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Allelopathic Medicinal Plants: 3. *Capparis spinosa* L.

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ABSTRACT

The genus *Capparis* (Capparidaceae) comprises more than 250 species. *C. spinosa* L. is found in Mediterranean regions (Iran, Turkey, Italy, Algeria and Morocco). It is a medicinal herb due to the presence of several chemical compound in its roots, leaves, buds, fruits and seed. In folk medicine it is used as anti-diabetic, anti-obesity, anti-hypertensive and antimicrobial, hence, traditionally used in diet. This is overview of botanical, chemical, pharmacological as well as genetic aspects of *C. spinosa* L. and explains the scientific basis and pharmacological uses.

Key words: Botany, Capers, *Capparis spinosa* L, Chemistry, Herbal plant, Medicinal plant, Pharmacology, Variation,

1. INTRODUCTION

The genus *Capparis* [Capparidaceae Family (Figure 1)] has more than 250 species in tropical and subtropical regions (62). *Capparis spinosa* L. is found in Mediterranean regions (Iran (48), Turkey (8), Italy (44), Algeria (15) and Morocco (60)]. It is a medicinal herb due to the presence of several chemical compounds (alkaloids, flavonoids, terpenes, essential oil, and antioxidant compounds) in its roots, leaves, buds, fruits and seeds. The leaves and flowers and roots are rich in polyphens and flavoids but the roots have low contents of acids (15). Monoterpenes are the main compounds in

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C. spinosa L. (8). It contains nutrients (Na, K, Ca, Mg and P) and essential elements in all caper parts (50)

Figure 1. *Capparis spinosa* plant (shrub, stem, leaves, flowers, bush)- Iran, Isfahan

C. spinosa L. has been traditionally used for diet and in folk medicine. Its buds and leaves have anti-diabetic and anti-hyperlipidemic effects (44), roots, stem barks, leaves and fruits have antimicrobial effects (1,33,47), leaves, buds and flowers contain anticarcinogenic activity (37), and aerial parts have antiviral (13) as well as antifungal effects (15,52). It also has anti-diabetic properties. Due to these properties, the infusion of the aerial parts of this plant has been used to treat rheumatism, toothache and cough (62). Native people used root and shoots to treat rheumatism. Furthermore, it is used against malaria and hemorrhoids (2), gastrointestinal infections and diabetes (45). Mehrzadi *et al.* (42) reported that *C. spinosa* L. is used for diabetes with no side effects. Its fruits

significantly reduce the triglyceride levels in diabetic patients (49). The endemic *C. spinosa* L. is one of the medicinal plants in Greek. It has been used to treat liver and kidney diseases (44). In recent decades, many researches were done on morphological, chemical and pharmacological aspects. This review summarizes the existing information to guide future researches.

2. MORPHOLOGY

Capers grow as small, perennial shrubs with both erect and pendulous branches, showcasing shades of green, red, or yellow, reaching up to 4 m. These branches can appear unramified or multiramified. Stipules, slightly curved or straight, come in antrorse or retrorse positions, ranging in hues from orange to yellow or green, measuring 6 mm in length (53). These stipules transform into spines, giving rise to the plant's name "Spinosa." The leaves, whether rounded, ovate, elliptical, obcordate, oblong, or lanceolate, display various bases (cordate or acute) and apexes (obtuse). Veins are subtle, and textures range from glabrous to pubescent and dense. A grooved or complete petiole is up to 2 cm in length. The noctiflorous flowers feature four white or pinkish-white petals, often oblong or obovate, accompanied by numerous stamens with 5 cm filaments and a 3-6 mm gynophore. The ellipsoidal fruit contains numerous reddish-brown seeds. The plant has adaptive nature, modifying its leaf, stem, and root structure to resist severe drought conditions, thriving in rocky slopes and pastures (53).

