*Capparis spinosa*:A Rich Source of Phenolic Compounds - A Comprehensive Review of Its Phytochemistry, Health Benefits, and Biotechnological Applications

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# Abstract

# Caper (*Capparis spinosa*) is a plant of significant socio-economic importance in the Mediterranean region which is traditionally used to fight various metabolic diseases. It has indeed long been recognized for its medicinal properties, notably attributed to its rich nutritional content and potent antioxidant activity due to phenolic compounds and other secondary metabolites. However, the commercial production of relevant secondary metabolites requires innovative approaches improving the biosynthesis of these metabolites to fulfill the industrial demand and mitigate the overexploitation of natural resources. For this end, different techniques such as cell suspension culture, hairy roots culture, biotic and abiotic elicitors supply as well as genetic engineering could be used to enhance the production of caper-derived secondary metabolites. In addition, omics tools including genomics, transcriptomics, metabolomics and proteomics can help to elucidate the biosynthetic pathway and altering the production of targeted metabolites. While this review first highlights the phytochemistry, ethno-pharmacological uses, and biological activities of caper, it also discusses the significance of *in vitro* culture systems, omics tools and metabolic engineering approaches to improve the production of caper-derived bioactive compounds.

# Keywords: *Capparis spinosa*, secondary metabolites, health benefits, biotechnological applications, *in vitro* culture

# Graphical Abstract

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1. Introduction

*Capparis spinosa* (*C. spinosa*) is a perennial thorny bush belonging to the *Capparaceae* family. The genus *Capparis* comprises approximately 150 species, with *C. spinosa* being represented by 12 subspecies (POWO, 2021). Taxonomic revisions have been conducted multiple times (Fici, 2017, 2015, 2014; Inocencio et al., 2006), but the precise taxonomic classification of this genus remains a subject of debate. *C. spinosa*, whichis predominantly found in the Mediterranean area (Fici, 2014), exhibits plesiomorphic traits (Fici, 2001) and significant heterogeneity (Mahmodi et al., 2022). Due to its numerous therapeutic properties, *C. spinosa* holds a primary place in traditional medicine, particularly in the treatment of diabetes (Bousta et al., 2014; Hachi et al., 2016; Kachmar et al., 2021; Karous et al., 2021; Katiri et al., 2017) and other ailments such as fever (Karous et al., 2021; Tlili et al., 2011a), digestive disorders (Mahboubi and Mahboubi, 2014; Motti, 2021), rheumatism, inflammatory disorders (Darwish and Aburjai, 2010; Ramdane et al., 2015), hypertension (Sher and Alyemeni, 2010; Tahraoui et al., 2007), anti-hemorrhoidal effects (Altundag and Ozturk, 2011; Mahboubi and Mahboubi, 2014), cancer (Jaradat et al., 2016; Moghadamnia et al., 2019; Taibi et al., 2021), and renal diseases (Ramdane et al., 2015).

Phytochemical studies have revealed that *C. spinosa* is rich in bioactive substances, including tetraterpenes, alkaloids, polyphenols, and fatty acids (Alkhaibari and Alanazi, 2022; Al-Tamimi et al., 2019; Mollica et al., 2019; Ouhammou et al., 2022; Saberi et al., 2022; Stefanucci et al., 2018; Tlili et al., 2011a, 2010; Yahia et al., 2020). Furthermore, pharmacological investigations have demonstrated its wide array of biological effects, and notably antioxidant activity, immune system modulation, and health benefits (Assadi et al., 2021; Darwish and Aburjai, 2010; Grimalt et al., 2022; Kalantari et al., 2018; Kirkan et al., 2021; Ouhammou et al., 2022; Rad et al., 2021; Rajhi et al., 2021), antidiabetic potential (Assadi et al., 2021; Hachi et al., 2016; Saleem et al., 2021; Vahid et al., 2017; Wojdyło et al., 2019), antibacterial activity (Di Lodovico et al., 2022; Rajhi et al., 2019; Ramdani et al., 2020; Zhu et al., 2022), anti-inflammatory effects (El Azhary et al., 2017; Hamuti et al., 2017; Kernouf et al., 2018; Rahimi et al., 2020; Zhou et al., 2010), cytotoxicity (Alkhaibari and Alanazi, 2022; Rakhshandeh et al., 2021; Saleem et al., 2021), gastroprotective properties (Al-Zubaidy and Khalil, 2022), neuroprotective effects (Tlili et al., 2017), as well as insecticidal and larval development inhibitory actions (Alkhaibari and Alanazi, 2022; Yan et al., 2022).

The objective of this review is to comprehensively explore the chemistry, pharmacology, and biotechnology of *C. spinosa* providing insights into potential avenues for development and guiding future research.

# 2. Botanical description

*C. spinosa* is a perennial bush, a creeping dicotyledon that can reach heights of up to 1 meter (Legua et al., 2013). The plant bears deciduous or semi-evergreen leaves, which are simple, alternate, leathery, oval, or elliptical in shape, measuring 2-5 cm in length. The leaves have a mucronate, obtuse, or emarginate apex and a rounded base, displaying an intense green color (Peter, 2006). The adaxial surface is glabrous or glabrescent, while the abaxial surface can be either glabrous or grayish pubescent (Fici, 2017). The leaf veins are not prominent (Inocencio et al., 2006), and the petiole is short, ranging from 0 to 2 cm, and can be grooved or entire (Chedraoui et al., 2017).

The stipular spines are pale yellow or orange, curved and rarely straight, mostly base-decurrent, narrowed, setaceous or spreading, often hooked and divaricate, and sometimes weakly developed or absent (Inocencio et al., 2006; Sozzi, 2001). The floral buds are acute, and the floral pedicels are thick, measuring 5 to 6.5 cm long (Inocencio et al., 2006). The flowers are hermaphroditic, 5-7 cm in diameter, solitary and axillary, scented (Kantsa et al., 2023), and noctiflorous. They are slightly zygomorphic, with 4 white or pinkish-white petals and 4 purplish, oblong, or oval sepals. The sepals are glabrous to pubescent on the outside, and the posterior part is more or less saccate (Fici, 2014; Sozzi, 2001).

The stamens are multiple, glabrous, and the filament length can extend up to 5 cm with a pink-purple tip. The purple anthers are nearly 2 mm long with acute apices (Fici, 2014; Sozzi, 2001). The gynophore measures 2 to 5 cm in length and might be pubescent at the base. The ovary is oval, ellipsoid, or cylindrical, consisting of several carpels, and the stigma is sessile or capitate (Decraene and Smets, 1997; Fici, 2014). The stems of *C. spinosa* are thick and short, and the twigs can be tortuous or straight, and may or may not have single hairs (Sozzi, 2001). The roots can reach lengths of 6-10 m (Sozzi et al., 2012).

The fruit is ellipsoidal, obovate, or oblong, and usually dehiscent with a thin, ribbed pericarp, containing red or greenish-yellow pulp (Fici, 2014). After ripening, the fruit splits open, revealing a reniform seed within a pale crimson mass, measuring between 3 and 4 mm wide (Melgarejo et al., 2009). The fruit can contain up to 500 seeds (Legua et al., 2013).

# Taxonomy, geographic distribution and ecological factors

Caper (*C. spinosa*) belongs to the *Capparis* taxonomic genus, which is a member of the *Capparidaceae* family (Inocencio et al., 2006), and which was originally defined by Carolus Linnaeus in his major work "*Species Plantarum*" published in 1753. Taxonomic classifications within the genus *Capparis* reflect its taxonomic complexity (Fici, 2015, 2014; Tutin et al., 1976; Zohary, 1960). Several researchers have conducted studies on genetic diversity, demonstrating a marked degree of polymorphism and genetic variation within this genus (Ahmadi and Saeidi, 2018; Aichi-Yousfi et al., 2016; Bourhim et al., 2021; Chibani et al., 2017; Gristina et al., 2014; Mahmodi et al., 2022; Rhimi et al., 2019; Saifi et al., 2011; Wang et al., 2016). The *C. spinosa* genome encompasses a total extent of 274.53 Mb, containing 21.577 protein-coding genes (Wang et al., 2022). The chloroplast genome, spanning 157.728 bp, contains 136 genes, of which 80 are protein-coding and 35 are RNA genes (Alzahrani et al., 2021).

*C. spinosa* is ubiquitous in the Mediterranean region, as well as in the Middle East, Central and Southwest Asia, the Pacific islands and Australia (Fig. 1) (Fici, 2015; Fici et al., 2022; Inocencio et al., 2006; Najafian et al., 2021; Özcan, 1999; Zarei et al., 2021). Among these, Morocco stands out as a key global player in the production and export of capers (Kdimy et al., 2022). Wild plants of caper have indeed shown a high resistance to the unfavorable conditions in the Mediterranean area (Abu-Shama, 2019) as well as to current climate disturbances and future projections (Ashraf et al., 2018). It should be noted that while the cultivation of *C. spinosa* is expanding within the Mediterranean region and has achieved significant success in several countries (Grimalt et al., 2022; Infantino et al., 2007), caper trade and traditional use remain heavily dependent on wild plant resources (Sottile et al., 2021; Tlili et al., 2011a).This dependence presents a risk of overexploitation of resources, which could be insufficient to meet market requirements for these plant species.

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**Fig. 1.** Distribution of *Capparis spinosa*. Occurrence data were collected from the Global Biodiversity Information Facility, which counts 10 408 occurrence points corresponding to 13 intraspecific *C. spinosa*. DOIs: https://doi.org/10.15468/dl.8ksrdy.

1. **Ethnobotanical studies**

As presented in Table 1, ethnobotanical studies have highlighted the widespread use of different parts of the *C. spinosa* plantin traditional medicine in the Mediterranean region, making it one of the most well-known plants in the *Capparidaceae* family (Alzahrani et al., 2021; Tlili et al., 2017). In Moroccan traditions, the plant is extensively used to treat diabetes (Bousta et al., 2014; Eddouks et al., 2002; Hachi et al., 2016; Jamila and Mostafa, 2014; Jouad et al., 2001; Katiri et al., 2017; Tahraoui et al., 2007; Ziyyat et al., 1997). Notably, the fruit has been employed as a decoction for this purpose in various regions of Morocco (Hachi et al., 2016; Katiri et al., 2017; Ziyyat et al., 1997), while the aerial part is used as an infusion for the same therapeutic purpose in the Central Middle Atlas region (Hachi et al., 2016). Additionally, in the Errachidia province of Morocco, flowers and fruits are prepared in maceration as remedies for diabetes and hypertension (Tahraoui et al., 2007), while in the Tarfaya region, decoctions are used for urolithiasis (Idm’hand et al., 2020). In the Taounate region of Northern Morocco, flowers and fruits are macerated to treat rheumatism (El-Hilaly et al., 2003). Moreover, fruits in decoction and/or powder are utilized in South-East of Morocco to address female infertility and menstrual disorders (Eddouks et al., 2020). In Southern Tunisia (Ouled Dabbeb) leaves and/or buds are traditionally used in decoction for diabetes, fever reduction, and diuretic effects (Karous et al., 2021). In Algeria, the population employs the roots, fruits, and flowers of *C. spinosa* in powder and/or decoction as anti-cancer agents and for the treatment of prostate enlargement (Taibi et al., 2021, 2020). In the Hoggar region of Algeria, aerial parts and leaves are used in decoctions, cataplasms, and/or infusions to combat rheumatism and renal diseases (Ramdane et al., 2015). Furthermore, in the Tassili N'ajjer region of Algeria, leaves are prepared in cataplasm form and used as remedies for rheumatism and headaches (Hammiche and Maiza, 2006). In Jordan, roots are employed in poultices to alleviate rheumatism (Darwish and Aburjai, 2010).

The leaf and root of the plant are also utilized as cataplasm for arthritis by the people of Jordan (Aburjai et al., 2007; Lev and Amar, 2002). In Turkey's Izmir province, the decoction of caper buds is employed to treat splenitis, hepatitis, diarrhea, and gastric ulcers (Ugulu et al., 2009). In Liguria, Italy, the buds are used in decoction to alleviate inflammation of the mouth (Cornara et al., 2009). In Southern Italy, buds and fruits are exploited for flavoring foods (Mattalia et al., 2020; Mautone et al., 2019). In Saudi Arabia, buds and leaves are used in decoctions to alleviate cold symptoms (Sher and Alyemeni, 2010). Other ethnobotanical studies suggest that *C. spinosa* can be used as a laxative (Singh and Lal, 2008), against respiratory infections (Mughal, 2008; Ouelbani et al., 2016), for skin problems (Ouelbani et al., 2016; Sargin et al., 2015), liver disorders, sexual dysfunction (Singh and Lal, 2008), and even against snakebites (Hosseini et al., 2022).

**Table 1**. Ethnomedicinal uses of *Capparis spinosa*.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Traditional applications | Research region | Part used | Method of preparation | References |
| Hypoglycemic | Oriental, Morocco | Fr | Decoction | (Kahouadji, 1995) |
| Diabetes | Northeastern, Morocco | Se | Powder | (Ziyyat et al., 1997) |
| Diabetes | Taroudant Province, Morocco | Fr | Decoction | (Katiri et al., 2017) |
| Diabetes | Fez–Boulemane, Morocco | Fr | N. R | (Jouad et al., 2001) |
| Hypertension, diabetes | Errachidia province, Morocco | Fl, Fr | Maceration | (Tahraoui et al., 2007) |
| Diabetes | Central Middle Atlas region, Morocco | Fr, Ap | Decoction/infusion | (Bousta et al., 2014; Hachi et al., 2016) |
| Diabetes, rheumatic pain, respiratory problems, dermatological affections, digestive tract disorders, helminthiasis, and kidney stones | Taza city region, Morocco. | Fr | Powder | (Kachmar et al., 2021) |
| Urolithiasis | Tarfaya, Morocco | Fr | Decoction | (Idm’hand et al., 2020) |
| Rheumatism | Taounate, Morocco | Fl, Fr | Maceration | (El-Hilaly et al., 2003) |
| Lymphoma | Morocco | Fr | Powder | (Kabbaj et al., 2012) |
| Female infertility, menstrual disorders | Southeast, Morocco | Fr | Decoction/ powder | (Eddouks et al., 2020) |
| Ease fever, diuretic, diabetes | Ouled Dabbeb, Southern Tunisia | Lv, bd | Decoction | (Karous et al., 2021) |
| Rheumatism, kidney diseases | Hoggar, Algeria | Lv, Ap | Decoction, poultice, infusion | (Ramdane et al., 2015) |
| Migraine, headache, joint pain | El Kantara, Algeria | Lv | Cataplasm | (Mechaala et al., 2022) |
| Cancers, prostate enlargement, breast, bone, prostate | Algeria | Fl, Fr, Rt | Powder, decoction | (Taibi et al., 2021, 2020) |
| Rheumatism, headache | Tassili N’ajjer, Algeria | Lv | Poultice | (Hammiche and Maiza, 2006) |
| Hypertension, diabetes | Saudi Arabia | Fr | Powder | (Sher and Alyemeni, 2010) |
| Cold | Bd, Lv | Decoction |
| Arthritis, painkillers, women’s barrenness | Jordan | Rt | N. R | (Lev and Amar, 2002) |
| Arthritis | Jordan | Lv | Poultice | (Aburjai et al., 2007) |
| Rheumatic | Jordan | Rt | Poultice | (Darwish and Aburjai, 2010) |
| Splenitis, hepatitis, diarrhea, gastric ulcer | Izmir province, Turkey | Buds | Decoction | (Ugulu et al., 2009) |
| Headache, anti-hemorrhoidal | East Anatolia, Turkey | Fr | Decoction, internal | (Altundag and Ozturk, 2011) |
| Emmenagogue, suppurating wound antiseptic | Hatay Province, Turkey | Fl, Lv | Infusion, paste | (Güzel et al., 2015) |
| Eczema, fungal itches | Manisa, Turkey | Bd, Fr, Rt | Decoction, eaten raw, mash | (Sargin et al., 2015) |
| Aromatize foods | South Italy | Bd | N. R | (Mautone et al., 2019) |
| Mouth inflammation | Liguria, Italy | Bd | Decoction | (Cornara et al., 2009) |
| Aromatize foods | Calabria, Southern Italy | Fr | Seasoning | (Mattalia et al., 2020) |
| Digestive | Italy | Buds | N. R | (Motti, 2021) |
| Laxative | Iran | Rt, Bd | Cataplasm | (Mehrnia et al., 2021) |
| Respiratory infections | Pakistan | Rt, Lv, Fr | N. R | (Mughal, 2008) |
| Mental disorder, tubercular glands, enlarged spleen | Northern Areas of Pakistan | Rt | N. R | (Afzal et al., 2009) |
| Liver disorder, sexual dysfunction | Western Himalaya | Sh, Fr | Powder, ripe fruit | (Singh and Lal, 2008) |
| Deafness | Golan Heights, West Bank | Rt | Oil | (Said et al., 2002) |
| Snake bite | Sarvabad, Kurdistan province, Iran | Fr | Cataplasm | (Hosseini et al., 2022) |

Ap: Aerial parts, Bd: Buds, Fl: Flowers, Fr: Fruits, Lv: Leaves, Rt: Roots, Se: Seeds, Sh: Shoots; N. R: Not reported.

