grade MeOH at a 1 mg/mL concentration. It was analyzed using an Agilent 1100 HPLC (Santa Clara, CA, USA) mounted with an Inertsil ODS-3 3 µm 3 × 100 mm column and using the following gradient: acetonitrile: mQ water (85:15, solvent B) and mQ water (solvent A) + 0.2% formic acid and 12 mM ammonium formate. One minute of 53% B was followed by a linear increase of B to 100% at 17 min and an isocratic elution at 18 min. The gradient was then reversed at 6 min followed by a stabilization after 3 min at a flow rate of 0.5 mL/min. The injected volume was 10 µL.

Then using an ESI-ion trap mass spectrometer (Esquire HCT ion trap mass spectrometer; Bruker, Rheinstetten, Germany), the fraction of interest was characterized. The ESI was operated in the positive mode. Mass spectrometer parameters were set as follows: capillary voltage -4500 V; endplate offset -500 V; nebulizer pressure 50 psi; dry gas flow rate 10 L/min; dry gas temperature 300 °C; skimmer 20.6 V; capillary exit 300 V; oct 1 DC 10 V; oct 2 DC 2.79 V; Lens 1–5.2 V; lens 2–72 V; oct RF 300 Vpp; trap drive 92.8. The scan range was optimized at 300–1250 m/z

2.6.4. **NMR**

The purified sample was diluted in D_2O with TSP as internal standard and 2D (^{1}H–^{13}C) NMR spectra were recorded at 300 K on a Bruker Avance NEO Ultrashield 700 Plus equipment operating at 700 MHz for ^{1}H and 175 MHz for ^{13}C and using a TCI cryo-probe (Rheinstetten, Germany).

For heteronuclear single quantum correlation (HSQC) experiments, the datasets were acquired with 1024 and 512 data points for the f2 (^{1}H) and f1 (^{13}C) dimensions, with spectral widths of 11161 and 38736 Hz, respectively. Eight scans were performed and the relaxation delay was fixed at 1 s.

Regarding heteronuclear multiple bond correlation (HMBC) experiments, the datasets were acquired with 4096 and 512 data points for the f2 (^{1}H) and f1 (^{13}C) dimensions, with spectral widths of 9091 and 38736 Hz, respectively. Thirty-two scans were performed and the relaxation delay was fixed at 1.5 s.

2.6.5. **Colorimetric Test**

In order to confirm the properties of the component, a colorimetric test based on Prior *et al.* (Prior et al., 2010) protocol was performed. The DMAC (4-dimethylaminocinnamaldehyde) test has proven to be effective when trying to quantify proanthocyanidins in plant extracts (Cunningham et al., 2002). A 0.1 mg/mL sample solution was prepared in pure ethanol. The DMAC solution was done following Prior's protocol: 0.01 g of DMAC was placed in a 10 mL volumetric flask and a solution of 36% hydrochloric acid, distilled water and pure ethanol (1:1:6) was added to the mark. The reaction was performed at room temperature: 100 µL of sample solution was placed in a spectrophotometric cell added with 500 µL of DMAC solution and read immediately at 640 nm.

3. Results and Discussion

3.1. Species Selection

Twenty-one species were selected after the ethnobotanical study in Mayotte (France) and their crude extracts obtained with methanol and dichloromethane were used for biological *in vitro* testing (data not shown). Among the 21 species tested, *Litchi chinensis* was the most promising, exhibiting high anti-tyrosinase and antioxidant activities (95.1 ± 0.06%, 84.8 ± 1.87%, respectively).

3.2. Bioguided Fractionation

The bio-guided successive fractionation steps are illustrated in the different chromatograms shown below (Fig. 17-19). In each chromatogram, the peak that was selected after each fractionation and biological activities evaluation (Tables 6–8) has been pointed out. In the first, fraction F10 was selected (Fig. 17) because of its biological activities (Table 6); in the second one, F10.3 was selected because of its biological activities (Table 7) (Fig. 18). The identification work took place on peak F10.3.3 (Fig. 19), and its biological activities can be found in table 8, obtained after the third fractionation/purification step.

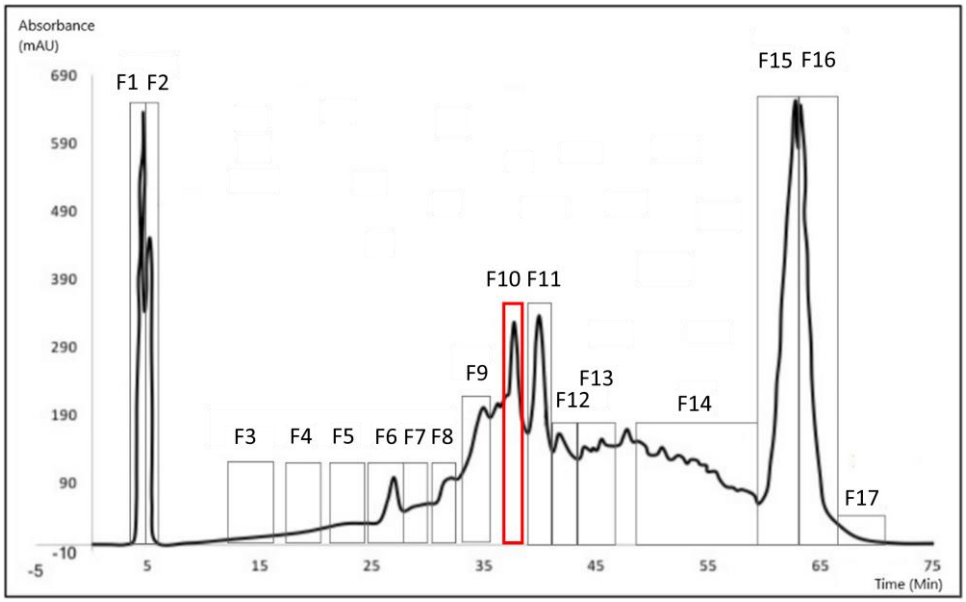

Figure 17: Chromatogram from the first fractionation process (preparative HPLC). Seventeen fractions were isolated. The peak of interest is F10 (RT = 37'49'') (shown in red).

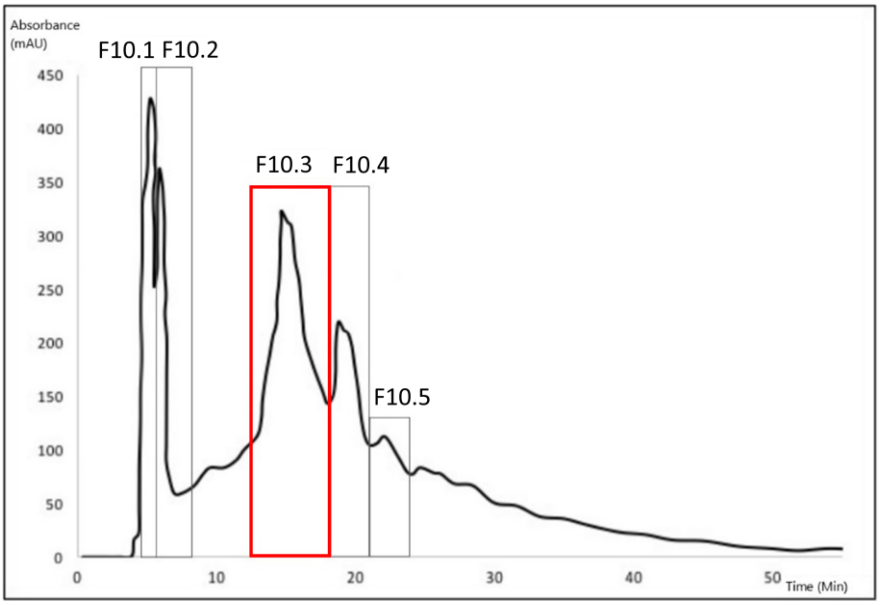

Figure 18: Chromatogram from the second fractionation process (preparative HPLC). Five fractions were isolated. The peak of interest is F10.3 (RT = 14'45'') (shown in red).

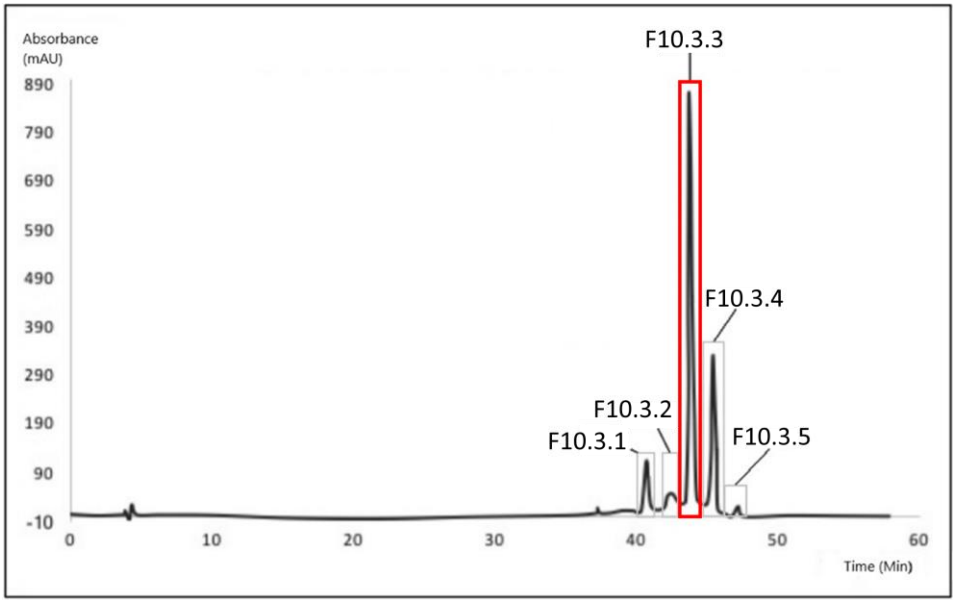

Figure 19*:* Chromatogram from the third fractionation process (analytical HPLC with fraction collector). Five fractions were isolated. The peak of interest is F10.3.3 (RT = 43'49'') (shown in red).

The Tables 6–8 present the relative anti-tyrosinase and antioxidant activities of each fraction collected respectively after one, two or three HPLC purification step(s). In Table 6, the fraction 10 is highlighted for its high anti-tyrosinase and antioxidant activities and was further fractionated into sub-fractions (Table 7) where fraction 10.3 was selected for the third fractionation step (Table 8). The molecular characterization took place on fraction 10.3.3.

Table 6: Relative activity shown by the fractions retrieved after the first purification process.

Fraction	DPPH		Tyrosinase	
	Inhibition %	SD %	Inhibition %	SD %
1	97.7	0.53	37.4	3.69
2	59.6	5.16	12.7	8.75
3	56.8	7.05	11.0	1.74
4	3.43	1.76	20.8	15.7
5	91.2	4.40	28.6	7.30
6	50.8	3.75	0.03	0.06
7	96.4	0.74	78.6	0.74
8	95.6	0.40	76.9	5.42
9	98.8	0.55	55.2	1.32
10	**97.1**	**0.72**	**87.4**	**0.85**
11	97.5	0.66	65.2	1.16
12	22.1	5.35	6.35	1.07
13	97.5	0.33	35.8	4.45
14	96.8	0.64	77.2	0.19
15	90.0	9.19	75.6	2.32
16	89.0	9.91	28.1	1.71
17	16.9	4.39	0.00	0.00

3.2.1. **Second Fractionation Activities**

Table 7*:* Relative activity shown by the fractions retrieved after the second purification process.

Fraction	DPPH		Tyrosinase	
	Inhibition %	SD %	Inhibition %	SD %
10.1	28.6	13.2	35.8	4.45
10.2	18.0	5.07	57.1	0.90
10.3	**72.6**	**10.2**	**82.4**	**0.87**
10.4	35.3	22.7	52.5	3.35
10.5	32.0	15.3	51.9	3.14

3.2.2. **Third Fractionation**

Table 8*:* Relative activity shown by the fractions retrieved after the third purification process.

Fraction	DPPH	Tyrosinase

	Inhibition %	SD %	Inhibition %	SD %
10.3.1	28.6	13.2	0.0	0.0
10.3.2	18.0	5.07	0.0	0.0
10.3.3	**72.6**	**10.19**	**8.44**	**1.59**
10.3.4	35.3	22.7	1.18	1.21
10.3.5	32.0	15.28	0.0	0.0

3.3.Molecular Characterization

Combining the three successive fractionation steps allowed us to obtain fraction 10.3.3 that was re-analyzed by analytical HPLC revealing a single peak with > 99% UV-purity. Starting from 20 g of litchi dry roots, we obtained around 9 mg of fraction 10.3.3 (protocol yield of 0.045 g/Kg DM).

3.3.1. **IR**

The most striking feature of the infrared spectrum (Fig. 20) is the intense and relatively broad band around 1600 cm^{-1}. Such an intense band is not expected from double bond stretching vibration but has been observed in molecules with 1,3-diketone moiety. The band is thought to result from the resonance and the formation of a strong hydrogen bond when one of the ketones enolizes. Carbonyl stretching bands are sometimes observed in 1,3-diketones infrared spectrum but the intensity of the bands is highly variable according to the molecular structure. 1,3-dihydroxy aromatic structures such as resorcinol and phloroglucinol also show an intense band around 1600 cm^{-1} and no intense band in the carbonyl region of the spectrum. This could suggest that the isolated molecule is a phenolic compound possessing −OH moieties in 1,3 positions. The occurrence of a small node at 3543 cm^{-1} suggests an intermolecular bonded −OH. The strong band at 1065 cm^{-1} can be explained by C-O stretching from ether bond.

