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Sustainable management of rosemary wastewater and essential oil in agri-environmental bioprocessing

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ABSTRACT

In agriculture, fragrant and medicinal plants offer significant untapped potential for generating biomass-derived materials, particularly from wastewater by-products. In this context, the present study investigates the chemical compositions, antioxidant capacities, antimicrobial properties, acute oral toxicity, and diabetes management potential of wastewater by-products and essential oil from *R. tournefortii* de Noé. Utilizing advanced analytical techniques, including ATR-FTIR, GC/MS, and HPLC-DAD, were employed to conduct the analyses. ATR-FTIR analysis revealed intricate molecular compositions in both the essential oil and wastewater, confirming terpenoids, phenolic acids, and other functional groups. GC/MS and HPLC-DAD identified dominant compounds in the essential oil, notably camphor (25.49%) and 1,8-cineole (18.03%), while the wastewater contained significant levels of hydroxycinnamic acids such as caffeic acid (23.51%) and rosmarinic acid (21.15%). In terms of bioactivity, the essential oil demonstrated robust antimicrobial effects, with inhibition zones up to 17.1 mm, whereas the wastewater exhibited moderate activity, with zones up to 15.15 mm. Additionally, antioxidant assessments revealed exceptional potency of the wastewater, with IC50 values of 0.046 ± 0.007 mg/mL for DPPH, 0.082 ± 0.013 mg/mL for ABTS, and 2.45 ± 0.71 mg/mL for the beta-carotene/linoleate model system, surpassing the essential oil. Furthermore, both the essential oil and wastewater showed significant inhibitory effects on pancreatic α-amylase, crucial for diabetes management, with wastewater demonstrating remarkable inhibition (IC50 = 0.48 ± 0.021 mg/mL). Acute oral toxicity assessment confirmed the safety of these components, alleviating concerns about potential adverse effects. In summary, these findings highlight the untapped potential and environmental significance of wastewater by-products as valuable resources, positioning *R. tournefortii* de Noé's essential oil and wastewater as promising agents for sustainable healthcare and environmental sustainability.

1. Introduction

Physiological processes generate free radicals, necessitating the neutralization provided by antioxidants, which play a crucial role in maintaining cellular balance (Zhang et al., 2023). However, weak defence mechanisms against oxidative stress, compounded by environmental factors like pollution, pose significant health risks, including metabolic disorders, chronic diseases, and cancer (Martinelli et al.,

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2020). Recognition of the role of free radicals in disease has prompted exploration into antioxidants, with aromatic plants such as rosemary showing promising potential (Qiu et al., 2024). Rosemary essential oil, dominating the global market with annual production between 150 and 200 tons, showcases its pharmacological prowess and extensive applications across industries such as agro-food industry, aromatherapy, and cosmetics (Bouammali et al., 2023). However, the ecological concerns associated with the production of rosemary essential oil via steam distillation, particularly concerning thermal pollution caused by wastewater by-products (de Elguea-Culebras et al., 2022), underscore the need for advanced extraction techniques that mitigate the environmental impact (Sartor et al., 2011).

Sustainability concerns regarding rosemary essential oil extend to the food industry as a whole, where about one-third of all food produced globally is lost or wasted - around 1.3 billion tons per year (Comunian et al., 2021). In addition to the economic implication of such loss, it also contributes to many environmental issues. As a result, there is a growing interest in valorizing food processing by-products as new raw materials or functional food ingredients under such circumstances. This approach has huge potential to make food production more sustainable, healthy, and economically feasible. The studies conducted related to using by-products of food items within food products state that it could enhance their antioxidant capacity by up to 50%, depending on the kind of by-product used, and decrease production cost by 20%–30% (Comunian et al., 2021). Such developments could result in the evolution of a multi-billion-dollar industry offering health-enhancing and sustainable foods. At the same time, agricultural by-products for instance, pomegranate peel and grape pomace already largely contribute to enhancing the nutritional quality of food products. The further valorization of such by-products may be added to these enhancing nutritional profiles and help attain the SDGs in the area of sustainable consumption and production with the additional advantage of creating novel income streams for small farmers in underdeveloped regions (Rasul, 2016).

The use of food and agricultural by-products also raises several safety issues. Chemical contaminants and pathogens risks have to be mitigated, as there are serious health hazards from by-products to consumers (Lau et al., 2021). For instance, the addition of coffee silverskin has already been proved to enhance the micronutrient profile in cereal-based products, but not much attention is paid to the microbiological safety of such additives. Such valorized products will have to meet high quality and safety standards. These are ensured by the establishment of very tight quality control that involves pathogen monitoring for a maximum count of less than 25 CFU/g of *Bacillus cereus* and an absence of Salmonella (Socas-Rodríguez et al., 2021). In addition, effective decontamination techniques and adherence to regulatory standards are necessary to guarantee the safety of these food products. While the potential of food by-products is huge, it is notable that a literature gap exists regarding proper safety evaluations, thus calling for further research in developing stringent safety standards and regulations.

In recent years, more attention has been paid to recycling waste from aromatic and medicinal plants (Naboulsi et al., 2023); a major role was developed in the valorization of by-products, such as rosemary waste (Gençdağ et al., 2021; Saha & Basak, 2020). The earlier studies about rosemary dealt with the extraction of bioactive polyphenols as a function of their antioxidant, antibacterial, and bioplaguicide properties (Santana-Méridas et al., 2014). Innovative applications have involved the re-use of rosemary's solid wastes as sheep fodder to improve the quality of the meat (Yagoubi et al., 2021) and distillation residues as natural antioxidants during preservation processes of the meat (Tibaoui et al., 2020). Despite all these developments, a huge research gap remains around the wastewater co-products from rosemary, mainly from *Rosmarinus tournefortii* de Noé. Most literature has concentrated on wastewater from *Rosmarinus officinalis* L., and its application is limited to a small scale (Ali et al., 2019), with a considerable understanding gap of the potential of rosemary wastewater from less-studied rosemary species (Wu et al., 2022).

This study critically addresses this gap by pioneering a comprehensive analysis of *Rosmarinus tournefortii* de Noé. It introduces novel assessments of its antioxidant, antimicrobial, antidiabetic potential, acute oral toxicity and molecule profile using HPLC-DAD, GC/MS and FTIR-ATR analysis. Another important innovation of this work is the comparative analysis of the wastewater by-products with the essential oil, using the same methodology, thus showing the particular properties and potential uses that these by-products can give. Moreover, a comparative study with the essential oil of the well-known species *R. officinalis* L. gives a benchmark that would allow an understanding of the distinctiveness of *R. tournefortii* de Noé. This comparative approach fills the knowledge regarding the two species of rosemary, but it also emphasizes the potential of by-products of a wastewater process as valuable, biomass-derived materials. Furthermore, this research also covers the main challenges of by-product valorization, taking into account the potential mitigation of environmental impacts as well as the evaluation of economic viability. By exploring these concerns, the study has brought out some important insights into the capacity of wastewater by-products in addressing the existing sustainability and economic issues by enhancing scientific knowledge and practical applications in functional food development and healthcare.

2. Materials and methods

2.1. Plant material harvesting and extraction

Fresh leaves of *Rosmarinus tournefortii* de Noé were gathered on March 13, 2020, while the plants were blooming, from the Megrez forest region in eastern Morocco (Ziani et al., 2023). The Forest Management Studies Service in Oriental, Morocco, confirmed the plant's identity. Following this, a pilot-scale steam distillation was conducted on the dried leaves to extract the essential oil. A 90 mm Whatman GF/A filter was employed to separate the wastewater by-products from the solid waste post-distillation, and a rotary evaporator was used to concentrate the product. Essential oil and wastewater by-products were stored in amber-coloured, sealed glass vials at 2 °C until analysis. The yield of essential oil and wastewater by-products was calculated using **Eq. (1)** and **Eq. (2)**, respectively. Where m_{EO} represents the mass of essential oil, M_s designates the mass of dried leaves, and M_{Ext} indicates the mass of wastewater by-products.

$$Essential\ oil\ yield\ (\%) = \frac{m_{EO}}{M_s} \times 100 \qquad (1)$$

$$Wastewater\ yield\ (\%) = \frac{M_{Ext}}{M_s} \times 100 \qquad (2)$$

2.2. Total polyphenol content

The determination of total phenolic content (TPC) in the wastewater produced during rosemary distillation was determined using a previously established method (Ćujić et al., 2016). Briefly, 1 mL of tenfold diluted Folin-Ciocalteau reagent was mixed with 0.2 mL of wastewater by-products. Following a 4-min incubation, 0.8 mL of sodium carbonate solution (0.0075 g/mL) was introduced. After incubating for 2 h at ambient temperature, the optical density at 760 nm was recorded using a UV–VIS spectrophotometer. The TPC was quantified in milligrams of gallic acid equivalent per gram of the dehydrated extract (mg GAE/g DW), with gallic acid serving as the reference standard.