**5. Nutritional value**

To date, *C. spinosa* remains a popular culinary plant in Mediterranean cuisine. Its various parts, including fruits, seeds, and flower buds are widely used in fermentation processes and as garnishes for salads, pizzas, and pasta, or as food supplements (Bacchetti et al., 2022; Tlili et al., 2017, 2011a). Caper berries have been reported to be a significant source of carbohydrates (5%), dietary components (3%), protein (2%), and fat (0.9%), with a moderate content of vitamin C (Allaith, 2016; Tlili et al., 2011b). Indeed, caper seeds contain a variety of nutritional components, including proteins, lipids, glycolipids, phospholipids, and carotenoids (El Amri et al., 2019; Yuldasheva et al., 2008). Additionally, *C. spinosa* seed oil is very rich in linoleic and oleic acids (Bodaghzadeh et al., 2021; Özcan et al., 2012) while other fatty acids, such as palmitic, palmitoleic, stearic, linolenic, and myristic acids, are also found in reasonable proportions (Akgül and Özcan, 1999; Bodaghzadeh et al., 2021; Giuffrida et al., 2002; Haciseferoğullari et al., 2011). Moreover, *C. spinosa* seed oil contains significant amounts of total sterols ranging from 4.9 to 10.0 g/kg, with sitosterol being the principal component, along with notable content of campesterol, stigmasterol, and delta-5-avenasterol (Matthäus and Özcan, 2005). Analyses have also confirmed that *C. spinosa* is rich in macro and oligo-elements (Aliyazicioglu et al., 2013; Duman and Özcan, 2014; Giuffrida et al., 2002). For instance, Aliyazicioglu et al. (2013) showed that mineral contents in *C. spinosa* varied as follows: Al, P, S, K, and Ca ranged from 0.5% to 5%, while Fe and Zn contents were 520 ppm and 250 ppm, respectively, with other elements exhibiting varying concentrations, including Cl (94 ppm), Ti (55 ppm), Mn (70 ppm), Ni (24 ppm), Cu (88 ppm), Br (11 ppm), Rb (79 ppm), Sr (40 ppm), and Pb (5 ppm). In another investigation, Grimalt et al. (2022) reported that young caper shoots have excellent biochemical characteristics, surpassing caper flower buds and fruits in nutritional value.

**6.** **Phytochemistry**

As with all medicinal plants, *C. spinosa* is rich in biologically active components including polyphenols, alkaloids and fatty acids (Table 2, Fig. 2 and Fig. 3). Some of these compounds, such as rutin, quercetin, kaempferol, and their derivatives, have drawn significant attention due to their therapeutic capacities and diverse chemical structures (Kianersi et al., 2020a; Shahrajabian et al., 2021).

For instance, Rajhi et al. (2019) demonstrated that methanolic extracts obtained by maceration from various parts of *C. spinosa* in Tunisia are rich in phenolic components, flavonoids, and tannins. Generally, the leave extract had the highest phenolic compound content with total phenolic content (77.7 mg gallic acid equivalent (GAE)/g of dry weight(DW)), flavonoids (39.6 mg quercetin equivalent (QE)/g DW), tannins (11.4 mg catechin equivalent (CE) /g DW), and anthocyanins (0.33 mg cyanidin-3-glucoside Eq/kg DW), while the lowest content was found in the roots (Rajhi et al., 2019). On the other hand, Safarzaei et al. (2020) revealed that ultrasound-assisted extraction of *C. spinosa* roots resulted in a total phenolic content of 14.96 mg/g with an aqueous solvent and 17.24 mg/g with an alcoholic solvent.

Various extracts of *C. spinosa* buds from Morocco, Italy, and Turkey showed differences in total phenolic and flavonoid compounds, ranging from 24.17 and 9.63 mg/g extract to 23.50 and 5.02 mg/g extract, respectively. Soxhlet extraction demonstrated higher phenolic compounds compared to decoction and microwave methods, with Moroccan buds exhibiting the highest level of this component (24.17 mg/g extract). Rutin was the predominant component in *C. spinosa* extracts, ranging from 96.42 to 7.36 μg/mg extract in the different extraction techniques (Stefanucci et al., 2018). Similarly, studies by Mollica et al. (2019) revealed that Soxhlet extract (17.96 mg GAE/g extract) of *C. spinosa* buds from Italy possessed a higher concentration of bioactive components compared to microwave and decoction extracts (14.59 mg GAE/g extract and 14.27 mg GAE/g extract, respectively). Rutin was also the major phenolic component with all extraction methods, with the highest content found in the microwave extract, at 10 μg/mg of extract.

In the work of Yahia et al. (2020), maceration aqueous extraction of *C. spinosa* leaves from five sites in the south of Tunisia exhibited the richest content of polyphenolic acids. The LC-MS analysis identified 7 phenolic acids, including quinic acid (1095.69 mg/g), gallic acid (185 mg/g), crypto-chlorogenic acid (122.5 mg/g), protocatechuic acid (32.11 mg/g), and *p*-coumaric, *trans*-ferulic, and syringic acids (27.11 mg/g, 7.55 mg/g, and 6.17 mg/g, respectively); salviolinic acid (99.87 mg/g) was exclusively found in the extract obtained through ultrasound-assisted extraction and catechin was the most abundant flavonoid in all extracts, with concentrations of 2269, 1991, and 1304 mg/g extract in maceration, reflux, and ultrasonic extracts, respectively. Other flavonoids detected included epicatechin (211.9 mg/g), rutin (20.37 mg/g), cynaroside (10.88 mg/g), quercetrin (13.80 mg/g), quercetin (68.92 mg/g), kaempferol (4.80 mg/g), and naringenin (3.12 mg/g) (Yahia et al., 2020).

Phytochemical analysis of caper aerial parts revealed the presence of hesperidin (72.93 mg/g), quercetin (1.34 mg/g), hyperoside (1.23 mg/g), and 4-hydroxybenzoic acid (0.92 mg/g) (Kirkan et al., 2021). Moreover, HPLC analysis of hydroalcoholic extracts showed that rutin and quercetin were the main components of Iranian *C. spinosa.* In leaves, the rutin content was 16.94 mg/g, and quercetin was 0.91 mg/g fresh weight (FW), while in fruits, the content was 1.02 mg/g for rutin and 0.1 mg/g FW for quercetin (Mohebali et al., 2018). Also, in Egypt, the HPLC analysis showed that quercetin and kaempferol were the main flavonoids for ethanolic extracts of caper buds, fruits, and leaves (Abu-Shama, 2019). Another study showed that the total phenolic compounds of caper flower buds varied depending on genotype and flower growth stage, with the nonpareil stage characterized by the most significant polyphenol content compared to other stages (Wojdyło et al., 2019). Grimalt et al. (2018) demonstrated that the stages of caper fruit development could affect the contents of total phenols and flavonoid compounds, with the thick stage being preferable for consumption.

In fact, investigations on commercial caper fruits from the Mediterranean (Tunisia, Morocco, Turkey, and Spain) indicated that the contents of phenolic compounds ranged from 1.15 to 2.24 g/100 g FW, while the contents of rutin varied from 0.15 to 0.73 g/100 g FW, and the total tocopherol content ranged from 0.7 to 2.55 mg/100 g FW. Additionally, all samples were found to contain an appreciable quantity of vitamin C, with the highest content of β-carotene recorded at 0.81 g/100 g FW (Tlili et al., 2011b). However, the fermentation treatment of caper buds and berries induced a decrease in some phenolic and flavonoid components, with derivatives of quercetin and kaempferol becoming the principal components after fermentation (Aksay et al., 2021; Jiménez-López et al., 2018; Lo Bosco et al., 2019). HPLC-DAD analysis of salt-fermented caper flower buds collected from different harvesting sites revealed significant variation in kaempferol and quercetin derivatives, with values ranging from 6.46 to 267.93 mg kaempferol equivalent/g FW and from 22.39 to 367.14 mg quercetin equivalent/g FW (Lo Bosco et al., 2019). Sonmezdag et al. (2019) showed that the fermentation process qualitatively and quantitatively modified total aroma and phenolic compositions, with the latter being lowered by 66% and 78%, respectively, during the fermentation process. GC-MS results for aroma compounds obtained from fresh and fermented caper samples showed a decrease from 62.616 µg/kg to 21.471 µg/kg (Sonmezdag et al., 2019).

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**Fig. 2.** Chemical structures of abundant *C. spinosa* components: a structural view of phenolic acids, flavonoids, and organic acids.

Furthermore, the content of the essential oils extracted from 10 caper fruits in Iran varied between 0.55 to 1.46%. The main components revealed by GC-MS were isopropyl isothiocyanate, methyl sulfonyl heptyl isothiocyanate, butyl isothiocyanate, γ-terpinene, and thymol (Alipour et al., 2021). A complete volatile compound profile of different parts of *C. spinosa* from southeastern Spain was realized using HS-SPME-GC/MS. A total of 43 volatile compounds were identified in caper shoots, while flowers contained 32 compounds, flower buds, leaves, and fruit contained 18, 10, and 6 volatile compounds, respectively, with isocyanates being the dominant component in all samples (Grimalt et al., 2021).

Moreover, studies have identified various alkaloids in *C. spinosa*, including capparisine A, B, C, 2-(5-hydroxymethyl-2-formylpyrrol-1-yl) propionic acid lactone, and *N*-(30-maleimidy1)-5-hydroxy-methyl-2-pyrrole formaldehyde, as well as flazine, capparin A, capparin B, and 1-H-indole-3-carboxaldehyde in fruits from China (Yang et al., 2010; Zhou et al., 2010). Fu et al. (2008) identified three new root alkaloids: capparispine, its glucosidic derivative, and cadabicine 26-*O*-*β*-D-glucoside hydrochloride. Saleem et al. (2021) reported the presence of compounds such as alkaloids, calystegin B2, cadabicin, 3-*O*-acetylhamayne, and michellamine B in the methanolic extracts of aerial parts of caper in Pakistan.

Additionally, caper extracts have been found to contain tannins, glucosinolates, saccharide derivatives, and terpenoids (Abu-Shama, 2019; Ascrizzi et al., 2016; Jiménez-López et al., 2018; Matthäus and Özcan, 2005; Nazer et al., 2021; Rajhi et al., 2021, 2019; Ramdani et al., 2020; Saleem et al., 2021; Yahia et al., 2020). Moreover, Al-Tamimi et al. (2019) demonstrated the presence of quaternary ammonium compounds, choline, and glycine betaine in roots and leaves of caper. The chemical composition of *C. spinosa* varies depending on several factors, such as the region where the plant was grown, the part of the plant used, the time of harvesting, and the extraction technique employed. Optimization of extraction parameters is crucial to ensure high yields and maximum purity of bioactive compounds extracted from *C. spinosa.* Various studies have explored optimal extraction conditions, including solvent selection, temperature, and extraction duration, to enhance the efficiency and quality of extracted secondary metabolites (Ara et al., 2014; Fattahi and Rahimi, 2016; Mazarei et al., 2017; Safarzaei et al., 2020). These efforts are necessary to improve the extraction efficiency of compounds such as rutin, quercetin, and kaempferol from caper.

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**Fig. 3.** Chemical structures of abundant volatile components in *C. spinosa.*

