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Review Article

Capparis spinosa L.: A Plant with High Potential for Development of Functional Foods and Nutraceuticals/Pharmaceuticals

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Abstract

Caper (*Capparis spinosa* L.), a drought tolerant plant belonging to genus Capparis of the family Capparidaceae is mainly distributed in arid and semi-arid regions of the tropical and subtropical world. The plant, as a potential source of valuable nutrients such as vitamins (especially vitamin C), digestible protein, reducing sugars and essential minerals is valued for human food. The fruit of this plant, being a rich source of high-value components, is usually pickled and added to salads, sauces and jams. The plant has been used traditionally to prevent and/or treat a number of health disorders such as diabetes, hepatitis, obesity and kidney problems. Besides uses as an ingredient for food and feed, the contents of bioactive phytochemicals such as terpenoids, alkaloids, glucosinolates, tocopherols, polyprenols, isothiocyanates, carotenoids and phenolics, have allowed to envisage potential applications of *C. spinosa* as a health promoter plant. A broad range of pharmacological activities such as antioxidant, cardiovascular, antimicrobial, anti-inflammatory, hepatoprotective, antipyretic, diuretic and hypoglycemic have been ascribed to different parts of *C. spinosa*. This comprehensive review describes the detailed profile of high-value nutrients and bioactives along with pharmacological and phyto-medicinal attributes of this multipurpose food plant with the aim to exploring its potential uses as ingredients for functional foods and nutraceutical/pharmaceutical industry.

Key words: Bioactives, caper, functional foods, glucinosinolates, medicinal uses, nutraceuticals

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INTRODUCTION

Plants have been valued as a rich source of medicinal and nutraceutical agents for centuries. In the new era, even though, around 25% of the modern drugs have been isolated from plant sources (WHO., 2013; Xu *et al*., 2015). Currently, there is a revival of interest in the use of herbal medicines world over particularly in the form of dietary supplements (Al Qura'n, 2008; Olsen and Larsen, 2003; Gilani and Atta-ur-Rahman, 2005). Diets rich in biologically-active phytochemicals not only provide nutrients, but are also known to reduce the risk of different diseases such as cancer, inflammation, cardiovascular and neurodegenerative diseases (Banerjee *et al*., 2011; Ahmed and Gilani, 2014; Kim *et al*., 2014).

Among valuable flora, wild plants have gained much attention because of their functional food and potential health benefits (Mcdougall and Stewart, 2005; Ndhlala *et al*., 2006; Stewart *et al*., 2007). According to an estimate, among 95000 wild plants, 7500 are used in phyto-medicines and 3900 are harvested to fulfill nutritional needs (Mishra *et al*., 2007). An important plant genus namely Capparis contains 250 species (Cronquist, 1981; Heywood, 1993; Mabberley, 1997; Hamed *et al*., 2007). Most plants belonging to genus Capparis are wild species and are distributed in arid and semi-arid dry lands of tropical and sub-tropical regions of the world (Hansen, 1991; Jiang *et al*., 2007). Several members of the Capparis genus have been recognized for their food and medicinal uses owing to their high nutritional value and strong antioxidant properties attributable to the presence of essential minerals, vitamins and high contents of phenolics and flavonoids (Yadav *et al*., 1997; Sharma *et al*., 2009; Duman *et al*., 2013). The potential folk medicinal and pharmaceutical uses of different caper species have been reviewed recently by our research group (Gull *et al*., 2015). Interestingly, different parts of caper species have been proposed to be effective as antihypertensive, anti-inflammatory, anti-asthmatic, anti-hyperlipidemic and antimicrobial agents (Mali *et al*., 2004; Purohit and Vyas, 2005, 2006; Eldeen and Staden, 2008; Chahlia, 2009; Castro *et al*., 2014a, b; Duman *et al*., 2013; Gull *et al*., 2015).

Among the Capparis species, *Capparis spinosa* L. is especially important due to its impressive nutritional and medicinal attributes (Cronquist, 1981; Heywood, 1993; Hamed *et al*., 2007; Gull *et al*., 2015). This plant is well known for the edible flower buds and the fruit (caper berries), both of which are frequently consumed as pickled. The fruit from this species is used to garnish pizza and also added to salads, sauces and jams (Panico *et al*., 2005; Musallam *et al*., 2011).

A number of folk medicinal and therapeutic properties have also been ascribed to different parts of *C. spinosa* which include the treatment of diabetes, high blood pressure and liver, spleen and kidney disorders (Baytop, 1984; Handa *et al*., 1986; Yaniv *et al*., 1987; Ziyyat *et al*., 1997; Calis *et al*., 1999; Azaizeh *et al*., 2003; Hussain *et al*., 2007; Taifour *et al*., 2011). Interestingly, the bark and fruit aqueous extracts from this species have been reported to act as diuretic, poultice, expectorant and astringent as well as they possess anti-inflammatory and antifungal activities (Al-Said *et al*., 1988; Ali-Shtayeh and Abu Ghdeib, 1999; Baytop, 1999; Calis *et al*., 1999; Eddouks *et al*., 2005; Hussain *et al*., 2007). The reported medicinal health functions and nutritional attributes of *C. spinosa* can be mainly attributed to the occurrence of alkaloids, glucosides, reducing sugars, essential fatty acids, organic acids, vitamin C, terpenoids, flavonoids and resins in the fruit and leaves of this species (Rastogi and Mehrotra, 1995; Joshi *et al*., 2011).

There is no comprehensive review available in the literature particularly focusing on the detailed medicinal uses, bioactive constituents, nutritional and pharmacological attributes of *C. spinosa*. Its wide spectrum of biological applications and folk medicinal uses inspired the authors to compile a comprehensive review, which covers the detailed profile of high-value nutrients and phytochemicals/bioactives as well as traditional medicinal and biological attributes of *C. spinosa* with the objective to explore potential applications of this multipurpose tree for the functional food and nutraceutical/pharmaceutical industry.

Taxonomy/distribution: *Capparis spinosa*, the caper bush, also known as flinders rose, is an economically vital plant among 250 species of genus Capparis of the family Capparidaceae (Fici, 2001). It is dicotyledonous perennial, 20-30 cm long creeping shrub, wildly distributed in semi-arid or arid areas of Southeast Asia, South-Western and Central Asia, Himalayas, Mediterranean, the Pacific Islands, East Africa, Madagascar and Australia (Rhizopoulou, 1990; Bakshi *et al*., 1999; Psaras and Sofroniou, 1999; Fici, 2001; Levizou *et al*., 2004). *Capparis spinosa* is widespread in drylands, deserts and rocky areas of India and Pakistan. It usually grows on bare rocks, cracks, crevices and sand dunes (Bakshi *et al*., 1999; Psaras and Sofroniou, 1999).