2.3. Vibrational characterization

The ATR examination was performed using a Jasco 4700-FTIR spectrometer to scrutinize the functional groups in the wastewater by-products (WRR) of *R. tournefortii* de Noé and its essential oil (REO)

(Ziani et al., 2024). The absorption spectrum was recorded across a wavelength span of 450–4000 cm^{-1}. This method provides a detailed examination of the molecular interactions and structural features of the samples, offering valuable insights into their chemical composition and potential uses.

2.4. Chemical overview of wastewater by-products

The analysis of the wastewater by-products derived from the distillation process of rosemary was conducted through high-performance liquid chromatography using the Waters Alliance™ e2695 XC HPLC System, maintained at a temperature of 30 °C. This analytical setup included a reverse phase C18 column (with dimensions of 5 μm, 250 mm × 4.6 mm) along with a Photodiode Array Detector. The wastewater by-products, prepared at a concentration of 6 mg/mL, were subsequently injected into the column at 20 μL, with a flow rate of 800 μL/min. This process followed a gradient of two solvents, with a few minor adjustments based on a previously described method (Liu et al., 2011). The separation of polyphenols was accomplished using a mobile phase gradient as follows: eluent A (water containing 0.2% formic acid) and eluent B (0.2% formic acid in acetonitrile). The gradient proceeded as outlined: 0–10 min, 70%–30% A; 10–15 min, 30%–70% A; 15–25 min, 30%–70% A; and 25–30 min, 70%–30% A. Detection occurred in the UV–vis range (280–330 nm). Identification of phenolic compounds in the rosemary wastewater by-products relied on their UV–VIS profiles and retention times, referenced against available standards and literature data.

2.5. Essential oil composition analysis

Rosmarinus tournefortii de Noé essential oil was analysed in a gas chromatograph with an RTX-5 Capillary Column with a dimethylpolysiloxane stationary phase containing 5% of a phenyl group (30 m × 0.25 mm, film thickness 0.25 μm) equipped with a mass selective detector (Hewlett Packard 6890) (Oualdi et al., 2023). The split injection technique was used, and a temperature of 250 °C was chosen for the ion source and interface. The GC oven was set at 50 °C for 1 min and then heated to 250 °C at 10 °C/min for 1 min. The pure helium mobile phase (99.99%) was the carrier gas for the separation at a flow velocity of 1.4 mL/min. The ionization energy used was 70 eV with an ionization current of 2 A. The mass spectra scan range was performed between 40 and 300 m/z. The chemical profile of rosemary essential oil was recognized by contrasting their holding times and their mass spectra. Linear interpolation of the holding times in a series of n-alkanes was used to calculate holding times, which were then compared to data from authenticated standards in the database. The mass spectra were contrasted with reference spectra discovered in databases, including those available from the National Institute of Standards and Technology (NIST), which encompass 147,198 compounds. LabSolutions software, version 2.5, was utilized for data collection and processing (Pokajewicz, 2023).

2.6. Antioxidant performance assessment

Antioxidant assays were conducted using standard techniques, including DPPH scavenging assay, ABTS cation radical assay, and Beta-carotene/linoleate model system. The DPPH method was executed following a recognized procedure (Santana-Méridas et al., 2014), which relies on the reduction of DPPH free radicals. To summarize, a mixture was created by combining 2 mL of a DPPH solution (4 mg/100 mL) with 0.5 mL of varying concentrations of both rosemary essential oil and wastewater. This mixture was thoroughly blended and left to incubate in the dark at room temperature for 60 min. The ability to neutralize free radicals was assessed by measuring the absorbance at 517 nm. The assessment of ABTS^{+} radical scavenging activity was carried out according to the procedure described (Różyło et al., 2023). To create the ABTS^{+} radical, equal volumes of potassium persulfate (2.45 mM) and ABTS solution (7 mM) were dispersed, and it was left in darkness for 14–16 h. Once this initial solution attained an optical density of 0.7 at 734 nm, it was weakened with ethanol. Subsequently, 0.1 mL of the rosemary samples were mixed with 2 mL of the diluted stock solution, and the absorbance was determined at a wavelength of 734 nm after a 6-min incubation period.

The beta-carotene/linoleate model system approach was used to examine the antioxidant efficacy of rosemary samples, following an established procedure (Rohman et al., 2021). The formulation of the beta-carotene/linoleic acid mixture in distilled water involved several steps: A blend was created by mixing 1 mL of a beta-carotene solution (20 mg/100 mL) with linoleic acid (0.02 mg) and tween 20 (0.2 mg). Following this, 30 mL of distilled water was introduced into the mixture, and it was subjected to ultrasonic treatment for 5 min. Afterwards, 4000 μL of the resulting emulsion solution was combined with 200 μL of the rosemary samples, and this mixture was then incubated in an aquatic heater at 50 °C for 120 min. The optical density was measured at t = 0 for the control formulation and at time point t = 120 min for both the control solution and the samples Employing a UV–VIS spectrophotometer set to 470 nm for measurement. The inhibition activity (%) in the DPPH and ABTS assays was determined using **Eq. (3)**, while the inhibition for the beta-carotene/linoleate model system assay was calculated using **Eq. (4)**.

$$Inhibition\ (\%) = \frac{A_N - A_{Ext}}{A_N} \times 100 \tag{3}$$

$$Beta - Carotene\ inhibition\ (\%) = \frac{A_{Ext}\ (120) - A_C\ (120)}{A_C(0) - A_C(120)} \times 100 \tag{4}$$

where A_N represents the absorbance of the negative control, and A_{Ext} denotes the absorbance of the extracts. Specifically, $A_{Ext}(120)$ indicates the absorbance of the extracts at 120 min, $A_C(120)$ refers to the absorbance of the control at 120 min, and $A_C(0)$ signifies the absorbance of the control at the initial time point of 0 min. The results obtained through linear regression analysis, are expressed as IC50 values, which indicate the concentration needed to achieve a 50% inhibition of the radicals. Ascorbic acid consistently functioned as the standard antioxidant and negative control in all conducted assays.

2.7. Exploring antimicrobial efficacy

The antimicrobial effectiveness of rosemary wastewater by-products and its essential oil was thoroughly assessed against a range of bacteria and fungi. For Gram-negative strains like *Escherichia coli* and *Pseudomonas aeruginosa*, as well as Gram-positive strains including *Listeria innocua* and *Staphylococcus aureus*, the antibacterial activity was examined. Additionally, the antifungal potency was evaluated against yeast species *Rhodotorula glutinis*, *Candida albicans*, and mold *Geotrichum* sp. The well-established agar diffusion method was employed for these analyses (Schönbächler et al., 2023). For experimental rigour, the strains were meticulously adjusted and diluted to achieve a standardized concentration of 0.5 McFarland, corresponding to 10^{6} CFU/mL for bacteria and yeast, and 10^{6} spores/mL for moulds. Subsequently, fresh cultures underwent prudent inoculation onto petri dishes after requisite dilution in Mueller-Hinton medium for bacteria and yeasts, and sterile saline solution for moulds (El Guerraf et al., 2023). The method entailed the strategic seeding of Mueller-Hinton agar with the targeted bacteria or fungi to facilitate the creation of consistent 6 mm diameter wells. Within these wells, precisely measured 10 μL volumes of samples, each prepared at a concentration of 2 mg/mL, were meticulously dispensed. After inoculation, the agar plates underwent a meticulously orchestrated incubation regimen: an initial 2-h interval at 4 °C, followed by an extended incubation at 30 °C for 24 h for bacteria, and at 25 °C for fungi. The assessment of the antimicrobial potential of rosemary samples hinged on the measurement of inhibition zone diameters within the agar gel. *Gentamicin* served as a positive control for bacteria, while *cycloheximide* functioned as a positive control for fungi.

2.8. *Pancreatic alpha-amylase inhibition*

The evaluation of alpha-amylase inhibitory activity in the wastewater by-products of *R. tournefortii* de Noé and its essential oil obtained by steam distillation was assessed using a prescribed method (Sun et al., 2017). In this procedure, each sample, at different concentrations (0.45, 0.90, 1.35, 1.8 and 2.25 mg/mL), or acarbose (positive control), was combined with pancreatic alpha-amylase enzyme solution (200 μL) and left to stand for 10 min at 37 °C. Following this initial incubation, a 1% starch solution was introduced to the mixture and re-incubated for an additional 15 min at the same temperature. To put an end to the response, 600 μL of DNSA reagent was included, and the resulting mixture was boiled in a water bath for 8 min. After cooling to room temperature, the blend was thinned by incorporating 1000 μL of distilled water before measuring its absorbance at 540 nm. The inhibition (%) was calculated according to **Eq. (5)**.

$$Pancreatic\ \alpha - amylase\ inhibition\ (\%) = \frac{A_C - A_{Ext}}{A_C} \times 100 \tag{5}$$

Where A_C is the control reaction's absorbance (without the inhibitor) and A_{Ext} is the reaction with inhibitor absorbance. The results were presented in the form of IC50 values, which signify the concentration needed to achieve a 50% inhibition of the enzyme's activity, determined through linear regression analysis of the percentage of activity versus the inhibitor concentration curves.