**Table 2.** Chemical Composition of extracts and essential oils of *Capparis spinosa.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Study area | Use section | Extracts/ Essential oils | Compound family | Compounds | References |
| Italy | Ap | methanol extract | flavonoids | rutin | (Mollica et al., 2017) |
| Italy | Bd | decoction, Soxhlet, microwave | phenolics, flavonoids | rutin, palmitic acid, naringenin | (Mollica et al., 2019) |
| Spain | Be | methanolic extracts | phenolics, flavonoids, saccharide derivative | epicatechin, quercetin, coumaric acid-*O*-hexoside, rutin, dihydrokaempferol-*O*-hexoside, epicatechin, isorhamnetin-*O*-rutinoside, glucocapparin | (Jiménez-López et al., 2018) |
| Spain | Bd | methanol extract | polyphenolics | quercetin, quercetin-3-*O*-rutinoside, kaempferol, myricetin, isorhamnetin,  *p*-coumaric acid, isorhamnetin-3-*O*-hexoside, myricetin-3-*O*-hexoside, 5-caffeoylquinic acid,  feruloylquinic acid, mono-rhamnoside, isorhamnetin-3-*O*-glucoside | (Wojdyło et al., 2019) |
| Turkey | Ap | methanol extract  ethyl acetate extract  aqueous extract | phenolics, flavonoids | quercetin, vanillic acid, *p*-coumaric acid, ferulic acid, syringic acid, hesperidin, hyperoside, protocatechuic acid, 4-hydroxybenzoic acid | (Kirkan et al., 2021) |
| Turkey | Bd, Be | methanol/water extract | phenolics, flavonoids | rutin, kaempferol, kaempferol-3-*O*-rutinoside, quercetin, quercetin-*O*-galloly-*O*-hexoside, iso-rhamnetin | (Aksay et al., 2021) |
| Turkey | Bd | purge and trap method, methanolic extract | volatile compounds, phenolic compounds | 2,3-butanedione, *α*-pinene, *β*-pinene, butanol, 3-carene, dl- limonene, methyl isothiocyanate, *p*-cymene, acetic acid, furfural, linalool, cresol, xylene, *p*-coumaric acid, caffeoylquinic acid, feruloylquinic acid, *p*-coumaroylquinic acid, kaempferol-3-*O*-rutinoside, kaempferol-3-*O*-glucoside, quercetin-3-*O*-glucoside, protocatechuic acid | (Sonmezdag et al., 2019) |
| Italy, Morocco, Turkey | Bd | decoction, microwave, Soxhlet, essential oils | phenolics, flavonoids, fatty acid | rutin, *α*-linoleic acid, palmitic acid, oleic acid, nonacosane, docosane, heptacosane, pentacosane | (Stefanucci et al., 2018) |
| Saudi Arabia, Italy | Rt and Lv | aqueous extract | alkaloids | stachydrine, choline, glycine betaine, homostachydrine, quaternary ammonium | (Al-Tamimi et al., 2019) |
| Tunisia | Lv | methanolic extract | phenolics, flavonoids, tannins | N. R | (Rajhi et al., 2019) |
| Tunisia | Lv | hydro-ethanolic extract, fractional extraction | phenolics, flavonoids, tannin | coumaran, 5-methylfurfural, furfural, protein | (Rajhi et al., 2021) |
| Tunisia | Lv | aqueous/ethanolic extracts | phenolics, flavonoids | vanillic acid, catechin acid, caffeic acid, rutin, quercetin, *p*-coumaric acid | (Aichi-Yousfi et al., 2016) |
| Tunisia | Lv | methanolic extracts | phenolics, flavonoids | gallic acid, vanillic acid, rutin, kaempferol, coumarin, epicatechin, catechin, luteolin, resveratrol | (Tlili et al., 2017) |
| Tunisia | Lv | maceration, refux, ultrasonic extractions | phenolics, flavonoids, tannin | quinic acid, gallic acid, crypto-chlorogenic acid, protocatechuic acid, *p*-coumaric acid, catechin, epicatechin, rutin, quercetin, kaempferol | (Yahia et al., 2020) |
| Egypt | Bd, Fr, Lv | ethanolic extracts | polyphenols, flavonoids, tannins, glycosides, alkaloids | quercetin, kaempferol, resorcinol, naphthaline | (Abu-Shama, 2019) |
| Pakistan | Ap, Rt | methanolic extract, dichloromethane extract | phenolics, flavonoids, glucosinolate, alkaloid | vanillic acid, syringic acid, kaempferol, robinin, robinetin, luteolin, tricetin 7-methyl ether 3′-glucoside-5′-rhamnoside, glucoputranjivin, glucocochlearin, gingerol, calystegin B2, cadabicine, 3-*O*-ace-tylhamayne, michellamine B, melanoxetin, 2.3-diMeO benzoic acid, 4-methoxyglucobrassicin | (Saleem et al., 2021) |
| Pakistan | Ap, Rt | aqueous methanol extract | phenolics, flavonoids | gallic acid, caffeic acid, sinapic acid, *p*-coumaric acid | (Gull et al., 2018) |
| Syria | Rt | hydroalcoholic extract | alkaloid | stachydrine | (Khatib et al., 2016) |
| Iran | Ap | hydro-ethanol extract | phenolics, flavonoids, alkaloid | quercetin, kaempferol derivatives,  rutin, capparine A, cappariloside A, flazine, *p*-coumaroyl quinic acid, chrysoeriol, guanosine, ginkgetin, sakuranetin | (Rahimi et al., 2020) |
| Iran | Fr | essential oil | volatile compounds | isopropyl isothiocyanate, methyl sulfonyl heptyl isothiocyanate, butylisothiocyanate, *α*-terpinene, thymol | (Alipour et al., 2021) |
| Iran | Fr | methanol /aqueous extract | tannins, flavonoids, terpenoids, glycosides, alkaloids | N. R | (Nazer et al., 2021) |
| Iran | Lv, Fr | hydroalcoholic extracts | flavonoids | rutin, quercetin | (Mohebali et al., 2018) |
| China | Fr | aqueous extract | phenolics, flavonoids, alkaloid | flazin, capparine A, capparine B, chrysoeriol, kaempferol, apigenin, thevetiaflavone, vanillic acid, 4-hydroxy-1H-indole-3-carboxaldehyde | (Zhou et al., 2010) |
| China | Fr | successive extracts | alkaloid | capparisine A, B and C, *N*-(30-maleimidy1)-5-hydroxymethyl-2-pyrrole formaldehyde, 2-(5-hydroxymethyl-2-formylpyrrol-1-yl) propionic acid lactone, | (Yang et al., 2010) |
| China | Rt | ethanol extract | alkaloid | cadabicine 26-*O*- β-D-glucoside hydrochloride, capparispine, capparispine 26-*O*- β-D-glucoside | (Fu et al., 2008) |
| Algeria | Ap | essential oils | fatty acid  , terpenoids,  alkanes | palmitic acid, octacosane, n-nonanal, 2,5-dimethoxy-*p*-cymene | (Ramdani et al., 2020) |
| Saudi Arabia | Ap | essential oils | aldehyde, terpenoids | limonene, methyl isothiocyanate, hexadecanoic acid | (Alkhaibari and Alanazi, 2022) |

Ap: Aerial parts, Be: Berries, Bd: Buds, Fr: Fruits, Lv: Leaves, Rt: Root; N. R: Not reported.

**7. Biological activities**

*In vitro* and *in vivo* investigations have substantiated caper traditional usage as a medicinal plant, providing evidence of its efficacy, and notably of its antioxidant, anti-diabetic and anti-inflammatory properties.

The antioxidant capacity of caper extracts has been confirmed using various methods, such as DPPH, FRAP, and ABTS assays (Aichi-Yousfi et al., 2016; Bodaghzadeh et al., 2021; Jiménez-López et al., 2018; Kirkan et al., 2021; Safarzaei et al., 2020; Sonmezdag et al., 2019; Yahia et al., 2020) (Table 3). Grimalt et al. (2022) notably reported the antioxidant activity of methanolic shoot extracts for different caper cultivars, with DPPH test results revealing values between 0.908 and 2.067 g Trolox/100 g DW. In another study, the *C. spinosa* leaf ethanolic extract showed powerful DPPH (77.80%; IC50 31.73 g/mL) and ABTS (IC50 value of 34.02 g/mL) activities compared to the five other taxa of the *Capparis* genus studied (Aichi-Yousfi et al., 2016). Yahia et al. (2020) also tested the antioxidant activity of aqueous leaf *C. spinosa* extracts prepared by maceration, reflux, and ultrasonic extractions using DPPH and ABTS assays. The maceration showed the greatest results for the DPPH test with an average reducing capacity EC50 of 74.02 mg/mL, followed by the reflux extract (57.65 mg/mL) and the ultrasonic-assisted extract (46.29 mg/mL). Furthermore, extraction by Soxhlet revealed the highest free radical scavenging capacity for both ABTS (124.15 mg TE/g) and DPPH (60.54 mg TE/g) assays, in contrast to the extracts obtained by decoction or microwave extraction (Mollica et al., 2019). Further studies by Kirkan et al. (2021) have indicated that methanolic extracts from *C. spinosa* aerial parts showed superior antioxidant properties to ethyl acetate and water extracts, as well as the richest polyphenolic components with 81.45 mg GAE/g and 36.57 mg RE/g, and the relative antioxidant capacity index (RACI) showed a maximum value of 1.20 for the methanolic extract, followed by water extract (-0.55) and ethyl acetate (-0.62), although high enzymatic inhibitory activity was recorded for ethyl acetate extracts. Analysis of *C. spinosa* hydroalcoholic extracts by the DPPH method revealed an antioxidant activity six times higher for the leaf extract than for the fruit extract (Rad et al., 2021). Another study indicated that *C. spinosa* hydroalcoholic leaf extract has a higher antioxidant activity than extracts obtained from fruits and seeds (IC50 = 1.41, 1.56, and 2.49 mg/ml, respectively) (Assadi et al., 2021). In addition, the antioxidant activity can vary depending on the development stage of *C. spinosa* fruits (Grimalt et al., 2018) and flowers (Wojdyło et al., 2019), as the activity at the nonpareil stage was significantly higher, with values of 6.92 mmol Trolox/100 g for the ABTS assay, of 7.51 mmol Trolox/100 g for the FRAP assay, and of 27.66 mmol Trolox/100 g for the ORAC assay. Kalantari et al. (2018) also showed that the *in vitro* antioxidant activity of *C. spinosa* hydroalcoholic leaf extract evaluated with DPPH and FRAP assays was higher (IC50 = 0.04 mg/mL and EC1 = 0.66 mg/mL) than the activities of the chloroformic (IC50 of DPPH = 0.04 mg/mL; EC1 of FRAP = 3.91 mg/mL) and ethyl acetate (IC50 of DPPH = 0.28 mg/mL; EC1 of FRAP = 15.90 mg/mL) extracts. In the same previous study, the hydroalcoholic extract showed good hepatoprotective activity against t-BHP (tert-butyl hydroperoxide)-induced liver toxicity in rats as the extract protected the liver against t-BHP-induced damage and significantly reduced serum enzyme activities, sleep time, and oxidative stress (Kalantari et al., 2018). Similarly, Tlili et al. (2017) demonstrated that the methanolic extract of *C. spinosa* leaves was able to counteract the increase in ALT (alanine aminotransferase), AST (aspartate aminotransferase), and LDH (lactate dehydrogenase) levels in CCL4-induced acute liver injury, and to limit malondialdehyde (MDA) formation in the liver, increase enzymatic antioxidant activities, and restore liver damage in rats. For nephroprotective activity in the same study, the methanolic extract significantly normalized renal biochemical parameters and repaired kidney damage caused by cisplatin treatment. Tir et al. (2019) also revealed that *C. spinosa* seeds' methanolic extracts can decrease the degree of tissue fibrosis, and biochemical analyses demonstrated the nephroprotective and hepatoprotective effects of *C. spinosa.* *In vitro* and *in vivo* analyses also showed that the caper fruit ethanolic extract significantly decrease hepatic cell apoptosis, improve the hepatic injury induced by triptolide, and inhibited the activity of choline kinase alpha in the rat liver (Yang et al., 2022).

The *in vitro* and *in vivo* anti-diabetic effect of *C. spinosa* has also been evaluated in a number of studies. Treatment of diabetic rats with a hydroalcoholic extract of *C. spinosa* leaves significantly reduced glucose intolerance and oxidative stress, and doses of 200 and 400 mg/kg improved fasting blood glucose levels (16% and 20%, respectively), a significant change in lipid profile for the 400 mg/kg dose, and a significant decrease in hepatic phosphoenolpyruvate carboxykinase of about 19%, an increase in acetyl-CoA carboxylase of about 40% (Assadi et al., 2021). The anti-diabetic activity of caper flower bud extract evaluated *in vitro* showed interesting activity for *α*-amylase with an IC50 value between 0.93 and 3.74 mg/ml and *α*-glucosidase at an IC50 value between 1.53 and 3.68 mg/ml, as well as for the ''gruesas'' stage, recorded the highest value (Wojdyło et al., 2019). In another investigation, *C. spinosa* methanolic extract showed very significant inhibition of *α*-amylase and *α*-glucosidase, for the aerial part with a value of 0.52 and 1.85 (mmol acarbose equivalent/g extract, respectively) and the root extract with an inhibitory value at 0.39 and 1.94 (mmol acarbose equivalent/g extract, respectively) (Saleem et al., 2021). Similarly, leaves and buds have anti-diabetic activities, and *in vitro* studies by Mollica et al. (2017) have demonstrated that decoction extracts of fresh buds and salted bud microwave extracts had the most significant inhibitory power on *α*-amylase and *α*-glucosidase, respectively. Indeed, *in vivo* administration of *C. spinosa* leaf powder or buds in STZ-induced diabetic rats normalized the biochemical profile, decreased blood glucose concentrations significantly, repaired liver and kidney damage with varying degrees of organ protection (Mollica et al., 2017). Yang et al. (2022) reported that the ethanolic extract of *C. spinosa* fruit displayed a hepatoprotective effect. The hepatotoxicity was induced by triptolide (TP) *in vitro* on AML-12 cell model and *in vivo* by injecting TP (1 mg/kg) to mice. The *in vitro* evaluation reveals that the survivability rate of AML-12 cells approached 100% by 16 mg/l treatment of *C. spinosa* extract, as well as the biochemical parameters were significantly decreased by different treatments of the extract (Yang et al., 2022).

The different *C. spinosa* organs have also anti-inflammatory properties, highlighted by both *in vivo* and *in vitro* studies (Table 3). As an example, Kernouf et al. (2018) showed that the oral treatment of rats having paw edema with *C. spinosa* bud methanolic extracts at 200 and 400 mg/kg inhibited edema by 52% to 69% compared to control. Additionally, treatment with 1 mg of extracts induced a 49% inhibition of the air pouch in mice (Kernouf et al., 2018). *In vitro* assays also indicated that 100 μg/mL of the extract was able to inhibit the production of TNF-*α*, IL-1β, LTB4, and to block the generation of superoxide anions released by blood mononuclear cells (Kernouf et al., 2018). In another *in vivo* study by El Azhary et al. (2017), it was shown that treatment with *C. spinosa* leaf extract significantly reduced contact hypersensitivity in Swiss mice compared to control with an inhibition percentage of 73.44%. *C. spinosa* alsoinduced a decrease in immune cell infiltration, vasodilation, and dermal thickness at the site of inflammation and inhibited cytokines. Similarly, *C. spinosa* fruit and root extracts have shown anti-inflammatory activity, suppressing pro-inflammatory cytokine expression, and can relieve pain associated with rheumatoid arthritis and osteoarthritis (Hamuti et al., 2017; Maresca et al., 2016).

Moreover, caper extracts have also been shown to have other biological activities (Table 3). For instance, aqueous extracts of *C. spinosa* flower buds showed antibacterial and antiviral effects against *staphylococcus* *aureus* (MIC 6.25%) and *Pseudomonas aeruginosa* (12.50%). *C. spinosa* also significantly reduced biofilm in Lubbock's chronic wound of *S. aureus* and *P. aeruginosa* with a percentage of 97.32% and 99.67%, respectively, but the aqueous extract of *C. spinosa* remains without action on *Candida albicans* (Di Lodovico et al., 2022). In the same way, Rajhi et al. (2019) demonstrated that the methanolic extract of fruits has antibacterial activity by the radial diffusion method; the results showed very significant inhibition against *S. aureus*, *Enterococcus faecalis, Escherichia* *coli*, *Salmonella*, and *P. aeruginosa* with diameters of 13, 12, 12, 10, and 10 mm, respectively. Also, *C. spinosa* fruits can disrupt the ultrastructure of protoscoleces and metacestode larvae of *Echinococcus granulosus* (Yan et al., 2022). *C. spinosa* essential oils can be used as a bioinsecticide against *Aedes aegypti* larvae as reported by Alkhaibari and Alanazi (2022) with an LC50 of 21.6 μg/mL, as well as *in vitro* tests revealing anti-plasmodial activity against *Plasmodium falciparum* and against *Leishmania major* (MRHO/IR/75/ER) with an IC50 of 7.4 μg/mL and IC50 of 9.1 μg/mL, respectively. Moreover, Al-Zubaidy and Khalil (2022) reported that *C. spinosa* ethanolic extract had good gastroprotective activity caused by indomethacin in rats, significantly increased prostaglandin E2 levels with a significant decrease in gastrin, TNF-*α*, and IL1-β, and significantly improved epithelial cell erosions. Furthermore, *C. spinosa* fruit aqueous extract has potential effects on ulcerative colitis as Zhu et al. (2021) showed *in vivo* that the extract improved the colonic histopathology of mice, increased protein gene levels in intestinal epithelial cells, and inhibited the expression of proinflammatory cytokines, as well as attenuating oxidative stress in the colon and improving the diversity of intestinal microbes. In addition, the hydroalcoholic extract of caper may be able to regulate sleep disorders *in vivo* in mice compared with diazepam (Rakhshandeh et al., 2021).