The plant has showy white or pinkish white, hermaphrodite, auxiliary and solitary (about 8 cm) flowers attached on the peduncle. Two spines (slightly curved at the end) are usually present at the base of ovate, round, fleshy, alternate or rarely opposite leaves. Fruit are oval shaped, approximately 3 cm long, greenish in color with red pulp.

Seeds are small in size, numerous, 1-3 cm broad, kidney-shaped and grayish brown (Sher and Alyemeni, 2010; Al-Soqeer, 2011)

Growth and flowering of this shrub starts from mid-April to end of September showing that it can tolerate high temperature (above 40°C) and low water availability. Interestingly, *C. spinosa* can grow well in nutrient deficient soils and saline areas under harsh environment and is relatively resistant to fire (Pugnaire and Esteban, 1991; Sakcali *et al*., 2008).

During the last few decades, the caper bush has been introduced as a specialized culture in some european countries. A high commercial value of caper plant led to a significant increase in both the area under cultivation and production yield of this typical species by the late 1980s. Capers are now commercially valuable plants cultivated in several parts of the world including Greece, Turkey, Italy, France, Spain and Morocco. These countries are big exporters while UK and USA are big importers (Musallam *et al*., 2011; Sozzi, 2001; Panico *et al*., 2005; Infantino *et al*., 2008).

Proximate composition: *Capparis spinosa* is a potential source of some basic dietary components for human nutrition. For example, the fruit of this species is reported to contain moisture (79%), ash (1.6%), protein (5.8%), fat (1.6%), crude fiber (5.4%) and important minerals such as calcium (871 ppm), magnesium (636 ppm), potassium (542 ppm), sodium (226 ppm), iron (13 ppm) and phosphorous (21 ppm) (Rodrigo *et al*., 1992). But the concentration of these nutrients is affected with regard to the nature of cultivar, time of cultivation/harvest and size of the fruit. Poly-unsaturated fatty acids contribute 50% of total fatty acids of the fruit lipids of this species (Rodrigo *et al*., 1992).

A monomeric protein with molecular mass 38 kDa showing some resemblance to imidazole glycerol phosphate synthase was separated from the seeds of *C. spinosa* using different chromatographic techniques. This protein was reported to repress the multiplication of hepatoma HepG2 cells, colon cancer HT 29 cells and breast cancer MCF-7 cells. It also exhibited the inhibition of HIV-I reverse transcriptase (Lam and Ng, 2009). Another dimeric protein, lectin having molecular mass 62 kDa has also been isolated from the seeds of *C. spinosa* and further purified by various chromatographic techniques. Inhibition of HIV-1 reverse transcriptase was reported by this protein (Lam *et al*., 2009). Similarly, proliferation of hepatoma HepG2 and breast cancer MCF-7 cells was inhibited by lectin (Lam *et al*., 2009).

The raw fruit of *C. spinosa* contains high contents of moisture, crude oil, fibers, sodium, potassium and phosphorous, which make this fruit more appropriate for pickling at un-ripened stage (Ozcan and Aydin, 2004). Different sized buds of *C. spinosa* have been investigated for their chemical composition in raw and pickled forms. Small buds are more preferred for processing than larger ones because of their high contents of flavonoids, lipids, protein and minerals (Na, K, Ca and Mg) (Giuffrida *et al*., 2002).

Traditional food/culinary uses: The flower buds (capers) and the fruit (caper berries) of *C. spinosa* due to having high nutritional status have been traditionally consumed as a seasoning or garnish. Capers are a common ingredient in mediterranean cuisine, especially, italian, cypriot and maltese. Moreover, in ancient Greece the caper had been used as a carminative (Megaloudi, 2005). The fruit is used to garnish pizza and also added to salads, sauces and jams (Panico *et al*., 2005; Musallam *et al*., 2011).

Both the caper buds and the fruit are often pickled in salt or in a salt and vinegar solution resulting in development of a pungent flavor resembling mustard oil (glucocapparin). During this, an enzymatic reaction leads to the formation of rutin and the presence of this flavonoid compound can be seen as crystallized white spots on the surfaces of caper buds. Capers are considered as a unique ingredient in Italian cuisine, especially in sicilian and southern italian cooking. These are usually utilized in salads, pasta sauces and meat dishes (Panico *et al*., 2005). On commercial basis capers are graded and sold based upon their size, with the smallest size being the most marketable. The pickled fruit can be served as a Greek mezze and snack in Menorca. Dried caper leaves are also used as a substitute for an enzyme, rennet, which is mostly employed during preparation of high-quality cheese (Panico *et al*., 2005; Musallam *et al*., 2011). In the current perspectives of malnutrition, especially in under-developed and developing countries, *C. spinosa* can be explored as a nutritious plant to serve rural communities.

Medicinal applications: According to WHO, herbal medicines are used to maintain health by more than 80% people of the world particularly in Africa and Asia along with some Western countries (Al Qura'n, 2008; Olsen and Larsen, 2003; Gilani and Atta-ur-Rahman, 2005). Besides treating ailments, phyto-medicines are widely used in cosmetics and as functional foods (Gilani and Atta-ur-Rahman, 2005; Rahmatullah *et al*., 2010).

Among other plant species of the genus Capparis, (*C. spinosa*) is recognized as a rich source of a wide array of medicinal compounds with proven pharmacological actions. Almost all species of Capparis have long been used in the

Unani (Greco-Arab) and Ayurvedic systems of medicines. However, *C. spinosa* is of particular importance due to the presence of several classes of medicinally important alkaloids along with potential antioxidant compounds (Bonina *et al*., 2002; Panico *et al*., 2005). The presence of a wide variety of nutrients including; lipids, protein, minerals and tocopherols in *C. spinosa* is well documented. Different parts of this plant have been reported to be used for the treatment of female infertility, infections, inflammations, allergies, heart, kidney and liver disorders. Examples of medicinal applications and pharmacological attributes of *C. spinosa* are listed in Table 1. The extracts from flowers, roots, stem, leaves and seeds of *C. spinosa* plant are biologically active and are used to treat several disorders (Yaniv *et al*., 1987; Ziyyat *et al*., 1997; Calis *et al*., 1999; Hussain *et al*., 2007). Important folk medicinal applications of different parts of *C. spinosa* are discussed below:

Fruits: Metabolic disorders including diabetes and cardiovascular complications are on the rise at the global level and it is not uncommon that diabetes is usually associated with hypertension (Jali *et al*., 2009). Both of these disorders are simultaneously treated by taking orally dried fruits of *C. spinosa* (Sher and Alyemeni, 2010). Fruits of *C. spinosa* are perhaps mostly used in folk medicines. The fruits have a number of traditional medicinal applications including; diuretic, expectorant and astringent activities (Gupta and Ali, 1997; Al-Said *et al*., 1988; Fici, 2001) and treatment of tuberculosis, atherosclerosis, hepatitis and kidney diseases (Bond, 1990). The fruit (dry powder) also acts as a tonic and used to expel worms from intestine and gas from stomach (Baytop, 1984; Hussain *et al*., 2007). Capers have demonstrated powerful antioxidant and anti-cancer properties (Inocencio *et al*., 2000). The hydrolysis products of indol-3-ylmethyl glucosinolates and potent flavonoids (rutin and quercetin) as well as selenium in capers have been linked with its antioxidant and anti-carcinogenic effects (Winter, 1978; Rosa *et al*., 1996; Inocencio *et al*., 2000).