3. GENETIC DIVERSITY

Molecular genetic studies of *C. spinosa* L. are limited and mostly focused on genetic diversity and structure of genotypes or populations from the different region using various molecular markers (Table 1). (5,17,41). Twelve new specific Chloroplast SSR (cpSSR) primer pairs were developed for *C. spinosa* L., which 80 developed primers showed multilocus patterns (58).

Table 1. Different Molecular markers used for genetic diversity of *Capparis spinosa* L.

No	Number of individual	Type of Molecular marker	Number of Molecular markers	Number of fragments (band)	% Polymorphic	Reference
1	1	cpSSR	12	multilocus patterns	multilocus patterns	58
2	90	RAPD, ISSR	20, 20	223, 85	98, 68	17
3	47	IRAP, ISSR	11, 13	153, 69	71.5, 82.04	10
4	3	ISSR	10	313	52.0	40
5	213	AFLP	3 combinations	750	84.8	5
6	92	ISSR	10	387	97.7	4
7	80	ISSR, SCoT	34, 10	127	85.04, 84.84	41
8	8 population	ISSR	7	190	36.51-100	20
9	108 (5 spp)	ISSR	10	5, 55	15.96, 85.44	48
10	3	ISSR, SCoT	5, 5	28, 40	64.28, 67.5	25

The phylogenetic relationships of 90 wild grown *C. spinosa* L. genotypes collected from 9 sampling sites of trans-Himalayan region were analyzed using 20 random amplified polymorphic DNAs (RAPDs) and 20 inter simple sequence repeats (ISSRs). The RAPD analysis produced 223 fragments of which 220 were polymorphic while, ISSR yielded 85 bands, of which all are found polymorphic (17). The high genetic diversity of *C. spinosa* L. and revealed both RAPD and ISSR markers, which are equally useful to study the genetic relationships of *Capparis* individuals.

Al- Safadi *et al.* (10) tested 11 Inter-retrotransposon amplified polymorphism (IRAP) primer combinations and 13 ISSR primers for genetic diversity of 47 samples of three *C. species* L. genotypes which were collected from 21 different locations in Syria. Eighty-four fragments were produced from ISSR primers which 69 fragments (82.04 %) were polymorphic. While, one hundred and fifty five fragments were amplified from IRAP primers and 109 (71.5 %) of them were polymorphic. The authors found that the genetic relationships among the studied genotypes through IRAP and ISSR markers combination, showed similar dendrogram as obtained from each single technique. Liu *et al.* (40) used 10 ISSR primers to assess the genetic diversity of ten natural populations of *C. spinosa* L. from 3 locations in North, Central, and South Xinjiang, China. The ISSR analysis produced 313 amplified DNA fragments, with 52 % of fragments being polymorphic. And 10 *C. spinosa* L. showed the high genetic diversity populations which are clustered into 3-Geographically distinct groups.

Three primer combinations of Amplified Fragment Length Polymorphism markers (AFLP) were used to analyse of 6-Tunisian *C. species* L., 213 accessions of Caper. Out of 750 fragments generated, 636 were polymorphic and 407 of them were restricted to a single species. (5). There is high genetic diversity in *C. spinosa* L. Ahmadi and Saeidi (4) analysed genetic diversity and population structure of 92 Iranian genepool of *C. spinosa* L. using Inter Simple Sequence Repeat (ISSR) markers. Ten ISSR primers were amplified 387 DNA fragments (bands) of which 378 (97.7%) were polymorphic. There was high genetic and genetic differentiation and low gene flow among populations. The genetic diversity of caper was recently provided (41). A set of 34 ISSR primers and Ten SCoT primers were used in their study. Eighty caper (*C. spinosa* L.) genotypes from the 12 regions of the central Zagros Mountains located in the west of Iran. ISSR primers produced a total of 108 polymorphic bands (85.04 %) from 127 bands while, SCoT primers produced a total of 165 polymorphic bands (86.84 %) from 190 bands in their genetic diversity study. The combined (ISSR+SCoT) markers did not provide more information of genetic diversity than single analysis of ISSR and SCoT. The levels of genetic variation in Moroccan *Capparis* population were due to 7-commercial ISSR primers (20). The polymorphism rate was found between 36.51 % to 100 %. The results of their study have shown that the majority of genetic diversity within species helps ensure long-term breeding success (20). Najafian *et al.* (48) reported highest level of genetic polymorphism (85.44 %) in *C. spinosa* L. Ten ISSR primers were used in 108 randomly collected plants from 20 geographical populations of Capparis species.