No significant cytotoxicity of *C. spinosa* essential oil was highlighted on J774A1 macrophage cells (CC50 value = 93.7 μg/mL) by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) colorimetric assay (Alkhaibari and Alanazi, 2022). Similarly, Saleem et al. (2021) showed that *C. spinosa* methanolic root extract had low toxicity against the MDA-MB-231 cell line. Also, the hydroalcoholic extract of *C. spinosa* revealed no cytotoxic effect on L929 fibroblast cells (LD50: 2.4 g/kg) (Rakhshandeh et al., 2021). On the other hand, it was highlighted that the *C. spinosa* flower bud extract can exert a cytotoxic effect, and that it induced greater oxidative stress in cancer cells (T24 cells and Caco-2 cells) than in normal cells (Bacchetti et al., 2022). *In vivo* acute toxicity studies on rats carried out by Mollica et al. (2017), Oudah et al. (2019), and Assadi et al. (2021) for the different extracts (fruits, leaves, and buds) of *C. spinosa* showed no mortality, even at the maximum doses.

# 8. Clinical Studies

Numerous clinical studies have corroborated the previously observed *in vivo* and *in vitro* biological activity of caper (Banerjee et al., 2011; Huseini et al., 2013; Khavasi et al., 2018, 2017; Rizza et al., 2010; Sardari et al., 2019). Banerjee et al. (2011) demonstrated that the use of *C. spinosa* as a component of a polyherbal formulation had a significant effect on antioxidant properties in geriatric patients compared to the control group. Similarly, Huseini et al. (2013) confirmed that the fruit of *C. spinosa* possesses anti-hyperglycemic properties, and the usage of 400 mg of extract showed a significant effect in patients with type 2 diabetes. Research by Khavasi et al. (2018, 2017) into the effects of capers in patients with non-alcoholic fatty liver revealed that the consumption of 40-50 grams of caper fruit pickles resulted in a significant decrease in serum ALT and AST levels. Additionally, a significant reduction in weight, body mass index, and disease severity was observed (Khavasi et al., 2017), suggesting that daily consumption of caper gherkins may play a preventive role against cardiovascular problems (Khavasi et al., 2018, 2017). Other studies by Sardari et al. (2019) showed that the consumption of 40-50 g of caper fruit pickles in combination with atorvastatin significantly lowered total cholesterol in patients with hyperlipidemia. Furthermore, topical use of *C. spinosa* significantly reduced radiation-induced skin disease, as found by Rizza et al. (2010).

**Table 3.** Biological activities of *Capparis spinosa*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Part used | Biological activities | Extracts | Experimental approach | Key results | Reference |
| Young shoots | Antioxidant activity | Methanolic extract | ABTS  DPPH  FRAP | 1.814 g TE/100 g DW  2.066 g TE/100 g DW  1.925 g TE/100 g DW | (Grimalt et al., 2022) |
| *C. spinosa* honey | Antioxidant activity | Ethanolic extract | ABTS  NO | IC50 = 11.5 ± 0.02 mg/mL  IC50= 20.7 ± 0.04 mg/mL | (El-Guendouz et al., 2017) |
| Diuretic activity | Administration of 1 g/kg honey to rats to evaluate effect on urine volume and excretion of sodium, potassium, and chloride | Significant increase in rat diuresis  Significantly increased urinary  No significant effect on plasma sodium, potassium levels or osmolarity |
| Leaves | Antioxidant activity | Hydro-alcoholic extract | DPPH  FRAP | IC50 = 0.034 ± 0.002 mg/mL  IC50 = 1.655 ± 0.122 mg/mL | (Kalantari et al., 2018) |
| Hepatotoxicity in rats induced by t-BHP | Pretreatment with 400 mg/kg of the hydroalcoholic fraction showed liver protection |
| Hepatoprotective activity |
| Leaves | Antioxidant activity | Hydro-ethanolic extract | DPPH  FRAP | DPPH inhibition :84.02%  FRAP: 4.275 mmol/g | (Rajhi et al., 2021) |
| Antifungal activity | Agar diffusion test | Highest inhibition (58.78%) of *A. niger* was achieved by the diethyl ether fraction |
| Different parts | Antibacterial activities | Methanolic extracts | By radial diffusion method was reported on five reference bacterial strains *(S. aureus, P. aeruginosa, E. coli, Salmonella and Enterococcus)* | Flowers have antibacterial activity against all five strains with inhibition diameters of 13, 12, 12, 10 and 10 mm, respectively | (Rajhi et al., 2019) |
| Antioxidant activities | Total antioxidant capacity  DPPH | Root extract: (175.7 ±2.3 mg EAA/g DW)  IC50 DPPH (Leaves) = 70.1±2.32 mg/mL |
| Fruit | Antioxidant activities | Hydro-ethanolic extracts | DPPH | IC50(leaves) = 1.41 ± 0.10 mg/mL  IC50 (fruits) = 1.56 ± 0.12 mg/mL  IC50 (seeds) = 2.49 ± 0.21 mg/mL | (Assadi et al., 2021) |
| Antidiabetic | Diabetic rats treated with 200 and 400 mg/kg | Increased levels of antioxidant enzymes Reduced glucose intolerance and blood sugar levels  Significant reduction in fasting blood glucose levels; non-significant decrease in HbA1c and hepatocyte nuclear factor 4*α* (HNF-4*α*) levels; significant decrease in hepatic phosphoenolpyruvate carboxykinase and increase in acetyl CoA carboxylase |
| Leaves | Antioxidant activities | Methanolic extract | DPPH  H2O2 scavenging activity | IC 50 = 43.031± 1.24 μg/mL  IC 50= 81.21± 1.28 μg/mL | (Tlili et al., 2017) |
| Nephroprotective and  hepatoprotective effects | CCl4 and cisplatin-induced hepatotoxicity in rats | Significant reduction in AST, ALT and LDH enzyme levels (136.5, 93.98 and 1032 U/L, respectively)  Significant increase in SOD activity (28.34) and slight increase in CAT and GPx activities (26.85 U/mg protein and 50.21 U/mg protein, respectively)  Protective effects were confirmed by histological examination |
| Flowers Buds | Antioxidant activity | Methanolic extract | ABTS  FRAP  ORAC | 6.92 ± 0.54 mmol Trolox/100 g  7.51 ± 0.11 mmol Trolox/100 g  27.66 ± 1.43 mmol Trolox/100 g | (Wojdyło et al., 2019) |
| Antidiabetic activity | *α*-amylase inhibitory  *α*-glucosidase inhibitory | IC50= 0.93 mg/mL  IC50 = 1.52 mg/mL |
| Cholinesterase’s inhibition | Inhibition of AChE  Inhibition of BuChE | AChE = 28.1% ± 2.0  BuChE = 33.8% ± 2.3 |
| Fruit | Hepatoprotective effects | Ethanolic extract | *In vitro* test: triptolide-induced AML-12 cell injury model.  *In vivo* test: acute liver injury in mice | Significantly inhibits arachidonate 5-lipoxygenase and choline kinase alpha in the liver  Significantly reduces apoptosis of liver cells and can improve liver damage  Significantly modification of metabolites pathways | (Yang et al., 2022) |
| Aerial parts | Insecticidal activity | Essential oils | Larvae of *Aedes Aegypti* | LC50= 21.6 ± 2.15 μg/mL | (Alkhaibari and Alanazi, 2022) |
| Antiplasmodial activity | *Plasmodium falciparum* K1 | IC50= 7.4 ± 0.89 μg/mL |
| Antileishmanial activity | *Leishmania major* (MRHO/IR/75/ER) | IC50= 9.1 ± 1.12 μg/mL |
| Cytotoxic effects | MTT assay: *J774A1 macrophage* cell*,* | CC50= 93.7 ± 4.54 μg/mL |
| Aerial parts | Gastroprotective effect | Ethanolic extract | Indomethacin-induced gastric ulcer in rats | Significantly increased of prostaglandin E2  Reduction of TNF-*α* and Interleukin-1-β levels | (Al-Zubaidy and Khalil, 2022) |
| Leaves | Antibacterial activities | Ethanolic extract | Disk diffusion method | *E. coli* Ф = 19.808 ± 0.755 mm  *S. aureus* Ф = 15.080 ± 0.417 mm | (Zhu et al., 2022) |
| Fruit | Anti-inflammatory activities | Ethanolic extract | Maturation of mice bone marrow dendritic cells | Significant inhibited pro-inflammatory cytokines  Significant inhibited tumor necrosis factor (TNF-*α*) initiated by LPS | (Hamuti et al., 2017) |
| Flower bods | Antimicrobial and Antiviral effects | Aqueous extract | Microdilution method  Evaluation of motility and biofilm formation | *S. aureus* MIC = 6.25%  *P. aeruginosa* MIC = 12.50%  *Candida albicans* no inhibition  Significant inhibition Lubbock chronic wound biofilm for both species *S. aureus* and *P. aeruginosa* | (Di Lodovico et al., 2022) |
| Fruit | Ulcerative colitis | Aqueous extract | Ulcerative Colitis (UC) induced by dextran sulfate sodium in mice | Reduced effect of CU on mouse colon histopathology  Reduced pro-inflammatory cytokines and oxidative stress  Increased expression levels of ZO-1 and Occludin  Improved intestinal microbial diversity and Firmicutes metabonomic | (Zhu et al., 2021) |
| Leaves | Anti-inflammatory activities | Methanol extract | Model of contact hypersensitivity in Swiss mice | Inhibited cytokine gene expression  Significantly induced a decrease in immune cell infiltration, vasodilation, and dermal thickness in the inflammatory site | (El Azhary et al., 2017) |
| Fruit | Larval development effect | Ethanolic extracts | Larvae of *Echinococcus granulosus* sensu stricto | Inhibited growth of larvae  Mortality = 100% and 82% 24h after treatment  Not Significantly Cytotoxicity | (Yan et al., 2022) |
| Aerial parts | Antioxidant activity | Methanol extract  Dichloromethane extract | DPPH  ABTS  FRAP  CUPRAC  TAC  Metal Chelating (MC) | DPPH = 30.48 ± 0 .37 mg TE/g extract  ABTS = 40.43 ± 3.33 mg TE/g extract  FRAP = 50.37 ± 2.42 FRAP mg TE/g extract  CUPRAC = 118.45 ± 1.69 mg TE/g extract  TAC = 75.79 ± 1.25 mg TE/g extract  MC= 2.51 ± 0.19 mg EDTA/g | (Saleem et al., 2021) |
| Root | DPPH = 28.45 ± 0.60 mg TE/g extract  ABTS = 40.55 ± 1.35 mg TE/g extract  FRAP = 42.82 ± 1 mg TE/g extract  CUPRAC = 96.89 ± 5.19 mg TE/g extract  TAC= 13.56 ± 1.05 mg TE/g extract  MC= 1.41 ± 0.09 mg EDTA/g |
| Aerial parts | Enzyme inhibition assays | AChE Inhibition  BChE Inhibition  Tyrosinase (TYR)  *α*-Amylase assay  *α*-Glucosidase assay | AChE = 4.06 ± 0.18 mg galantamine equivalent/g extract  BChE =5.58 ± 0.45 mg galantamine equivalent/g extract  TYR = 135.52 ± 0.76 mg kojic acid equivalent/g extract  *α*-Amylase =0.77 ± 0.02 mmol acarbose equivalent/g extract  *α*-Glucosidase = 1.85 ± 0.06 mmol acarbose equivalent/g extract |
| Root | AChE = 4.71 ± 0.14 mg galantamine equivalent/g extract  BChE = 4.13 ± 0.17 mg galantamine equivalent/g extract  TYR = 139.78 ± 0.95 mg kojic acid equivalent/g extract  *α*-Amylase = 0.57 ± 0.04 mmol acarbose equivalent/g extract  *α*-Glucosidase = 1.94 ± 0.01 mmol acarbose equivalent/g extract |
| Aerial parts | Cytotoxic effects | MTT assay: MDA-MB 23  MCF-7 cells | Viability = 55.72%  Viability = 55.36% |
| root | Viability = 48.46%  Viability = 73.81% |
| Aerial parts | Hypnotic activity | Hydro-alcoholic extract | In mice in comparison with diazepam | Significantly augmented induced sleeping time | (Rakhshandeh et al., 2021) |
| Cytotoxic effects | MTT assay: l929 cells using | LD50= 2.4 g/kg  Not Significantly Cytotoxicity |
| Flower buds | Anti-inflammatory activities | Methanolic extract | Carrageenan Induced Edema  Air pouch inflammation models | Inhibition = 69%  Inhibition = 48.92% | (Kernouf et al., 2018) |

# *In vitro* production of *Capparis spinosa* secondary metabolites

The biosynthesis of secondary metabolites in *C. spinosa* is subject to the influence of multiple factors, among which the geographical location, genetic diversity, and environmental conditions, which have significant effects on both the quality and quantity of these bioactive compounds (Mahmodi et al., 2022; Pegiou et al., 2023; Qaderi et al., 2023). *In vitro* culture offers numerous advantages in terms of plant preservation, enhanced production of metabolites, and synthesis pathway manipulation (Chandran et al., 2023; Mohaddab et al., 2022; Vivek et al., 2023). Furthermore, the excessive exploitation of wild plant resources may result in notable alterations in phytochemical composition, including certain components that remain to be characterized (Sottile et al., 2021). Moreover, techniques such as cell culture, cell suspension, and hairy culture facilitate the augmentation of secondary metabolite production and provide a means for transitioning to large-scale production through the utilization of bioreactors (Fig. 4) (Andrade et al., 2021; Bouzroud et al., 2023; Rohini and Rajasekharan, 2022; Sreelekshmi et al., 2023).

Une image contenant texte, capture d’écran, diagramme, conception

Description générée automatiquement

**Fig. 4.** Overview of the different steps for *in vitro* production of secondary metabolites using cell culture and hairy root culture.

In the existing scientific literature, several articles have studied cell culture as an alternative strategy for secondary metabolite production in *C. spinosa* (Duran and Issah, 2022; Kianersi et al., 2020a; Wang et al., 2007; Yin et al., 2014). Typically, callus formation in plants is initiated by the application of auxins and/or cytokinins (Ikeuchi et al., 2013). However, to successfully induce callus formation and stimulate the synthesis of secondary metabolites *in vitro* in *C. spinosa,* it is essential to determine the optimal combination and concentration of these phytohormones, as well as the selection of the appropriate explant. Previous studies by Yin et al. (2014), Wang et al. (2007), and Liu et al. (2011) have reported that leaf explants and their treatment with 2,4-dichlorophenoxyacetic acid (2,4-D , 1.0 mg/L) and 6-benzylaminopurine (BAP, 1.5 mg/L) were optimal for callus induction and subsequent subculture. The results of GC-MS analyses demonstrate a significant resemblance in the volatile profile, fatty acid composition, acid ester composition, and carboxylic acid composition between callus, suspension cultures of *C. spinosa* and *C. spinosa* seeds and fruits (Yin et al., 2014). Furthermore, Liu et al. (2011) observed a progressive elevation in the total unsaturated fatty acid content of *C. spinosa* suspension cells treated with less than 12% polyethylene glycol, accompanied by a decrease in the level of total saturated fatty acids.