Roots and root bark: The root-bark of *C. spinosa* has versatile medicinal applications and acts as analgesic, diuretic, expectorant, anthelmintic, antihaemorrhoidal, aperient, depurative, deobstruent, emmenagogue, vasoconstrictive and tonic (Chiej, 1984). The paste from the root bark of *C. spinosa* plant is reported to be used as a tonic to treat skin diseases (Sher and Alyemeni, 2010). The root bark of this species has been used as a remedy for cold, liver, spleen and kidney disorders and constipation. Moreover, in Greece, herbal tea made from caper young shoots and root is considered to be beneficial against rheumatism (Baytop, 1984; Hussain *et al*., 2007). Aghel *et al.* (2007) reported that gout, anemia and dropsy can also be treated by taking water-decoction of root bark of *C. spinosa.*

Flowers and leaves: The steam of boiling leaves of *C. spinosa* has been inhaled since a long time by females to improve fertility (Bailey and Dannin, 1981). The flowers of *C. spinosa* are used to treat gout and arthritis (Ageel *et al*., 1986; Fu *et al*., 2008). The flowers are also used to lower blood pressure and for diuretic and tonic applications (Baytop, 1984; Calis *et al*., 1999). Moreover, aqueous extract from the aerial parts of *C. spinosa* is reported to inhibit the growth of fungus

Table 1: Medicinal uses and pharmacological attributes of different parts of *C. spinosa*

Plant part/extract	Medicinal uses	References
Methanolic extract of flowering buds	Anti-inflammatory, chondroprotective, antiallergic and antihistaminic	Bonina *et al.* (2002) and Panico *et al.* (2005)
Whole plant	Anti-diabetic, hypolipidemic, hepatoprotective, antifungal, dermatosis, urolithiasis, anti-arthritis, anti-coagulant, odynolysis, memory protective, anti-inflammatory, tonic, anthelmintic, expectorant, cardioprotective, anti-haemorrhoidal, aperients and for treatment of sciatica and trigeminal pains and anemia	Ageel *et al.* (1986), Yaniv *et al.* (1987), Mahasneh *et al.* (1996), Al-Said *et al.* (1988), Eddouks *et al.* (2004), Mishra *et al.* (2007), Yang *et al.* (2008) and Sher and Alyemeni (2010)
Aqueous extract of plant	Anti-lipidemic, hypoglycemic, anti-obesity, antifungal, antibacterial, antihypertensive, diuretic, hepatoprotective and antidiabetic	Handa *et al.* (1986), Yaniv *et al.* (1987), Ziyyat *et al.* (1997), Calis *et al.* (1999), Ali-Shtayeh and Abu Ghdeib (1999), Mahasneh (2002), Eddouks *et al.* (2005), Ali *et al.* (2007) and Lemhadri *et al.* (2007)
Butanol extract	Antifungal and antibacterial	Baytop (1984) and Inocencio *et al.* (2000),
Capers	Anti-inflammatory, diuretic, expectorant, astringent, anti-tuberculosis, antisclerosis, urolithic, vermifuge, carminative, anti-arthritis and anti-diabetic antihypertensive	Germano *et al.* (2002), Mahasneh (2002), Hussain *et al.* (2007), Sher and Alyemeni (2010), Feng *et al.* (2011) and Zhou *et al.* (2011)
Roots	Hepatoprotective and to treat cold remedies, spleen problems, kidney diseases, constipation, dropsy, anemia, arthritis and gout	Baytop (1984), Shirwaikar *et al.* (1996), Hussain *et al.* (2007) and Sher and Alyemeni (2010)
Leaves	To treat cold, pain, female infertility, diarrhea, dysentery and for expulsion of kidney stones	Bailey and Danin (1981), Sher and Alyemeni (2010) and Bhoyar *et al.* (2011)
Stem	Used to treat paralysis and toothache, liver disorders and diabetes	Prashar and Kumar (1994), Chopra *et al.* (1996) and Baijal *et al.* (2004)

(Ali-Shtayeh and Abu Ghdeib, 1999) and is also used for the treatment of liver disorders (Handa *et al*., 1986), diabetes (Yaniv *et al*., 1987; Ziyyat *et al*., 1997) and high blood pressure (Calis *et al*., 1999). A decoction of leaves and buds of *C. spinosa* is considered to be useful against common cold and headache (Bailey and Dannin, 1981; Sher and Alyemeni, 2010).

Whole plant: The whole plant of *C. spinosa* is used as antifungal agent and for its antioxidant, anti-inflammatory and odynolytic properties (Yang *et al*., 2008). The plant is also used in folk medicine to treat hepatitis, diabetes, urolithiasis, rheumatism and arthritis. The whole plant extracts can be employed as memory enhancer and anticoagulant as well (Yang *et al*., 2008) in India and Morocco, people use *C. spinosa* as an antibacterial (Singh *et al*., 2002), anti-proliferative (Nakano *et al*., 1998) and anti-ulcerogenic (Khayyal *et al*., 2001) agent. Multiple medicinal uses ascribed to different parts of *C. spinosa* support the potential utilization of this species for the development of nutraceuticals and safer phyto-medicines to improve health status of the consumers (Singh *et al*., 2002; Yang *et al*., 2008).

Pharmacological attributes: Caper has been well studied for its multiple biological activities supported by the presence of a wide array of bioactive such as alkaloids, steroids, terpenoids, flavonoids and tocopherols (Aghel *et al*., 2007; Ali *et al*., 2007; Zhou *et al*., 2011; Bhoyar *et al*., 2011). The details on individual pharmacological activities of *C. spinosa* are discussed below:

Anti-diabetic activity: Diabetes is one of the major health problems in the world and particularly in Middle-East and South-Asia (Jali *et al*., 2009; Harlev *et al*., 2013; Muhammad *et al*., 2015). The treatment of diabetes requires a life-long use of multiple drugs resulting in multiple side-effects in addition to the high cost of medication. Currently, due to revival of interest in optimal nutrition, there is much focus on the use of plant based functional foods and nutraceuticals as alternative therapies for health improvement and disease control (Shahidi, 2009).

Herbal remedies have been extensively used for the treatment of diabetes (Bhuvaneswari and Krishnakumari, 2012). For example, the aqueous extract of fruit of *C. spinosa* was found to decrease glucose to normal level in the blood of rats with diabetes induced by streptozotocin. Glucose level did not decrease in the control (normal) rats indicating that glucose lowering pathway may not depend upon secretion of insulin (Eddouks *et al*., 2004). In another study, the aqueous extract of *C. spinosa* was found to be effective against diabetes in obese rats (Lemhadri *et al*., 2007).