2.9. *Acute oral toxicity evaluation*

The acute oral toxicity assessment of *Rosmarinus tournefortii* de Noé steam distillation wastewater and its essential oil was conducted on albino mice, both female and male, in accordance with the protocols approved by the animal laboratory at the Department of Biology, Mohammed I University (Faculty of Science-Oujda, Morocco), following the guidelines established by the Organization for Economic Cooperation and Development. The well-being of the animals was maintained in compliance with the Guide for the Care and Use of Laboratory Animals as outlined by the US National Institutes of Health in 2012 (Costa et al., 2011). The healthy mice were divided into seven groups, each consisting of 3 females and 3 males. The first group, designated as the control group, received distilled water orally, while the remaining groups were administered ascending doses of essential oil (500, 1000, and 2000 ppm body weight). Before the oral treatment, the animals were weighed and subjected to an overnight fast, with access to water provided without restrictions. Over 14 days, the mice were closely monitored for 2 h daily to observe any signs of toxicity and behavioural abnormalities.

3. Results and discussion

3.1. *Total polyphenol content*

Polyphenols, extensively researched plant secondary metabolites, significantly contribute to the nutritional value of plant-based diets and their positive impact on human health (Bouakline et al., 2023). In our analysis of wastewater by-products from the steam distillation of *Rosmarinus tournefortii* de Noé, a yield of 24.65% was obtained, revealing a total phenolic content of 98.8 ± 1.098 mg AGE/g DW. Moreover, the literature reports that *Rosmarinus officinalis* L. species wastewater contains 2.77 mg GAE/mL using the same process (Celano et al., 2017). In contrast, other studies have reported 108.10 ± 0.26 mg GAE/g (Luca et al., 2023) and 129 ± 6.45 mg GAE/mL using a different process, specifically hydrodistillation (Gonzalez-Rivera et al., 2023). Furthermore, comparing the TPC of wastewater with solid waste extracted with water from *Rosmarinus officinalis* L., the solid waste showed a total phenolic content of 53.1 mg GAE/g (Christaki et al., 2022), contrasting with our previous study's findings of 100.84 ± 0.20 mg GAE/g for *Rosmarinus tournefortii* de Noé using hydrodistillation process (Ziani et al., 2023). This variability may arise from factors such as distillation time, temperature, and solvent effects.

Notably, comparing the wastewater by-products with the solid waste from hydro distillation and steam distillation processes underscores distinct differences in total phenolic content, highlighting the significant role of direct water contact in enhancing phenolic extraction. This discrepancy may stem from the hydrodistillation process's direct immersion in water, enhancing phenolic extraction, unlike in steam distillation. Generally, when comparing the TPC using the same studied process (steam distillation), wastewater by-products of *Rosmarinus tournefortii* de Noé exhibit a higher TPC than *Rosmarinus officinalis* L. While there is no established classification for high/low phenol values, some authors suggest that natural extracts can be considered rich in phenolic compounds when their total phenol content exceeds 20 mg GAE/g DW (Raghuvanshi et al., 2022). Taking this criterion into account and considering the literature data mentioned earlier, our results fall within the expected range.

3.2. *The finger-print characteristic*

The chemical structures of REO and WRR were investigated using attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy, revealing the individual bands as illustrated in Fig. 1. The REO spectrum exhibits prominent bands between 1030 and 1135 cm^{-1}, which are caused by the non-planar C-H wagging vibrations of terpenoids. Peaks occurring within the range of 1190 to 1035 cm^{-1} correspond to C-O stretching vibrations found in carbohydrates. The zone between 1700 and 1500 cm^{-1} indicates C=C bending, while the bands around 2900 cm^{-1} are due to aromatic C-H bending vibrations. The O-H stretching of carboxylic acids is observed between 3000 and 2500 cm^{-1}. These results align with existing studies, which describe the FTIR spectrum of rosemary essential oil as exhibiting terpenoid characteristics, such as C-H stretching (~2900 cm^{-1}), C=O stretching (~1700 cm^{-1}), broad O-H stretching (~3400 cm^{-1}), and C-O stretching (~1100 cm^{-1}). This confirms the presence of these functional groups in our

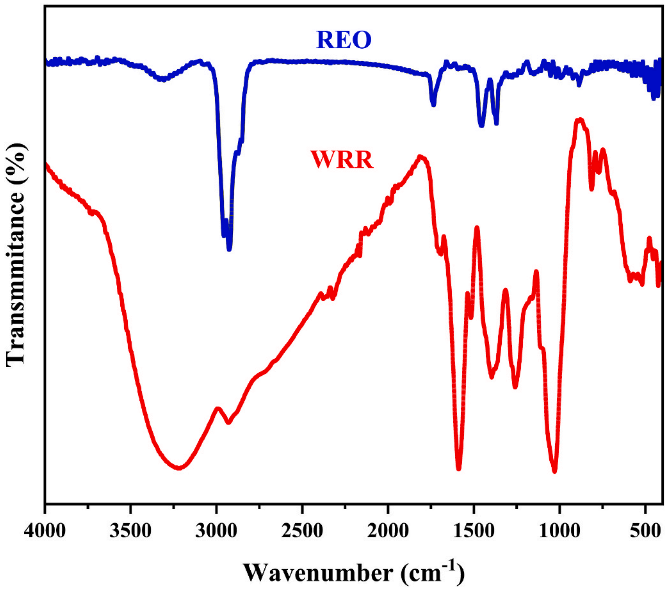

Fig. 1. ATR-FTIR spectra of *R. tournefortii* de Noé steam distillation wastewater by-products (WRR) and its essential oil (REO).

analysed samples (Volić et al., 2018).

On the other hand, the ATR-FTIR spectrum of WRR reveals a complex molecular composition characterized by distinct functional groups. The prominent broad peak around 3300-3400 cm^{-1} indicates hydroxyl groups, suggesting the presence of alcohols of phenolic compounds. A sharp peak at approximately 1700 cm^{-1} denotes the presence of carbonyl groups, typical of ketones, aldehydes, or carboxylic acids. Additionally, significant stretching vibrations of C-H in the vicinity of 2800–3000 cm^{-1} point to aliphatic hydrocarbons, while C=C stretching vibrations around 1600-1500 cm^{-1} suggest aromatic or unsaturated structures. Furthermore, the multiple peaks between 1200 and 1000 cm^{-1} indicate the presence of C-O bonds, typical in ethers, esters, and alcohols. These observations are consistent with the literature, which reports similar bands for these functional groups (Agatonovic-Kustrin et al., 2021). Distinct stretching vibrations of carbonyl groups (C=O) at 1687 cm^{-1} and 1655 cm^{-1}, characteristic of carboxylic acids and esters, are observed in compounds like rosmarinic acid and carnosic acid. Our findings also show carbonyl groups around 1700 cm^{-1}, corroborating the literature (Ziani et al., 2024). The presence of aromatic ring (C=C) stretching vibrations at 1605 cm^{-1} confirms the presence of phenolic acids such as caffeic acid derivatives. Additionally, methoxyl groups (C-H), identified through stretching vibrations at 2925 cm^{-1} and 2854 cm^{-1}, suggest the presence of lignin and other diterpenoids, which is also supported by our data showing similar C-H stretching bands.

3.3. *Phenolic profile of wastewater by-products*

To analyse the chemical composition of polyphenols within the wastewater by-products of *Rosmarinus tournefortii* de Noé steam distillation, a comprehensive phenolic profile assessment was conducted using HPLC-DAD. This analysis was conducted utilizing established HPLC-DAD methodologies and drawing upon data referenced in the existing literature. Reference standards, including gallic acid, chlorogenic acid, epicatechin, caffeic acid, and rosmarinic acid, were employed to validate the identification of molecules by contrasting their retention times and UV–Vis's spectra with literature and the reference data. Additionally, extensive studies were reviewed to identify other phenolic compounds by matching their elution patterns to data described in the literature. As indicated in Table 1 and represented in Fig. 2(a), a total of ten phenolic compounds, categorized into four different groups, were provisionally recognized in the wastewater by-products of rosemary distillation: two hydroxybenzoic acids (1 and 4), four hydroxycinnamic acids (3, 7, 8, and 9), two flavan-3-ols (2 and 5), and one flavone (10). Table 1 also displays the percentage area of the different compounds in rosemary water distillation, with phenolic acids representing the predominant compounds at over 80%, comprising 50.9% hydroxycinnamic acids and 32.97% hydroxybenzoic acids, followed by flavan-3-ols and flavone at 12.07% and 1.21%, respectively.