In another study by Duran and Issah (2022), it was demonstrated that a medium containing 10.74 μM of 1-naphthaleneacetic acid (NAA), 4.44 μM of BAP, and 0.1 μM of strigolactone GR24 promotes the formation of callus in *C. spinosa.* Additionally, HPLC analyses showed an improvement in the production of rutin, quercetin, and chlorogenic acid compared to the control. Similarly, the application of elicitors in callus culture can enhance the production of secondary metabolites, as shown by studies by Kianersi et al. (2020a,2020b) which indicate that rutin levels were increased by the application of salicylic acid and stimulated the expression of rutin-related genes. Moreover, analysis of the aromatic compounds in the callus unveiled the presence of sulfur compounds (66.97-87.53%), aldehydes (4.88-7.90%), ketones (0.34-19.3%), hydrocarbons, and derivatives (0.56-5.8%), alcohols (1.62-6.08%), and other compounds (0.61-2.37%), with methyl isothiocyanate identified as the predominant compound (Duran and Issah, 2022).

Hairy root cultures have recently emerged as a highly practical alternative approach to producing secondary metabolites (Alcalde et al., 2022; Malarz et al., 2023) as it has demonstrated robustness in generating bioactive components of interest, often yielding comparable or higher quantities compared to intact plant systems (Andrade et al., 2021). The rapid growth and genetic stability of hairy root cultures provide them with an advantage over cell cultures (Gabr et al., 2021; Pietrosiuk et al., 2022). Moreover, hairy root culture exhibits significant potential for biomass production, making it well-suited for large-scale synthesis of bioactive compounds in bioreactors while ensuring the conservation of plant resources (Gantait and Mukherjee, 2021; Sonkar et al., 2023). Multiple studies have successfully induced hairy roots in various plant species, including *Rindera graeca* (Graikou et al., 2021; Sykłowska-Baranek et al., 2023), *Thymus daenensis* (Alamholo and Soltani, 2023), *Atropa belladonna* (Singh et al., 2021), *Withania somnifera* (Karami et al., 2023), *Hybanthus enneaspermus* (Sathish et al., 2023), *Hyoscyamus muticus* (Abdelkawy et al., 2023), *Perilla frutescens* (Yan et al., 2023), and *Calendula officinalis* (Rogowska et al., 2023). The primary metabolites produced by hairy roots have demonstrated significant biological activity.

To date, no published studies have explored the use of biotechnological tools such as cell culture and hairy root culture to produce secondary metabolites from *C. spinosa*. However, this plant possesses a wealth of significant bioactive compounds, including phenolic compounds, flavonoids, and alkaloids. It is conceivable that harnessing these components through these biotechnological techniques could meet the specific requirements of the pharmaceutical industries. The large and sustainable production of economically significant plant secondary metabolites requires innovative interventions at different scales of production and development processes (Motolinía-Alcántara et al., 2021). Plant biotechnological approaches can be of significant importance to increase the production of suitable secondary metabolites using a plethora of *in vitro* culture systems (Mohaddab et al., 2022), which may be optimized through diverse approaches such as the modification of culture media, supplementation with elicitors and precursors, selection of high-yielding cell lines, biotransformation, hairy root culture, immobilization and permeabilization of plant cells, and metabolic engineering (Abdulhafiz et al., 2022; Bouzroud et al., 2023; Dias et al., 2016; Fazili et al., 2022; Mukhopadhyay, 2023).

Metabolic engineering is a powerful tool that can increase the production of plant secondary metabolites to achieve a sustainable supply (Mipeshwaree Devi et al., 2023) by altering their biosynthetic pathway in cell culture or in the whole plant (Verpoorte et al., 2002). Furthermore, metabolic engineering could be helpful to optimize the production of desired compounds; nevertheless, the secondary metabolites of plants are generally controlled by complex and interconnected metabolic pathways, which make it difficult to manipulate their biosynthesis. These biosynthetic pathways may include also different physiological aspects associated with the transport and accumulation of metabolites, which make the regulatory genes promising targets to upgrade the pathway of suitable metabolite (Verpoorte et al., 2002).

Several strategies are used to alter the biosynthetic capacity of plant cells to enhance the synthesis of desired compounds, which include overexpression of rate-limiting enzymes involved in the synthesis of the targeted molecule, downregulation of competing pathways, alteration of transcription factors, upregulation of transporters of secondary metabolites (Bagal et al., 2023; Halder and Roy, 2023; Yue et al., 2016). In fact, previous studies reported the utility of these techniques to manipulate the biosynthesis of different plant-derived phytochemicals endowed with important biological activity such as phytocannabinoids (Hesami et al., 2022), camptothecin (Fan et al., 2022), and diverse anticancer compounds (Changxing et al., 2020).

Hence, it could be useful to employ these strategies to optimize the production of specialized metabolites in *C. spinosa*. As previously discussed, this medicinal plant possesses an arsenal of health-promoting compounds that could be targeted for strategic valorization. However, limited studies have been conducted to explore the genetic basis of the biosynthesis of metabolites of significant importance. In a recent study (Kianersi et al., 2020a) using qRT-PCR reported that the upregulation of four genes (4-coumaroyl CoA ligase (4CL), flavonoid 3′-hydroxylase (F3′H), flavonol synthase (FLS), and flavonol-3-O-glucoside L-rhamnosyltransferase (RT)) was associated with the increased accumulation of rutin, therefore, these genes play a significant role in the biosynthesis of rutin in *C. spinosa* and could be targeted by different genetic engineering approaches to increase the production of rutin. The same authors, in another study, have also highlighted the upregulation of FLS-encoding gene at the vegetative stage in the leaves of caper treated with methyl jasmonate and salicylic acid; however, RT was upregulated at the fresh fruiting stage (Kianersi et al., 2020b). The latter results would be a starting point for investigations targeting the valorization of Caper as a valuable source of rutin and quercetin that may be used in different industrial applications. In addition to rutin and quercetin, *C. spinosa* possesses several others bioactive compounds with diverse biological activity such ginkgetin, capparine, catechin, luteolin, coumarin, resveratrol, syringic acid, etc. that can be targeted by different biotechnological approaches for enhancing their production; therefore, future studies are needed to dissect the gene regulatory network governing the synthesis of these metabolites of interest in caper.

For a tangible application of metabolic engineering to modulate the biosynthesis of the desired metabolite, a deep understanding of biosynthetic pathways is required. In this regard, omics tools such as genomics, transcriptomics, proteomics, and metabolomics could play a pivotal role in identifying genes, gene regulatory networks, and proteins involved in the biosynthesis and accumulation of secondary metabolites (Acharjee et al., 2022; Kumari et al., 2022). Furthermore, in recent years, genome editing tools like zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 (Cas9) have emerged as powerful methods for the precise alteration of genes involved in the biosynthetic pathways of targeted metabolites (Mipeshwaree Devi et al., 2023). Smart exploitation of technological advances in omics area and genome editing tools could be a pragmatic way for the strategic valorization of caper by the identification of metabolic routes of targeted metabolites; this requires interdisciplinary research and collaborative efforts of researchers from different fields.

# Conclusion

Caper is one of the most widely recognized medicinal plants in various regions and has been traditionally used in conventional medicinal systems to treat a range of diseases, particularly diabetes and inflammation. Phytochemical investigations have revealed that *C. spinosa* contains a diverse array of chemical compounds, such as phenolic acids, flavonoids, and alkaloids, which may vary according to environmental conditions and vegetative stages. Pharmacological tests have substantiated the traditional uses of caper due to its richness in secondary metabolites, and particularly phenolic compounds. *In vivo* and/or *in vitro* pharmacological studies on different parts of *C. spinosa* have indicated several therapeutic effects, including antidiabetic, antibacterial, cytotoxic, gastroprotective, and anti-inflammatory activities. Additionally, promising pharmacological effects against oxidative stress-related disorders, notably diabetes, inflammation, and cancer, have been revealed. However, future investigations are necessary to explore anticancer effects, pharmacodynamics of studied activities, and toxicological studies on animal models.

Furthermore, caper holds considerable socio-economic importance in several countries such as Morocco, Spain, Turkey, and others. In light of its potential, caper cultivation can be seen as an agricultural strategy to address the challenges posed by climate change in the Mediterranean region. To achieve this objective, genetic research to determine taxonomy and the development of specific agronomic approaches for caper are required. In fact, the collection, conservation, and screening of caper genetic resources is primordial to select and develop future caper cultivars endowed with superior agronomic traits of breeders and farmers interests. The development of improved caper genotypes could help in increasing the production and the profitability of this crop. However, at present there is limited research related to genetic improvement and the development of adapted cultivars with relevant traits. Therefore, the implementation of breeding programs of caper would be helpful in order to speed up the delivery of improved cultivars of caper, increase productivity, and prevent the overexploitation of natural resources.

Moreover, as discussed above, caper possesses a plethora of bioactive compounds; hence, the integration of biotechnological tools represents a promising, sustainable, and eco-friendly alternative that can support the pharmaceutical industry's demands and contribute to reducing the overexploitation of natural resources. However, for efficient commercial production, scientific approaches assessing the profitability and stability of secondary metabolite production, as well as modeling large-scale production, are essential. In conclusion, the extensive pharmacological and chemical studies on *C. spinosa* have highlighted its potential as a valuable source of therapeutic compounds. Exploiting this potential will not only aid in expanding the pharmacological applications but also contribute to the socio-economic development of regions where caper is cultivated. By employing a multidisciplinary approach encompassing genetic research, and biotechnological tools we can harness the full potential of caper and pave the way for its integration into modern medicine and industries, while also ensuring the preservation of natural resources.

**CRediT authorship contribution statement**

**Marouane Mohaddab:** conceptualization, investigation, data curation, methodology, software, writing-original draft, writing-review & editing, visualization. **Manon Genva**: supervision, conceptualization, writing-review & editing. **Malika Fakiri:** supervision, writing-review & editing. **Younes El-Goumi:** supervision, writing-review & editing. **Abdelmonim Zeroual:** investigation, data curation, writing - review & editing. **Marie-Laure Fauconnier:** supervision, investigation, validation, methodology, writing – review & editing.

**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.

**Data Availability**

Not applicable.

**References**

Abdelkawy, A.M., Alshammari, S.O., Hussein, H.-A.A., Abou El-Enain, I.M., Abdelkhalek, E.S., Radwan, A.M., Kenawy, S.K., Maaty, D.A., Abed, N.N., Sabry, S., 2023. Effect of silver nanoparticles on tropane alkaloid production of transgenic hairy root cultures of hyoscyamus muticus l. And their antimicrobial activity. Sci. Rep. 13, 10397.

Abdulhafiz, F., Mohammed, A., Reduan, M.F.H., Kari, Z.A., Wei, L.S., Goh, K.W., 2022. Plant cell culture technologies: A promising alternatives to produce high-value secondary metabolites. Arab. J. Chem. 15, 104161.

Aburjai, T., Hudaib, M., Tayyem, R., Yousef, M., Qishawi, M., 2007. Ethnopharmacological survey of medicinal herbs in Jordan, the Ajloun Heights region. J. Ethnopharmacol. 110, 294–304.

Abu-Shama, H.S., 2019. Effect of caper (*Capparis spinosa*) extracts as a natural antimicrobial agent. J. Food dairy sci. 10, 209–216.

Acharjee, S., Kumar, R., Kumar, N., 2022. Role of plant biotechnology in enhancement of alkaloid production from cell culture system of *Catharanthus roseus*: A medicinal plant with potent anti-tumor properties. Ind. Crops Prod. 176, 114298.

Afzal, S., Afzal, N., Awan, M.R., Khan, T.S., Gilani, A., Khanum, R., Tariq, S., 2009. Ethno-botanical studies from Northern Pakistan. J Ayub Med Coll Abbottabad 21, 52–7.

Ahmadi, M., Saeidi, H., 2018. Genetic diversity and structure of *Capparis spinosa L*. In Iran as revealed by ISSR markers. Physiol. Mol. Biol. Plants 24, 483–491.

Aichi-Yousfi, H., Meddeb, E., Rouissi, W., Hamrouni, L., Rouz, S., Rejeb, M.N., Ghrabi-Gammar, Z., 2016. Phenolic composition and antioxidant activity of aqueous and ethanolic leaf extracts of six Tunisian species of genus *Capparis–Capparaceae*. Ind. Crops Prod. 92, 218–226.

Akgül, A., Özcan, M., 1999. Some compositional characteristics of capers (*Capparis spp,*) seed and oil. Grasas Aceites 50, 49–52.

Aksay, O., Selli, S., Kelebek, H., 2021. LC-DAD-ESI-MS/MS-based assessment of the bioactive compounds in fresh and fermented caper (*Capparis spinosa*) buds and berries. Food Chem. 337, 127959.

Alamholo, M., Soltani, J., 2023. Agrobacterium rhizogenes-mediated transformation as a means for induction of hairy roots and secondary metabolites in thymus daenensis. Biol. Bull. 1–7.

Alcalde, M.A., Perez-Matas, E., Escrich, A., Cusido, R.M., Palazon, J., Bonfill, M., 2022. Biotic elicitors in adventitious and hairy root cultures: A review from 2010 to 2022. Molecules 27, 5253.

Alipour, F., Nabigol, A., Nabizadeh, E., 2021. Variation in volatile organic compounds in fruits of Iranian *Capparis spinosa* L. Accessions. Saudi J. Biol. Sci. 28, 4664–4667.

Aliyazicioglu, R., Eyupoglu, O.E., Sahin, H., Yildiz, O., Baltas, N., 2013. Phenolic components, antioxidant activity, and mineral analysis of *capparis spinosa* L. Afr. J. Biotechnol. 12, 6643–6649.

Alkhaibari, A.M., Alanazi, A.D., 2022. Chemical composition and insecticidal, antiplasmodial, and anti-leishmanial activity of *Capparis spinosa* essential oil and its main constituents. Evid. Based Complement. Alternat. Med. 2022.

Allaith, A.A.A., 2016. Assessment of the antioxidant properties of the caper fruit (*Capparis spinosa* L.) From Bahrain. J. Assoc. Arab Univ. Basic Appl. Sci. 19, 1–7.

Al-Tamimi, A., Khatib, M., Pieraccini, G., Mulinacci, N., 2019. Quaternary ammonium compounds in roots and leaves of *Capparis spinosa* L. From Saudi Arabia and Italy: investigation by HPLC-MS and 1H NMR. Nat. Prod. Res. 33, 1322–1328.

Altundag, E., Ozturk, M., 2011. Ethnomedicinal studies on the plant resources of east Anatolia, Turkey. Procedia-Soc. Behav. Sci. 19, 756–777.

Alzahrani, D., Albokhari, E., Yaradua, S., Abba, A., 2021. The complete plastome sequence for the medicinal species *Capparis spinosa* L.(*Capparaceae*). Gene Rep. 23, 101059.

Al-Zubaidy, A.A., Khalil, A.M., 2022. Gastroprotective effect of *Capparis spinosa* on indomethacin-induced gastric ulcer in rats. Arch. Razi Inst. 77, 1437–1445.

Andrade, M., Ribeiro-Santos, R., Sanches, S.A., 2021. Exploring Plant Cells for the Production of Compounds of Interest. Explor. Plant Cells Prod. Compd. Interest 145–170.

Ara, K.M., Karami, M., Raofie, F., 2014. Application of response surface methodology for the optimization of supercritical carbon dioxide extraction and ultrasound-assisted extraction of *Capparis spinosa* seed oil. J. Supercrit. Fluids 85, 173–182.

Ascrizzi, R., Cioni, P.L., Giusti, G., Pistelli, L., Flamini, G., 2016. Patterns in volatile emission of different aerial parts of caper (*Capparis spinosa* L.). Chem. Biodivers. 13, 904–912.