Anti-inflammatory activity: Non-steroidal anti-inflammatory drugs (NSAIDs), although effective in reducing pain, are associated with increased risk of gastric ulcer. Similarly, the expensive and selective COX-2 inhibitors are still not free from side effects (Fries, 1991; Emery *et al*., 1999). However, safer and cheaper drugs can be developed from medicinal plants (Gilani and Atta-ur-Rahman, 2005; Ikram, 1983; Gautam and Jachak, 2009). The alcoholic extracts of *C. spinosa* showed strong anti-inflammatory activity inhibiting paw edema in rats (Al-Said *et al*., 1988). This anti-inflammatory activity of the alcoholic extracts was linked to the presence of polyprenols like cappaprenol-12, cappaprenol-13 and cappaprenol-14 containing 12, 13 and 14 isoprenoid units, respectively. Other researchers reported that aqueous and chloroform extracts of *C. spinosa* also showed a remarkable anti-inflammatory activity against carrageenan-induced paw edema in rats (Ageel *et al*., 1986; Zhou *et al*., 2010).

In a recent study, secreted placental alkaline phosphatase (SEAP) reporter assay was used to measure the anti-inflammatory effect of biflavonoids, isoginkgetin and ginkgetin separated from fruit of *C. spinosa* based on nuclear factor-kappa B (NF-κB) activation. Studies revealed that ginkgetin was more potent than isoginkgetin with IC_{50} value of 7.5 μM indicating it a good NF-κB inhibitor (Zhou *et al*., 2011). Furthermore, the fruit of *C. spinosa* was extracted in aqueous-ethanol to study its anti-arthritic effect in rats. The extract showed anti-arthritic and anti-inflammatory activities. Bioactive phytochemicals isolated from the active fraction of the tested extract were identified as stachydrine, *p*-hydroxy benzoic acid, 5 (hydroxymethyl) furfural, bis(5-formylfurfural) ether, daucosterol, uracil and α-*D*-fructofuranosides methyl (Feng *et al*., 2011). Based on these reports it appears that *C. spinosa* plant is a good source for isolation of natural anti-inflammatory agents.

Antioxidant activity: Synthetic antioxidants, although effectively used in the food industry, have been reported to have some side effects. Therefore, there is a need to replace synthetic antioxidants by plant-based safer natural antioxidants (Anwar *et al*., 2015). Antioxidants present in medicinal plants capture and neutralize reactive oxygen species and free radicals and thus protect body from cancer, cardiovascular and degenerative disorders (Kalim *et al*., 2010; Saeed *et al*., 2014).

Likewise, *C. spinosa* contains different natural antioxidants including; phenols, rutin, carotenoids and tocopherols in significant quantities, which are helpful in scavenging free radicals and imparting medicinal benefits (Prakash *et al*., 2007; Mozaffarieh *et al*., 2003). Antioxidant activity of the methanolic extract of *C. spinosa* leaves has

been assessed by 1,1-diphenyl-2-picrylhydrazyl (DPPH), 2,2-azinobis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and Ferric Reducing Antioxidant Power (FRAP) assays. The extract showed very good antioxidant capacity with average IC_{50} values 73.0 and 34.0 μg mL^{-1} in DPPH and ABTS assays, respectively. Total antioxidant content assessed by using FRAP assay ranged from 83.43-87.14% at 0.1 mg mL^{-1} concentration. While phenolic content of extract was determined to be 21.42-27.62 mg GAE g^{-1} dry weight (Bhoyar *et al*., 2011).

In another investigation, the infusions of *C. spinosa* were prepared by boiling the plant stalks and flower tops with water for 30 min and evaluated for their antioxidant activity before and after *in vitro* digestion. The samples were found to have good antioxidant potential as assessed by DPPH free radical scavenging, β-carotene bleaching and copper-induced oxidation of human LDL assays. A number of antioxidant compounds including; cinnamoylquinic acid derivatives along with rutin, kaempferol 3-*O*-rutinoside and isorhamnetin 3-*O*-rutinside were confirmed in the infusion by HPLC/UV-Vis-DAD/ESI-MS (Siracusa *et al*., 2011).

In another *in vivo* study, hot water extract of *C. spinosa* was found to show a strong antioxidant activity against lead mediated lipid peroxidation in model rats (Al-Soqeer, 2011). Antioxidant activity of methanolic extract of buds of *C. spinosa*, carried out using tests like ascorbate/Fe^{2+}-mediated lipid peroxidation, DPPH and autoxidation of Fe^{2+} ion in the presence of bathophenanthroline disulfonate, confirmed that this activity was due to phenolic contents. In the same study, participation of glucosinolates in antioxidant activity was excluded by removing these compounds from methanolic extract and performed the assays again. The HPLC analysis of the hydrolyzed sample confirmed that the buds contained 0.39% of a potent flavonoid, rutin (Germano *et al*., 2002).

Bonina *et al.* (2002) investigated that methanolic extract of flowering buds of *C. spinosa* has strong *in vitro* and *in vivo* antioxidant activity followed by DPPH assay, peroxidation induced by the water-soluble radical initiator 2,2'-azobis(2-amidinopropane) hydrochloride of mixed dipalmitoyl phosphatidyl choline/linoleic acid unilamellar vesicles (LUVs) (LP-LUV test) and UV-induced peroxidation of phosphatidyl choline multi lamellar vesicles (UV-IP test). Characterization of the extract by chromatographic and spectroscopic techniques revealed the presence of quercetin derivatives, kaempferol, ferulic acid, cinnamic acid, caffeic acid and *p*-cumaric acid. The presence of these phenolic compounds was strongly linked to the antioxidant properties of *C. spinosa*.

According to Tesoriere *et al.* (2007), the flower buds of *C. spinosa* also exhibited a strong antioxidant potential, which was measured by different assays. Total phenolic contents of flower buds were estimated to be 4.19 mg of gallic acid equivalents, while total antioxidant potential using [2,2-azinobis(3-ethylbenzothiazoline-6-sulfonic acid)] diammonium salt (ABTS) cation radical decolorization assay was 25.8 μmol of Trolox equivalents. Meanwhile, hydrophilic extract of flower buds of *C. spinosa* inhibited lipid oxidation in red meat up to level of 70-280 μM GAE (Tesoriere *et al*., 2007). Skin sclerosis, initiated by reactive oxygen species, was treated by applying ethanolic extract of *C. spinosa* fruits. The tested ethanolic extract caused a significant reduction in the generation of reactive species like O_{2-}, H_2O_2, etc. Interestingly, a decrease in expression of P-ERK1/2 and Ha-Ras, as well as apoptosis was also recorded in the same experiments (Cao *et al*., 2010).