Recently, endemic varieties among three Egyptian *C. spinosa* L.; canescens, deserti, inermis were identified using two marker approaches including inter simple sequence repeat (ISSR) and start codon targeted polymorphism (25). Five primers for each

approach were analysed. ISSR and SCoT primers generated 28 and 40 bands overall, respectively. Polymorphism levels ranged between 64.28 to 67.50 % with ISSR and SCoT examination, respectively (25).

4. CHEMICAL COMPOSITION

A number of components have been identified in *C. spinosa* L., including alkaloids (26,65), flavonoids (45,56), terpenoids (55), volatile oils and fatty acids (16,45). Chemical composition of *C. spinosa* L. summarized in Table 2.

4.1. Alkaloids: The aromatic content of *C. spinosa* L. from Italy shows 22. 2 % aldehydes (55). While, Aliyazicioglu *et al*. (8) isolated 18.2 % aldehyde from *C. spinose* L. of Turkey and Benachour *et al.* (16) reported aldehydes as major component (19.74 ± 7.74 %). The various alkaloids in *C. spinosa* L. isolated from fruits was tetrahydroquinoline acid (65), and from roots were: capparispine, cadabicine 26-O-β-D-glucosidehydrochloride and capparispine 26-O-β-D-glucoside (27). The fruit contained new alkaloids such as : capparisine A , capparisine B, capparisine C, 2-(5-hydroxymethyl-2-formylpyrrol-1-yl) propionic acid lactone, N-(3/ -maleimidyl)-5-hydroxymethyl-2-pyrrole formaldehyde (64).

4.2. Flavonoids: *C. spinosa* L. is rich source of flavonoids. Several groups (14,34,44,56) have found the flavonoids content in many regions. Total flavonoid was determined 10.17-11.67 mgGAE/g extract in *C. spinosa* L. (45). Its different parts contained various amount of flavonoids derivatives. The most abundant flavonoid rutin was found in both buds and fruits (54,56). Quercetin and kaempferal were isolated from the buds of caper (54), while various glycosides were identified in the fruits and arial parts of the plant (56). Argentieri *et al*. (14) isolated kaempferol, Kaempferol rutinoside and Kaempferol rhamnosyl-rutinoside from the fruits and buds. Li *et al.* (39) identified flavone derivatives (sakuranetin, wogonin and oroxylin). In addition, Isoginkgetin and ginkgetin were also found in caper by Zhou *et al.* (66).

Table 2. Some important chemical constituents isolated from *Capparis spinosa* L.

No	Chemical Family	Geographical Distribution	Compound Name	Plant parts Used	Ref
1	Alkaloids	China	Tetrahydroquinoline acid	Fruit	65
2	Alkaloids	China	Capparispine	Root	27
3	Alkaloids	China	Capparispine 26-O-β-D-glucoside	Root	27
4	Alkaloids	China	Cadabicine 26-O-β-D-glucosidehydrochloride	Root	27
5	Alkaloids	China	Capparisine A	Fruit	64
6	Alkaloids	China	Capparisine B	Fruit	64
7	Alkaloids	China	Capparisine C	Fruit	64
8	Alkaloids	China	2-(5-Hydroxymethyl-2-formylpyrrol-1-yl) propionic acid lactone	Fruit	64
9	Alkaloids	China	N-(3/ -Maleimidyl)-5-hydroxymethyl-2-pyrrole formaldehyde	Fruit	64
10	Flavonoids	Spain	Rutin	Bud and Fruit	54