Ashraf, U., Chaudhry, M.N., Ahmad, S.R., Ashraf, I., Arslan, M., Noor, H., Jabbar, M., 2018. Impacts of climate change on *Capparis spinosa* L. Based on ecological niche modeling. Peerj 6, e5792.

Assadi, S., Shafiee, S.M., Erfani, M., Akmali, M., 2021. Antioxidative and antidiabetic effects of *Capparis spinosa* fruit extract on high-fat diet and low-dose streptozotocin-induced type 2 diabetic rats. Biomed. Pharmacother. 138, 111391.

Bacchetti, T., Campagna, R., Sartini, D., Cecati, M., Morresi, C., Bellachioma, L., Martinelli, E., Rocchetti, G., Lucini, L., Ferretti, G., 2022. *C. Spinosa* l. Subsp. Rupestris phytochemical profile and effect on oxidative stress in normal and cancer cells. Molecules 27, 6488.

Bagal, D., Chowdhary, A.A., Mehrotra, S., Mishra, S., Rathore, S., Srivastava, V., 2023. Metabolic engineering in hairy roots: An outlook on production of plant secondary metabolites. Plant Physiol. Biochem. 107847.

Banerjee, P., Maity, S., Das, T., Mazumder, S., 2011. A double-blind randomized placebo-controlled clinical study to evaluate the efficacy and safety of a polyherbal formulation in geriatric age group: A phase IV clinical report. J. Ethnopharmacol. 134, 429–433.

Bodaghzadeh, A., Alirezalu, K., Amini, S., Alirezalu, A., Domínguez, R., Lorenzo, J.M., 2021. Fatty acid composition, phytochemicals and antioxidant potential of *Capparis spinosa* sedes. Grasas Aceites 72, e430–e430.

Bourhim, T., Chakhchar, A., Lamaoui, M., El Kharrassi, Y., Alaoui, A., El Modafar, C., Ibnou Ali El Alaoui, M., Hsissou, D., 2021. Morphological characterization and assessment of genetic diversity of natural Moroccan populations of *Capparis spinosa*. Acta Physiol. Plant. 43, 1–10.

Bousta, D., Boukhira, S., Aafi, A., Ghanmi, M., el Mansouri, L., 2014. Ethnopharmacological Study of anti-diabetic medicinal plants used in the Middle-Atlas region of Morocco (Sefrou region). Int. J. Pharma Res. Health Sci. 2, 75–79.

Bouzroud, S., El Maaiden, E., Sobeh, M., Merghoub, N., Boukcim, H., Kouisni, L., El Kharrassi, Y., 2023. Biotechnological Approaches to Producing Natural Antioxidants: Anti-Ageing and Skin Longevity Prospects. Int. J. Mol. Sci. 24, 1397.

Chandran, S., Raghu, A.V., Mohanan, K.V., 2023. *In vitro* conservation of rare, endangered, and threatened plants, in: Conservation and Sustainable Utilization of Bioresources. Springer, pp. 391–408.

Changxing, L., Galani, S., Hassan, F., Rashid, Z., Naveed, M., Fang, D., Ashraf, A., Qi, W., Arif, A., Saeed, M., 2020. Biotechnological approaches to the production of plant-derived promising anticancer agents: An update and overview. Biomed. Pharmacother. 132, 110918.

Chedraoui, S., Abi-Rizk, A., El-Beyrouthy, M., Chalak, L., Ouaini, N., Rajjou, L., 2017. *Capparis spinosa* L. In a systematic review: A xerophilous species of multi values and promising potentialities for agrosystems under the threat of global warming. Front. Plant Sci. 8, 1845.

Chibani, F., Skouri-Gargouri, H., Salem, A.B., Ghorbel, A., Zoghlami, N., 2017. Using genetic structure data and phylogenetic criteria in attributing prioritization scores for conservation of spontaneous *Capparis spinosa* L. Populations from Tunisia. J. Nat. Conserv. 37, 96–105.

Cornara, L., La Rocca, A., Marsili, S., Mariotti, M.G., 2009. Traditional uses of plants in the Eastern Riviera (Liguria, Italy). J. Ethnopharmacol. 125, 16–30.

Darwish, R.M., Aburjai, T.A., 2010. Effect of ethnomedicinal plants used in folklore medicine in Jordan as antibiotic resistant inhibitors on Escherichia coli. BMC Complement. Altern. Med. 10, 1–8.

Decraene, L.R., Smets, E.F., 1997. Evidence for carpel multiplications in the Capparaceae. Belg. J. Bot. 59–67.

Di Lodovico, S., Bacchetti, T., D’Ercole, S., Covone, S., Petrini, M., Di Giulio, M., Di Fermo, P., Diban, F., Ferretti, G., Cellini, L., 2022. Complex Chronic Wound Biofilms Are Inhibited *in vitro* by the Natural Extract of Capparis spinose. Front. Microbiol. 13, 832919.

Dias, M.I., Sousa, M.J., Alves, R.C., Ferreira, I.C., 2016. Exploring plant tissue culture to improve the production of phenolic compounds: A review. Ind. Crops Prod. 82, 9–22.

Duman, E., Özcan, M.M., 2014. Mineral contents of seed and seed oils of Capparis species growing wild in Turkey. Environ. Monit. Assess. 186, 239–245.

Duran, R.E., Issah, H., 2022. The impact of strigolactone GR24 on *Capparis spinosa* L. Callus production and phenolic compound content. Plant Cell Tissue Organ Cult. PCTOC 149, 197–204.

Eddouks, M., Hebi, M., Ajebli, M., 2020. Medicinal Plants and gyneco-obstetric disorders among women in the South East of Morocco. Curr. Womens Health Rev. 16, 2–17.

Eddouks, M., Maghrani, M., Lemhadri, A., Ouahidi, M.-L., Jouad, H., 2002. Ethnopharmacological survey of medicinal plants used for the treatment of diabetes mellitus, hypertension and cardiac diseases in the south-east region of Morocco (Tafilalet). J. Ethnopharmacol. 82, 97–103.

El Amri, N., Errachidi, F., Bour, A., Bouhaddaoui, S., Chabir, R., 2019. Morphological and Nutritional Properties of Moroccan *Capparis spinosa* Seeds. Sci. World J. 2019, 8594820. Https://doi.org/10.1155/2019/8594820

El Azhary, K., Tahiri Jouti, N., El Khachibi, M., Moutia, M., Tabyaoui, I., El Hou, A., Achtak, H., Nadifi, S., Habti, N., Badou, A., 2017. Anti-inflammatory potential of *Capparis spinosa* L. In vivo in mice through inhibition of cell infiltration and cytokine gene expression. BMC Complement. Altern. Med. 17, 1–12.

El-Guendouz, S., Al-Waili, N., Aazza, S., Elamine, Y., Zizi, S., Al-Waili, T., Al-Waili, A., Lyoussi, B., 2017. Antioxidant and diuretic activity of co-administration of *Capparis spinosa* honey and propolis in comparison to furosemide. Asian Pac. J. Trop. Med. 10, 974–980.

El-Hilaly, J., Hmammouchi, M., Lyoussi, B., 2003. Ethnobotanical studies and economic evaluation of medicinal plants in Taounate province (Northern Morocco). J. Ethnopharmacol. 86, 149–158.

Fan, X., Lin, X., Ruan, Q., Wang, J., Yang, Y., Sheng, M., Zhou, W., Kai, G., Hao, X., 2022. Research progress on the biosynthesis and metabolic engineering of the anti-cancer drug camptothecin in Camptotheca acuminate. Ind. Crops Prod. 186, 115270.

Fattahi, M., Rahimi, R., 2016. Optimization of extraction parameters of phenolic antioxidants from leaves of *Capparis spinosa* using response surface methodology. Food Anal. Methods 9, 2321–2334.

Fazili, M.A., Bashir, I., Ahmad, M., Yaqoob, U., Geelani, S.N., 2022. *In vitro* strategies for the enhancement of secondary metabolite production in plants: A review. Bull. Natl. Res. Cent. 46, 1–12.

Fici, S., 2017. A taxonomic revision of the genus Capparis (Capparaceae) in New Caledonia. N. Z. J. Bot. 55, 407–423.

Fici, S., 2015. A taxonomic revision of the *Capparis spinosa* group (*Capparaceae*) from eastern Africa to Oceania. Phytotaxa 203, 24–36.

Fici, S., 2014. A taxonomic revision of the *Capparis spinosa* group (*Capparaceae*) from the Mediterranean to Central Asia. Phytotaxa 174, 1–24.

Fici, S., 2001. Intraspecific variation and evolutionary trends in *Capparis spinosa* L.(*Capparaceae*). Plant Syst. Evol. 228, 123–141.

Fici, S., Averyanov, L.V., Sy, D.T., 2022. An Updated Checklist of the Genus Capparis L. (Capparaceae) in Vietnam, including a New Species from Hon Tre Island. Plants 11, 3402. Https://doi.org/10.3390/plants11233402

Fu, X.P., Wu, T., Abdurahim, M., Su, Z., Hou, X.L., Aisa, H.A., Wu, H., 2008. New spermidine alkaloids from *Capparis spinosa* roots. Phytochem. Lett. 1, 59–62.

Gabr, A.M., Mabrok, H.B., Sytar, O., Smetanska, I., 2021. Recent advances toward development of plant cell culture process for sustainable production of lignans and their health benefits. Explor. Plant Cells Prod. Compd. Interest 249–289.

Gantait, S., Mukherjee, E., 2021. Hairy root culture technology: applications, constraints and prospect. Appl. Microbiol. Biotechnol. 105, 35–53.

Giuffrida, D., Salvo, F., Ziino, M., Toscano, G., Dugo, G., 2002. Initial Investigation On Some Chemical Constituents Of Capers (*Capparis spinosa* L.) From The Island Of Salina. Ital. J. Food Sci. 14.

Graikou, K., Damianakos, H., Ganos, C., Syklowska-Baranek, K., Jeziorek, M., Pietrosiuk, A., Roussakis, C., Chinou, I., 2021. Chemical profile and screening of bioactive metabolites of *Rindera graeca* (A. Dc.) Bois. & Heldr.(*Boraginaceae*) *in vitro* cultures. Plants 10, 834.

Grimalt, M., Hernández, F., Legua, P., Almansa, M.S., Amorós, A., 2018. Physicochemical composition and antioxidant activity of three Spanish caper (*Capparis spinosa* L.) Fruit cultivars in three stages of development. Sci. Hortic. 240, 509–515.

Grimalt, M., Hernández, F., Legua, P., Amorós, A., Almansa, M.S., 2022. Antioxidant activity and the physicochemical composition of young caper shoots (*Capparis spinosa* L.) Of different Spanish cultivars. Sci. Hortic. 293, 110646.

Grimalt, M., Sánchez-Rodríguez, L., Hernández, F., Legua, P., Carbonell-Barrachina, Á.A., Almansa, M.S., Amorós, A., 2021. Volatile profile in different aerial parts of two caper cultivars (*Capparis spinosa* L.). J. Food Qual. 2021, 1–9.

Gristina, A.S., Fici, S., Siragusa, M., Fontana, I., Garfì, G., Carimi, F., 2014. Hybridization in *Capparis spinosa* L.: Molecular and morphological evidence from a Mediterranean island complex. Flora-Morphol. Distrib. Funct. Ecol. Plants 209, 733–741.

Gull, T., Sultana, B., Anwar, F., Nouman, W., Mehmood, T., Sher, M., 2018. Characterization of phenolics in different parts of selected Capparis species harvested in low and high rainfall season. J. Food Meas. Charact. 12, 1539–1547.

Güzel, Y., Güzelşemme, M., Miski, M., 2015. Ethnobotany of medicinal plants used in Antakya: a multicultural district in Hatay Province of Turkey. J. Ethnopharmacol. 174, 118–152.

Hachi, M., Ouafae, B., Hachi, T., Mohamed, E.B., Imane, B., Atmane, R., Zidane, L., 2016. Contribution to the ethnobotanical study of antidiabetic medicinal plants of the Central Middle Atlas region (Morocco). Lazaroa 37, 1–11.

Haciseferoğullari, H., Özcan, M.M., Duman, E., 2011. Biochemical and technological properties of seeds and oils of *Capparis spinosa* and *Capparis ovata* plants growing wild in Turkey. J. Food Process. Technol. 2.

Halder, M., Roy, S., 2023. Current Status of Metabolic Engineering of Medicinal Plants for Production of Plant-Derived Secondary Metabolites, in: Medicinal Plants: Biodiversity, Biotechnology and Conservation. Springer, pp. 819–869.

Hammiche, V., Maiza, K., 2006. Traditional medicine in Central Sahara: pharmacopoeia of Tassili n’ajjer. J. Ethnopharmacol. 105, 358–367.

Hamuti, A., Li, Jinyu, Zhou, F., Aipire, A., Ma, J., Yang, J., Li, Jinyao, 2017. *Capparis spinosa* fruit ethanol extracts exert different effects on the maturation of dendritic cells. Molecules 22, 97.

Hesami, M., Pepe, M., Baiton, A., Jones, A.M.P., 2022. Current status and future prospects in cannabinoid production through *in vitro* culture and synthetic biology. Biotechnol. Adv. 108074.

Hosseini, S.H., Sadeghi, Z., Hosseini, S.V., Bussmann, R.W., 2022. Ethnopharmacological study of medicinal plants in Sarvabad, Kurdistan province, Iran. J. Ethnopharmacol. 288, 114985.

Huseini, H.F., Hasani-Rnjbar, S., Nayebi, N., Heshmat, R., Sigaroodi, F.K., Ahvazi, M., Alaei, B.A., Kianbakht, S., 2013. *Capparis spinosa* L.(Caper) fruit extract in treatment of type 2 diabetic patients: a randomized double-blind placebo-controlled clinical trial. Complement. Ther. Med. 21, 447–452.

Idm’hand, E., Msanda, F., Cherifi, K., 2020. Ethnobotanical study and biodiversity of medicinal plants used in the Tarfaya Province, Morocco. Acta Ecol. Sin. 40, 134–144.

Ikeuchi, M., Sugimoto, K., Iwase, A., 2013. Plant Callus: Mechanisms of Induction and repressionopen.

Infantino, A., Tomassoli, L., Peri, E., Colazza, S., 2007. Viruses, fungi and insect pests affecting caper. Eur. J. Plant Sci. Biotechnol. 1, 170–179.

Inocencio, C., Rivera, D., Obón, M.C., Alcaraz, F., Barreña, J.-A., 2006. A systematic revision of capparis section Capparis (Capparaceae) 1, 2. Ann. Mo. Bot. Gard. 93, 122–149.

Jamila, F., Mostafa, E., 2014. Ethnobotanical survey of medicinal plants used by people in Oriental Morocco to manage various ailments. J. Ethnopharmacol. 154, 76–87.

Jaradat, N.A., Shawahna, R., Eid, A.M., Al-Ramahi, R., Asma, M.K., Zaid, A.N., 2016. Herbal remedies use by breast cancer patients in the West Bank of Palestine. J. Ethnopharmacol. 178, 1–8.

Jiménez-López, J., Ruiz-Medina, A., Ortega-Barrales, P., Llorent-Martínez, E.J., 2018. Phytochemical profile and antioxidant activity of caper berries (*Capparis spinosa* L.): Evaluation of the influence of the fermentation process. Food Chem. 250, 54–59.