The chemical structures corresponding to peaks 1, 2, 3, 7, and 9 were positively identified as gallic acid, epicatechin, chlorogenic acid, caffeic acid, and rosmarinic acid, respectively, in accordance with the reference standards. This identification was consistent with previous studies on rosemary (Bendif et al., 2017). Peak 4 was identified as protocatechuic acid glycoside based on its UV–Vis spectrum with λ_{max} values of 220.0 and 281.2 nm, closely matching the spectrum patterns described in the literature for the same plant (Vallverdú-Queralt et al., 2014). Peak 5 was tentatively assigned as gallocatechin, given its UV spectra ranging from 283 to 335 nm, which closely resembled the values observed in our investigation (283, 334 nm). Moreover, the two UV absorption spectra exhibited identical patterns, suggesting that peak 5 could be attributed to gallocatechin (Gonelimali et al., 2018). Peak 8 was likely Yunnaneic acid F, as indicated by its spectra maxima at 275.3 nm, a characteristic feature consistent with spectra maximal detected in various studies (de Almeida Gonçalves et al., 2018). Peak 10 was identified as apigenin, a flavone, as it exhibited maximum values of 268.2 and 339.7 nm, which closely align with previously reported values (Santana-Méridas et al., 2014).

Comparing our results with the literature data, only four published outcomes (Celano et al., 2017; de Elguea-Culebras et al., 2023; Luca et al., 2023; Wollinger et al., 2016) focusing on the chemical profile of the wastewater resulting from the distillation process of rosemary, specifically centred around the *Rosmarinus officinalis* L. species. Our findings align with reports indicating the predominance of polar compounds, particularly flavonoids and phenolic acids (Luca et al., 2023). However, only the presence of rosmarinic acid and slight traces of carnosol were observed, potentially due to the duration of the distillation process (Wollinger et al., 2016). In contrast, other researchers (Celano et al., 2017; de Elguea-Culebras et al., 2023) noted the detection of the entire family of phenolic compounds, encompassing phenolic diterpenes, which are moderately polar compounds and typically extracted only with organic solvents, in the wastewater by-products. Despite the extensive research on *R. officinalis* L., no studies have yet explored the wastewater by-products of the *R. tournefortii* de Noé species. The lack of substantial data concerning the wastewater by-products of rosemary steam distillation underscores the potential for further exploration of our findings in forthcoming research endeavours.

3.4. *Essential oil chemical profile*

Steam distillation of freshly harvested *Rosmarinus tournefortii* de Noé leaves, collected from the woodland area of Megrez in the eastern part of Morocco, yielded a pale-yellow oil with an appealing fragrance, at a yield of 2.01% (w/w). The intricate blend of secondary metabolites was described using gas chromatography-mass spectrometry (GC-MS). As

Table 1
Phenolic compounds identification of *R. tournefortii* de Noé wastewater by-products steam distillation.

Peak	Retention time (min)	Tentative identification	Molecular formula	Family	Peak area (%)	UV–Visλmax (nm)	Reference
1	2.13	Gallic acid	$C_7H_6O_5$	Hydroxybenzoic acid	0.92	268.2–280	Al-Juhaimi et al. (2024)
2	2.66	Epicatechin	$C_{15}H_{14}O_6$	Flavan-3-ol	7.82	251.6, 326.5, 363.5	Ziani et al. (2024)
3	3.03	Chlorogenic acid	$C_{16}H_{18}O_9$	Hydroxycinnamic acid	4.94	283.6, 325.3, 330	Achour et al. (2021)
4	3.27	Protocatechuic acid-glycoside	$C_{13}H_{16}O_9$	Hydroxybenzoic acid	32.05	220.9, 281.2,	Vallverdú-Queralt et al. (2014)
5	3.66	Gallocatechin	$C_{15}H_{14}O_7$	Flavan-3-ol	4.25	283.6, 313, 334.9	Gonelimali et al. (2018)
6	4.43	Caffeic acid	$C_9H_8O_4$	Hydroxycinnamic acid	23.51	274.1, 328.9	Ziani et al. (2023)
7	6.08	Yunnaneic acid F	$C_{29}H_{26}O_{14}$	Hydroxycinnamic acid	1.33	275.3	de Almeida Gonçalves et al. (2018)
8	6.52	Rosmarinic acid	$C_{18}H_{16}O_8$	Hydroxycinnamic acid	21.15	331.3	Ziani et al. (2024)
9	9.32	Apigenin	$C_{27}H_{30}O_{15}$	Flavone	1.21	268.2, 339.7	Santana-Méridas et al. (2014)

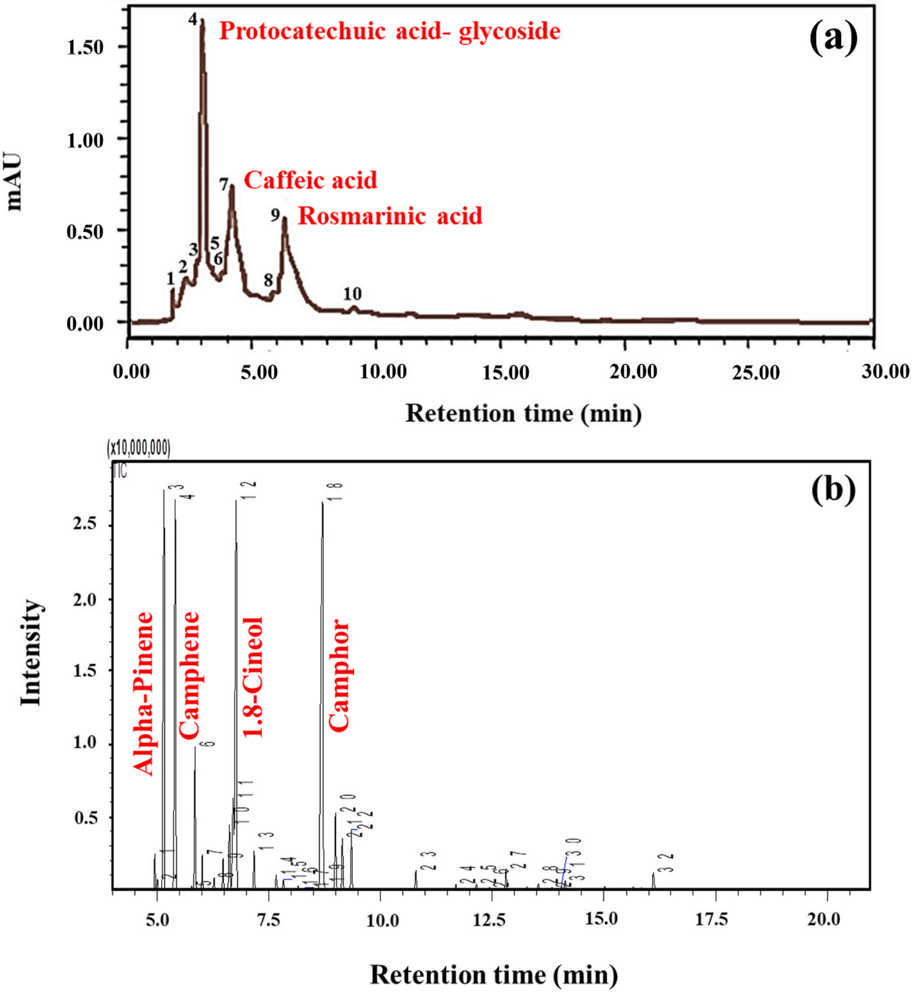

Fig. 2. (a) HPLC-DAD chromatogram and **(b)** Gas chromatography-mass spectroscopy (GC-MS) of *R. tournefortii* de Noé wastewater by-products and essential oil, respectively.

demonstrated in Table 2 and spectra represented in Fig. 2(b), a total of 32 compounds have been tentatively identified, collectively accounting for 99.91% of the total oil content. These compounds are classified into four groups: monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpene hydrocarbons, and oxygenated sesquiterpenes. Predominant compounds are concentrated within the groups of oxygenated monoterpenes and monoterpene hydrocarbons. Among these, camphor emerges as the most abundant constituent, constituting 25.49% of the essential oil, followed by eucalyptol (1.8-cineole) at 18.03%, alpha-pinene at 15.96%, and camphene at 15.14%. Additionally, minor monoterpenes such as beta-pinene (4.27%), D-limonene (3.88%), and borneol (2.62%) are also present.