11	Flavonoids	Spain	Quercetin	Bud and Fruit	54
12	Flavonoids	Spain	Kaempferal	Bud and Fruit	54
13	Flavonoids	Egypt	Glycosides	Fruit and other part	56
14	Flavonoids	Italy	Kaempferol	Aerial parts and seeds	14
15	Flavonoids	Italy	Kaempferol rutinoside	Aerial parts and seeds	14
16	Flavonoids	Italy	Kaempferol rhamnosyl-rutinoside	Aerial parts and seeds	14
17	Flavonoids	China	Sakuranetin	Arial part	39
18	Flavonoids	China	Wogonin	Arial part	39
19	Flavonoids	China	Oroxylin	Arial part	39
20	Flavonoids	China	Isoginkgetin	Arial part	66
21	Flavonoids	China	Ginkgetin	Arial part	66
22	Terpenes	Algeria	Sesquiterpenes	Arial part	16
23	Terpenes	Algeria	Monoterpenes	Arial part	16
24	Terpenes	Turkey	A-Terpinolene	Fruit	8
25	Terpenes	Italy	Acyclic sesquiterpene	Bud	55
26	Terpenes	Italy	4-terpineol	Bud	55
27	Terpenes	Switzerland	Linalool	Bud	21
28	Terpenes	Switzerland	β-ionone	Bud	21
29	Essential oil	Jordan	Isopropyl isothiocyanate	Aerial part	11
30	Essential oil	Jordan	Methyl isothiocyanate	Aerial part	11
31	Essential oil	Jordan	Butyl isothiocyanate	Arial part	11
32	Essential oil	Jordan	3-p-Menthene	Arial part	11
33	Essential oil	Jordan	2-Butenyl isothiocyanate	Arial part	11
34	Essential oil	Jordan	3-Methylthio-1-hexanol	Arial part	11
35	Essential oil	Turkey	Benzyl alcohol	Fruit	8
36	Essential oil	Turkey	Octanoic acid	Fruit	8
37	Essential oil	Turkey	Benzoic acid	Fruit	8
38	Essential oil	Turkey	A-terpinolene	Fruit	8
39	Essential oil	Turkey	Carvacrol	Fruit	8
40	Essential oil	Turkey	Zingerone	Fruit	8
41	Essential oil	Turkey	4-Fluoro benzaldehyde	Fruit	8
42	Essential oil	Italy	Docosane	Fresh leaf, buds	45
43	Essential oil	Italy	Nonacosane	Fresh leaf, buds	45
44	Essential oil	Italy	Hexadecanoic acid	Fresh leaf, buds	45
45	Essential oil	Algeria	Palmitic acid	Arial part	16
46	Essential oil	Algeria	Nonanal-n	Arial part	16
47	Essential oil	Algeria	Cymene-2,5-dimethoxy-ara	Arial part	16
48	Essential oil	Algeria	Octacosane	Arial part	16
49	Essential oil	Saudi Arabia	Methyl isothiocyanate	Arial part	9
50	Essential oil	Saudi Arabia	Hexadecanoic acid	Arial part	9
51	Essential oil	Saudi Arabia	Limonene	Arial part	9
52	Essential oil	China	Hypoxanthine	Fruit	26
53	Essential oil	China	Uracil	Fruit	26
54	Essential oil	Algeria	Nonanal-n-Cymen 2,5 dimethoxy para-Dodecanal	Arial part	16
55	Essential oil	Algeria	Nonanal-n-Hexadecanoic acid-tetracosane	Arial part	16
56	Essential oil	Algeria	Tetracosane-n-pentyl furane-2-octacosane	Arial part	16

4.3. Terpenes: Sesquiterpenes and monoterpenes are common in *C. spinosa*, in plants growing in Mediterranean area (16). Aliyazicioglu *et al.* (8) reported that terpenes constitute in *C. spinosa* contain 4.4 % of the aroma and the major representative was α-Terpinolene, while Romeo *et al.* (55) determined that terpenes constituted 5.8 % of the aroma. They detected five sesquiterpenes (C-15) and 10 monoterpenes (C-10) in capers which were the most important being the acyclic sesquiterpene trans-nerolidol, followed by the monoterpene 4-terpineol. The monoterpene linalool and the sesquiterpene β-ionone were the only terpenes in caper varieties from Morocco (21).