Jouad, H., Haloui, M., Rhiouani, H., El Hilaly, J., Eddouks, M., 2001. Ethnobotanical survey of medicinal plants used for the treatment of diabetes, cardiac and renal diseases in the North centre region of Morocco (Fez–Boulemane). J. Ethnopharmacol. 77, 175–182.

Kabbaj, F., Meddah, B., Cherrah, Y., Faouzi, E., 2012. Ethnopharmacological profile of traditional plants used in Morocco by cancer patients as herbal therapeutics. Phytopharmacology 2, 243–256.

Kachmar, M.R., Naceiri Mrabti, H., Bellahmar, M., Ouahbi, A., Haloui, Z., El Badaoui, K., Bouyahya, A., Chakir, S., 2021. Traditional knowledge of medicinal plants used in the Northeastern part of Morocco. Evid. Based Complement. Alternat. Med. 2021.

Kahouadji, M.S., 1995. Contribution à une étude ethnobotanique des plantes médicinales dans le Maroc oriental. Diplôme d’études Supér. 3ème Cycle Univ. Mohamed Ier.

Kalantari, H., Foruozandeh, H., Khodayar, M.J., Siahpoosh, A., Saki, N., Kheradmand, P., 2018. Antioxidant and hepatoprotective effects of *Capparis spinosa* L. Fractions and Quercetin on tert-butyl hydroperoxide-induced acute liver damage in mice. J. Tradit. Complement. Med. 8, 120–127.

Kantsa, A., Garcia, J.E., Raguso, R.A., Dyer, A.G., Steen, R., Tscheulin, T., Petanidou, T., 2023. Intrafloral patterns of color and scent in *Capparis spinosa* L. And the ghosts of its selection past. Am. J. Bot. 110, e16098.

Karami, M., Naghavi, M.R., Nasiri, J., Farzin, N., 2023. Methyl jasmonate and β-cyclodextrin shake hands to boost withaferin A production from the hairy root culture of Withania somnifera.

Karous, O., Ben Haj Jilani, I., Ghrabi-Gammar, Z., 2021. Ethnobotanical study on plant used by semi-nomad descendants’ community in Ouled Dabbeb—Southern Tunisia. Plants 10, 642.

Katiri, A., Barkaoui, M., Msanda, F., Boubaker, H., 2017. Ethnobotanical survey of medicinal plants used for the treatment of diabetes in the Tizi n’Test region (Taroudant Province, Morocco). J Pharmacogn Nat Prod 3, 2472–0992.

Kdimy, A., El Yadini, M., Guaadaoui, A., Bourais, I., El Hajjaji, S., Le, H.V., 2022. Phytochemistry, biological activities, therapeutic potential, and socio-economic value of the caper bush (*Capparis spinosa* l.). Chem. Biodivers. 19, e202200300.

Kernouf, N., Bouriche, H., Kada, S., Messaoudi, D., Assaf, A.M., Senator, A., 2018. Anti-inflammatory and immuno-modulatory effects of *Cpparis spinosa* flower bud extract. Annu. Res. Rev. Biol. 1–11.

Khatib, M., Pieraccini, G., Innocenti, M., Melani, F., Mulinacci, N., 2016. An insight on the alkaloid content of *Capparis spinosa* L. Root by HPLC-DAD-MS, MS/MS and 1H qnmr. J. Pharm. Biomed. Anal. 123, 53–62.

Khavasi, N., hosein Somi, M., Khadem, E., Faramarzi, E., Ayati, M.H., Fazljou, S.M.B., Torbati, M., 2017. Effect of daily caper fruit pickle consumption on disease regression in patients with non-alcoholic fatty liver disease: A double-blinded randomized clinical trial. Adv. Pharm. Bull. 7, 645.

Khavasi, N., Somi, M., Khadem, E., Ayati, M.H., Torbati, M., Fazljou, S.M.B., 2018. Daily consumption of the *Capparis spinosa* reduces some atherogenic indices in patients with non-alcoholic fatty liver disease: A randomized, double-blind, clinical trial. Iran. Red Crescent Med. J. 20.

Kianersi, F., Abdollahi, M.R., Mirzaie-asl, A., Dastan, D., Rasheed, F., 2020a. Biosynthesis of rutin changes in *Capparis spinosa* due to altered expression of its pathway genes under elicitors’ supplementation. Plant Cell Tissue Organ Cult. PCTOC 141, 619–631.

Kianersi, F., Abdollahi, M.R., Mirzaie-Asl, A., Dastan, D., Rasheed, F., 2020b. Identification and tissue-specific expression of rutin biosynthetic pathway genes in *Capparis spinosa* elicited with salicylic acid and methyl jasmonate. Sci. Rep. 10, 8884.

Kirkan, B., Ceylan, O., Sarikürkcü, C., Bektas, T., 2021. Phenolic profile, antioxidant and enzyme inhibitory activity of the ethyl acetate, methanol and water extracts of *Capparis spinosa* L. Int. J. Second. Metab. 8, 337–351.

Kumari, K., Kumar, S., Jha, A.K., Kumar, N., 2022. Biotechnological intervention in genetic improvement and regulation of secondary metabolites production in *Ocimum sanctum* L. Ind. Crops Prod. 187, 115329.

Legua, P., Martínez, J. J., Melgarejo, P., Martínez, R., Hernández, Fca., 2013. Phenological growth stages of caper plant (*Capparis spinosa* L.) According to the Biologische Bundesanstalt, Bundessortenamt and chemical scale. Ann. Appl. Biol. 163, 135–141. Https://doi.org/10.1111/aab.12041

Lev, E., Amar, Z., 2002. Ethnopharmacological survey of traditional drugs sold in the Kingdom of Jordan. J. Ethnopharmacol. 82, 131–145.

Liu, W., He, Y., Xiang, J., Fu, C., Yu, L., Zhang, J., Li, M., 2011. The physiological response of suspension cell of *Capparis spinosa* L. To drought stress. J Med Plants Res 5, 5899–5906.

Lo Bosco, F., Guarrasi, V., Moschetti, M., Germanà, M.A., Butera, D., Corana, F., Papetti, A., 2019. Nutraceutical Value of Pantelleria Capers (*Capparis spinosa* L.). J. Food Sci. 84, 2337–2346.

Mahboubi, M., Mahboubi, A., 2014. Antimicrobial activity of *Capparis spinosa* as its usages in traditional medicine. Herba Pol. 60.

Mahmodi, N., Sharifi-Sirchi, G.-R., Cheghamirza, K., 2022. Evaluation of molecular and morphological diversity of caper (*Capparis spinosa* L.). Genet. Resour. Crop Evol. 69, 1509–1534.

Malarz, J., Yudina, Y.V., Stojakowska, A., 2023. Hairy Root Cultures as a Source of Phenolic Antioxidants: Simple Phenolics, Phenolic Acids, Phenylethanoids, and Hydroxycinnamates. Int. J. Mol. Sci. 24, 6920.

Maresca, M., Micheli, L., Mannelli, L.D.C., Tenci, B., Innocenti, M., Khatib, M., Mulinacci, N., Ghelardini, C., 2016. Acute effect of *Capparis spinosa* root extracts on rat articular pain. J. Ethnopharmacol. 193, 456–465.

Mattalia, G., Paolo, C., Pieroni, A., 2020. The virtues of being peripheral, recreational, and transnational: local wild food and medicinal plant knowledge in selected remote municipalities of Calabria, Southern Italy. Ethnobot. Res. Appl. 19.

Matthäus, B., Özcan, M., 2005. Glucosinolates and fatty acid, sterol, and tocopherol composition of seed oils from *Capparis spinosa* Var. *Spinosa* and *Capparis ovata* Desf. Var. Canescens (Coss.) Heywood. J. Agric. Food Chem. 53, 7136–7141.

Mautone, M., De Martino, L., De Feo, V., 2019. Ethnobotanical research in Cava de’tirreni area, Southern Italy. J. Ethnobiol. Ethnomedicine 15, 1–21.

Mazarei, F., Jooyandeh, H., Noshad, M., Hojjati, M., 2017. Polysaccharide of caper (*Capparis spinosa* L.) Leaf: Extraction optimization, antioxidant potential and antimicrobial activity. Int. J. Biol. Macromol. 95, 224–231.

Mechaala, S., Bouatrous, Y., Adouane, S., 2022. Traditional knowledge and diversity of wild medicinal plants in El Kantara’s area (Algerian Sahara gate): An ethnobotany survey. Acta Ecol. Sin. 42, 33–45.

Mehrnia, M., Akaberi, M., Amiri, M.S., Nadaf, M., Emami, S.A., 2021. Ethnopharmacological studies of medicinal plants in central Zagros, Lorestan Province, Iran. J. Ethnopharmacol. 280, 114080.

Melgarejo, P., Legua, P., Martinez, J.J., Martinez-Font, R., Hernandez, F., 2009. Preliminary characterization of sixty one caper clones (*Capparis spinosa* L.). Acta Hortic.

Mipeshwaree Devi, A., Khedashwori Devi, K., Premi Devi, P., Lakshmipriyari Devi, M., Das, S., 2023. Metabolic engineering of plant secondary metabolites: prospects and its technological challenges. Front. Plant Sci. 14, 1171154.

Moghadamnia, Y., Kani, S.N.M., Ghasemi-Kasman, M., Kani, M.T.K., Kazemi, S., 2019. The anti-cancer effects of *Capparis spinosa* hydroalcoholic extract. Avicenna J. Med. Biotechnol. 11, 43.

Mohaddab, M., El Goumi, Y., Gallo, M., Montesano, D., Zengin, G., Bouyahya, A., Fakiri, M., 2022. Biotechnology and *in vitro* culture as an alternative system for secondary metabolite production. Molecules 27, 8093. Https://doi.org/10.3390/molecules27228093

Mohebali, N., Shahzadeh Fazeli, S.A., Ghafoori, H., Farahmand, Z., mohammadkhani, E., Vakhshiteh, F., Ghamarian, A., Farhangniya, M., Sanati, M.H., 2018. Effect of flavonoids rich extract of *Capparis spinosa* on inflammatory involved genes in amyloid-beta peptide injected rat model of Alzheimer’s disease. Nutr. Neurosci. 21, 143–150.

Mollica, A., Stefanucci, A., Macedonio, G., Locatelli, M., Luisi, G., Novellino, E., Zengin, G., 2019. Chemical composition and biological activity of *Capparis spinosa* L. From Lipari Island. South Afr. J. Bot. 120, 135–140.

Mollica, A., Zengin, G., Locatelli, M., Stefanucci, A., Mocan, A., Macedonio, G., Carradori, S., Onaolapo, O., Onaolapo, A., Adegoke, J., 2017. Anti-diabetic and anti-hyperlipidemic properties of *Capparis spinosa* L.: *in vivo* and *in vitro* evaluation of its nutraceutical potential. J. Funct. Foods 35, 32–42.

Motolinía-Alcántara, E.A., Castillo-Araiza, C.O., Rodríguez-Monroy, M., Román-Guerrero, A., Cruz-Sosa, F., 2021. Engineering considerations to produce bioactive compounds from plant cell suspension culture in bioreactors. Plants 10, 2762.

Motti, R., 2021. Wild plants used as herbs and spices in Italy: An ethnobotanical review. Plants 10, 563.

Mughal, T.A., 2008. Ethnomedicinal studies of flora of southern Punjab and isolation of biologically active principles (phd Thesis). Lahore College For Women University, Lahore, Pakistan.

Mukhopadhyay, R., 2023. Micropropagation for the Improved Production of Secondary Metabolites. Plants Bioreact. Ind. Mol. 161–184.

Najafian, S., Mehregan, I., Iranbakhsh, A., Assadi, M., Fici, S., 2021. Species delimitation in Capparis (Capparaceae): Morphological and molecular. Genetika 53, 609–627.

Nazer, M.R., Jahanbakhsh, S., Ebrahimi, K., Niazi, M., Sepahvand, M., Khatami, M., Kharazi, S., 2021. Cytotoxic and antileishmanial effects of various extracts of *Capparis spinosa* L. Turk. J. Pharm. Sci. 18, 146.

Oudah, S.K., Al-Salih, R.M., Gusar, S.H., Roomi, A.B., 2019. Study of the role of polyphenolic extract of *Capparis spinosa* L. Leaves as acute toxicity and antibacterial agent. Plant arch. 09725210 19.

Ouelbani, R., Bensari, S., Mouas, T.N., Khelifi, D., 2016. Ethnobotanical investigations on plants used in folk medicine in the regions of Constantine and Mila (North-East of Algeria). J. Ethnopharmacol. 194, 196–218.

Ouhammou, M., Adnany, E.M.E., Mourjane, A., Hammou, H.A., Bouchdoug, M., Jaouad, A., Mahrouz, M., 2022. Physico-chemical analysis and antioxidant activity of Moroccan caper leaves (*Capparis spinosa* L.). Euro-Mediterr. J. Environ. Integr. 7, 407–414.

Özcan, M., 1999. Pickling and storage of caperberries (Capparis spp.). Z. Für Leb. -Forsch. A 208, 379–382.

Özcan, M.M., Kanbur, G., Endes, Z. Leyha, Er, F., 2012. Fatty acid compositions of some oil-bearing plant seeds. Anal. Chem. Lett. 2, 235–239.

Pegiou, S., Raptis, P., Zafeiriou, I., Polidoros, A.N., Mylona, P.V., 2023. Genetic diversity and structure of *Capparis spinosa* L. Natural populations using morphological and molecular markers. J. Appl. Res. Med. Aromat. Plants 34, 100487.

Peter, K.V., 2006. Handbook of herbs and spices (Vol. 3). Abingt. Hall Abingt. Cambridgecb16ah Wood Head Publ. Ltd.

Pietrosiuk, A., Budzianowska, A., Budzianowski, J., Ekiert, H., Jeziorek, M., Kawiak, A., Kikowska, M., Krauze-Baranowska, M., Królicka, A., Kuźma, Lukasz, 2022. Polish achievements in bioactive compound production from *in vitro* plant cultures. Acta Soc. Bot. Pol. 91.

POWO, 2021. Plants of the World Online. Facilitated by the Royal Botanic Gardens, Kew. Published on the Internet.

Qaderi, M.M., Martel, A.B., Strugnell, C.A., 2023. Environmental Factors Regulate Plant Secondary Metabolites. Plants 12, 447.

Rad, M.K., Ghani, A., Ghani, E., 2021. *In vitro* effects of *Capparis spinosa* L. Extract on human sperm function, DNA fragmentation, and oxidative stress. J. Ethnopharmacol. 269, 113702.

Rahimi, V.B., Rajabian, A., Rajabi, H., Vosough, E.M., Mirkarimi, H.R., Hasanpour, M., Iranshahi, M., Rakhshandeh, H., Askari, V.R., 2020. The effects of hydro-ethanolic extract of *Capparis spinosa* (*C. Spinosa*) on lipopolysaccharide (LPS)-induced inflammation and cognitive impairment: Evidence from in vivo and *in vitro* studies. J. Ethnopharmacol. 256, 112706.

Rajhi, I., Ben Dhia, M.T., Abderrabba, M., Ouzari-Hadda, I., Ayadi, S., 2019. Phytochemical screening, *in vitro* antioxidant and antibacterial activities of methanolic extracts of Capparis Spionsa L. Different parts from Tunisia. J. Mater. Environ. Sci. 10, 234–43.

Rajhi, I., Hernandez-Ramos, F., Abderrabba, M., Ben Dhia, M.T., Ayadi, S., Labidi, J., 2021. Antioxidant, Antifungal and Phytochemical Investigations of *Capparis spinosa* L. Agriculture 11, 1025.