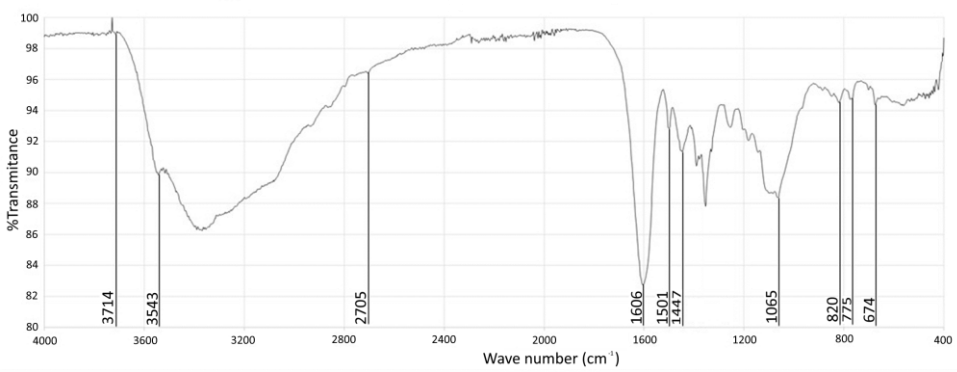

Figure 20: FTIR spectrum.

3.3.2. **Mass Spectrometry**

Based on the mass spectrum (Fig. 21), signal at 1153.1 m/z corresponded to $[M + H]^+$, indicating a monoisotopic mass of 1152.1 Da for the purified molecule. When compared to the literature, the observed parent ion is in line with the observations of (Lv et al., 2015; Xu et al., 2010) and suggests a proanthocyanidin tetramer with two B-type bonds and one A-type bond (Fig. 23). The following information obtained from the mass spectrum was consistent with that conclusion. Signal at 1001.1 corresponded to the loss of an hydroxyvinylbenzenediol unit $[M + H - 152]^+$, as previously described by Enomoto H. et al., 2020 (Enomoto et al., 2020). The most abundant ion of the mass spectrum (865.2 m/z) was formed by quinone methide fission which caused the loss of the first epicatechin unit linked with a single B-type 5–4' bond. The 865.2 m/z ion thus corresponded to an epicatechin trimer $[M + H - 288]^+$. Sodium adduct of the latter is also reported at 887.2 m/z $[M + Na - 288]^+$, as well as the formation of an ion resulting from a water molecule loss to the trimer at 847.2 m/z $[M + H - 288 - H_2O]^+$. The signal at 713.2 was produced following the loss of a hydroxyvinylbenzenediol unit from the epicathechin trimer $[M + H - 288 - 152]^+$. Specific fragment ions at 575.1 and 865.2 allowed to elucidate the position of the A-type double 5–4'/2-O-3' (Fig. 23) as those fragments are produced when the A-type bond is placed between the second and the third epicatechin units (Gross et al., 2012; Lin et al., 2014).

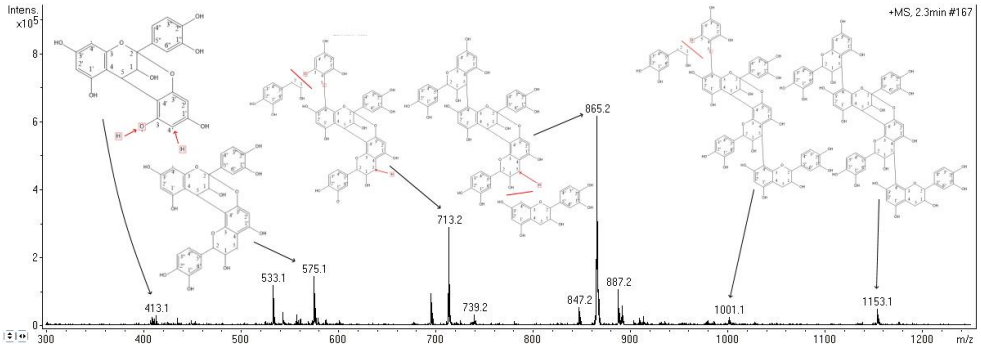

Figure 21: MS spectra of the purified molecule recorded in the positive mode.

3.3.3. **NMR**

Based on its 2D ^{1}H-^{13}C HSQC spectrum (Fig. 22), the isolated substance possesses at least eight unsaturated or aromatic C-H (green circle, Fig. 22). The HSQC and HMBC spectra (Fig. S1–S5) comparison revealed that the molecule also contains several unsaturated quaternary carbon atoms (154, 144, 131, 108, 106, 99 ppm). The quaternary C around 154 and 144 ppm are supposed to be linked to O in opposition to the 99 ppm and 130 ppm ones. The molecule does not seem to possess ketone, aldehyde or carboxylic acid moieties but includes an aliphatic part as suggested by several HSQC C-H signals (yellow, blue and red circles in Fig. 22) and a CH_2 signal (grey circle in Fig. 22). From HSQC and HMBC data, this saturated structure is likely a heterocycle containing one oxygen atom. Several signals support the connection of the heterocycle to two aromatic structures: ^{1}H at 5.55 ppm coupled to ^{13}C at 115, 119

and 130 ppm; ^{1}H at 2.8 and 2.7 ppm coupled to ^{13}C at 154 and 100 ppm. A more detailed allocation of HMBC signals is provided in Supplementary Materials (Fig. S6).

NMR data thus confirm that the molecule is a catechin derivative. This complies with the techniques used when isolating and purifying the compound (Delaunay et al., 2002; Lv et al., 2015) as well as when comparing to the available literature on the phytochemistry of Litchi (Ibrahim & Mohamed, 2015).

If the catechin structure seems relevant, there are still too many signals corresponding to aromatic C-H, non-aromatic hydroxylated C-H and non-aromatic C-H. As suggested by mass spectrometry, several elements of NMR spectra support that the molecule is an oligomer, probably a tetramer from the repetitive patterns observed in HSQC and HMBC experiments:

In HSQC, four signals are observed for non-aromatic hydroxylated C-H (red circle, Fig. 22).

In HMBC, four aromatic ^{1}H (two around 6.9 ppm and two around 6.8 ppm) are also coupled to ^{13}C with a common pattern (131; 144 ppm).

In HSQC, the presence of signals at 4.2; 27 and 4.3; 36 ppm (Fig. 22, yellow circle) can be explained if several catechin units are linked together since unpolymerized catechin should only display CH_2 signals in this area of the spectrum.

In HMBC, the B-type bond between units is confirmed by the coupling of ^{1}H at 4.3 ppm with ^{13}C at 154, 153, 151, 108, 106, 77 and 71 ppm. Signals at 4.3; 154,153 and 151 ppm correspond to H5 coupled to C1', C3 and C3'. The coupling of H5 with C4 and C4' are also expected and probably correspond to signals at 4.3; 108 and 106 ppm, respectively (HMBC spectrum in Fig. S5).

The presence of an A-type bond in the molecule is also confirmed by NMR data. Two distinct chemical shifts are attributed to carbon C2: 77–78 ppm and 99 ppm. The increased chemical shift (99 ppm) of carbon C2 (Fig. 23) is consistent with its involvement in an A-type bond which implies an additional bond to an oxygen atom.

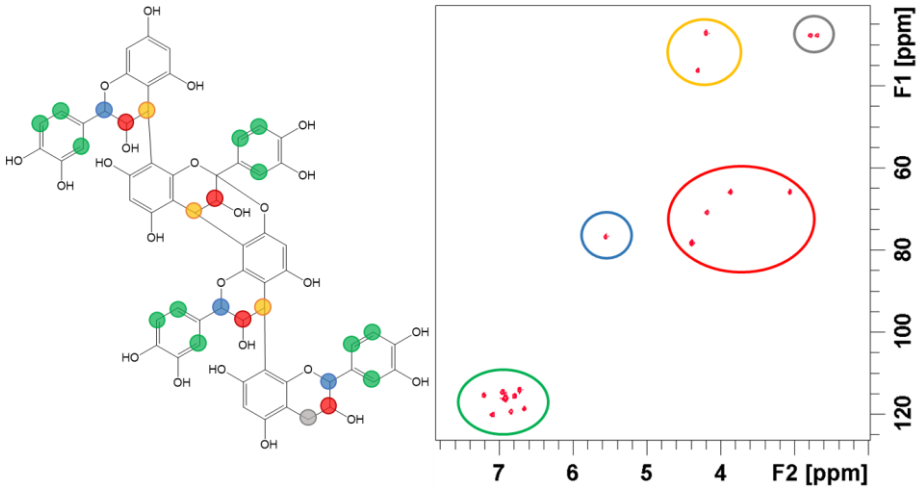

Figure 22*:* Two-dimensional *heteronuclear single quantum correlation (*HSQC) NMR spectrum of the isolated compound (right) and its hypothetical chemical structure (left). The structure proposal is based on both NMR and mass spectrometry data.

Using the NMR results coupled with IR results and the typical mass fragments, the isolated molecule is a proanthocyanidin composed of four catechins as seen in Fig. 20.

3.3.4. **UV**

As mentioned in the work of Hümmer & Schreier, 2008 (Hümmer & Schreier, 2008), the presence of proanthocyanidin is characterized by a peak around 200–220 nm and a peak at 278 nm, this information is aligned with the UV spectra obtained from the isolated molecule (data not shown).

3.3.5. **Colorimetric Test**

The absorbance of the blanks and the sample were as follows:

Table 9: Absorbance at 640 nm of the fraction 10.3.3 in contact with 4-dimethylamincinnamaldehyde (DMAC).

Observation	MeOH	DMAC 1mg/mL	HCl + EtOH	Sample	Sample + DMAC
Optical density	0.00 ± 0.00	0.13 ± 0.00	0.00 ± 0.00	0.24 ± 0.00	0.46 ± 0.08

Based on the works of (Lv et al., 2015; Payne et al., 2010; Wang et al., 2016), the compound reacts with DMAC, in a way that allows us to confirm the procyanidin nature of the compound as well as the presence of A linkage

Finally, when comparing all the available information, the isolated compound is a A-type procyanidin tetramer with the following structure: EC -->B --> EC --> A -->EC --> B --> EC where EC stands for epicatechin, B stands for a single 5-4’ bond and A stands for a double 5-4’/2-O-3’ bond (Fig. 23).

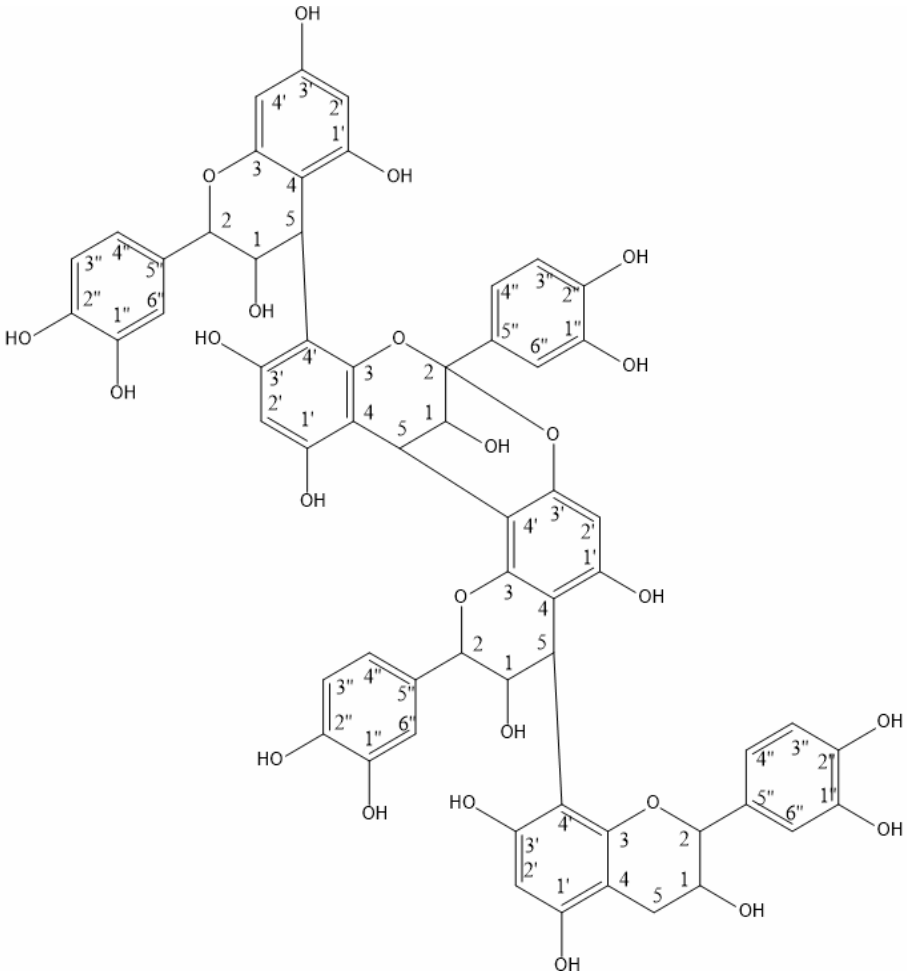

Figure 23: Purified compound from the roots of L. chinensis.

When comparing the determined structure to the available literature, a compound showing similar structure and mass is (2*R*,3*R*,4*S*,8*R*,14*R*,15*R*)-2,8-Bis(3,4-dihydroxyphenyl)-10-[(2*R*,3*R*,4*R*)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-3,5,7-trihydroxy-2H-1-benzopyran-4-yl]-4-[(2*R*,3*S*)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-3,5,7-trihydroxy-2H-1-benzopyran-8-yl]-3,4-dihydro-8,14-methano-2H,14H-1-benzopyrano[7,8-d][1,3]benzodioxocin-3,5,11,13,15-pentol or cinnamtannin D_2 (CAS registry number 97233-47-1). This molecule was previously described in peanut skin (*Arachis hypogaea* L., Fabaceae) (Tatsuno et al., 2012).