According to the literature data, the chemical profile of *R. tournefortii* de Noé growing in the eastern part of Morocco closely mirrors those previously reported in the literature, aligning with populations from Spain (Soriano Cano et al., 1993), Algeria (Bendif et al., 2017, 2018; Najar et al., 2020), and Morocco (Elamrani et al., 2000; Tahri et al., 2014). Indeed, these studies have demonstrated that the primary constituents of the essential oil are monoterpene camphor ketone, 1.8-cineole oxide, alpha-pinene, and camphene hydrocarbons. The proportion of the first component ranges from 17.3% to 39.27%, 16.9%–37.8%, and 26.7%–30.7% in Morocco, Algeria, and Spain, respectively. The composition of 1.8-cineole oxide varies from 2.24% to 6.73%, 1% to 17.4 %, and 6.9%–13.5% for the same countries. Regarding alpha-pinene, its content spans from 0.63% to 14.33%, 0.4%–17.8%, and 12.4%–17.3%, while camphene hydrocarbons range from 11.6% to 19.7%, 0.5%–15.6%, and 13.4%–16.3% in Morocco, Algeria, and Spain, respectively. In terms of the essential oil composition of the previously studied Algerian populations, research revealed a slightly distinct profile (Bensouici et al., 2020). This profile was characterized by its richness in 1.8-cineole and its relatively low content of camphor (1.455%) and camphene (1.21%).

Conversely, in the eastern region of Morocco, a different profile was observed, featuring minor proportions of 1.8-cineole (2.24%) and alpha-pinene (0.63%), with elevated levels of beta-pinene (14.72%) and gamma-terpinene (10.09%) (Tahri et al., 2014). Based on the information above, *Rosmarinus tournefortii* de Noé essential oil can be classified as the camphor chemotype, which is the sole chemotype identified thus far for this species. In contrast, various chemotypes of *Rosmarinus officinalis* L. have been distinguished based on the predominant component among alpha-pinene, 1.8-cineole, camphor, and verbenone (Bendif et al., 2017). The chemical profile of *Rosmarinus tournefortii* de Noé essential oil is determined by various factors such as harvest time, flowering stages, and geographical location (Sharifi-Rad et al., 2020). Among the most prominent balsamic periods when rosemary essential oils attain maximum concentration and quality are autumn and spring. Furthermore, stress conditions during these periods can lead to an improvement in the quality of the oil. The flowering stage affects the synthesis of secondary metabolites, resulting in variations in essential oil composition due to physiological changes (Li & Zidorn, 2022). In addition, geographical factors such as soil type, climate and altitude affect the accumulation of key compounds such as α-pinene, camphor

Table 2
Chemical profile of *R. tournefortii* de Noé essential oil.

Peak	Compounds	Retention time (min)	Area (%)
	Monoterpene hydrocarbons		**46.469**
1	Tricyclene	4.948	0.97
2	alpha-Thujene	5.003	0.30
3	alpha-Pinene	5.151	15.96
4	Camphene	5.405	15.14
5	Sabinene	5.770	0.09
6	beta-Pinene	5.847	4.27
7	beta-Myrcene	6.008	0.89
8	alpha-Phellandrene	6.273	0.33
9	4-Carene	6.474	0.86
10	beta-Cymene	6.618	2.31
11	D-Limonene	6.700	3.88
	Oxygenated monoterpenes		**51.21**
12	Eucalyptol	6.767	18.03
13	gamma-Terpinene	7.169	1.09
14	2-Carene	7.665	0.46
15	beta-Linalool	7.826	0.35
16	Fenchol	8.152	0.13
17	alpha-Campholenal	8.307	0.06
18	Camphor	8.703	25.49
19	Camphene hydrate	8.739	0.20
20	Borneol	8.990	2.62
21	4-Terpinenol	9.146	1.68
22	alpha-Terpineol	9.348	1.83
23	Bornyl acetate	10.790	0.59
24	alpha-Terpineol acetate	11.685	0.16
	Sesquiterpene hydrocarbons		**1.58**
25	Copaene	12.146	0.18
26	Methyleugenol	12.428	0.07
27	Caryophyllene	12.806	0.66
28	Copaene	13.530	0.21
29	alpha-Muurolene	13.832	0.09
30	gamma-Muurolene	14.046	0.13
31	delta-Cadinene	14.130	0.31
	Oxygenated sesquiterpenes		**0.66**
32	alpha-Bisabolol	16.107	0.66
	Total		**99.919**

and borneol, resulting in distinct chemical profiles (Formica et al., 2024). It is therefore the interaction of these factors that determines the quality and yield of rosemary essential oil.

3.5. *Harnessing nature defenders: antioxidant feats*

Plant polyphenols and essential oils, products of plant secondary metabolism, act as antioxidants, combating lipid oxidation and offering chemo-preventive benefits. The investigation assesses the antioxidant properties of wastewater obtained from *R. tournefortii* de Noé's steam distillation wastes and the identified essential oil as natural additives. To evaluate antioxidant activity, three established methods were used: radical quenching through ABTS and DPPH assays, as well as the Beta-carotene/linoleate model system. DPPH and ABTS are standard techniques for the analysis of free radical scavengers. Nevertheless, the non-physiological conditions of these methods are their drawbacks that may not be relevant to the biological issue. DPPH can be a source of error due to the high radical concentrations and ABTS may not be able to detect the effects of some compounds (Kusznierewicz et al., 2021). In order to overcome these limitations and validate the findings, the beta-carotene model system was incorporated. This method thus allows the antioxidant efficacy to be evaluated in a more realistic biological environment by checking the oxidation fading of beta-carotene in an emulsion, which might be biased by other components, yet, still, the antioxidant will be the main cause (Chen et al., 2020). Thus, the joint application of DPPH, ABTS, and beta-carotene procedures brings about comprehensive and validated antioxidant efficacy measurement.

The antioxidant capacities of the developed bioactive compounds are shown in Table 3, compared with those of ascorbic acid (AA). The remarkable performance of the wastewater by-products in all evaluation methods is particularly striking, characterized by IC50 scavenging inhibition values (0.046 ± 0.007, 0.082 ± 0.013, 2.45 ± 0.71 mg/mL for DPPH, ABTS, and the Beta-carotene/linoleate model system, respectively), signifying their higher antioxidant activity than essential oil (6.8 ± 0.15, 11.7 ± 1.26, 29.2 ± 1.25 mg/mL for DPPH, ABTS, and the Beta-carotene/linoleate model system, respectively). This alignment with literature data observed in *R. officinalis* L. species underscores the supremacy of the wastewater by-products (DPPH: 0.16,408 g TE/g; ABTS: 0.17,976 g TE/g) over the essential oil (DPPH: 3.70 ± 0.43 mg TE/g; ABTS: 32.05 ± 0.12 mg TE/g).

Table 3
Evaluating the antioxidant efficacy of *R. tournefortii* de Noé wastewater by-products and essential oil.

Sample	Assessing antioxidant Potency: IC50 as a Key Metric		
	DPPH (mg/mL)	ABTS (mg/mL)	Beta carotene/linoleate model system (mg/mL)
Essential oil	6.8 ± 0.15	11.7 ± 1.26	29.2 ± 1.25
Wastewater	0.046 ± 0.007	0.082 ± 0.013	2.45 ± 0.71
Ascorbic acid	0.01 ± 0.015	0.05 ± 0.008	1.82 ± 0.026

Moreover, to enhance the antioxidant capacities of wastewater by-products from rosemary, antioxidant assays were conducted, reporting values of 16.21 ± 2.1 μg/mL for DPPH (Celano et al., 2017). In addition, 1.8 and 2.2 μmol TE/100 mL for DPPH and ABTS, respectively, were discovered (de Elguea-Culebras et al., 2023). These observations stem from the complex tapestry of chemical compositions. HPLC-DAD and GC-MS analyses highlight that the wastewater by-products were mainly composed of phenolic acids, with hydroxycinnamic acids representing 50.9% and hydroxybenzoic acids comprising 32.97%, while the essential oil is characterized by a significant presence of oxygenated monoterpenes (51.21%) and monoterpene hydrocarbons (46.46%). This diversity opens the way to interesting explorations.

In addition, a study highlights that the antioxidant activity of hydroxycinnamic acids is associated with lower bond dissociation energy (BDE) values compared to hydroxybenzoic acids, which explains their greater reactivity (Olszowy, 2019). Here, the distinctive antioxidant prowess of phenolic acids unfolds due to the resonant interaction of phenolic hydroxyl groups attached to aromatic rings, facilitating the easy donation of hydrogen atoms to quench free radicals. On the other hand, while some oxygenated monoterpenes also carry hydroxyl groups, their antioxidant activity depends on complex factors such as hydroxyl group location, accompanying functional groups and overall chemical structure (Wojtunik et al., 2014). Although oxygenated monoterpenes with hydroxyl groups can confer antioxidant potential through hydrogen atom donation, they cannot achieve the same level of reactivity and efficacy as phenolic acids, renowned for their high antioxidant efficacy. In conclusion, the robust inhibitory effect of the water residue primarily stems from the presence of dominant hydroxycinnamic acids, namely caffeic and rosmarinic acids. On the other hand, the essential oil's reactivity is influenced by the prevalent oxygenated monoterpenes, specifically camphor and 1.8 cineole.