In another study, hydro-distilled essential oils isolated from flower buds and leaves of *C. spinosa* were evaluated for antioxidant attributes by applying DPPH scavenging, thiobarbituric acid and β-carotene bleaching assays and copper induced oxidation of human low-density lipoprotein. Essential oils showed low free radical scavenging activity in DPPH assay but high antioxidant activity in β-carotene bleaching and thiobarbituric acid assays (Kulisic-Bilusic *et al*., 2010). *Capparis spinosa* hence can be explored as potential plant for isolation of natural antioxidants to be uses in food systems to prevent degenerative diseases.

Cardiovascular activity: The major cause of mortality in the world is cardiovascular diseases. The prevalence of cardiovascular diseases is increasing at a rapid rate and can be minimized by exercise and optimal nutrition (Stampfer *et al*., 2000; Weisburger, 2000; Hu and Willet, 2002; AHA., 2004; Ding and Mozaffarian, 2006). Medicinal plants can contribute to the prevention and control of such civilization diseases. The aqueous extract of *C. spinosa*, when given to hypertensive rats at a dose of 150 mg kg^{-1} for 20 days, decreased systolic blood pressure considerably along with increase in potassium, sodium and chloride concentrations in urine without affecting plasma angiotensin converting enzyme and renin activities, indicating that the blood pressure lowering effect of the plant was possibly due to its diuretic activity (Ali *et al*., 2007).

Hepatoprotective activity: Viral and drug-induced hepatitis is one of the major health issues in developing countries such as Pakistan and India. Unfortunately, the hepatitis treatment is very expensive and beyond the reach of a large population in these countries in addition to its miserable side-effects. On

the other hand, phytomedicines are traditionally used by the locals to treat liver disorders (Gilani and Atta-ur-Rahman, 2005; Yaeesh *et al*., 2010; Muhammad *et al*., 2015). One of such popular herbal formulations is Liv-52, which contains 65 mg of *C. spinosa*. It is widely used for different types of hepatitis (Kolhapure and Mitra, 2004; Bardhan *et al*., 1985). When *C. spinosa* was studied for its possible hepatoprotective effect in rats, the results were encouraging (Gadgoli and Mishra, 1999). In an earlier study, the aqueous extract of aerial parts of *C. spinosa* showed a notable hepatoprotective effect in carbon tetrachloride (CCl_4) and paracetamol induced hepatitis in rats (Gadgoli and Mishra, 1999). Likewise, ethanolic extract of root bark of *C. spinosa* was evaluated for its hepatoprotective activity in rats and was found to protect liver from injury caused by CCl_4 and lowered the alanine transaminase and aspartate transaminase levels in the blood (Aghel *et al*., 2007). Petroleum ether, ethanol and ethyl acetate extracts of bark of *C. spinosa* roots were evaluated for their hepatoprotective activity in rats where hepatitis was induced by CCl_4. All the tested extracts reduced serum transaminases, petroleum ether extract being the most effective indicating that *C. spinosa* has a significant potential to treat hepatitis (Shirwaikar *et al*., 1996). In another study, thioacetamide induced liver damage was cured by *C. spinosa* extract (Yusufoglu *et al*., 2014).

Antimicrobial activity: Due to long term use of synthetic drugs, antimicrobial resistance is a growing concern, therefore, development of new safer antibiotics is highly required (Alves *et al*., 2012). Plants containing bioactives such as flavonoids, terpenoids, alkaloids and tannins are reported to possess antimicrobial activity (Bouzada *et al*., 2009; Sher, 2009).

The antimicrobial activity of aqueous, ethanol and butanol extracts of *C. spinosa* was assessed in different studies. The results have shown that aqueous and ethanol extracts had low while butanol extract had high antimicrobial activity when tested against Gram negative and Gram positive bacteria including; *E. coli*, *P. aeruginosa*, *S. typhimurium*, *B. cerreus* and *S. aureus* and fungi such as; *C. albicans*, *F. oxysporum* and *A. flavus*. The results were comparable to standard antimicrobials such as chloramphenicol, tetracycline and nalidixic acid (Mahasneh, 2002). In another study, the aqueous extract of *C. spinosa* showed a significant antifungal activity against *M. canis* and *T. violaceum* (Ali-Shtayeh and Abu Ghdeib, 1999). These studies support the potential uses of *C. spinosa* plant for the isolation of natural antimicrobial agents to treat infectious diseases.

Antiviral and anti-tumor activity: There is a limited number of anti-viral drugs available, while resistance of virus against currently available antiviral drugs is on the rise (De Clercq, 1993). Thus, there is a high demand for searching new plant-based antiviral drugs (McCutcheon *et al*., 1995).

The species *C. spinosa*, is reported to be a potential source of natural anti-viral and anti-tumor agents due to containing a wide array of bioactives. In this regard, methanolic extract of buds of *C. spinosa* inhibited the multiplication of HSV-2 in human peripheral blood mononuclear cells. The extract also prevented the extracellular virus release and improved immunity against HSV-2 infection by regulating the expression of proinflammatory cytokines[140]. Moreover, proteins isolated from the seeds of *C. spinosa* repressed the multiplication of hepatoma HepG2 cells, colon cancer HT29 cells and breast cancer MCF-7 cells. It also exhibited the inhibition of HIV-1 reverse transcriptase (Lam and Ng, 2009; Lam *et al*., 2009). The aqueous extract of flower buds of *C. spinosa* was used to study genotoxic and anti-mutagenic effects induced by ethyl methane sulphonate on root tip meristem of *Allium cepa* L. Meristem cells were treated with ethyl methane sulphonate for 2 h before the application of different concentrations of the aqueous extract. Subsequently, meristem cells from *A. cepa* were stained with aceto-orcein after squashing. The results showed a remarked reduction in mitotic index and chromosomal aberrations (Sultan and Celik, 2009).

Cholesterol lowering and anti-obesity: One of the major causes of cardiovascular diseases is the high cholesterol and triglycerides levels in plasma (Castelli, 1988; Moreyra *et al*., 2005). Similarly, obesity which leads to metabolic syndrome is a growing concern in many countries (Popkin, 2001; Grundy, 2004). Unfortunately, pharmaceutical medicine has limited therapeutic success and offers only symptomatic relief with life-long use of multiple medicines. Such medication is not only expensive but also causes multiple side-effects. Hence, life-style modifications and herbal remedies are contemplated as an alternative option.

Dietary fibers and plant materials can minimize LDL-cholesterol and reduce the chances of cardiovascular diseases (Anderson *et al*., 1999). An important plant in this regard is *C. spinosa*. Aqueous extract of *C. spinosa* was administered to rats orally, which significantly reduced blood cholesterol level. The extract also decreased lipids level in the rats suffering from diabetes (Eddouks *et al*., 2005). In another study (Lemhadri *et al*., 2007), it was demonstrated that the aqueous extract of *C. spinosa* could be used to reduce obesity, though further investigation is required to confirm the results.