4. Conclusions

This work is part of a bigger study aiming to identify compounds of interest in the wide flora available in the Comoros archipelago. In this specific case, an anti-tyrosinase activity is interesting when willing to treat issues such as melasma (Arrowitz et al., 2019). This kind of skin condition implies the local application of compound is destined to regulate melanogenesis. Treatments used nowadays can be very dangerous as they often contain hydroquinone and steroids. Those compounds have shown adverse effects such as dermatitis, black and blue skin pigmentation, blindness, skin thinning, bruises and stretch marks. This means that there is room for effective treatment without any adverse effect especially when taken for a long period of time, as it is often requested for those types of diseases (Burger et al., 2016). In addition, the antioxidant potency of the samples were tested, as it is also beneficial when working with topical treatments. Through a bio-guided purification followed by molecular characterization of extracts from the roots of *Litchi chinensis* Sonn., the structure of cinnamtannin D2 responsible for the biological activity was obtained. It is the first time that this class of compounds was highlighted in *L. chinensis'* roots. Lychee roots appear to be a promising source of raw material that could be used for the development of effective skin treatment. The fact that *L. chinensis* roots are used in this study may raise questions in terms of the plant's conservation. However, technologies exist to enhance the value of root plant compounds (Ghanem et al., 2011). In the end, our study has allowed the purification and the characterization of a proanthocyanidin A-type in *L. chinensis* roots for the first time. This study also revealed a consensus among the chemical structure, biological activities and the traditional uses of *Litchi* roots in Mayotte to treat skin pigmentation issues and soften the skin.

Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1, Figure S1: 1D ^{1}H NMR spectrum of the isolated compound, Figure S2: 2D HMBC NMR spectrum of the isolated compound, Figure S3: 2D HMBC NMR spectrum of the isolated compound, Figure S4: 2D HMBC NMR spectrum of the isolated compound, Figure S5: 2D HMBC NMR spectrum of the isolated compound, Figure S6: Allocation of 2D HMBC NMR signals of the isolated compound.

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6

GENERAL DISCUSSION

1. Review of traditional practices in the Comoros archipelago

The first part of this work identified a non-exhaustive list of plants used traditionally in the Comoros archipelago and then compared this information with a broader geographic area (the islands of the Indian Ocean) in order to highlight which plants might be of interest for the development of skin care products. A total of 207 different species coming from 80 different families put on the list. These data were compared with the RII (Relative Importance Index) which led to an observation regarding the species' number of uses; *e.g.* (*Plectranthus amboinicus* (Lour.) Spreng.) has 21 uses among the islands of the Indian Ocean but does not show a high consensus regarding its uses among the different areas. Other specimens with less known application, such as *Acalypha lyallii* Baker, tend to show a higher use consensus among the islands of the Indian Ocean. Likewise, concerning the data generated by Bennett and Prance, they discussed the number of species used for one or more body systems and compared this information with the origin of the species entering their work (Bennett & Prance, 2000).

In this work, the origin is not considered; however, the conclusions obtained from the RII are similar and allow for an indication of the versatility of uses for a specific species regardless of its origin. When looking at other studies using the RII, they have generally been used, "*to identify the most important species to a given culture, compare differences between the historical documented and contemporary importance of species and to test hypothesis related to the use, knowledge and conservation of medicinal plants*" (Albuquerque et al., 2006). In this work the intended outcome for the use of the RII is related to the known uses. This indicator was used in the review as it is applicable with secondary data and is less sensitive to a small number of informants (Albuquerque et al., 2006). In addition, the information available in the literature did not allow us to use other indicators such as the informant agreement ratio (IAR). Quantitative ethnobotany indicators all have advantages and limitations. For instance, the RIA gives information about the consensus regarding the use category but not about the importance of the species on its own. The RII on its own will allow for the identification of species with the greatest absolute number of uses; however, this indicator cannot be correlated with cultural importance (Albuquerque et al., 2006). Another important piece of information learned from this work is that some differences of use occurred between the different islands of the Comoros archipelago leading to the conclusion that ethnobotanical data from that region could not be taken as a whole but that each island needs to be studied separately. A simple hypothesis concerning these differences might reside in the current tension building between the Comorian immigrants and the Mahorans. One might think that such immigration would bring some knowledge from the Comoros to the island However, considering the risks encountered by those attempting the crossing, the elderly might not be the ones most prone to attempt the trip. As this disappearing knowledge is mainly retained by the older part of the population, there is very little chance that traditional knowledge would have travelled between the islands because of this new immigration crisis.

2. Ethnobotanical study

The second part of this work focused our research on a specific island of the Comoros archipelago. As mentioned by Barthelat and Viscardi (Fabien Barthelat & Viscardi, 2012), from a biodiversity point of view, Mayotte is one of the richest in the world. In addition, the location of the island being on the Dutch and Portuguese spice routes, between the 15th and 17th centuries implies influences from European countries, Asian countries, and African countries (Arnold, 2014; Barendse, 2016). With these overlapping influences, it is likely that they would develop varied uses of many different species within a limited area (374km²). An ethnobotanical study targeting Mayotte was concluded to be valuable and therefore conducted. The information collected during the two infield missions were first compared to the available data and then used to broaden the scope of the said data. Throughout this work the 4 conditions mentioned by Trotter and Logan (Trotter & Logan, 1986) on ethnobotanical principles were used as guidelines. A total of 249 answers were collected, leading to the identification 69 taxa. The interviewees were selected based on their reputation among the islands as keepers of knowledge. During the interviews, the age of the interviewees was recorded, and some observations were made. Interviewees of up to 25 years old (n=5) could name around 6 different species linked to traditional uses in cosmetics. Informants between 26 and 50 years old (n=9) could mention around 13 different species linked to traditional uses in cosmetics. Those between 51 and 80 (n=6) could name around 8 different species linked to traditional uses in cosmetics and the two informants age over 80 gave 11 and 15 different species linked to traditional uses in cosmetics. The tendencies observed show that the youngest interviewees had the least amount of knowledge. The second category knowledge-wise was the group of people between 50 and 80. A hypothesis regarding this phenomenon resides in the fact that this category of people could rely on their elders and therefore did not see the point in learning such knowledge. In addition, at that time Mayotte was undergoing political changes (Idriss, 2013) and people might have been more concerned by other matters. The third category knowledge-wises encompasses the people between 25 and 50 and the elderly. A hypothesis regarding them could be that there has been a regain of interest in such knowledge linked to a global interest for more “natural” products and people in the active life category might have seen an opportunity to develop a trade. The only two informants who were over 80 years old illustrate the disappearance of this ancestral knowledge. Even with this regain of interest by the middle-aged population, there is a tendency of the younger population to abandon this traditional knowledge. Such a situation emphasizes the need for works like the present one to be carried out not only in the hope of finding new species for the development of medicines but also to prevent this cultural richness from disappearing.

When comparing the data gathered in the ethnobotanical study with the data available in the literature, some consensus in the use of some species was observed, as based on Trotter and Logan’s (Trotter & Logan, 1986) statement, saying that if there is some sort of consensus, the chances for a real effectiveness are higher. It was interesting to compare observed consensus with the biological activities mentioned in this work.

28 species were already known for their traditional usage only on the Island of Mayotte and, as mentioned in the review, their use was confirmed during the ethnobotanical study. Among these species *Aloes mayotteensis* A. Berger, *Cordia subcordata* Lam. and *Senna singueana* (Delile) Lock. were known for their traditional uses in connection with the biological activities studied in this work which were, respectively: redness, dermal reactions, and acne. As mentioned by (Arican et al., 2005) acne can be linked to oxidative stress. Skin redness is an indicator used to study inflammatory reactions (Korting et al., 1993). As for dermal reactions, it is a very generic statement that could be linked to any of the activities studied in this work.

3. Biological activity evaluation

The original aim of this work was to identify some plant species with activities of interest for skin care medicine development. Whilst looking for the most active specie we also kept in mind the real usability of the plants considering the technical limitations of the Island. The three tests used in this work can be dived in two categories: the DPPH test which is a non-enzymatic test only based on the stoichiometry of the oxidation reaction and the anti-tyrosinase and anti-lipoxygenase evaluation which are both linked to enzymatic activities.

In comparison with other antioxidant tests such as the ABTS or the FRAP tests, the DPPH has the advantage of being fast and tolerating the use of organic solvents whereas the FRAP or ABTS have the advantage of being more stable and provide a complement to the data gained by doing the DPPH test. (Roy et al., 2010) also established that when using the DPPH test in an aqueous buffer, there is a risk of observing a pro-oxidant effect linked to the synthesis of ROS, which confirmed our choice of working with 100% organic solvent for our extractions

As mentioned by (Ozgen et al., 2006) in order to establish the TAC (total antioxidant capacity), complementing the DPPH test with the ABTS test is recommended. Another test known as the ORAC test has been used widely to evaluate antioxidant activities of plant extract. In a study carried out by (Roy et al., 2010) where ORAC was compared to DPPH, the DPPH gave generic good results regardless of the different polyphenol composition of the tea extract used for the test, whereas the ORAC test was strongly influenced by the different types of polyphenol found in the tea extract , reinforcing our hypothesis that even if not as precise as other test, the DPPH is a good generic test for global antioxidant estimation. As the aim of our work was to isolate plants of interest within a huge number of very diverse samples (bark, root, flowers, leaves, fruits, etc.), extracted with the same organic solvent, a generic test allowing for a differentiation regardless of the sample type was the obvious go-to even if it meant the loss of information such as amounts and types of compounds involved in the observed antioxidant reaction.

The second activity of interest was more linked to the aesthetic aspect of skin treatment as it aimed at identifying species that could cure or prevent skin pigmentation issues (melasma, post inflammatory hyperpigmentation, freckles or lentigines). Between the biosynthesis of eumelanin and pheomelanin there is a common pathway that is induced by tyrosinase. *Ergo* we focused our effort on finding a way to inhibit

its action to prevent the synthesis of melanin. This test was therefore selected as a tool to differentiate the species with potential anti-tyrosinase activities from species without any anti-tyrosinase activities. When talking about skin tone correction, one cannot ignore that in some places around the world, a general lighter tone is considered more aesthetically pleasing, especially for populations with Fitzpatrick skin phototypes IV to VI. This leads to the abuse use of skin lightening creams, sometimes inducing serious adverse effects such as irritation as well as exogenous ochronosis and confetti like leukoderma or occupational vitiligo (Dadzie & Petit, 2009; Westerhof & Kooyers, 2005). The development of skin tone corrective medicine is a dangerous process as there is a real medicinal requirement linked to the wellbeing for the patients; however there is always the risk of incorrect treatment practices which could lead to severe side effects. In this work we were hoping to find a compound that would have a real effectiveness on the skin pigmentation, with as few side effect as possible so that, even if it were used erroneously, it would not cause effects other than the ones linked to a lower concentration of melanin units, mainly the decrease of broadband UV absorbent activity, antioxidant activity and radical scavenging activity (Brenner & Hearing, 2008).

The last targeted biological activity of this work was the inhibition of the lipoxygenase enzyme. The biosynthesis pathway linked to this enzyme generate inflammatory precursors known as leukotrienes. By inhibiting its activity, the samples were expected to act as anti-inflammatory products. In the specific context of a screening of many samples from many different origin, the use of soybean lipoxygenase as model was chosen as this test has the advantage of being easy to implement, the reagents are relatively affordable, in addition it has been used as model for human lipoxygenase analysis in other works (Mahesha et al., 2007; Ribeiro et al., 2014; Srivastava et al., 2016). Once the primary selection has been undertaken the activity needs to be confirmed using standard anti-inflammatory tests. Due to observable deleterious effect in classical NSAID (non-steroidal anti-inflammatory drugs) the search for new compound with anti-inflammatory properties is ever so necessary.

There is a clear link between the three targeted biological activities. The DPPH tests gives an idea of the radical scavenging properties of the tested sample. Melanin is a radical scavenging promotor and a protective compound against UV's deleterious effects. Among those, inflammation is probably the first defense mechanism that will be initiated by the body. All three activities are strongly linked to the presence of ROS (reactive oxygen species). Human cell viability is strongly influenced by the oxidative stress it undergoes. This stress is managed by the balance between pro-oxidative compounds such as ROS (Reactive oxygen species) and antioxidant compound (Jones, 2008). The inflammation pathway is redox sensitive and thus is influenced by the presence or absence of ROS. These compounds are constantly produced as an unwanted by-product of the aerobic metabolism. However, to avoid oxidative stress and its deleterious effects the body has Its own defense mechanism (Surh et al., 2005). Among the antioxidant compounds found in the body melanin plays an important role (Glassford et al., 2007; Nofsinger et al., 2002; Sarna, 1992). By preventing the synthesis of melanin through tyrosinase inhibition, there is a risk of generating oxidative stress and promoting an unwanted inflammatory reaction. Therefore in the search for a treatment for skin tone correction, it was important to ensure that the balance

between antioxidant and prooxidant was kept, while avoiding potential adverse effects. The third activity of interest resides in the anti-inflammatory properties of the compounds. The researched activity could cause a decrease in the antioxidant capacity of the cells, leading to an accumulation of ROS. As mentioned by (Mohagheghpour et al., 2000; Page et al., 2011), ROS are responsible for the appearance of pro-inflammatory cytokine whose pathway is also promoted by the presence of leukotrienes (Doherty et al., 2013); *ergo* finding a compound that could inhibit tyrosinase activity and simultaneously interact with the leukotriene induced inflammatory pathways and prevent the loss of equilibrium in the oxidative state of the cell was established as a good way to limit the risk of any adverse effects of the treatment.