3.6. *Microbial battleground*

The antimicrobial activity analysis for *R. tournefortii* de Noé distillation wastewater by-products and its essential oil against bacteria, pathogenic fungi, and moulds is presented in Table 4, utilizing the agar diffusion method. The wastewater by-products exhibited moderate antibacterial inhibition, with inhibition zones ranging from 8.25 to 10.55 mm for gram-negative bacteria (*P. aeruginosa* and *E. coli*) and gram-positive bacteria (*L. innocua* and *S. aureus*). Additionally, *Candida albicans* displayed an inhibition zone of 9.45 mm. The wastewater by-products also showed remarkable inhibition against *Rhodotorula*

Table 4
Microbial inhibition zones of *R. tournefortii* de Noé wastewater by-products and essential oil.

Sample	Inhibition's diameter measurement (mm)						
	Bacteria gram -		Bacteria gram +		Yeasts		Moulds
	P. aeruginosa	*E. coli*	*L. innocua*	*S. aureus*	*Rhodotorula glutinis*	*Candida albicans*	*Geotrichum sp*
Wastewater	9.45 ± 0.63	10.55 ± 0.63	8.25 ± 0.35	9.6 ± 0.56	15.15 ± 1.20	9.45 ± 0.63	12.8 ± 0.28
Essential oil	–	15.25 ± 0.51	14.6 ± 0.22	12.34 ± 0.15	17.1 ± 0.19	14.1 ± 0.75	13.2 ± 0.1
C^+	22.75 ± 0.35	22.25 ± 0.21	22.3 ± 0.98	25.75 ± 0.35	22.6 ± 0.56	29.85 ± 1.06	23.1 ± 0.98

Note: C^+: Gentamicin and cycloheximide.

glutinis and *Geotrichum* sp., with inhibition zones of 15.15 mm and 12.8 mm, respectively. In contrast, the essential oil demonstrated significantly stronger inhibitory effects, with inhibition diameters of 15.25 mm for *E. coli*, 14.6 mm for *L. innocua*, 12.34 mm for *S. aureus*, 17.1 mm for *Rhodotorula glutinis*, 14.1 mm for *Candida albicans*, and 13.2 mm for *Geotrichum* sp. This is attributed to the high composition of volatile compounds, including eucalyptol (18.03%), camphor (25.49%), alpha-Pinene (15.96%), and camphene (15.14%), in the essential oil. This was followed by a disturbance in the plasma membrane structure of microbial cells that led to increased membrane permeability and consequently a loss in cytoplasm (Fig. 3). The nature of these compounds as volatile improved their diffusing capability through the microbial cells (Fan et al., 2023), hence improving their antimicrobial activity in relation to the non-volatile compounds present in the wastewater by-products.

Literature comparisons reveal similar findings. Significant antibacterial activity of rosemary essential oil has been reported, with inhibition zones ranging from 14.5 to 18 mm for *E. coli*, 7.5 mm for *P. aeruginosa*, and 13–16.5 mm for *K. pneumoniae*, as well as significant activity against gram-positive bacteria (Zaouali et al., 2010). Furthermore, the strong antimicrobial potential of rosemary essential oil against both gram-positive and gram-negative bacteria has also been confirmed (Olivas-Méndez et al., 2022), reinforcing its value as a natural antimicrobial agent. In contract, further studies indicate varied antimicrobial activities of rosemary by-products and extracts. For instance, moderating responses to *A. flavus* (29%) and *P. verrucosum* (28%) were observed in wastewater by-products from hydrodistillation of *R. officinalis* L. (de Elguea-Culebras et al., 2023). Additionally, negligible antimicrobial activity (MIC >250 mg/L) was reported for these by-products, suggesting limited efficacy of hydrophilic compounds (Luca et al., 2023). Similarly, minimal activity of rosemary extract against gram-negative bacteria, including *P. aeruginosa*, was found (Gonelimali et al., 2018; Lešnik et al., 2021). In contract, higher antifungal activity was observed in the hydrophilic fraction of rosemary and the efficacity of rosemary water extract against *Penicillium* sp. and *P. purpurogenum*, with inhibition ratios of 21% and 12 mm, respectively, was reported (Li et al., 2022; Othman et al., 2020).

To improve the antimicrobial property of *R. tournefortii* de Noé wastewater by-products, the chemical modification of the main phenolic compounds, namely protocatechuic acid-glycoside, caffeic acid, and rosmarinic acid, should be emphasized. These changes would, in principle, enhance their solubility, stability, and bioactivity to increase their antimicrobial efficiency compared to the base oil (Olszewska et al., 2020). Importantly, the mixture of essential oils may yield a synergistic effect that enhances their antimicrobial properties. However, these combinations must be subjected to thorough optimization and validation to guarantee that such alterations lead to improvements without any detrimental effects or reduction in efficacy (Li et al., 2022). Such prioritization of increasing antimicrobial effectiveness hereby underlines a substantial need for further investigation of compound optimization and their combinations. Formulation of such agents may hugely enhance the antimicrobial performance of the by-products, facilitating applications across a wide range. Studies on analogous molecules provide additional insights. For instance, flavone apigenin has been identified as a potential antibacterial and antifungal agent (Ono & Fujimori, 2011), while other compounds, such as flavan-3-ols,

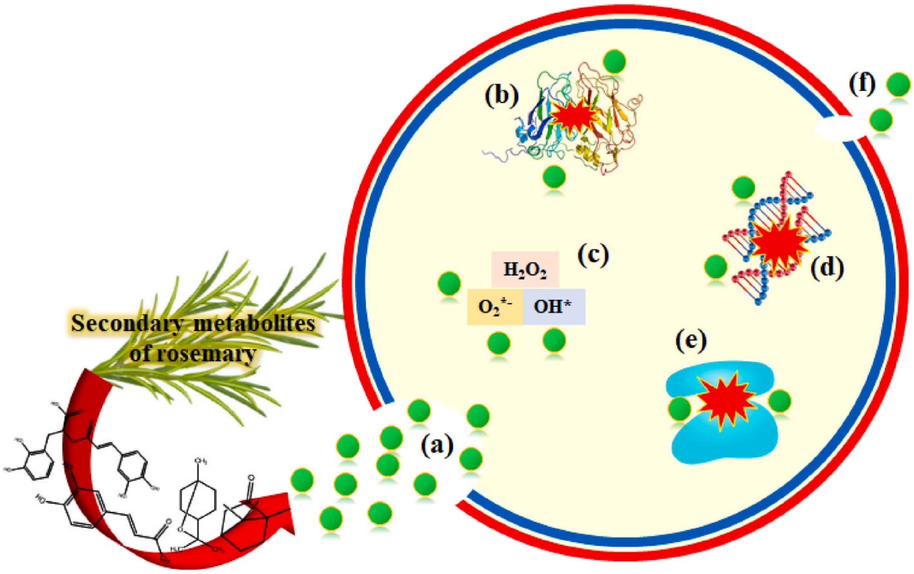

Fig. 3. A model showcases how secondary metabolites may exhibit potential antibacterial actions including; (a) Causing cell membrane disruption, resulting in the release of intracellular contents, (b) Engaging with proteins within the bacterial cells, (c) Generating reactive oxygen species (ROS), (d) Interacting with bacterial DNA, (e) Hindering ribosome function, which results in impaired protein synthesis and (f) Leading to the formation of membrane irregularities when exposed to secondary metabolites.

hydroxycinnamic and hydroxybenzoic acids, exhibit varying antimicrobial proprieties influenced by the presence of hydroxyl and methoxy functional groups (Asif et al., 2016; Jeong et al., 2014). These results shed light on the unique mechanisms of action of essential oils and point to possible routes for enhancing the activity of by-products from wastewater by targeted chemical modifications.