Rakhshandeh, H., Rashidi, R., Vahedi, M.M., Khorrami, M.B., Abbassian, H., Forouzanfar, F., 2021. Hypnotic activity of *Capparis spinosa* hydro-alcoholic extract in mice. Recent Pat. Food Nutr. Agric. 12, 58–62.

Ramdane, F., Mahammed, M.H., Hadj, M.D.O., Chanai, A., Hammoudi, R., Hillali, N., Mesrouk, H., Bouafia, I., Bahaz, C., 2015. Ethnobotanical study of some medicinal plants from Hoggar, Algeria. J. Med. Plants Res. 9, 820–827.

Ramdani, M., Lograda, T., Chalard, P., 2020. Chemical composition and antibacterial activities of *Capparis spinosa* essential oils from Algeria. Biodiversitas J. Biol. Divers. 21.

Rhimi, A., Mnasri, S., Ben Ayed, R., Bel Hajj Ali, I., Hjaoujia, S., Boussaid, M., 2019. Genetic relationships among subspecies of *Capparis spinosa* L. From Tunisia by using ISSR markers. Mol. Biol. Rep. 46, 2209–2219.

Rizza, L., D’Agostino, A., Girlando, A., Puglia, C., 2010. Evaluation of the effect of topical agents on radiation-induced skin disease by reflectance spectrophotometry. J. Pharm. Pharmacol. 62, 779–785.

Rogowska, A., Pączkowski, C., Szakiel, A., 2023. Modifications in steroid and triterpenoid metabolism in Calendula officinalis plants and hairy root culture in response to chitosan treatment. BMC Plant Biol. 23, 1–18.

Rohini, M.R., Rajasekharan, P.E., 2022. Scale-up production of bioactive compounds using bioreactors, in: Nutraceuticals Production from Plant Cell Factory. Springer, pp. 69–81.

Saberi, M., Kamali, N., Tarnian, F., Sadeghipour, A., 2022. Investigation Phenol, Flavonoids and Antioxidant Activity Content of *Capparis spinosa* in Three Natural Habitats of Sistan and Baluchestan Province, Iran. J. Rangel. Sci. 12, 191–204. Https://doi.org/10.30495/rs.2022.682941

Safarzaei, A., Sarhadi, H., Khodaparast, M.H.H., Shahdadi, F., Dashipour, A.R., 2020. Optimization of aqueous and alcoholic extraction of phenolic and antioxidant compounds from Caper (*Capparis spinosa* L.) Roots assisted by ultrasound waves. Zahedan J. Res. Med. Sci. 22.

Said, O., Khalil, K., Fulder, S., Azaizeh, H., 2002. Ethnopharmacological survey of medicinal herbs in Israel, the Golan Heights and the West Bank region. J. Ethnopharmacol. 83, 251–265.

Saifi, N., Ibijbijen, J., Echchgadda, D., 2011. Genetic diversity of caper plant (Capparis ssp.) From North Morocco. J. Food Agric. Environ. 9, 299–304.

Saleem, H., Khurshid, U., Sarfraz, M., Ahmad, I., Alamri, A., Anwar, S., Alamri, A.S., Locatelli, M., Tartaglia, A., Mahomoodally, M.F., 2021. Investigation into the biological properties, secondary metabolites composition, and toxicity of aerial and root parts of *Capparis spinosa* L.: An important medicinal food plant. Food Chem. Toxicol. 155, 112404.

Sardari, S., Fallahi, F., Emadi, F., Davati, A., Khavasi, N., Gholamifesharaki, M., Esmaeili, S.S., 2019. Daily consumption of caper fruit along with atorvastatin has synergistic effects in hyperlipidemic patients: Randomized Clinical trial. Galen Med. J. 8, e1345.

Sargin, S.A., Selvi, S., Lopez, V., 2015. Ethnomedicinal plants of sarigöl district (manisa), Turkey. J. Ethnopharmacol. 171, 64–84.

Sathish, S., Vasudevan, V., Karthik, S., Pavan, G., Siva, R., Manickavasagam, M., 2023. Precursor feeding enhances L-Dopa production in hairy root culture of *Hybanthus enneaspermus* (L.) F. Muell. Biologia (Bratisl.) 78, 913–923.

Shahrajabian, M.H., Sun, W., Cheng, Q., 2021. Plant of the Millennium, Caper (*Capparis spinosa* L.), chemical composition and medicinal uses. Bull. Natl. Res. Cent. 45, 1–9.

Sher, H., Alyemeni, M.N., 2010. Ethnobotanical and pharmaceutical evaluation of *Capparis spinosa* L, validity of local folk and Unani system of medicine. J Med Plants Res 4, 1751–1756.

Singh, K.N., Lal, B., 2008. Ethnomedicines used against four common ailments by the tribal communities of Lahaul-Spiti in western Himalaya. J. Ethnopharmacol. 115, 147–159.

Singh, S., Pandey, P., Akhtar, M.Q., Negi, A.S., Banerjee, S., 2021. A new synthetic biology approach for the production of curcumin and its glucoside in Atropa belladonna hairy roots. J. Biotechnol. 328, 23–33.

Sonkar, N., Shukla, P.K., Misra, P., 2023. Plant Hairy Roots as Biofactory for the Production of Industrial Metabolites. Plants Bioreact. Ind. Mol. 273–297.

Sonmezdag, A.S., Kelebek, H., Selli, S., 2019. Characterization of aroma-active compounds, phenolics, and antioxidant properties in fresh and fermented capers (*Capparis spinosa*) by GC-MS-olfactometry and LC-DAD-ESI-MS/MS. J. Food Sci. 84, 2449–2457.

Sottile, F., Caltagirone, C., Peano, C., Del Signore, M.B., Barone, E., 2021. Can the caper (*Capparis spinosa* L.) Still be considered a difficult-to-propagate crop? Horticulturae 7, 316.

Sozzi, G.O., 2001. Caper bush: botany and horticulture. Hortic. Rev.-Westport Then N. Y.- 27, 125–188.

Sozzi, G.O., Peter, K.V., Babu, K.N., Divakaran, M., 2012. Capers and caperberries, in: Handbook of Herbs and Spices. Elsevier, pp. 193–224.

Sreelekshmi, R., Swapna, T.S., Siril, E.A., 2023. *In Vitro* Secondary Metabolite Production for Sustainable Utilization of Endangered Medicinal Plants, in: Conservation and Sustainable Utilization of Bioresources. Springer, pp. 451–471.

Stefanucci, A., Zengin, G., Locatelli, M., Macedonio, G., Wang, C.-K., Novellino, E., Mahomoodally, M.F., Mollica, A., 2018. Impact of different geographical locations on varying profile of bioactives and associated functionalities of caper (*Capparis spinosa* L.). Food Chem. Toxicol. 118, 181–189.

Syklowska-Baranek, K., Gawel, M., Kuźma, Lukasz, Wileńska, B., Kawka, M., Jeziorek, M., Graikou, K., Chinou, I., Szyszko, E., Stępień, P., 2023. Rindera graeca (A. DC.) Boiss. & Heldr.(Boraginaceae) *in vitro* Cultures Targeting Lithospermic Acid B and Rosmarinic Acid Production. Molecules 28, 4880.

Tahraoui, A., El-Hilaly, J., Israili, Z.H., Lyoussi, B., 2007. Ethnopharmacological survey of plants used in the traditional treatment of hypertension and diabetes in south-eastern Morocco (Errachidia province). J. Ethnopharmacol. 110, 105–117.

Taibi, K., Abderrahim, L.A., Boussaid, M., Taibi, F., Achir, M., Souana, K., Benaissa, T., Farhi, K.H., Naamani, F.Z., Said, K.N., 2021. Unraveling the ethnopharmacological potential of medicinal plants used in Algerian traditional medicine for urinary diseases. Eur. J. Integr. Med. 44, 101339.

Taibi, K., Abderrahim, L.A., Ferhat, K., Betta, S., Taïbi, F., Bouraada, F., Boussaid, M., 2020. Ethnopharmacological study of natural products used for traditional cancer therapy in Algeria. Saudi Pharm. J. 28, 1451–1465. Https://doi.org/10.1016/j.jsps.2020.09.011

Tir, M., Feriani, A., Labidi, A., Mufti, A., Saadaoui, E., Nasri, N., Khaldi, A., El Cafsi, M., Tlili, N., 2019. Protective effects of phytochemicals of *Capparis spinosa* seeds with cisplatin and ccl4 toxicity in mice. Food Biosci. 28, 42–48.

Tlili, N., Elfalleh, W., Saadaoui, E., Khaldi, A., Triki, S., Nasri, N., 2011a. The caper (*Capparis* L.): Ethnopharmacology, phytochemical and pharmacological properties. Fitoterapia 82, 93–101.

Tlili, N., Feriani, A., Saadoui, E., Nasri, N., Khaldi, A., 2017. *Capparis spinosa* leaves extract: Source of bioantioxidants with nephroprotective and hepatoprotective effects. Biomed. Pharmacother. 87, 171–179.

Tlili, N., Khaldi, A., Triki, S., Munné-Bosch, S., 2010. Phenolic compounds and vitamin antioxidants of caper (*Capparis spinosa*). Plant Foods Hum. Nutr. 65, 260–265.

Tlili, N., Nasri, N., Khaldi, A., Triki, S., Munné-bosch, S., 2011b. Phenolic compounds, tocopherols, carotenoids and vitamin C of commercial caper. J. Food Biochem. 35, 472–483.

Tutin, T.G., Heywood, V.H., Burges, N.A., Valentine, D.H., Walters, S.M., Webb, D.A., 1976. Flora Europaea: Plantaginaceae to Compositae (and Rubiaceae). Cambridge university press.

Ugulu, I., Baslar, S., Yorek, N., Dogan, Y., 2009. The investigation and quantitative ethnobotanical evaluation of medicinal plants used around Izmir province, Turkey. J. Med. Plants Res. 3, 345–367.

Vahid, H., Rakhshandeh, H., Ghorbani, A., 2017. Antidiabetic properties of *Capparis spinosa* L. And its components. Biomed. Pharmacother. 92, 293–302.

Verpoorte, R., Contin, A., Memelink, J., 2002. Biotechnology for the production of plant secondary metabolites. Phytochem. Rev. 1, 13–25.

Vivek, A.S., Riyas, C.T., Swapna, T.S., 2023. Enhanced Secondary Metabolite Production for Drug Leads, in: Conservation and Sustainable Utilization of Bioresources. Springer, pp. 473–504.

Wang, L., Fan, L., Zhao, Z., Zhang, Z., Jiang, L., Chai, M., Tian, C., 2022. The *Capparis spinosa* var. Herbacea genome provides the first genomic instrument for a diversity and evolution study of the Capparaceae family. Gigascience 11, giac106.

Wang, Q., Zhang, M.-L., Yin, L.-K., 2016. Genetic diversity and population differentiation of *Capparis spinosa* (*Capparaceae*) in Northwestern China. Biochem. Syst. Ecol. 66, 1–7.

Wang, Y.T., Gan, L., Liu, W., Yu, L.J., Li, M.T., 2007. Research on the callus inducing and the cell growth and metabolism characteristics of *Capparis spinosa* L. Coll. Life Sci Technolo Huazhong Univ Sci Technolo Wuhan China 7, 1779–1783.

Wojdyło, A., Nowicka, P., Grimalt, M., Legua, P., Almansa, M.S., Amorós, A., Carbonell-Barrachina, Á.A., Hernández, F., 2019. Polyphenol compounds and biological activity of caper (*Capparis spinosa* L.) Flowers buds. Plants 8, 539.

Yahia, Y., Benabderrahim, M.A., Tlili, N., Hannachi, H., Ayadi, L., Elfalleh, W., 2020. Comparison of three extraction protocols for the characterization of caper (*Capparis spinosa L*.) Leaf extracts: evaluation of phenolic acids and flavonoids by liquid chromatography–electrospray ionization–tandem mass spectrometry (LC–ESI–MS) and the antioxidant activity. Anal. Lett. 53, 1366–1377.

Yan, M., Li, J., Liu, H., Yang, N., Chu, J., Sun, L., Bi, X., Lin, R., Lv, G., 2022. *In vitro* efficacy of *Capparis spinosa* extraction against larvae viability of Echinococcus granulosus sensu stricto. J. Vet. Med. Sci. 84, 465–472.

Yan, Y., Huang, X., Shen, Q., Hu, R., Wang, P., Yan, M., Di, P., Wang, Y., 2023. Establishment of hairy roots culture of Perilla frutescens L. And production of phenolic acids.

Yang, T., Wang, C., Chou, G., Wu, T., Cheng, X., Wang, Z., 2010. New alkaloids from *Capparis spinosa*: Structure and X-ray crystallographic analysis. Food Chem. 123, 705–710.

Yang, T., Wang, Y.-L., Zhang, Y.-L., Liu, Y.-T., Tao, Y.-Y., Zhou, H., Liu, C.-H., 2022. The protective effect of *Capparis spinosa* fruit on triptolide-induced acute liver injury: A metabolomics-based systematic study. J. Funct. Foods 90, 104989.

Yin, Y., He, Y., Liu, W., Gan, L., Fu, C., Jia, H., Li, M., 2014. The durative use of suspension cells and callus for volatile oil by comparative with seeds and fruits in *Capparis spinosa* L. Plos One 9, e113668.

Yue, W., Ming, Q., Lin, B., Rahman, K., Zheng, C.-J., Han, T., Qin, L., 2016. Medicinal plant cell suspension cultures: pharmaceutical applications and high-yielding strategies for the desired secondary metabolites. Crit. Rev. Biotechnol. 36, 215–232.

Yuldasheva, N.K., Ul′ chenko, N.T., Glushenkova, A.I., 2008. Lipids of *Capparis spinosa* seeds. Chem. Nat. Compd. 44, 637–638.

Zarei, M., Seyedi, N., Maghsoudi, S., Nejad, M.S., Sheibani, H., 2021. Green synthesis of Ag nanoparticles on the modified graphene oxide using *Capparis spinosa* fruit extract for catalytic reduction of organic dyes. Inorg. Chem. Commun. 123, 108327.

Zhou, H., Jian, R., Kang, J., Huang, X., Li, Y., Zhuang, C., Yang, F., Zhang, L., Fan, X., Wu, T., 2010. Anti-inflammatory effects of caper (*Capparis spinosa* L.) Fruit aqueous extract and the isolation of main phytochemicals. J. Agric. Food Chem. 58, 12717–12721.

Zhu, P., Wang, Y., Zhang, X., 2022. Preparation and characterization of electrospun nanofibre membranes incorporated with an ethanol extract of *Capparis spinosa* L. As a potential packaging material. Food Packag. Shelf Life 32, 100851.

Zhu, X., Yang, Y., Gao, W., Jiang, B., Shi, L., 2021. *Capparis spinosa* alleviates DSS-induced ulcerative colitis via regulation of the gut microbiota and oxidative stress. Evid. Based Complement. Alternat. Med. 2021.

Ziyyat, A., Legssyer, A., Mekhfi, H., Dassouli, A., Serhrouchni, M., Benjelloun, W., 1997. Phytotherapy of hypertension and diabetes in oriental Morocco. J. Ethnopharmacol. 58, 45–54.

Zohary, M., 1960. The species of Capparis in the Mediterranean and the Near Eastern Countries. Bull. Res. Counc. Isr. 49–64.