4.4. Essential oils: Different chemical composition of essential oil of *C. spinosa* L has been reported. Qualitative and quantitative differences between the components were observed in *C. spinosa*. These differences may be due to different reasons such as plant chemotype or nutritional status, climatic and genetic factors. Al-Shayeb *et al.* (11) extracted 92.89 % of the total oil content of *C. spinosa* L. and found isopropyl isothiocyanate (28.92 %), methyl isothiocyanate (25.60 %), butyl isothiocyanate (16.65 %), 3-p-menthene (3.08 %), 2-butenyl isothiocyanate (2.24 %) and 3-methylthio-1-hexanol (2.03 %) as major constituents of essential oils. Aliyazicioglu *et al.* (8) reported the major volatile of buds such as: benzyl alcohol, octanoic acid, benzoic acid, α-terpinolene, carvacrol, zingerone and 4-fluoro benzaldehyde. Mollica *et al.* (45) founded that docosane (20.42 %) was the major component in the studied essential oil, followed by nonacosane (16.72 %) and hexadecanoic acid (14.22 %), while palmitic acid (38.19 %), nonanal-n (12.61 %), cymene-2,5-dimethoxy-ara (8.94 %) and octacosane (5.49 %) were the major components in Benachour et al. (16) study. Bodaghzadeha *et al.* (18) reported the oil content in the seeds ranged from 16 to 27 %. In the recent study by Alkhaibari and Alanazi (9) main components of *C. spinosa* L. were observed as: methyl isothiocyanate, hexadecanoic acid, and limonene. Furthermore, hypoxanthine and uracil compounds were isolated from *C. spinosa* L. (Capparidaceae) fruit (27). The result of essential oils constituents of Benachour *et al.* (16) study, showed the presence of three chemotypes: the chemotype of Nonanal-n-Cymen 2,5 dimethoxy para-Dodecanal, the chemotype of Nonanal-n-Hexadecanoic acid-tetracosane and the chemotype Tetracosane-n-pentyl furane-2-octacosane.

4.5. Other compounds: Givianrad *et al. (*29) isolated the polyunsaturated FA (PUFA) of the seed oil amounted to 49 % of the total FA, while the monounsaturated and saturated FA (MUFA and SAFA) amounted to 38 % and 13 %, respectively. Total fatty acid in *C. spinosa*, growing in Algeria, was 38.95 %. (16). Mollica *et al.* (45) reported that, palmitic acid (51.95 %) was determined as major fatty acid in the oil of fermented buds, followed by stearic (15.72 %) and linoleic acids (10.08 %). Recently Bodaghzadeha *et al.* (18) reported the presence of fatty acids in the seed oil composition of *C. spinosa* species was linoleic acid (45–50 %) followed by oleic acid (30-39 %), palmitic acid (2-8 %) and stearic acid (2-3 %).

5. PHARMACOLOGICAL ACTIVITIES

Pharmacological activities of *C. spinosa* L. are summarized in Table 3. *C. spinosa* L. is very imperative and safe herbal medicine used as anti-diabetic, antibacterial, antifungal, antiviral, anti-inflammatory and anticarcinogenic (13,42,51,60).