Following the analysis for the previously mentioned activities, a list of 11 species showed promising *in vitro* activities. When comparing these species with the observed consensus from the primary part of this work, we can conclude that going through the valorization of traditional knowledge to target species of interest is still a good way of working. Among the species collected following the ethnobotanical study, an undeniable link could be made between the sample with the most promising results and the statistical analysis used to target the species worth studying. The following species stood out in both cases: *Persea americana* Mill., *Zingiber zerumbet* (L.) Roscoe ex Sm., *Litchi chinensis* Sonn., and *Syzygium aromaticum* (L.) Merr. &L.M. Perry, reinforcing the principle established by (Trotter & Logan, 1986)

Out of the 21 tested species, 11 showed significant activities. Out of those 11 species, 7 were known from previous ethnobotanical works as having potential activities linked to the three activities studied in this work. The 4 remaining issued from the ethnobotanical study realized in carrying out this work. Starting with a total of 69 species identified during the ethnobotanical study, to which were added the species identified in previous ethnobotanical work done in the surrounding island, 7% showed some significant activities.

4. Phytochemical study

From the several selection steps that occurred previously, one last reducing step was applied. The idea behind this process was to target a sample that would give us a high chances of isolating a compound. The sample also had to be original, in a sense that it had not been the subject of previous phytochemicals studies. The last criteria was linked to the accuracy and feasibility of the analysis. Out of the 11 species that showed significant activities, several samples had multiple activities of interest: *Acalypha hispida* dried and fresh leaves as well as *Acalypha wilkesiana* dried leaves had a good DPPH reducing activity and significant lipoxygenase inhibitory properties, *Acalypha wilkesiana* fresh leaves had a good DPPH reducing activity and significant tyrosinase inhibitory properties, *Cananga odorata* dried leaves and *Lantana camara* dried leaves showed some DPPH reduction activity as well as some significant lipoxygenase inhibitory properties, *Leea guineensis* dried fruits had a good DPPH reducing activity as well as a significant tyrosinase inhibitory activity, *Erythroxylum corymbosum* dried leaves had a good DPPH reducing activity and a significant lipoxygenase inhibitory activity. The dried leaves of *Litchi chinensis* were the only sample to show some significant DPPH reducing activity, some significant tyrosinase inhibitory activity and a

little lipoxygenase inhibitory activity. *Litchi chinensis* dried root was interesting as it had never been studied and presented some significant DPPH reducing activity and some significant tyrosinase inhibitory properties and *Syzigium aromaticum* dried leaves showed some good DPPH reducing properties and some significant tyrosinase inhibitory activity. When looking at the literature, most active species had been subject to phytochemical analysis explaining the observed activities. The only sample not studied were the root of *Litchi chinensis.*

The root of *Litchi chinensis* was selected to undergo the phytochemical analysis; this sample, in addition to presenting significant activities towards tyrosinase and as antioxidant, had never been studied. Other organs of this plant had been studied as the fruit has been consumed for hundreds of years. In the work of (Ibrahim & Mohamed, 2015), more than 10 different references give to the Litchi fruit the following properties: rich sources of flavonoids, tannins, anthocyanins, phenolic acids, triterpenes, and sterols and they also contain 15.7% polyphenol monomer ((+)-catechin and (-)-epicatechin and 13.3% polyphenol dimer (procyanidin B2).They are the main ingredient of oligonol, a flavanol-rich litchi extract processed to convert high-molecular weight proanthocyanidins into low molecular weight proanthocyanidins to improve bioavailability. In addition, the fruits and seeds possess a number of bioactivities including hypoglycemic, anticancer, antibacterial, anti-hyperlipidemic, antiplatelet, antiviral, protection against oxidative stress, prevention and treatment of hyperuricemia, reduction of fatigue and visceral fat. They have shown some inflammation reducing properties following exercise (Ibrahim & Mohamed, 2015).

Throughout the bio-guided fractionation, the biological activity of each newly generated fraction was monitored. The amounts resulting from the different fractionation did not allow for accurate weighing. Therefore, the observed activity was reported on the general amount of plant powder used for the initial extraction. If no significant differences could be seen between the different fractions, the fractions underwent dilution steps until differences could be observed. In this way, if processing did not give information on what fraction is more active from a same dose perspective, the differences observed could be explained either because the compounds in the targeted fraction were more potent or because the amount of compound was higher in one specific fraction. As the initial aim of this thesis was to target plants with biological activities to be used in the development of a simple formulation, as long as relative activity allowed for some differentiation between fractions, the significantly active fraction could move forward through the purification process. Regarding the evolution of DPPH relative activity through the different fractions, the most potent fraction showed a 25% loss of activity between the first and second fractionation but did not show any loss of activity between the second and third purification steps. Such phenomenon could be explained because some of the active compounds got lost during the purification steps. However, if this was the case, similar loss of activity should have been observed between the second and third purification step. Another hypothesis could be the presence of an additive effect linked to the more complex composition of the less purified fraction. When looking at the relative activities for the second and third fractionation, the isolated peak with the highest relative activity is surrounded by compounds showing activities that roughly match the observed loss of activity between the first and second fractionation steps. Such additive effects have been observed

when measuring antioxidant activity of catechins and epicatechins alone or mixed with α-tocopherol (Yin et al., 2012). When looking at the evolution of the anti-tyrosinase activities, there is very little loss of activity between the first and second fractionation. This observation leads towards the hypothesis that there was no loss of compound between the first and second fractionation and that the observed difference for the DPPH activity resides in an additive phenomenon. When looking at the differences of anti-tyrosinase activity between the second and third fractionation, however, there is a strong loss of activity. As no tested peak in the last fractionation showed any activity, the following hypothesis remains: in the case of additive activity, the compound responsible for most of the activity is not detectable by the means used for the purification and thus was lost during the purification process, leading to this important loss of activity. Another hypothesis resides in the presence of a synergistic activity between the selected compound and the other compound (detected or not). The suspicion of a synergistic effect is hard to confirm due to the different mechanisms linked to enzymatic inhibition. Even if synergistic effects have been observed with mixtures of polyphenol, it is more common to encounter an additive phenomenon (Yu et al., 2019). This being said, there was still some anti-tyrosinase activity.

In order to identify the compound of interest, first its UV purity (HPLC-DAD) had to established. Due to the known limitations of this technique, the final compound also underwent IR, NMR and MS analysis. Together these techniques gave us more assurance of the actual purity of the compound. Through the IR spectra some non-attributed bands could be seen if the compound wasn't sufficiently pure except in the case of "similar" compound contamination. As for the MS spectra, if the compound were not pure, unattributable ions would have been observed, and this was not the case. The NMR analysis also gives a good idea of the presence of potential impurities except if they lack hydrogen atoms or carbon atoms, as is the case for salts. By cross-referencing the results originating from these techniques with the literature we could establish that the compound was sufficiently pure. Through this process we could confirm the statement that the isolated compound was responsible for the observed activities and we also could establish its nature. It was identified as proanthocyanidin (2R,3R,4S,8R,14R,15R)-2,8-Bis(3,4-dihydroxyphenyl)-10-[(2R,3R,4R)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-3,5,7-trihydroxy-2H-1-benzopyran-4-yl]-4-[(2R,3S)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-3,5,7-trihydroxy-2H-1-benzopyran-8-yl]-3,4-dihydro-8,14-methano-2H,14H-1-benzopyrano[7,8-d][1,3]benzodioxocin-3,5,11,13,15-pentol also known as cinnamtannin D2 (CAS registry number 97233-47-1). This molecule was previously described in peanut skin (*Arachis hypogaea* L.) (Tatsuno et al., 2012) Considered from a wider perspective, angle, proanthocyanidins are part of the flavonoid class. These compounds, being secondary metabolites, are widely distributed throughout the plant kingdom (S Kumar et al., 2012; Park et al., 2011). Due to the numerous available hydroxyl substitutions, they tend to be very reactive with prooxidant compounds such as peroxides, superoxides , hydroxyl radicals, singlet oxygen, and alpha-oxygen (Cao et al., 1997). The USDA has identified 68 different species containing proanthocyanidins: some of the most known species being cinnamon (*Cinnamomum sp.*) (Mateos-Martín et al., 2012), aronia fruit (*Aronia sp.*), cocoa beans (*Theobroma cacao*), and grapes (*Vitis sp.*) (Souquet et al., 1996). In

addition to their capacity to react with ROS, these compounds have shown efficacity as tyrosinase inhibitors.

As mentioned by (Chai et al., 2015), proanthocyanidins found in avocado (*Persea americana*) fruits were potent, reversible, and competitive-type anti tyrosinase agents. This activity is suspected to be caused by the fact that bioactivity capacity of plant proanthocyanidins depends upon their structure, especially their degree of polymerization (Lee et al., 2007; Zhou et al., 2011); in their work, crude extracts containing up to 36 mer proanthocyanidins were tested. As they did not separate the extract into different polymer sizes, one cannot directly link this information to the observed efficacity of the isolated tetramer from this work. However, within all the polymers present in that specific work, the presence of tetramerous compound is probable and thus is in accordance with the observed anti-tyrosinase activity observed in this work.

In another study aiming to establish the anti-tyrosinase potency of wood samples it was shown that in addition to the phenolic hydroxylation pattern, the tyrosinase inhibition capacity also depends on the presence of 5,7-dihydroxyphenyl structure in the A-ring and a 3,4-dihydroxyphenyl structure in the B-ring (Takagi & Mitsunaga, 2003). This work is in accordance with our finding as our compound originates from the roots of *L. chinensis* and cinnamtannin D2 contains the same a-ring and b-ring structure.

Yet another study aimed to identify the potential anti-tyrosinase activity of extracts of cherimoya pericarps. Proanthocyanidins were extracted and purified and showed promising activities as tyrosinase inhibitors. The inhibition process was suspected to be competitive as the proanthocyanidins' structure was similar to tyrosinase's substrate (Chai et al., 2017).

Some work was also done on the proanthocyanidins found in kiwi fruits (*Actinidia chinensis)*, it was also established that these compounds were active as tyrosinase inhibitors. The inhibition was suspected to be mixed and competitive and it was also established that these proanthocyanidins could effectively scavenge DPPH confirming the observed antioxidant activity of the isolated cinnamtannin D2 (Chai et al., 2014).

In this work the isolated compound is not destined to be used in its purified form. As mentioned previously the aim of this work is to investigate and to work towards finding simple formulations using available plant material on the island of Mayotte. However, as this compound has been identified as being among the compounds responsible for the observed activities, it should be tested from a toxicological point of view to ensure it does not present any adverse effects. When looking at the literature, no toxicological studies have been conducted on this specific compound. In general plant phenolic compounds have been understudied when it comes to toxicity evaluations (Galati & O'Brien, 2004). When looking at the potential toxicity of remedies issuing from traditional medicine, they have the advantage of the empiric testing dating from their original uses. In addition, this plant extract is meant to be used with little or no transformation apart from shredding, leading to a very complex compound mixture that needs to be evaluated as is. Finally, one can never be sure of the total innocuity of a specific treatment as all humans are different and some people might develop specific conditions such as allergies and intolerances.

In the end, proanthocyanidins have proven to be effective as tyrosinase inhibitors; the inhibition type seems to be competitive as the tyrosinase's substrate has a similar structure. However for cinnamtannin D2 it still needs to be confirmed. In addition, proanthocyanidins are strongly related to the management of ROS and the maintenance of the oxidative balance throughout the body. It's clear that there is some real potential in researching these compounds when working on the development of medicines and cosmetics.

7

GENERAL CONCLUSION & PERSPECTIVES

This work has allowed us to have insight into traditional uses of plants for medicine and cosmetics in some Islands of the western part of the Indian Ocean, mainly in the Comoros archipelago and Mayotte. Through the realization of several infield missions, we were able to observe how fragile this ancestral knowledge still is and how valuable it is for the locals. By doing this work, we were hoping to valorize it locally as well as for a broader audience. The infield work realized on Mayotte allowed us to identify and collect species used traditionally. During this process, part of the collected material ended up in the collection of the CBNM (Concervatoire Botanique National du Mascarin) herbaria, thereby contributing to their local work. These first steps were crucial as we were trying to find plants of interest on an island rich with more than 1300 different species. From there, our different investigations reduced this number to 207, then to 69, to finally reach a number of collected species of 21, for a total of 89 different samples, comprising roots, flowers, leaves, bark, fruits and wood, depending on the seasonal availability.

The following steps of this work resided in finding the most potent sample with biological activities related to skin care treatment. The selected activities were anti-lipoxygenase, antioxidant and anti-tyrosinase. The aim when looking for such biological activities was to find species with good potential against skin inflammation and ageing as well as activities regarding pigmentation issues. The 89 samples were submitted to the activity analysis, then using Tukey's grouping method, and based on the observed results as well as the available information in the literature, *Litchi chinensis* was selected to undergo more in-depth analysis. The final step of this work was the identification of the isolated compound using NMR, MS, IR, UV and colorimetric tests. The identified compound is known as cinnamtannin D2; it is a tetramerous proanthocyanidin with a double bond between group 2 and 3.

From this point forwards, only questions remain.

To confirm our findings, and to gain some knowledge on the observed activities, the extracted compound should be tested against standards. The compound isolated in this work is not available commercially, however other proanthocyanidin are available and could be used for some research on structure linked activities.

When generating a higher amount of Cinnamtanin D2 by scaling up the extraction process, one could also work on the evaluation of exact dose dependent activities, and establish the toxicity linked to this specific compound.