Phytochemicals: It is well understood that the biological activities of plants and their formulations are due to the

presence of a wide variety of phytochemicals such as alkaloids, steroids, terpenoids, polyphenols and tocopherols among others (Joshi *et al*., 2011). *Capparis spinosa* is rich in a wide variety of biologically active compounds including natural antioxidants (phenolic acids, flavonoids, tocopherols), alkaloids, polyprenols, glucosinolates and reducing sugars along with several essential minerals, proteins and lipids. Fruit of *C. spinosa* has been well studied for its phytochemical constituents and found to contain alkaloids (0.74%), glucosides (0.083%), fats (3.75%), ascorbic acid (13.5%), reducing sugars (32.9%), resins (23.75%) and organic acids (14.1%) (Rastogi and Mehrotra, 1995). The potential biological activities and medicinal functions of different parts of *C. spinosa* can be attributed to the presence of different bioactives. Figure 1 presents the chemical structures of selected high-value bioactive phytochemicals identified in different parts of *C. spinosa.*

Flavonoids: Several important flavonoids have been identified in *C. spinosa* including rutin (quercetin 3-rutinoside), quercetin 3-glucoside-7-rhamnoside, quercetin 7-rutinoside, kaempferol-3-glucoside, kaempferol-3 rutinoside and kaempferol-3-rhamnorutinoside (Winter, 1978). Rutin is a versatile and potential antioxidant flavonoid that has several biological applications with no toxicity. It has been reported to decrease blood pressure, permeability of vessels and risk of arteriosclerosis along with its hypolipidemic and hepatoprotective activities (Pathak *et al*., 1991; Lima *et al*., 1999; Janbaz *et al*., 2002). Interestingly, *C. spinosa* is a rich source of rutin. In this regard, Ramezani *et al.* (2008) conducted a detailed study for the quantification of rutin from leaves, flowers and fruits of *C. spinosa*. From the extract (50% ethanol), rutin was separated by Thin Layer Chromatography (TLC), identified by UV light (254 nm) and further authenticated and quantified by the HPLC/UV method. The amount of rutin in leaves, fruit and flowers of *C. spinosa* was determined to be 61.09, 6.03 and 43.72 mg 100 g^{-1} of dried powder, respectively (Ramezani *et al*., 2008).

Previously, it was reported that methanolic extract of aerial parts of *C. spinosa* contained a novel flavonoid, quercetin 3-O-[6''-α-l-rhamnosyl-6''-β-d-glucosyl]-β-D-glucoside along with some known flavonoids such as rutin, quercetin 3-O-glucoside, quercetin 3-O-glucoside-7-O-rhamnoside, kaempferol-3-rutinoside and kaempferol-3-rhamnorutinoside (Rodrigo *et al*., 1992; Sharaf *et al*., 2000). Sharaf *et al*. (1997) also reported that leaves and stems of *C. spinosa* (extracted with 70% ethanol) contained quercetin-3-rutinoside, quercetin-7-rutinoside, kaempferol-3-rutinoside and quercetin 3- glucoside-7-rhamnoside. In another study, powdered fruit of *C. spinosa* was extracted with water. Ethanol eluted fractions contained eight new along with five known compounds out of which apigenin, kaempferol and the vetiaflavone were noted to be flavonoids (Zhou *et al*., 2010).

In a recent study, structurally diverse bioflavonoids (isoginkgetin, ginkgetin and sakuranetin) were isolated for the first time from the fruit of *C. spinosa* and their structures were confirmed by spectroscopic techniques (Zhou *et al*., 2011). In another study, HPLC coupled with a diode-array detector was used to evaluate quercetin 3-rutinoside, kaempferol 3-rutinoside and kaempferol 3-rhamnosyl-rutinoside and aglycones (quercetin and kaempferol) in brined flower buds of *C. spinosa*. According to the analysis the brined buds only contained quercetin and kaempferol. Meanwhile, total flavonoids and aglycones in flower buds available in market were estimated to be 5.18 and 3.86 mg g^{-1} of fresh caper, respectively (Inocencio *et al*., 2000). It can be inferred that *C. spinosa* is a potential plant to be explored as a viable source for extraction of antioxidant flavonoids for food and therapeutic uses.

Alkaloids: It is worth mentioning that *C. spinosa* is a rich source of different classes of alkaloids which include spermidine, indole and pyrrole alkaloids along with indol-aldehyde and indol-nitrile type derivatives. Several new alkaloids and their glycosides have also been identified in *C. spinosa*. For example, three new spermidine alkaloids including capparispine, capparispine 26-O-β-D-glucoside and cadabicine 26-O-β-D-glucoside hydrochloride were separated from the roots of *C. spinosa* and their structures were confirmed by NMR spectroscopy (Fu *et al*., 2008). Figure 2 shows two novel spermidine alkaloids identified in the roots of *C. spinosa*.

Furthermore, three novel alkaloids, capparisine A, capparisine B and capparisine C and two known alkaloids, 2-(5-hydroxymethyl-2-formylpyrrol-1-yl) propionic acid lactone and *N*-(3 -maleimidy1)-5-hydroxymethyl-2-pyrrole formaldehyde were isolated from the fruit of *C. spinosa* (Fig. 3). The isolated alkaloids were purified by the column chromatography, solvent separation and preparative TLC and their structures were confirmed by the spectroscopic and X-ray crystallographic techniques (Yang *et al*., 2010).

Mature fruit of *C. spinosa* was also shown to contain two glucose containing 1H-indole-3-acetonitrile compounds, 1H-indole-3-acetonitrile 4-O-β-glucopyranoside and 1H-indole-3-acetonitrile 4-O-β-(6-O-β-glucopyranosyl)-glucopyranoside, as confirmed by advanced spectroscopic techniques (Calis *et al*., 1999). According to a recent report, powdered fruit of *C. spinosa* (extracted with 70% ethanol and