5.1. Anti-diabetic and anti-hyperlipidemic activities: Eddouks *et al.* (23) reported the anti-hyperglycemic activity of aqueous extracts of *C. spinosa* L. in diabetic rats. In other study, Sharma *et al.* (57) demonstrated the action of alkaloids from capper on diabetes and their multiple therapeutic effects in mice. Mollica *et al.* (44) found that rutin is the major flavonoids in methanolic extracts of leave and buds. *C. spinosa* L. and rutin inhibited the α-glucosidase and α-amylase enzymes in rat.

Table 3. Pharmacological activities of *Capparis spinosa* L.

No	Pharmacological Activity	Geog. distribution	Plant parts Used	Animal Model	Extract/ compound Evaluated	Ref
1	Anti-diabetic and anti-hyperlipidemic activities	Morocco	Arial part	Rat	Aqueous extract	23
2	Anti-diabetic and anti-hyperlipidemic activities	India	Fruit	Mice	Aqueous extract	57
3	Anti-diabetic and anti-hyperlipidemic activities	Italy	Leave and buds	Mice	Methanolic/ Aqueous extracts	44
4	Anti-diabetic and anti-hyperlipidemic activities	Iran	Fruit	Human	Aqueous extract	32
5	Anti-diabetic and anti-hyperlipidemic activities	Iran	Arial part	Human	Aqueous extract	42
6	Antioxidant activity	Italy	Buds	-	Methanolic extracts	19
7	Antioxidant activity	Italy	Buds	Mice	Methanolic extracts	28
8	Antioxidant activity	Algeria	Leaves, flowers, fruit, seed, root	-	Methanolic extracts	15
9	Antioxidant activity	Iran	Fruit and leaves	-	Methanolic extracts	22
10	Antibacterial and antifungal activities	Jordan	Flowering aerial parts	-	Hydrodistillation	11
11	Antibacterial and antifungal activities	Jordan	Flowers and bud	-	Crude extract fractions	47
12	Antibacterial and antifungal activities	Morocco	Arial part	-	Ethanol and Methanolic extract	60
13	Antibacterial and antifungal activities	Algeria	Aerial parts	-	Hydrodistillation	16
14	Antibacterial and antifungal activities	Iraq	Leaves	-	Methanolic extracts	12
15	Antibacterial and antifungal activities	Israel	Stem and leave	-	Ethanolic and aqueous extracts	1
16	Antibacterial and	Tunisia,	Aerial	-	Ethanol	52

	antifungal activities		parts		extraction	
17	Antiviral and Immunomodulatory Effect	Italy	Buds	-	Methanolic extract	13
18	Antiviral and Immunomodulatory Effect	China	Seed	-	Aqueous extrac	38
19	Antiviral and Immunomodulatory Effect	Croatia	Leaves and buds	-	Methyl isothiocyanate extract	37
20	Anti-inflammatory activity	Italy	Bud	-	Methanolic extract	51
21	Anti-inflammatory activity	Morocco	Leave	Mice	Methanolic extracts	24
22	Anti-inflammatory activity	Algeria	Bud	-	Methanolic extracts	36
23	Hepatoprotective activity	Iran	Roots	Mice	Ethanolic extract	3
24	Hepatoprotective activity	Iran	Leave	-	Methanolic extracts	35
25	Hepatoprotective activity	Algeria	Fruits and leaves	-	Methanolic extracts	6
26	Hepatoprotective activity	Tunisia	Seed	Mice	Methanolic extracts	61
27	Hepatoprotective activity	Iraq	Fruit	-	Aqueous extract	7
28	Neurodegenerative effects	India	Bud	Mice	Aqueous extract	30
29	Antiplasmodial activity	Saudi Arabia	Bud	-	Methyl isothiocyanate extract	9

5.2. Antioxidant activity: The methabolic extract of *C. spinosa* L. showed significant antioxidant effects which can be related to the high level of phenolic compounds (19,28). Moreover, it has good antioxidant potential and capacity to scavengs free radicals (15). Total antioxidant capacities of *C. spinosa* L. fruit and leaves were 1.96 mmol Fe2+/L, and 1.65 mmol Fe2+/L respectively, (22). Its protective effects are due to richness in phenolic, tocopherols and carotenoids compounds, leading to anti-oxidative property (46,59).