Prior to using the findings of this work for the observed properties, several tasks must be undertaken. A toxicological assessment needs to be implemented. Such analyses are strongly influenced by the means in which the substance is used. Whether the final product is based on the purified molecule or on crude *L. chinensis'* root extract will strongly influence the toxicological evaluation. Once the harmlessness of the crude extract and its different levels of purification have been proven, the following step resides in investigating the effective *In vivo* activity of the compound. As this compound is destined to be used topically, bioavailability and real effectiveness should be evaluated accordingly. The traditional way to evaluate such activities lies in the use of animal testing. As such practices are more and more decried, a lead could reside in the use of "artificial skin".

If some *in vivo* effectiveness is observed, then work must be undertaken towards finding the ideal formulation. Considering the island of Mayotte's resources and infrastructure, valorizing such a product should require the simplest of formulations. By keeping this potentially new industry as simple as possible, it would be accessible to most of the population in the island. The search for the ideal formulation should also include active compound bioavailability, skin penetration optimization aspects and shelf life aspects. The texture and the scent of the final product should be enjoyable and avoid compounds with potential allergenic properties. In this formulation process, one can imagine using more than one species of interest in the final mixture. In this work other plants have proven to be effective but were not studied to ascertain that no adverse effect would come from them; why not broaden the composition of the final product with other locally available species.

In the case of the emergence of a new industry, other aspects need to be considered. As the compound of interest resides in the roots of the litchi tree, how harvesting them be carried out while keeping the trees healthy? Should new agricultural methods be developed to harvest the fruits as well as the roots? How can this be implemented in Mayotte?

As observed for the different industries that were developed in Mayotte over the years; when a crop gives rise to an industry, the population will plant the crops regardless of the ecological impact. Therefore, while exploring the possibilities towards developing an industry around the roots of litchi, the sustainability of such an industry needs to be considered. The first reason is obviously linked to the environment, the second reason is more linked to history. At first Mayotte produced sugar cane but this industry did not last. Then Mayotte produced ylang-ylang, and this industry also collapsed after several years.

In conclusion, if any industry is initiated following this work, it is crucial that the persons responsible for our findings are recognized. By this I mean, the keepers of knowledge and all the informants who freely agreed to share what they knew, so that we could bring this work to completion.

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9

SUPPLEMENTAL DATA

1. Publication list

1 – Articles as first author

Saive, M., Frederich, M. and Fauconnier, M.-L. (2020) 'Plants used in traditional medicine in the Comoros archipelago: a review', Biotechnologie, Agronomie, Société et Environnement. Presses Agronomiques de Gembloux, 24(2), pp. 117–141.

Saive, M., Frederich, M. and Fauconnier, M.-L. (2018) 'Plants used in traditional medicine and cosmetics in Mayotte Island (France): An ethnobotanical study', Indian Journal of Traditional Knowledge, 17(4).

Saive, M. *et al.* (2020) 'Identification of a Proanthocyanidin from Litchi Chinensis Sonn. Root with Anti-Tyrosinase and Antioxidant Activity', *Biomolecules*. Multidisciplinary Digital Publishing Institute, 10(9), p. 1347.

Saive, M. et al. (2020) 'Study of the cosmetic potential uses of plants from Mayotte as skin care agents through the screening of their biological activities', Cosmetics. (Submitted)

2 – Articles as co-author

Souhir, K. et al. (2020) 'Influence of climate variation on phenolic composition and antioxidant capacity of Medicago minima populations', Scientific Reports (Nature Publisher Group). Nature Publishing Group, 10(1).

Guo, X. et al. (2020) 'Aptamer-based biosensor for detection of mycotoxins', Frontiers in Chemistry. Frontiers Media SA, 8.

Serteyn, L. et al. (2020) 'Changes of feeding behavior and salivary proteome of Brown Marmorated Stink Bug when exposed to insect-induced plant defenses', Arthropod-Plant Interactions. Springer, 14(1), pp. 101–112.

Nea, F. *et al.* (2019) 'A new chemotype of Lantana rhodiensis Moldenke oil from Côte d'Ivoire: chemical composition and biological activities', *Industrial Crops and Products*. Elsevier.

Tanoh, E. A. *et al.* (2019) 'Antioxidant and lipoxygenase inhibitory activities of essential oils from endemic plants of Côte d'Ivoire: Zanthoxylum mezoneurispinosum Ake Assi and Zanthoxylum psammophilum Ake Assi', *Molecules*. Multidisciplinary Digital Publishing Institute, 24(13), p. 2445.

3 – Poster

Changes of feeding behavior and salivary proteome of Brown Marmorated Stink Bug when exposed to insect-induced plant defenses. Serteyn, Laurent; Ponnet, Lola; Saive, Matthew et al. Poster (2020, January 31)

New essential oils with interesting biological activities from endemic plants of Côte d'Ivoire: Zanthoxylum mezoneurispinosum and Zanthoxylum psammophilum. Tanoh, Amenan Evelyne; Nea, Fatimata; Kenne Kemene, Tierry et al. Poster (2019, February 04)

Interaction between Halyomorpha halys Stål and its host plant: induced defense and feeding behavior. Serteyn, Laurent; Ponnet, Lola; Saive, Matthew et al. Poster (2018, July)

Screening of mahoran plants for cosmetic applications. Saive, Matthew; Frederich, Michel; Fauconnier, Marie-Laure. Poster (2016, June 01)

Phytochemical Study of Plants of Interest for Cosmetics in Mayotte. Saive, Matthew; Fauconnier, Marie-Laure; Danflous, Jean-Paul. Poster (2014, December 16)

Identification of Pentalonia nigronervosa‘s bacterial endosymbionts and study of their implication on the Banana Bunchy Top Virus transmission efficiency. De Clerck, Caroline; Saive, Matthew; Francis, Frédéric et al. Poster (2012, May 22)

4 – Oral communication

Criblage de plantes Mahoraise pour des usages cosmétiques. Saive, Matthew; Fauconnier, Marie-Laure. Communication orale (2016, June 24)

Etude phytochimique de plantes d'intérêt cosmétique à Mayotte. Saive, Matthew. Allocution et communication diverse (2014)

2. Appendix from Chapter 2

Appendix 1:This Table listes all the mentioned issues recorded during the bibliographical review (in bold) and classes it into a category of issue (normal format). For instance, Dermatomycosis has been classified in skin issue.

abdominal syndrom	**brucellosis**	**eye disease (1/2)**	**lice**	dermatitis
abdominal pain	brucellosis	eye disease	lice	dermatomycosis
colic	**burns**	eye diseases	**liver disease**	**skin issue(2/2)**
epigastric	burns	eye infections	liverdisease	dermatosis
epigastric pain	**cardiac pain**	eye irritation	**lupus**	eczema
stomach ache	cardiac pain	glaucoma	lupus	erysipelas
stomach aches	chest pain	trachoma	**malaria**	herpes
stomach cramps	**cervicalgia**	**fertility**	malaria	impetigo
stomach disease	cervicalgia	female fertility	**malformation**	irritation
stomach disorders	**cholera**	infertility	malformation	irritations due to continuous rubbing
stomach pain	cholera	prevent miscarriage	spinal curvature	itch
stomach ulcer	**choleretic**	prevents smiscarriage	**mouth disease (1/2)**	nettle-rash
stomachpain	choleretic	sterility	aphthous stomatitis	pimple
upset stomach	**contusion**	women sterility	children’s oral mycoses	psoriasis
abortive	bruising	**fever**	dental pain	purpura
abortive	contusion	child fever	gingivitis	redness
abscess	**cosmetic**	febrifuge	oral inflammation	ruff
abscess	beauty mask	fever	**mumps**	scars
acne	cosmetic	inflammatory fever	mumps	skin

acne

allergy

allergy

anaemia

anaemia

asthenia

chronic fatigue

fatigue

fatigue during pregnancy

analgesic

ache

analgesic

antalgic

diffuse pain

local analgesic

localized pain

localized pain.

pain

pain in the lower body

pain of the limbs inside the bone

antifungal

antifungal

cosmetics

cough

cough

cramp

cramp

cyst

cyst

depurative

depurative

diuretic

dysuria

purgative

diabetes

diabetes

evolved diabetes

diarrhoea

bloody diarrhoea

diarrhoea

dysentery

dismenorrhoea

dismenorrhoea

dysmenorrhea

typhoid fever

fracture

fractures

furuncles

anthrax

boils

furuncle

furuncles

gastro intestinal syn-drom

colitis

colitis

constipation

digestive

flatulence

gastralgia

gastric pains

gastric ulcer

gastritis

heartburn

heartburn

hiccup

indigestion

myalgia

muscle pain

muscular inflammation

muscular pain

myalgia

nausea

antiemetic

vomiting

nervous disorder

nervous disorder

neuralgia

night incontinence

night incontinence

nightmares

nightmares

nose bleed

epistaxis

nose bleed

oedema

oedema

pelada

pelada

skin disease

skin diseases

skin infection

skin infections

skin lesion

skin smoothing

varicose ulcer

warts

throat disease

angina

bronchitis

infected throat

pharyngitis

phlegm

sore throat

throat illness

tonic

fortifying

fortifying gum

stimulant

tonic

tooth ache

fungal infections
mycoses

anti-inflammatory

emollient for sprains
inflammation
nodes
painful swelling
soreness
sores
sprain
sprain joint
swelling
swollen feet
swollen spleen

antimicrobial

antimicrobial
colibacillus

antiseptic

antiseptic
disinfectant
infected wound
panaris

dysmenorrhoea
heavy periods
hypermenorrhoea
leucorrhoea
menstrual disorder
painful menstruation
painful periods
premenstrual tension

dystocia

dystocia
help expel the placenta after childbirth
oxytocic
parturition
post partum pain
postpartum treatment
pregnancy disorder

ear issue

ear aches
ear pain
ear washings
painful ear
suppurative otitis

influenza
intestinal illness
laxative
loss of appetite
nausea

haemorrhoids

haemorrhoids

head ache

cephalalgia
child severe head ache
facial neuralgia
headache
migraine

impotence

erectile dysfunction
impotence
impotency
sexual asthenia
sexual incapacity

insect bite

caterpillar sting
insectbites

poisoning

poisoning
poisons

psychomotor issue

psychomotor development delay
psychomotor disability

pulomnary issue

emphysema

relaxing agent

anxiety
convulsion
epilepsy
epilepsy
heart pounding
hyperactivity
hyperactivity in children
hypertension
hypotensive
insomnia
relaxing agent
sedative
stress

odontalgia
toot hache
tooth decay
tooth diseases
toothache

tuberculosis

tuberculosis

ulcers

ulcers

urogenital infection

bladder problem
cystitis
gonorrhoea
gynaecological diseases
hydrocele
orchitis
pelvic pain
syphilis
urethral flow
urinary disorder
urinary infection
urinary inflammation

paronychia
whitlow

aphrodisiac

aphrodisiac

arthritis

arthritis
articular pain
articular pain in the lower part of thebody
joint pain
joint pain linked to childbirth

asthma

asthma

astringent

astringent

back ache

backache
backpain
low back pain
lumbago
sciatic
sciatica
sciatica.

external parasitism

maggot
mange
scabies
tineacapitis

bad luck

bad luck

bleeding

bleeding
bleeding umbilical wound
cicatrizing
cut
cuts
fresh cut
haemorrhages
haemostatic
healing wounds
injury
vulnerary
wounds

eye disease (1/2)

blepharitis

sting of centipede

internal parasitism

amoebiasis
amoebic disease
anthelminthic
ascaris
cococsidiosis
cysticercose
deworming
foot fleas
giardiase
internal parasitism
intestinal parasites
intestinal parasitism
intestinal worm
tenia
worms

jaundice

jaundice

kidney issue

kidney pain
kidney stones

tensions
work overload

respiratory disease

nasal congestion
respiratory disease
rhinitis
rhinorrhoea
shortness of breath
sinusitis
whooping cough

rheumatism

rheumatism

sadness

sadness

scurvy

scurvy

sudorific

sudorific

skin issue(1/2)

blisters
chap
child’s eczema

urogenital infection
uterus disease
vaginal infection
vaginal prolapsed
vulvar pruritus

uterine prolapses

uterine prolapses

vertigo

benign positional vertigo
dizziness
faint
giddiness
syncope
vertigo
vitiligo

water retention

water retention

weaning

weaning

body aches	blindness	renal inflammation	childhood eczema
body aches	cataract	**laxative**	dermal reaction linked to allergies
breast-feeding issue	conjunctivitis	chronic constipation	dermalreaction
better lactation	eye		

3. Appendix from Chapter 3

Appendix 2: Semi-structured report card used during the infield interviews

DATE :

Fiche d'enquête

Informateur :
Langue :
Commune :
Village :
Profession :
Revenu moyen :

Sexe :
Age
Etat civil :
Religion :
Niveau d'éducation :

N°	Nom vernaculaire	Partie utilisée	Rôle ciblé	Région Géographique	Posologie
1					
2					
3					
4					
5					
6					
7					
8					
9					