3.7. *Alpha-amylase inhibition*

Elevated oxidative stress is a key factor in diseases like type 2 diabetes mellitus (T2DM), affecting many worldwide (Bouakline et al., 2024). T2DM disrupts insulin, raising glucose levels. Current IDF estimates predict a rise to 783 million affected by 2045 (Ali et al., 2006). Managing hyperglycemia involves inhibiting enzymes like alpha-glucosidase and alpha-amylase. However, conventional drugs have reversible side effects (Cardullo et al., 2021). In the search for alternatives, researchers are turning to plant-based natural compounds due to their potential across culinary, pharmaceutical, and cosmetic applications (Bursal et al., 2020). Consequently, the study aims to evaluate the effect of wastewater by-products and essential oil on alpha-amylase inhibition, exploring their potential as safer alternatives. The results depicted in Fig. 4 reveal that both the wastewater by-products and the essential oil exhibit inhibitory effects lower than that of the reference drug, acarbose. However, upon closer examination, the wastewater by-products emerge as remarkably potent, showcasing inhibition ranging from 36.4% to 90.05%, thereby even surpassing the inhibitory potential of the essential oil. In contrast, the essential oil demonstrates comparatively weaker inhibitory activity, ranging from 7.21% to 54.2%, when contrasted with the potent acarbose. Noteworthy is the significantly higher concentration (1.88 ± 0.016 mg/mL) required by the essential oil to achieve a 50% reduction in enzyme activity, which is approximately five times greater than the potency of acarbose (IC50 = 0.48 ± 0.021 mg/mL). Intriguingly, the wastewater by-products emerge as an exceptional contender, requiring only 0.95 ± 0.022 mg/mL to achieve the same 50% enzyme reduction, highlighting its remarkable efficacy that is roughly twice as efficient as acarbose.

The high efficacy of the wastewater by-products may be attributed to their unique chemical composition, particularly high content of phenolic acids and flavonoids, some of which are recognized for their potential to be a strong inhibitor of enzymes (Şöhretoğlu & Sari, 2020). Compared to the major ingredients present in the essential oil, like 1.8 cineole and camphor, the hydroxycinnamic acids in these by-products have conjugated C=C double bonds and multiple hydroxyl (-OH) groups that are responsible for strong binding and inhibitory action at the active site of the enzyme (Kumar & Goel, 2019). The reason for this might be that the essential oil has reduced efficacy based on the difference in chemical composition. Phenolic acids such as caffeic acid, were reported to inhibit α-amylase quite effectively, with an IC50 of 0.4 mM. However, their activity could be reduced significantly by substitutions, such as the deletions of hydroxyl or methoxy groups in the structure (Sun et al., 2019). Flavonoids, on the other hand, are more potent α-amylase inhibitors with an IC50 value of 1.18 mg/mL and contribute majorly to the bioactivity of the herbal product (Irondi et al., 2017). In a similar connection, flavonoids without the -OCH3 substitution at the -OH are generally found to exhibit higher α-amylase inhibitory action (Giuberti et al., 2020).

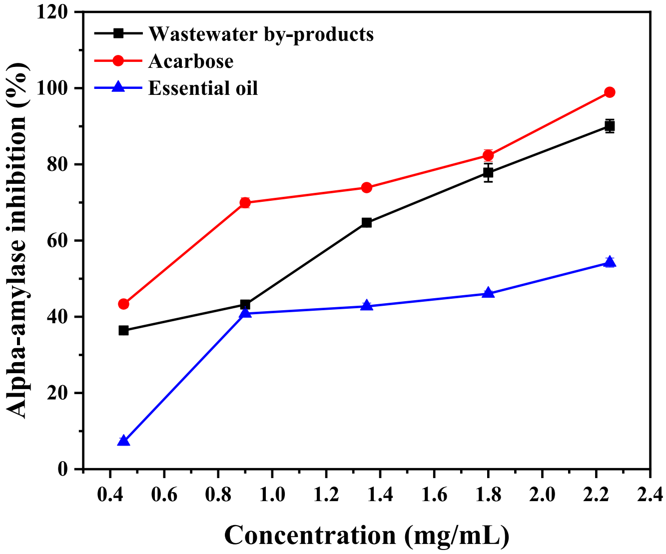

Fig. 4. Exploring alpha-amylase inhibition of *R. tournefortii* de Noé wastewater by-products and essential oil.

Integrating previously published data enriches our understanding of rosemary species' antidiabetic effects. For instance, conflicting results have been reported regarding *R. tournefortii* de Noé essential oil, with some researchers finding no antidiabetic effect as tested against α-Glucosidase (Bensouici et al., 2020). However, the essential oil from another species of rosemary, *R. Officinalis* L., attained the highest level of inhibition (0.39 mmol ACAE/g) for alpha-amylase, surpassing the wastewater by-products from steam distillation (Luca et al., 2023). This study found the wastewater by-products to have 0.06 mmol ACAE/g, which is six times lower in potency than the essential oil. Expanding the discussion to the application of bioactive molecules from rosemary, a study investigated the effect of rosemary water extract on α-amylase enzymes in yoghurt samples (Akan et al., 2022). The study observed an increase in α-amylase inhibitory activity during the storage period, reaching maximum values on day 28. The α-amylase inhibitory activity ranged from 26% to 37%, highlighting the efficacy of rosemary phenolic compounds.

The observed variations may only be ascribed to the unique chemical components of each rosemary species. In the essential oil of *R. Officinalis* L., 1.8 cineole emerges as the primary component, while *R. tournefortii* de Noé is dominated by camphor. This suggests that 1.8 cineole has a more pronounced effect compared to camphor (Ehrnhöfer-Ressler et al., 2013). The main compound in *R. Officinalis* L. wastewater by-products couldn't be detected, limiting analysis to the identified chemical composition. The prevalent family dominance leads to the detection of an equivalent presence of phenolic acids and flavonoids. In contrast, *R. tournefortii* de Noé wastewater by-products exhibit more than 80% of the total compounds as phenolic acids, which may justify the differences observed.

3.8. *Acute oral toxicity*

Understanding the acute oral toxicity of substances holds paramount importance in assessing their safety profile when consumed, thereby guiding regulatory decisions and shaping public health policies (Strickland et al., 2023). This critical research aids in determining safe dosage levels, potential adverse effects, and overall health risks, ensuring the well-being of both humans and animals. The examination of *R. tournefortii* Noé's steam distillation wastewater by-products and essential oil underscores the significance of such investigations in promoting health-conscious consumption. Through meticulous oral administration, the study encompassed a range of doses (0.5, 1, and 2 g/kg) and durations (from 48 h to 14 days), consistently revealing the absence of acute poisoning symptoms or fatalities among the mice subjects. This comprehensive two-week investigation closely monitored their eating habits, general behaviour, and body weights, reaffirming the lack of observable adverse effects.

Focusing on the essential oil, the literature review unveils an exploration into the toxicity of camphor, a prominent monoterpenic constituent of this oil. Previous studies have demonstrated its toxicity in female mice, with notable alterations in hepatic enzyme functions observed after administration at 300 mg/kg/day for 20 days (Dosoky &

Setzer, 2021). Additionally, the lethal dose range in humans has been reported to be between 5 and 20 g and 50–550 mg per kilogram (Wojtunik-Kulesza, 2022). Parallel research illustrated camphor's toxicity, revealing its efficacy in combating stored product beetles, yielding mortality rates ranging from 70% to 100% in *T. castaneum*, along with potent repellent qualities, showing repellency rates spanning 80%–100% (Obeng-Ofori et al., 1998). Despite camphor's prominence within our essential oil, our meticulous investigation showcases its inherent non-toxic nature. The pivotal role of camphor, constituting up to 26% of our essential oil, suggests the potential presence of other modulating compounds collectively contribute to the oil's diminished toxicity of the essential oil. This comparison draws parallels to the well-established non-toxicity of *R. Officinalis* L. essential oil (Alavi et al., 2021; Kiran & Prakash, 2015).

Meanwhile, the assessment of the wastewater by-products presents a counterpoint to prior research (Wang & Wang, 2021), which suggested acute oral toxicity in female Wistar rats and aged balb-c mice exposed to aqueous rosemary extract at 2000 mg/kg (Guldiken et al., 2021). Contrarily, our meticulous study recorded no mortality or any clinical indications of toxicity throughout the 14 day monitoring period. This finding is further supported by observations of no adverse effects on mice behaviour following the administration of rosemary in a polyherbal formulation at a dose of 5000 mg/kg (Abutaha et al., 2021). As the chemical constitution of the wastewater by-products from, it is notable that the wastewater from *Rosmarinus tournefortii* de Noé steam distillation remains relatively unexplored within the literature. Thus, a new course is charted by juxtaposing the discoveries with data derived from studies involving the wastewater by-products of *Rosmarinus tournefortii* de Noé, thereby capitalizing on shared compound components. This innovative approach illuminates our findings in a novel light and offers a profound context for interpretation.