5.3. Antibacterial and antifungal activities: Crude extract of aerial parts of *C. spinosa* L. exhibited *in-vitro* antibacterial activity and inhibited the *Staphylococcus epidermidis* and *Streptococcus faecalis* (11). Its flowers and floral bud extract showed antibacterial activity against *Streptococcus faecalis* and *Escherichia coli* (47). *C. spinosa* L. extract killed some pathogenic strains such as *Staphylococcus aureus*, *Escherichia coli* and *Klebsilla pneumonia* (60). Benachour *et al.* (16) reported that its concentrated oil was most effective against all gram-positive and gram- negative bacteria, except *E. coli* which was resistant to this oil. Arean *et al.* (13) showed that, *E. coli*, *K. pneumonia*, *S. aureus*, *S. pidermidis* and *S. typhi* are very sensitive to extracts of *C. spinosa* L. Ethanol and aqueous extracts of stem and leaf of *C. spinosa* L. used to treat and prevent infections

caused by *E. coli*, *S. aureus*, *K. pneumoniae* and *Candida albicans* (1). Moreover Rajhi *et al.* (52) brought attention to the antifungal activity of the caper leave extract against *Aspergillus niger*.

5.4. Antiviral and Immunomodulatory effects: HSV-1 and HSV-2 virus cause severe problems in immunodeficient patients. Arena *et al.* (13) reported that methanolic extract of *C. spinosa* L. flower buds may treat HSV-2 infections in immunocompromised hosts. Lam and Ng (38) stated that a protein simila to imidazoleglycerol phosphate synthase isolated from the seed extract of *C. spinosa* L. showed anti-proliferate activity against tumor cells and inhibited activity of HIV-1 reverse transcriptase. Moreover, methyl isothiocyanate extracts of leaves and flower buds of *C. spinosa* L., whose anticarcinogenic activity was analyzed, and inhibited the human colon carci-noma cell line, HT-29 (37). Some studies showed that the tocopherols and phenolic compounds play an important role against cancer and tumor cells (31).

5.5. Anti-inflammatory activity: Panico *et al.* (51) showed that the cytokine of the caper extract had an anti-inflammatory effect on human chondrocytes cultures. El Azhary *et al.* (24) displayed methanol extract of the caper leaves reduced the edema inhibition (%) to 1.07 g/kg dose. The extract of caper flower bud reduced the edema inflammation. Similarly, Kernouf *et al.* (36) revealed its anti-inflammatory activity. These finding confirmS the traditional use of caper plants as anti-inflammatory (51).

5.6. Hepatoprotective activity: Aghel *et al.* (3) reported the anti-Hepatoprotective activity of *Caparis spinosa* L., the ethanolic extract of root protected mice from hepato cellular injury. Similarly, Kalantari *et al.* (35) discovered the hepatoprotective activity of ethanol leaf extract of *C. spinosa* L. against tert-butyl hydroperoxide (T-BHP) as a liver damage inducer. In other study of Aichour *et al. (*6) demonstrated the decrease of serum enzyme levels from hepatoprotective activities. Tir *et al.* (61) observed the protection effects of Caper seed extract on the toxicity, confirmed by the histopathological studies with a decrease in the degree of tissue fibrosis. Ali Al-Nuani and Kadhim (7) investigated the effects of aqueous fruit extract of Caper on two detoxification enzymes that reduced the cytochrome P450 2E1. Based on these findings, Caper could be considered an adjuvant agent in hepatoprotective.

5.7. Other activities: Aqueous extract of *C. spinosa* L. buds inhibited neurodegenerative effects and improved the learning, memory and cognitive abilities in mice (30). The methyl isothiocyanate extract of *C. spinosa* L. showed insecticidal, antiplasmodial, anti-leishmanial and cytotoxic activity. These methyl isothiocyanate extracts had hexadecanoic acid and limonene, which displayed insecticidal, activity against healthy 4th-instar larvae of *A. aegypti*, and anti-leishmanial, activity against chloroquine-resistant *P. falciparum* K1 strain, and antiplasmodial activity against L. major amastigotes (9).