Appendix 3: Herbaria specimens

N° PART	TAXON ORIGINEL	FAMILLE ORIGINELLE	TAXON	FAMILLE	NOM VERNACULAIRE
MAO0 0041	*Tamarindus indica* L.	Fabaceae	*Tamarindus indica* L.	Fabaceae	Waju oua malavuni (Sm), Madiro kakazo (Sb), Waju urehaginy
MAO0 0042	*Lawsonia inermis* L.	Lythraceae	*Lawsonia inermis* L.	Lythraceae	Hina hina ndziche, Hina ndrume (Sm), Mwina vavi (Sb)
MAO0 0043	*Pandanus mayotteensis* H. St.John	Pandanaceae	*Pandanus mayotteensis* H. St.John	Pandanaceae	Sari mlula, Sari mlua masera (Sm), Sari droa (Sb)
MAO0 0044	*Kalanchoe pinnata* (Lam.) Pers.	Crassulaceae	*Kalanchoe pinnata* (Lam.) Pers.	Crassulaceae	Meawani (Sm), Sodifafa (Sb)
MAO0 0045	*Erythroxylum lanceum* Bojer	Erythroxylaceae	*Erythroxylum lanceum* Bojer	Erythroxylaceae	Loangati mena vavi (Sb)
MAO0 0046	*Adansonia digitata* L.	Malvaceae	*Adansonia digitata* L.	Malvaceae	Mbuiu (Sm), Boio (Sb)
MAO0 0047	*Leea guineensis* G.Don	Vitaceae	*Leea guineensis* G.Don	Vitaceae	Fu la radi (Sm), Sadrakidraki lahi (Sb)
MAO0 0048	*Acalypha hispida* Burm.f.	Euphorbiaceae	*Acalypha hispida* Burm.f.	Euphorbiaceae	Moukiana mkomba (Sb)
MAO0 0049	*Acalypha wilkesiana* Müll.Arg.	Euphorbiaceae	*Acalypha wilkesiana* Müll.Arg.	Euphorbiaceae	Mshiha wa kima
MAO0 0050	*Persea americana* Mill.	Lauraceae	*Persea americana* Mill.	Lauraceae	M'zavoca (Sm), Zavoca(Sb)
MAO0 0051	*Litchi chinensis* Sonn.	Sapindaceae	*Litchi chinensis* Sonn.	Sapindaceae	
MAO0 0052	*Litsea glutinosa* (Lour.) C.B.Rob.	Lauraceae	*Litsea glutinosa* (Lour.) C.B.Rob.	Lauraceae	Mzavocamaro (Sm), Zavocamaro (Sb)
MAO0 0053	*Syzygium aromaticum* (L.) Merr. & L.M.Perry	Myrtaceae	*Syzygium aromaticum* (L.) Merr. & L.M.Perry	Myrtaceae	Karafou (Sm et Sb)

MAO0 0054	*Cananga odorata* (Lam.) Hook.f. & Thomson	Annonaceae	*Cananga odorata* (Lam.) Hook.f. & Thomson	Anno-naceae	Ilang Ilang (Sm), langilangi (Sb)
MAO0 0055	*Aloe mayottensis* A. Berger	Asphodelaceae	*Aloe mayottensis* A. Berger	Asphode-laceae	Chizia mlili (Sm), Sakoankankini (Sb)
MAO0 0056	*Paullinia* L.	Sapindaceae	*Paullinia pinnata* L.	Sapinda-ceae	M'hotso m'hotso (Sm), Vahi mari ranha (Sb)
MAO0 0057	*Lantana camara* L.	Verbenaceae	*Lantana camara* L.	Ver-benaceae	M'bwasera M'rimba, Davoum'ba (Sm), Fatsiki madani, Wavu n'kalaga (Sb)
MAO0 0136	*Myristica fragans*	Myristicaceae	*Myristica fragans* Houtt.	Myristi-caceae	Koukou manga (Sm, Sb), Muscadier

4. Appendix from Chapter 4

Appendix 4: List of collected sample.

Species	Organ	Species	Organ
Acalypha hispida	Dried wood	*Litsea glutinosa*	Dried wood
	Fresh leaves		Dried bark
	Dried leaves		Fresh leaves
	Fresh flowers		Dried leaves
	Dried flowers		Dried roots
Acalypha wilkesiana	Dried wood	*Myristica fragrans*	Dried seeds
	Fresh leaves	*Pandanus mayottensis*	Dried wood
	Dried leaves		Fresh leaves
	Dried roots		Dried leaves
Adansonia digitata	Dried wood		Fresh fruits
	Dried seeds		Dried fruits
Aloes Mayottensis	Fresh leaves		Dried roots
	Dried leaves	*Paullinia pinnata*	Fresh leaves
	Dried roots		Dried leaves
Cananga odorata	Dried wood		Dried liana
	Dried leaves		Dried aerial root
	Fresh flowers		Dried roots
	Dried flowers	*Persea americana*	Dried wood
	Dried roots		Fresh leaves
Erythroxylum corymbosum	Dried wood		Dried leaves
	Fresh leaves		Fresh pit
	Dried leaves		Dried pit
	Dried roots		Dried roots
Erythroxylum lanceum	Dried wood	*Sesamum indicum*	Dried seeds
	Fresh leaves	*Syzygium aromaticum*	Dried wood
	Dried leaves		Fresh leaves
	Dried roots		Dried leaves
Kalanchoe pinnata	Fresh leaves		Dried roots
	Dried leaves	*Tamarindus indica*	Dried wood
	Dried roots		Fresh leaves
Lantana camara	Dried wood		Dried leaves
	Fresh leaves		Dried roots

	Dried leaves	*Zingiber zerumbet*	Floral water
	Dried fruits		Fresh leaves
	Dried roots		Dried leaves
Lawsonia inermis	Dried wood		Fresh flowers
	Fresh leaves		Dried flowers
	Dried leaves		Floral stem
	Dried roots		Fresh rhizomes
Leea guineensis	Dried wood		Dried rhizomes
	Fresh leaves		Dried stem
	Dried leaves		
	Dried fruits		
	Dried roots		
Litchi chinensis	Dried wood		
	Fresh leaves		
	Dried leaves		
	Dried roots		

Table S 1: Lipoxygenase inhibition activity results for the plant extracts at the first dilutions (N = number of replicates). Results were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%																
Sample	N	Average	Grouping													
Acalypha hispida Dried flower	3	99,05	A													
Erythroxylum corymbosum Dried leaf	3	98,83	A													
Acalypha wilkesiana Dried leaf	3	96,70	A	B												
Zingiber zerumbet Dried leaf	3	92,36	A	B	C											
Cananga odorata Fresh flower	3	90,64	A	B	C	D										
Zingiber zerumbet Dried flower	3	88,92		B	C	D										
Zingiber zerumbet Stem	3	88,66		B	C	D	E									
Lantana camara Dried leaf	3	85,19			C	D	E	F								
Cananga odorata Dried leaf	3	82,82				D	E	F	G							
Leea guineensis Dried root	3	79,94					E	F	G	H						
Acalypha hispida Dried leaf	3	78,51						F	G	H	I					
Erythroxylum lanceum Dried leaf	3	74,49							G	H	I					
Litchi chinensis Dried wood	3	72,50								H	I					
Zingiber zerumbet Fresh rhizom	3	70,85									I	J				
Cananga odorata Dried root	3	62,69										J	K			
Zingiber zerumbet Fresh leaf	3	60,23											K	L		
Lawsonia inermis Dried root	3	58,54											K	L		
Persea americana Dried pit	3	51,57												L	M	
Zingiber zerumbet Flower stem	3	45,04													M	N
Litsea glutinosa Dried root	3	42,55														N

Paullinia pinnata Dried root	3	37,88		N	O		
Zingiber zerumbet Fresh flower	3	33,70			O	P	
Acalypha hispida Dried root	3	33,62			O	P	
Erythroxylum corymbosum Fresh leaf	3	31,22			O	P	
Acalypha wilkesiana Dried root	3	30,30			O	P	
Paullinia pinnata Dried liana	3	27,87				P	
Tamarindus indica Dried root	3	9,21					Q

Table S 2: Lipoxygenase inhibition activity results for the plant extracts at the first dilutions (N = number of replicates). Results were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%

Sample	N	Average	Grouping				
Zingiber zerumbet Dried leaf	3	68,73	A				
Zingiber zerumbet Dried flower	3	62,84	A				
Zingiber zerumbet Stem	3	55,90		B			
Myristica fragrance Dried seed	3	38,19			C		
Zingiber zerumbet Fresh rhizom	3	32,03			C	D	
Acalypha hispida Dried flower	3	31,15				D	
Acalypha hispida Dried leaf	3	26,54				D	
Litchi chinensis Dried leaf	3	16,18					E
Persea americana Dried pit	3	13,92					E

Table S 3: Lipoxygenase inhibition activity results for the plant extracts at the third dilutions (N = number of replicates). Results were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%

Sample	N	Average	Grouping		
Zingiber zerumbet Fresh rhizom	3	55,73	A		
Acalypha hispida Dried leaf	3	26,13		B	
Zingiber zerumbet Dried flower	3	21,81		B	

Table S 4: Antioxidant activity results (DPPH assay) for the plant extracts at the first dilutions (N = number of replicates). Results were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%

Sample	N	Average	Grouping										
Erythroxylum corymbosum Dried leaf	3	99,97	A										
Acalypha hispida Fresh flower	3	99,96	A	B									
Erythroxylum lanceum Dried root	3	99,94	A	B									
Lantana camara Fresh leaf	3	99,91	A	B									
Erythroxylum corymbosum Dried wood	3	99,89	A	B									
Erythroxylum corymbosum Fresh leaf	3	99,68	A	B	C								
Acalypha hispida Fresh leaf	3	99,21	A	B	C	D							
Erythroxylum lanceum Dried leaf	3	99,04	A	B	C	D	E						
Acalypha wilkesiana Dried root	3	97,83	A	B	C	D	E	F					
Erythroxylum lanceum Dried wood	3	97,36	A	B	C	D	E	F	G				
Myristica fragrans Dried seed	3	97,02	A	B	C	D	E	F	G	H			
Acalypha wilkesiana Fresh leaf	3	96,49	A	B	C	D	E	F	G	H	I		
Cananga odorata Dried root	3	96,35	A	B	C	D	E	F	G	H	I		
Paullinia pinnata Dried leaf	3	96,29	A	B	C	D	E	F	G	H	I		
Cananga odorata Dried flower	3	96,10	A	B	C	D	E	F	G	H	I	J	
Adansonia digitata Dried wood	3	95,55	A	B	C	D	E	F	G	H	I	J	K

Leea guineensis Dried root	3	94,86	A	B	C	D	E	F	G	H	I	J	K	L	
Syzygium aromaticum Fresh leaf	3	94,86	A	B	C	D	E	F	G	H	I	J	K	L	
Leea guineensis Dried fruit	3	94,51	A	B	C	D	E	F	G	H	I	J	K	L	
Persea americana Dried root	3	94,50	A	B	C	D	E	F	G	H	I	J	K	L	
Paullinia pinnata Dried liana	3	94,50	A	B	C	D	E	F	G	H	I	J	K	L	
Litchi chinensis Dried root	3	94,28	A	B	C	D	E	F	G	H	I	J	K	L	
Acalypha hispida Dried wood	3	94,28	A	B	C	D	E	F	G	H	I	J	K	L	
Leea guineensis Fresh leaf	3	94,25	A	B	C	D	E	F	G	H	I	J	K	L	
Kalanchoe pinnata Fresh leaf	3	94,21	A	B	C	D	E	F	G	H	I	J	K	L	
Litchi chinensis Dried wood	3	94,00	A	B	C	D	E	F	G	H	I	J	K	L	
Persea americana Dried pit	3	93,68		B	C	D	E	F	G	H	I	J	K	L	
Paullinia pinnata Dried aerial root	3	93,50			C	D	E	F	G	H	I	J	K	L	
Lawsonia inermis Fresh leaf	3	93,33				D	E	F	G	H	I	J	K	L	
Lawsonia inermis Dried leaf	3	93,27				D	E	F	G	H	I	J	K	L	
Pandanus mayottensis Dried fruit	3	93,14				D	E	F	G	H	I	J	K	L	
Syzygium aromaticum Dried wood	3	93,05				D	E	F	G	H	I	J	K	L	
Paullinia pinnata Dried root	3	92,91					E	F	G	H	I	J	K	L	M
Litchi chinensis Dried leaf	3	92,64						F	G	H	I	J	K	L	M
Lantana camara Dried leaf	3	92,40						F	G	H	I	J	K	L	M
Leea guineensis Dried leaf	3	92,31						F	G	H	I	J	K	L	M
Litchi chinensis Fresh leaf	3	92,19						F	G	H	I	J	K	L	M
Leea guineensis Dried wood	3	92,18						F	G	H	I	J	K	L	M

Persea americana Fresh pit	3	91,99		F	G	H	I	J	K	L	M	N							
Paullinia pinnata Fresh leaf	3	91,90		F	G	H	I	J	K	L	M	N							
Persea americana Fresh leaf	3	91,87		F	G	H	I	J	K	L	M	N							
Litsea glutinosa Dried bark	3	91,31			G	H	I	J	K	L	M	N							
Pandanus mayottensis Fresh fruit	3	91,05				H	I	J	K	L	M	N							
Acalypha wilkesiana Dried leaf	3	90,98				H	I	J	K	L	M	N							
Persea americana Dried leaf	3	90,95				H	I	J	K	L	M	N							
Cananga odorata Dried leaf	3	90,87				H	I	J	K	L	M	N							
Lawsonia inermis Dried root	3	90,31					I	J	K	L	M	N							
Lawsonia inermis Dried wood	3	90,30					I	J	K	L	M	N							
Acalypha hispida Dried flower	3	89,82						J	K	L	M	N							
Cananga odorata Fresh flower	3	89,78							K	L	M	N							
Zingiber zerumbet Fresh flower	3	89,61							K	L	M	N							
Persea americana Dried wood	3	88,91								L	M	N	O						
Litsea glutinosa Fresh leaf	3	86,66									M	N	O	P					
Tamarindus indica Dried leaf	3	85,80										N	O	P	Q				
Kalanchoe pinnata Dried leaf	2	82,38											O	P	Q	R			
Tamarindus indica Fresh leaf	3	80,39												P	Q	R			
Acalypha hispida Dried leaf	3	80,13													Q	R			
Litsea glutinosa Dried leaf	3	78,64														R			
Pandanus mayottensis Dried root	3	64,81															S		
Litsea glutinosa Dried wood	3	62,24															S		