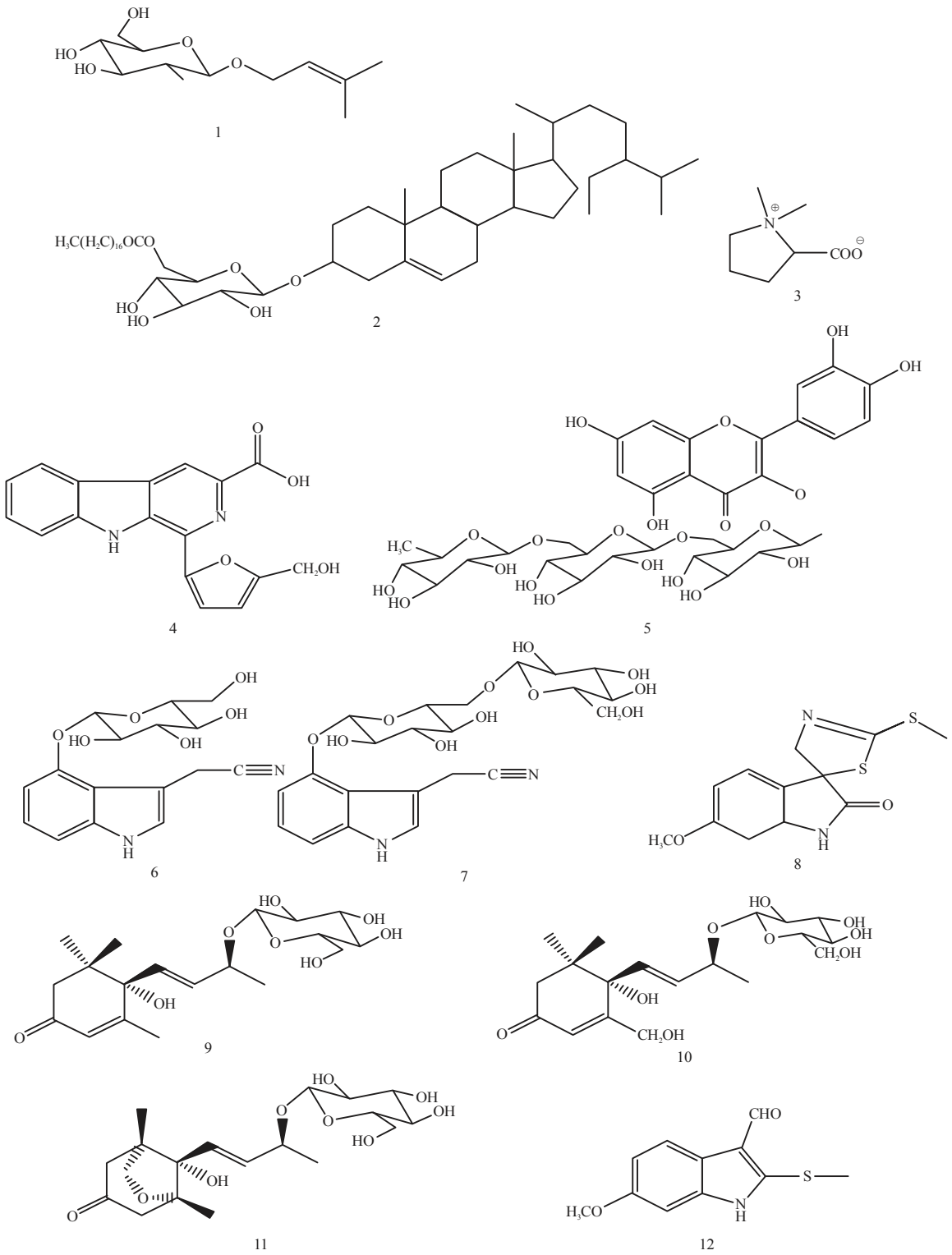

Fig. 1: Some important secondary metabolites of *C. spinosa*: 3-Methyl-2-butenyl-β-glucoside (1), β-Sitosterylglucoside-6'-octadecanoate (2), Stachydrine (3), Flazen (4), Quercetin 3-O-[6 "-α-l-rhamnosyl-6"-β-d-glucosyl]-β-d-glucoside (5), Cappariloside A (6), Cappariloside B (7), Capparine A (8), (+)-(6S,9S)-9-O-β-D-gluc opyranosyloxy-6-hydroxy-3-oxo-α-ionol (corchoionoside C, (6S,9S)-roseoside) (9), Spionoside A (10), Spionoside B(11) and Capparine B (12)

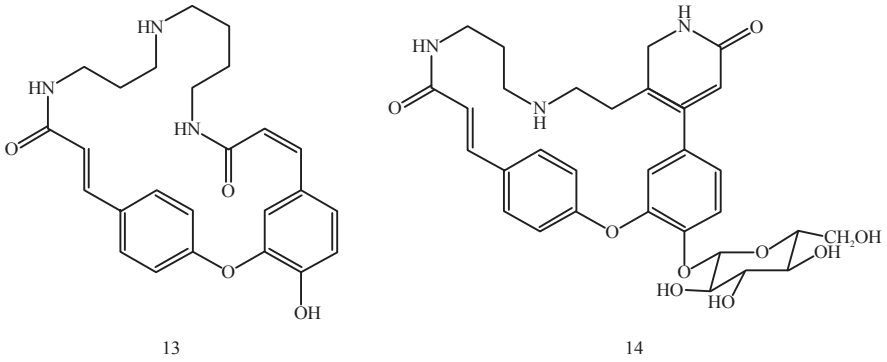

Fig. 2: Capparispine (13) and Capparispine 26-O-β-d-glucoside (14)

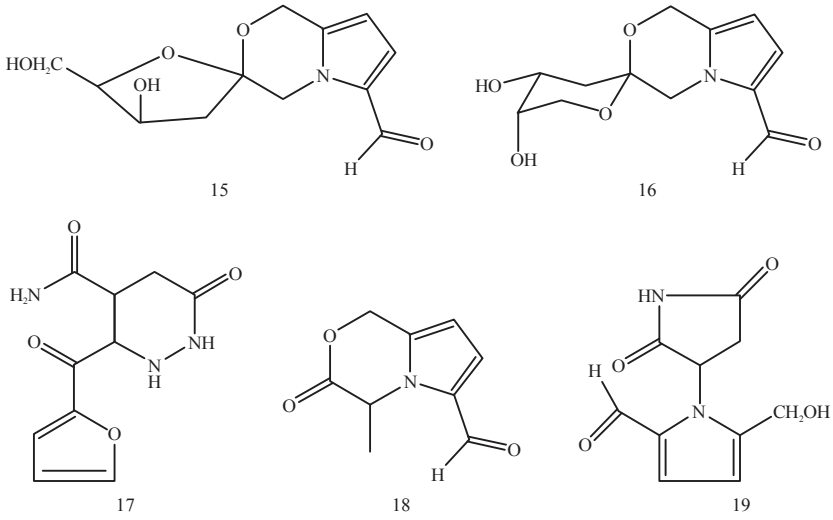

Fig. 3: Capparisine A (15), Capparisine B (16), Capparisine C (17), 2-(5-hydroxymethyl-2-formylpyrrol-1-yl) propionic acid lactone (18) and *N*-(3 -maleimidy1)-5-hydroxymethyl-2-pyrrole formaldehyde (19)

diluted with water and sulphuric acid) was found to have an important alkaloid cappariloside A along with hypoxanthine, uracil and adenosine (Fu *et al*., 2007). Other alkaloid compounds in the fruit of *C. spinosa* include flazin, guanosine, capparine A, capparine B, 1H-indole-3-carboxaldehyde and 4-hydroxy-1H-indole-3-carboxaldehyde (Zhou *et al*., 2010).