6. MEDICINAL USES

The medicinal properties of *C. spinosa* L. have been documented in numerous papers. Historically the people used *C. spinosa* L. roots, leaves, buds, fruits, bark and seeds for several medicinal purposes and to treat diseases such as: diabetes, cancer, rheumatism, Alzheimer and liver problems.

6.1. Diabetes: *C. spinosa* L. fruit significantly decreases the triglyceride levels in diabetic patients (32). On the other hand, Mehrzadi *et al.* (42) reported that *C. spinosa* L. is used to treat diabetes mellitus in special formulation with no side effects.

6.2. Cancer: The extraction of *C. spinosa* L. seed had shown anti-proliferate activity to tumor cells and inhibitory activity to HIV-1 reverse transcriptase (37). *C. spinosa* L. extract killed some pathogenic strains (16) and it can be used as an instant herbal antibiotic in some diseases.

6.3. Alzheimer: The extract of caper flower bud reduces the edema inflammation (51). These finding represents that this plant can be used to treat rheumatism disease.

6.4. Liver problems: The extract of caper plant can play a role in Alzheimer's disease by inhibiting the destructive effects on the nervous system (30). Moreover, fruit extract of Caper effect on important enzymes in liver and could be considered an adjuvant agent in hepatoprotective (7).

It is also used to treat rheumatism, toothache and cough (62). Furthermore, it used against malaria and hemorrhoids (2), gastrointestinal infections and diabetes (45).

7. FUTURE LINES OF RESEARCH

Numerous studies have investigated caper, yet its biochemical and pharmacological mechanisms remain elusive. Transcriptome sequencing (RNA-seq) has emerged as a valuable tool to explore volatile and nonvolatile metabolite biosynthesis in fruits, but limited data exist on volatile-related genes and enzymes in caper. Additionally, the specific roles of individual allelochemicals remain unclear, indicating the complexity of the issue. Therefore, further comprehensive research is needed to elucidate these mechanisms and the functions of individual allelochemicals. Furthermore, molecular genetic studies of *C. spinosa* L. have primarily focused on genetic diversity and structure, neglecting SSR discovery in *Caparis spinosa*. Thus, identifying SSR markers for *Caparis species* warrants attention as a key research focus.

8. CONCLUSIONS

The *Capparis spinosa* provides a wide range of research possibilities. The phytochemical studies identified different components which showed their phytochemical aspects. The main constituents of this plant are alkaloids, flavonoids, terpenoids, volatile oils and fatty acids. Moreover, Pharmacological activities including: anti-diabetic, antibacterial, antifungal, antiviral, anti-inflammatory and anticarcinogenic, support the use of this plant for human healthcare from ancient time and to find new pharmacological actions. Mechanisms of these pharmacological activities are not totally elucidated and few clinical trials have been performed until now. Although genetic data is one of the key factor for variation within crops, few data are available about the genetic diversity of *C. spinosa*. ISSR, AFLP, IRAP and RAPD molecular markers were used for genetic diversity in *C. spinosa.* The development of different genetic study methods for *C. spinosa* may reveal important information about the genome of this medicinal plant and the genes involved in some of its medicinal substances.

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AUTHOR'S CONTRIBUTION

Elmira Ziya Motalebipour: conceptualization, methodology, writing- original draft preparation and editing. Akbar Pirestani: data curation, writing- review and editing

DECLARATION

The authors declare that they have no conflict of interest to report in this paper.

ETHICAL APPROVAL

The authors declare that the study was carried out following scientific ethics and conduct. However, this study did not involve any use of animals, hence no ethical approval has been obtained from the concerned committee.

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