Litsea glutinosa Dried root	3	60,13	S							
Zingiber zerumbet Dried leaf	3	59,18	S	T						
Tamarindus indica Dried wood	3	58,58	S	T						
Aloes mayottensis Dried root	3	53,21		T	U					
Lantana camara Dried fruit	3	51,92			U					
Erythroxylum lanceum Fresh leaf	3	50,25			U					
Zingiber zerumbet Dried flower	3	49,18			U					
Pandanus mayottensis Dried leaf	3	47,57			U					
Aloes Mayottensis Dried leaf	3	31,24				V				
Zingiber zerumbet Fresh rhizom	3	26,45				V	W			
Pandanus mayottensis Fresh leaf	3	21,87					W	X		
Zingiber zerumbet Fresh leaf	3	21,67					W	X		
Kalanchoe pinnata Dried root	3	18,23						X	Y	
Cananga odorata Dried wood	3	16,65						X	Y	
Lantana camara Dried root	3	16,39						X	Y	
Acalypha wilkesiana Dried wood	3	15,35							Y	
Lantana camara Dried wood	3	12,50							Y	

Table S 5: Antioxidant activity results (DPPH assay) for the plant extracts at the second dilutions (N = number of replicates). Re-sults were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%										
Sample	N	Aver-age	Grouping							
Acalypha hispida Fresh leaf	3	98,76	A							
Erythroxylum corymbosum Fresh leaf	3	98,54	A	B						
Acalypha hispida Dried flower	3	96,86	A	B	C					
Erythroxylum corymbosum Dried leaf	3	95,77	A	B	C	D				
Acalypha wilkesiana Dried leaf	3	94,99	A	B	C	D	E			
Leea guineensis Dried fruit	3	94,62	A	B	C	D	E	F		
Leea guineensis Dried root	3	94,55	A	B	C	D	E	F		
Syzygium aromaticum Fresh leaf	3	94,36	A	B	C	D	E	F		
Leea guineensis Fresh leaf	3	93,92	A	B	C	D	E	F		
Lawsonia inermis Fresh leaf	3	93,91	A	B	C	D	E	F		
Acalypha wilkesiana Dried root	3	93,71	A	B	C	D	E	F		
Litchi chinensis Dried wood	3	93,47	A	B	C	D	E	F		
Persea americana Dried root	3	93,34	A	B	C	D	E	F		
Acalypha wilkesiana Fresh leaf	3	93,30	A	B	C	D	E	F		
Acalypha hispida Fresh flower	3	93,27	A	B	C	D	E	F		
Litchi chinensis Dried root	3	93,26	A	B	C	D	E	F		
Litchi chinensis Dried leaf	3	92,95	A	B	C	D	E	F	G	
Leea guineensis Dried leaf	3	92,76	A	B	C	D	E	F	G	

Persea americana Dried leaf	3	92,58	A	B	C	D	E	F	G									
Persea americana Fresh pit	3	92,32		B	C	D	E	F	G									
Lawsonia inermis Dried leaf	3	92,31		B	C	D	E	F	G									
Syzygium aromaticum Dried wood	3	91,79			C	D	E	F	G									
Lantana camara Dried leaf	3	89,71				D	E	F	G									
Paullinia pinnata Dried root	3	89,39				D	E	F	G									
Paullinia pinnata Dried leaf	3	89,20					E	F	G									
Persea americana Fresh leaf	3	89,12					E	F	G									
Acalypha hispida Dried leaf	3	88,36						F	G	H								
Lawsonia inermis Dried root	3	86,63							G	H	I							
Paullinia pinnata Dried aerial root	3	82,12								H	I							
Cananga odorata Dried leaf	3	81,67									I							
Paullinia pinnata Dried liana	3	73,33										J						
Persea americana Dried pit	3	65,31											K					
Litchi chinensis Fresh leaf	3	62,58											K					
Lantana camara Fresh leaf	3	55,48												L				
Erythroxylum lanceum Dried wood	3	52,26												L	M			
Adansonia digitata Dried wood	3	49,57												L	M			
Tamarindus indica Dried leaf	3	48,75													M			
Kalanchoe pinnata Fresh leaf	3	40,24														N		
Erythroxylum corymbosum Dried wood	3	38,45														N	O	
Erythroxylum lanceum Dried root	3	37,71														N	O	P
Persea americana Dried wood	3	36,16														N	O	P

Cananga odorata Fresh flower	3	35,01								N	O	P					
Myristica fragrans Dried seed	3	33,76									O	P					
Paullinia pinnata Fresh leaf	3	31,38										P	Q				
Leea guineensis Dried wood	3	26,62											Q	R			
Pandanus mayottensis Fresh fruit	3	23,15												R			
Kalanchoe pinnata Dried leaf	2	22,45												R			
Pandanus mayottensis Dried fruit	3	20,57												R	S		
Erythroxylum corymbosum Dried root	2	20,55												R	S	T	
Litsea glutinosa Fresh leaf	3	14,33													S	T	U
Pandanus mayottensis Dried root	3	13,67														T	U
Aloes Mayottensis Dried leaf	3	12,01															U
Erythroxylum lanceum Fresh leaf	3	9,69															U
Pandanus mayottensis Dried leaf	3	8,07															U
Zingiber zerumbet Dried flower	3	6,81															
Cananga odorata Dried wood	3	3,13															

Cananga odorata Fresh flower																	
Myristica fragrans Dried seed																	
Paullinia pinnata Fresh leaf																	
Leea guineensis Dried wood																	
Pandanus mayottensis Fresh fruit																	
Kalanchoe pinnata Dried leaf																	
Pandanus mayottensis Dried fruit																	
Erythroxylum corymbosum Dried root																	
Litsea glutinosa Fresh leaf																	
Pandanus mayottensis Dried root																	
Aloes Mayottensis Dried leaf																	
Erythroxylum lanceum Fresh leaf																	
Pandanus mayottensis Dried leaf																	
Zingiber zerumbet Dried flower																	
Cananga odorata Dried wood																	

Table S 6: Antioxidant activity results (DPPH assay) for the plant extracts at the third dilutions (N = number of replicates). Results were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%

Sample	N	Average	Grouping							
Leea guineensis Dried leaf	3	45,91	A							
Litchi chinensis Dried leaf	3	43,10	A							
Litchi chinensis Dried root	3	42,39	A	B						
Acalypha wilkesiana Fresh leaf	3	41,78	A	B						
Lawsonia inermis Dried leaf	3	37,80		B	C					
Syzygium aromaticum Fresh leaf	3	36,53			C					
Acalypha hispida Dried flower	3	35,97			C					
Acalypha hispida Fresh leaf	3	27,45				D				
Acalypha hispida Fresh flower	3	26,83				D				
Leea guineensis Fresh leaf	3	26,48				D	E			
Lawsonia inermis Fresh leaf	3	26,38				D	E			
Leea guineensis Dried fruit	3	26,07				D	E			
Persea americana Dried leaf	3	26,02				D	E			
Erythroxylum corymbosum Dried leaf	3	22,67				D	E	F		
Tamarindus indica Dried leaf	3	21,83					E	F		
Syzygium aromaticum Dried wood	3	18,49						F	G	
Acalypha wilkesiana Dried leaf	3	17,86						F	G	
Acalypha hispida Dried leaf	3	16,39							G	
Persea americana Dried pit	3	7,81								H

Erythroxylum corymbosum Dried wood		3		3,06						H	I	
Leea guineensis Dried wood		3		2,65							I	

Table S 7: Anti-tyrosinase activity results for the plant extracts at the first dilutions (N = number of replicates). Results were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%												
Sample	N	Ave-rage	Grouping									
Litchi chinensis Dried leaf	3	98,57	A									
Leea guineensis Dried fruit	3	93,28	A	B								
Leea guineensis Fresh leaf	3	91,53	A	B	C							
Leea guineensis Dried root	3	89,82	A	B	C	D						
Syzygium aromaticum Dried leaf	3	89,74	A	B	C	D						
Lawsonia inermis Dried root	3	87,69		B	C	D						
Syzygium aromaticum Fresh leaf	3	86,22		B	C	D						
Litchi chinensis Dried root	3	84,83		B	C	D	E					
Persea americana Dried leaf	3	82,05			C	D	E					
Persea americana Dried root	3	80,10				D	E					
Lawsonia inermis Dried leaf	3	80,07				D	E					
Litchi chinensis Dried wood	3	75,61					E	F				
Paullinia pinnata Dried leaf	3	68,99						F	G			
Kalanchoe pinnata Fresh leaf	3	66,18						F	G	H		
Adansonia digitata Dried wood	3	64,91							G	H	I	
Paullinia pinnata Dried root	3	63,91							G	H	I	

Persea americana Fresh leaf	3	62,84	G	H	I												
Litchi chinensis Fresh leaf	3	62,36	G	H	I												
Persea americana Fresh pit	3	60,80	G	H	I	J											
Acalypha hispida Fresh leaf	3	60,20	G	H	I	J											
Lawsonia inermis Fresh leaf	3	59,63	G	H	I	J											
Acalypha wilkesiana Fresh leaf	3	59,01		H	I	J											
Paullinia pinnata Dried aerial root	3	56,23		H	I	J	K										
Lantana camara Fresh leaf	3	54,99			I	J	K										
Paullinia pinnata Dried liana	3	51,78				J	K	L									
Persea americana Dried pit	3	51,64				J	K	L									
Tamarindus indica Fresh leaf	3	51,33				J	K	L									
Erythroxylum lanceum Dried wood	3	48,76					K	L	M								
Persea americana Dried wood	3	47,22					K	L	M	N							
Litsea glutinosa Dried root	3	44,81						L	M	N							
Pandanus mayottensis Dried aerial root	3	44,07						L	M	N	O						
Erythroxylum corymbosum Dried root	3	43,89						L	M	N	O	P					
Acalypha hispida Dried flower	3	43,69						L	M	N	O	P	Q				
Syzygium aromaticum Dried wood	3	43,47						L	M	N	O	P	Q				
Cananga odorata Fresh flower	3	40,55							M	N	O	P	Q	R			
Acalypha hispida Dried root	3	40,17							M	N	O	P	Q	R			
Aloes mayottensis Mucilage	3	39,15							M	N	O	P	Q	R	S		
Zingiber zerumbet Dried rhizom	3	38,77								N	O	P	Q	R	S		
Paullinia pinnata Fresh leaf	3	34,12									O	P	Q	R	S	T	

Tamarindus indica Dried root	3	34,08	P	Q	R	S	T			
Cananga odorata Dried root	3	33,85		Q	R	S	T			
Zingiber zerumbet Fresh leaf	3	31,72			R	S	T	U		
Zingiber zerumbet Flower stem	3	30,59			R	S	T	U		
Zingiber zerumbet Stem	3	29,61				S	T	U		
Erythroxylum corymbosum Dried wood	3	29,40				S	T	U		
Syzygium aromaticum Dried root	3	28,46					T	U	V	
Cananga odorata Dried wood	3	27,51					T	U	V	
Zingiber zerumbet Fresh rhizom	3	26,71					T	U	V	
Zingiber zerumbet Floral water	3	26,14					T	U	V	
Zingiber zerumbet Dried flower	3	24,76					T	U	V	
Pandanus mayottensis Fresh leaf	3	22,70						U	V	
Aloes mayottensis Dried leaf	3	18,85							V	

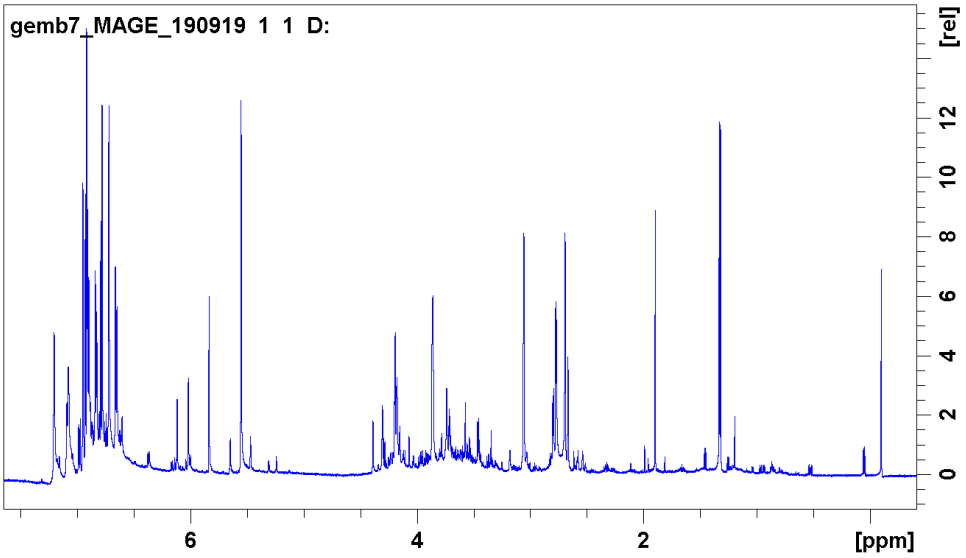
Table S 8: Anti-tyrosinase activity results for the plant extracts at the second dilutions (N = number of replicates). Results were statistically analyzed using Tukey's grouping test.