3.9. *Challenges and future outlook*

3.9.1. *Innovative waste utilization*

The use of innovative waste utilization in the development of functional foods is a transformative approach that should respond to issues of both resource efficiency and environmental sustainability. Converting food processing by-products and waste streams into high-value, health-promoting ingredients has enormous economic and health benefits. This is key to the application of advanced extraction and reclamation technologies. Supercritical fluid extraction (SFE), enzymatic-assisted extraction (EAE), ultrasound-assisted extraction (UAE) and fermentation-assisted extraction (FAE) have become examples of such innovations. For example, grape pomace containing 15% of the phenolic compounds and 60% of dietary fibres may be valorized to increase the extraction yields by up to 30% over the conventional ones with SFE and UAE (Coelho et al., 2020). These improved yields keep the antioxidant characteristics of these molecules and hence maintain their suitability as dietary supplements and functional foods. The same is true for EAE and FAE in the upcycling of agro-industrial by-products from the residues of vegetables and spent coffee grounds. The EAE can enhance the extraction of phenolic compounds by as much as 50%, while spent coffee grounds with 5%–10% chlorogenic acids will be upcycled to prebiotics and other healthful compounds for the human diet (Vilas-Franquesa et al., 2024).

The next important development is the valorization of food-processing wastewater. Technologies such as membrane filtration have proven that more than 85.6% of proteins can be recovered from potato-starch wastewater, which will help to improve the nutritional value of foods (Lee & Stuckey, 2022). This nutrient-rich wastewater also makes an excellent medium for microalgae cultivation, resulting in the production of proteins and omega-3 fatty acids at a productivity level of 20–30 g/m^2/day. In addition to the above, the breakdown of complex organic compounds makes it easy to conversion of such compounds in the wastewater into bioactive ingredients, for instance, antioxidant peptides from whey proteins show up to 90% radical scavenging activity (Lee & Stuckey, 2022).

Indeed, the use of fruit and vegetable biowaste brings into the limelight the issue of waste valorization. Such biowastes, having a high content of phenol compounds and dietary fibres, can be subjected to treatment, for instance, water and acid extraction, for efficiencies of up to 19.89 g/g (Oliveira et al., 2023). In fact, strong antioxidant activities have been demonstrated in these recovered compounds, where over 90% of the free radicals are inhibited, hence accounting for savings in the production costs by about 20%. An example is the seafood waste from prawn and shrimp shells, which provide good sources of functional food ingredients using the process of enzymatic hydrolysis (Tkaczewska et al., 2024). Hydrolysates from the shells are rich in essential amino acids and have high antioxidant activity for fortified snacks and protein beverages. Stated differently, the combination of food processing by-products and waste streams with innovative state-of-the-art technologies creates value out of waste into food, improving its nutritive and functional characteristics (He et al., 2023). In this scenario, the development goes beyond critical issues in waste management and sustainable development, answering an emerging demand from the public that is showing increasing awareness and responsibility for healthy and green-oriented choices in food (Gupta et al., 2022). Continuous integration and development of these technologies will be essential in advancing sustainable food systems and further economic growth in the food industry.

3.9.2. *Circular economy practices*

The circular economy is a good foundation on which to scale up the sustainability goals in the development of functional food, given its economic and environmental benefits. The valorization of citrus by-products, from which high-value compounds are recovered, goes on to include flavanones and essential oils. This allows the creation of up to 22.9 mg/g of hesperidin and over 80% oil from citrus peels within an hour, thus leaving very low waste of around 80% of processes for citrus fruits (Panwar et al., 2021). In the sector of dairying, the model of the circular economy is perfectly aligned with the recommendations in the Sustainable Development Goals by reimagining the agro-industrial side streams, for example, grape skins and seeds left over from wine production increase the content of fibre and antioxidants in dairy products by 25%–30% of the side streams (Granato et al., 2022). The process hereby upholds SDG 2: zero hunger and SDG 3: good health and well-being, directly aligning with SDG 12: responsible production and consumption. There is an additional potential of reducing food wastage by 30% with effective utilization in dairy processing, hence resulting in increased profitability of 10%–15% for dairy companies.

These circular business models underpin the need for technical innovation and flexible logistics, and often require co-investment in R&D. The economic feasibility of such business models relies on the competitiveness of the produced bio-based products; the investment in the early-up phase is usually 30%–50% of the overall project costs (Donner et al., 2021). Therefore, public subsidies are needed in the early stages to reduce such costs, while close collaboration with research organizations and local stakeholders can increase operational efficiency by 20%–30%. In the aquaculture sector, more than in any other sphere, valorization of by-products, especially within regions like Galicia, increases economic yield by 30% through the recovery of valuable biomolecules, such as collagen and omega-3 fatty acid, from fish waste (Fraga-Corral et al., 2022). However, there is a high cost in facing the regulations and approvals and the time needed to be realized. These challenges involve issuing affected policy frameworks and the need for enhanced stakeholder commitment if the full potential of circular bio-economy practices is to be exploited. Food waste biorefineries show great expectations to gain economic and environmental benefits (Pal & Suresh, 2016). Although many valorization pathways are still laboratory-scale, the scaling of such processes will bring significant reductions in landfill utilization, lower greenhouse gas emissions, and sustain resource management. For instance, estimates are approximately \$10.25 a ton for some landfill substrates and transportation costs may weigh heavily in determining profitability (Caldeira et al., 2020). Therefore, strong logistical platforms and life cycle assessments need to be developed to attain efficient collection and processing at the same time.

Valorization of vegetable and fruit wastes offers opportunities coupled with challenges. Reduction of 30% of lettuce waste through anaerobic digestion and novel extraction methodologies might decrease about 72 tons per year in CO_2-equivalent emissions. High initial investment and advanced technologies requiring energy could act as a barrier (Plazzotta et al., 2020). Therefore, the economic feasibility issues must be resolved to enable the wide diffusion of FVW valorization practices. In summary, circular economy applied to functional food development is more sustainable, innovative and offers economic growth. Further research investment, enabling policies, and collaboration among the chain stakeholders will be necessary to have food system transformation toward more sustainability and resilience in overcoming the challenges identified above, as well as to capture these benefits.

4. Conclusion

This study highlights the exceptional promise of *Rosmarinus tournefortii* de Noé wastewater by-products, emphasizing their profound utility and superior advantages compared to essential oil as the principal product. Through comprehensive analysis, a wealth of potential applications emerges, extending beyond conventional boundaries. ATR-FTIR analysis reveals that the essential oil contains terpenoids, while the wastewater shows phenolic acids and other functional groups. The determination of camphor and 1,8-cineole was conducted using GC-MS, while caffeic acid and rosmarinic acid were quantified by HPLC-DAD. Investigations into the antioxidant potential of both the essential oil and wastewater by-products demonstrated the wastewater's exceptional ability to combat free radicals and shield against oxidative damage. This is evident in the impressive IC50 values (0.046 ± 0.007 mg/mL for DPPH and 0.082 ± 0.013 mg/mL for ABTS), showcasing its superior antioxidant capabilities compared to the essential oil. Additionally, the wastewater's remarkable antimicrobial efficacy against various bacteria, particularly *Rhodotorula glutinis*, underscores its practical utility in antimicrobial applications. The wastewater exhibited moderate antibacterial inhibition with diameters of 8.25–10.55 mm against gram-negative (*P. aeruginosa* and *E. coli*) and gram-positive bacteria (*L. innocua* and *S. aureus*), as well as a 9.45 mm inhibition zone against *Candida albicans*. In contrast, the essential oil showed stronger inhibitory effects, with inhibition diameters up to 17.1 mm for *Rhodotorula glutinis*. A significant finding is the wastewater's substantial inhibition of pancreatic α-amylase (IC50 = 0.48 ± 0.021 mg/mL), a key enzyme relevant to diabetes management. These results open wide the possibility for the exploitation of wastewater by-products in functional food development, with great potential based on their potent antioxidant and antimicrobial activities. In this way, they could be used as functional ingredients and enhance food quality while at the same time prolonging its shelf life. Examples of practical applications include the use in food packaging material formulations or the development of preservative systems, or natural additives in processed foods. Such applications not only encourage the sustainable production of food but also contribute to low-cost waste management. Their safety, efficacy and cost-reducing ability underline their economic exploitability into functional food products. These by-products are turning such waste into valuable ingredients, therefore contributing to both environmental and economic challenges by providing practical innovative solutions beneficial to both the food and health sectors.

CRediT authorship contribution statement

Imane Ziani: Writing – original draft, Visualization, Investigation, Data curation, Conceptualization. **Hamza Bouakline:** Writing – original draft, Visualization, Investigation. **Saliha Bouknana:** Writing – original draft, Resources, Formal analysis. **Nour Eddine Bentouhami:** Writing – review & editing, Software, Methodology. **Farooq Sher:** Writing – review & editing, Project administration, Funding acquisition. **Sabah Ansar:** Writing – review & editing, Funding acquisition. **Marie-Laure Fauconnier:** Writing – review & editing, Supervision, Resources, Funding acquisition. **Mohamed Bnouham:** Writing – review & editing, Validation, Resources. **Ali El Bachiri:** Writing – original draft, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

Data will be made available on request.

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