Grouping information based on Tukey's method configured with a confidence level of 95%

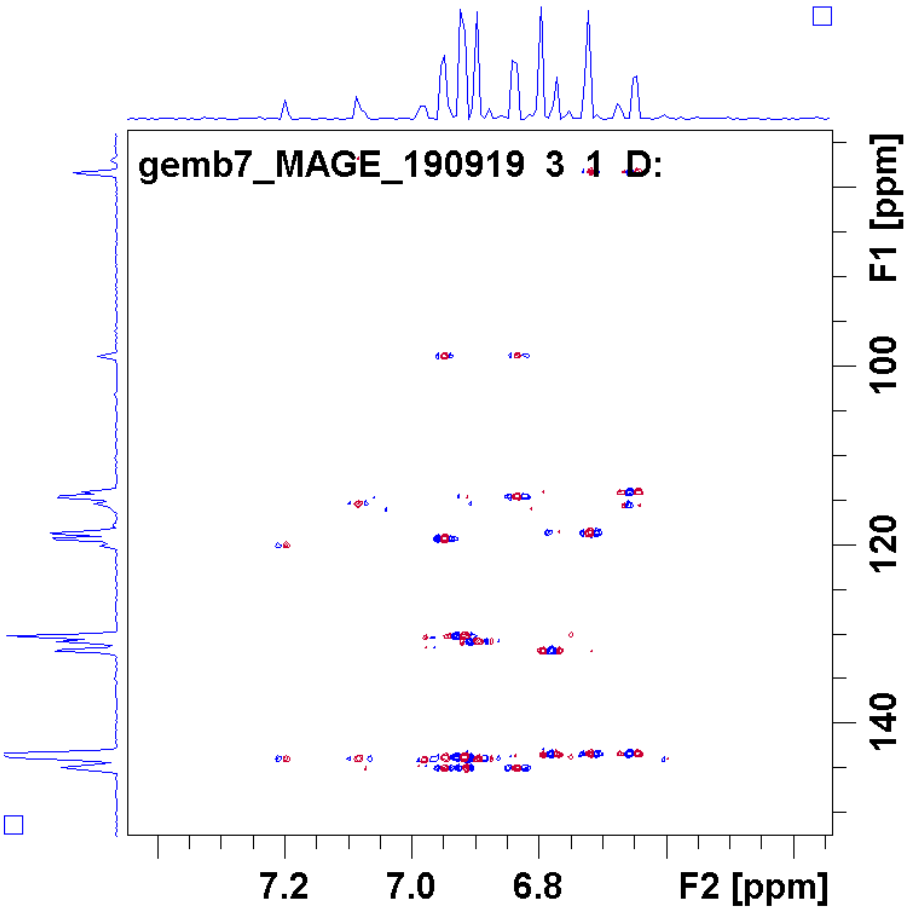
Sample	N	Average	Grouping			
Litchi chinensis Dried leaf	3	51,36	A			
Leea guineensis Dried fruit	3	45,45		B		
Litchi chinensis Dried root	3	42,29		B		
Persea americana Dried root	3	27,49			C	
Syzygium aromaticum Dried leaf	3	27,28			C	
Persea americana Fresh pit	3	18,69				D
Acalypha wilkesiana Fresh leaf	3	16,26				D

5. Appendix from Chapter 5

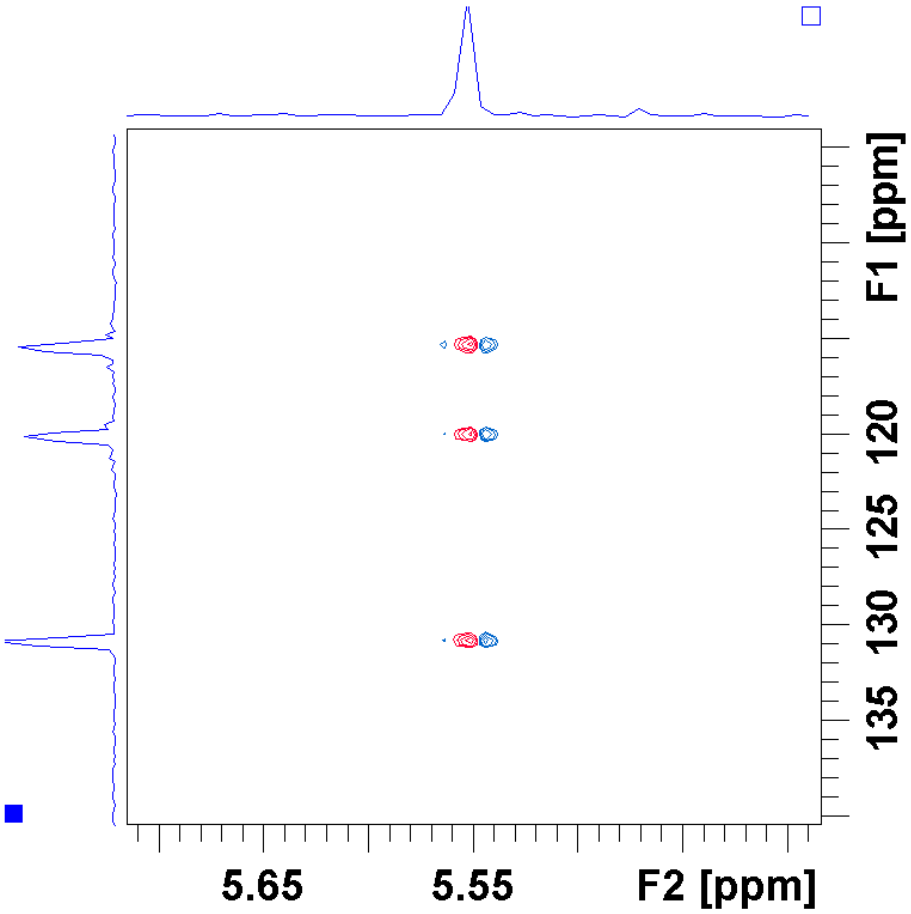
Supplementary material



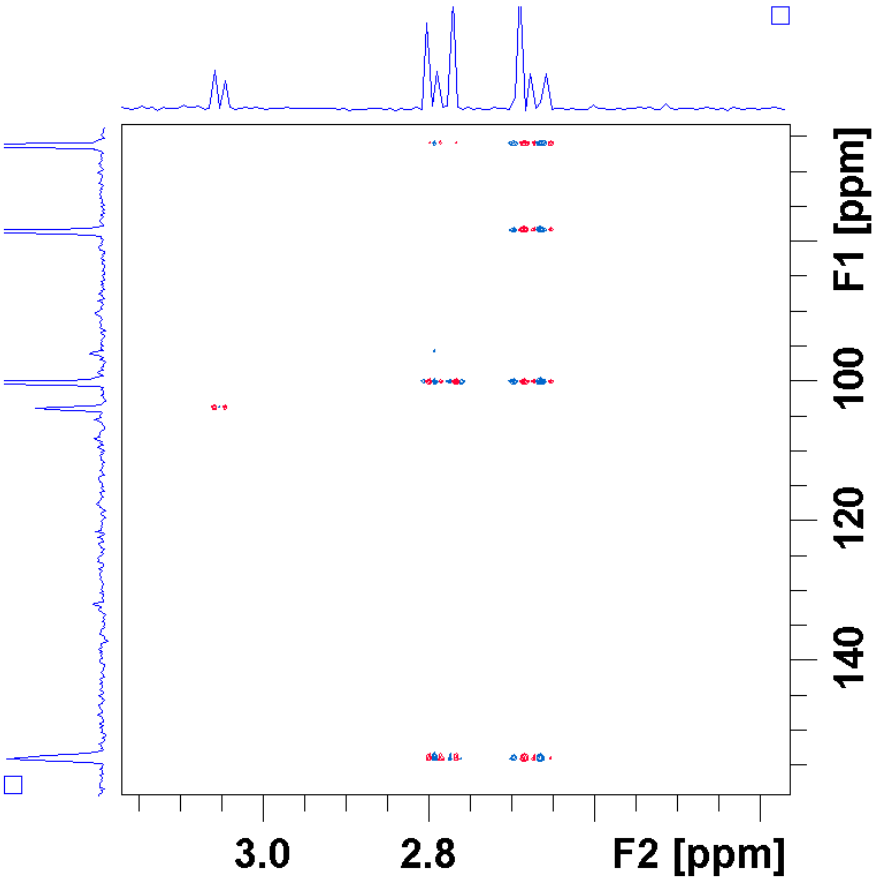
Supplementary figure 1 : 1D ^{1}H NMR spectrum of the isolated compound.



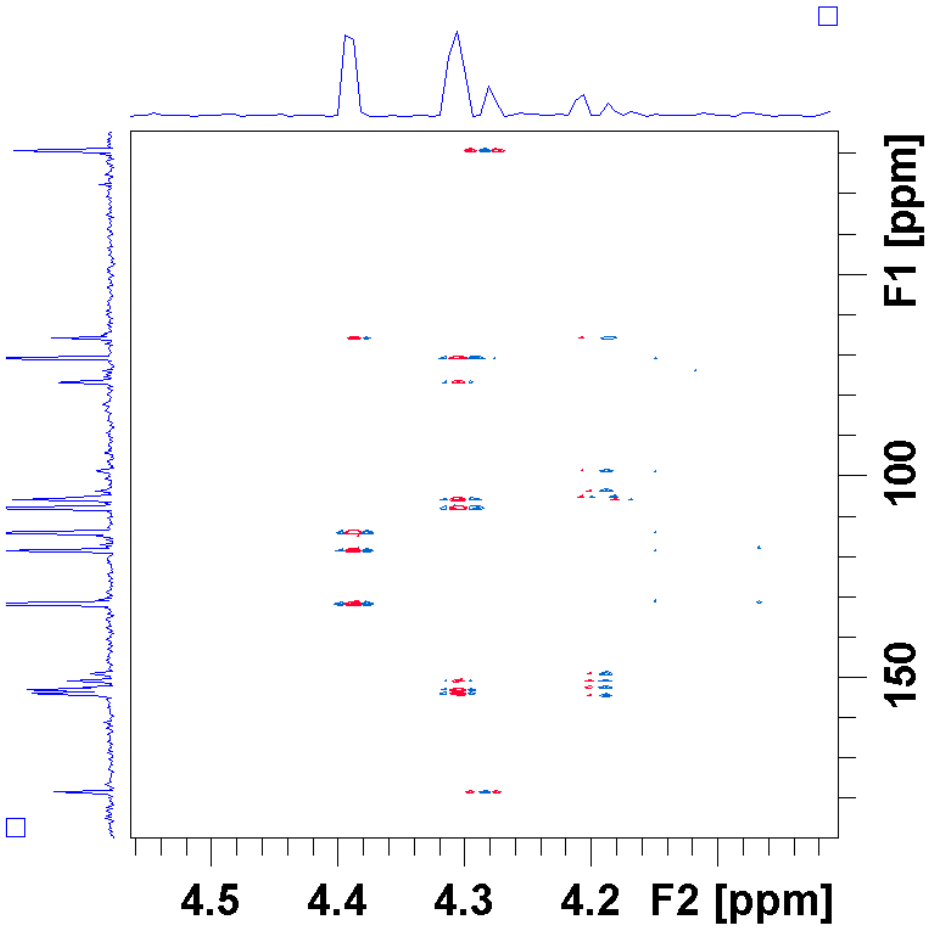
Supplementary figure 2: 2D HMBC NMR spectrum of the isolated compound.



Supplementary figure 3 : 2D HMBC NMR spectrum of the isolated compound.

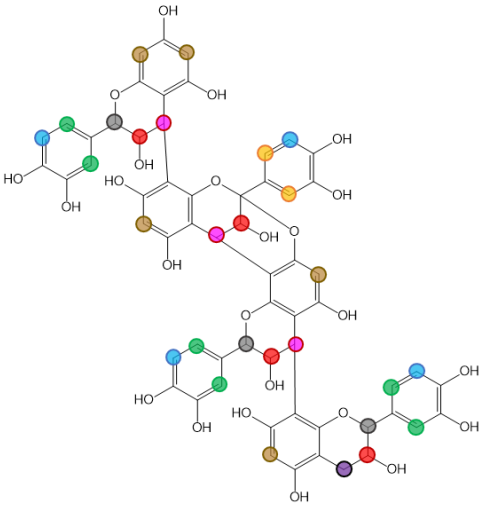


Supplementary figure 4 : 2D HMBC NMR spectrum of the isolated compound.



Supplementary figure 5 : 2D HMBC NMR spectrum of the isolated compound.

Line	Colour	^{1}H chemical shift (ppm)	$^{2}J_{CH}$ and $^{3}J_{CH}$ coupled ^{13}C chemical shift (ppm)
1		7.2	144,120, 77
2		7.1	144, 116, 77
3		7.0	144, 119, 99
4		6.9	144, 131
5		6.9	144, 131
6		6.8	144,131
7		6.8	144, 131
8		6.8	144, 115, 99
9		6.7	144, 119, 78
10		6.6	144, 115, 78
11		5.8	105*
12		5.6	131, 120, 115
13		4.4	131, 119, 113, 66
14		4.3	154, 153, 151, 108, 106, 77, 71
15		4.2	149, 99, 66
16		3.9	100, 78
17		3.1	104
18		2.8	154, 100, 66
19		2.7	154, 100, 78, 66



Supplementary figure 6: allocation of 2D HMBC NMR signals of the isolated compound. Allocation color indicates the position where the corresponding ^{1}H is attached to the structure. Chemical shifts were rounded leading to identical HMBC signals in some cases. * : this proton signal is perfectly visible in the 1D ^{1}H NMR spectrum and can be unambiguously attributed to an aromatic structure, however no corresponding C-H signal can be observed in 2D HSQC NMR spectrum. In HMBC, a very weak signal is observed.