Essential oils and terpenoids: Essential oils, hydro-distilled products isolated from different parts of plants, are gaining much recognition as potential ingredients of functional foods, pharmaceuticals and cosmo-nutraceuticals due to their multiple medicinal and biological activities (Hussain *et al*., 2008, 2013). In particular, essential oils are popular for their antimicrobial, insecticidal, antiviral, antioxidant and food flavoring and preservative properties (Hussain *et al*., 2008, 2013; Karpouhtsis *et al*., 1998; Rusenova and Parvanov, 2009).

Capparis spinosa is rich in essential oil as reported by several studies. The flower buds and leaves of *C. spinosa* were used to extract essential oil by hydro-distillation in a clevenger-type apparatus. The GC-MS analysis of the essential oil revealed the presence of isothiocyanate (92.06%), sec-butyl isothiocyanate (0.25%), butyl isothiocyanate (0.38%), benzeneacetaldehyde (0.23%), benzeneacetonitrile (0.4%), E-β-ionone (0.5%), methyl methylsalicilate (0.17%), benzyl isothiocyanate (0.74%) and 3-hexenyl benzoate (0.27%) (Kulisic-Bilusic *et al*., 2010). Previously, it has been reported that *C. spinosa* essential oil contained 145 compounds when analyzed by HS-SPME/GC-MS. Among those, aldehydes (22.2%) and ketones (8.42%) are most abundant classes followed by sulphur compounds (8.42%). The plant also contained five sesquiterpenes and ten monoterpenes (Romeo *et al*., 2007). From Jordanian *C. spinosa*, γ-sitosterylglucoside-6'-octadecanoate and 3-methyl-2-

butenyl-γ-glucoside were also isolated[164]. Moreover, isothiocyanates, n-alkanes, terpenoids, a phenyl propanoid, an aldehyde and a fatty acid were isolated from the leaf oil of *C. spinosa.* The fruit and root oils also contained methyl, isopropyl and sec-butyl isothiocyanates (Afsharypuor *et al*., 1998).

In another study, extraction of essential oil via steam-distillation was carried out from dried fruit of *C. spinosa*. Out of 53 essential oil compounds identified by capillary GC-MS method, the main twelve compounds were found to be (Z,Z)-9,12-octadecadienoic acid (26.40%), hexadecanoic acid (15.35%), octadec-9-enoic acid (11.41%), 1,2-benzene dicarboxylic acid-bis(2-methylpropyl) ester (5.77%), di-(2-ethylhexyl) phthalate (4.41%), 2-methoxy-phenol (2.94%), tetradecanoic acid (2.67%), dodecanoic acid (2.47%), (Z,Z)-9,12-octadecadienoic acid-methyl ester (2.03%), *Z*-11-Hexadecenoic acid (1.86%), 1-(1H-pyrrol-2-yl)-ethanone(1.04%) and hexadecanoic acid-methyl ester (1.02%). These twelve compounds accounted for 77.37% of total separated compounds of the essential oil (Bai *et al*., 2007). Presence of a considerable amount of essential oil rich in diverse classes of chemical constituents, advocates that this species can be commercially exploited for essential oil production and its utilization in pharmaceutical, food and cosmo-nutraceutical industry leading to value-addition.

Lipid components: Plant lipids, being a potential source of essential fatty acids and natural antioxidant tocols and phytosterols, are another important class of bioactives with multiple functionalities (Anwar *et al*., 2008). The seeds of *C. spinosa* fruit have oil content varying between 27.3-37.6 g 100 g^{-1}. The fruit seed oil contains fatty acids (linoleic acid 24.6-50.5%, oleic acid 10%, vaccenic acid 30%), tocopherols (γ-tocopherol 124.3-1944.9 mg 100 g^{-1}, δ-tocopherol 2.7-269.5 mg 100 g^{-1} and α-tocopherol 0.6-13.8 mg 100 g^{-1}), total sterols (4.96-10.0 g kg^{-1}) and glucosinolates (42.6-88.9 μmol g^{-1}). Among the oil sterols, β-sitosterol (60%) is most abundant followed by campesterol (16%) and stigmasterol (10%) (Matthaus and Ozcan, 2005).

Tlili *et al.* (2009a) investigated the composition of fatty acids, tocopherols and carotenoids in the fruit seed oil of Tunisian caper (*C. spinosa*). According to the results, the seed oil contents of *C. spinosa* fruits ranged from 23.25-33.64% dry weight basis. The seed oil contained appreciable amount of tocopherols (ca. 628 mg 100 g^{-1}) and carotenoids (ca. 457 μg 100 g^{-1}). The occurrence of fatty acids such as oleic acid (45.82%), linoleic acid (25.37%), palmitic acid (15.93%), palmitoleic acid (4.55%) and stearic acid (4.06%) alongwith γ-tocopherol (ca. 92%), α-tocopherol (ca. 4%), δ-tocopherol (ca. 2%) and β-carotene (ca.375 μg 100 g^{-1}) was established in the tested seed oil (Tlili *et al*., 2009a).

Tlili *et al.* (2011), reported the contents of protein, lipid, aliphatic and triterpenic alcohols in the caper (*C. spinosa*) seeds. The amount of total protein and lipids was noted to be 27 and 33%, respectively. Aliphatic alcohols including hexadecanol, octadecanol and tetracosanol were determined as high as 45 mg kg^{-1} of total lipophilic substances. The amount of triterpenic alcohols such as citrostadienol, β-amyrin, gramisterol, cycloartanol and 2,4 methylcycloartenol was estimated to be 396.82 mg kg^{-1} with octadecanol (28 mg kg^{-1}) and citrostadienol (170 mg kg^{-1}) as the major compound.

In a similar study by Yili *et al.* (2006), extraction of lipids from the roots of *C. spinosa* was carried out using a mixture of chloroform and methanol (1:1 v/v) and the yield found to be 0.54% of total raw material. The analysis of the extracted lipids, after elution through a column using chloroform, showed the presence of neutral lipids, hydrocarbons, esters of sterols and high-molecular-weight fatty acids, triacylglycerides, free fatty acids, free sterols and aliphatic alcohols. Monogalactosyldiglycerides, sterolglycosides, cerebrosides, esters of sterolglycosides and digalactosylglycerides were found to be the main classes of glycolipids when separated from a column using acetone as a mobile phase, whereas methanol fraction mainly contained phosphatidylinosites, phosphatidylcholines and phosphatidylethanolamines (Yili *et al*., 2006). The lipids extracted from the epigeal parts of *C. spinosa* were found to contain hydrocarbons (5.4%), sterol and triterpenol components (18.6%), triacylglycerols (28.7%), free fatty acids (32.5%) and triterpenols (2.1%) as the neutral lipids while N-acyl- phosphatidylethanolamines (14.6%), N-acyl-lyso-phosphatidylethanolamines (6.7%), phosphatidylglycerols (26.1%), phosphatidylcholine (16.5%), phosphatidylethanolamines (20.4%), phosphatidylinositols (12.8%) and phosphatidic acid (2.8%) were identified as phospholipids. Glycolipids, esters of sterol glycosides (12.8%), sterol glycosides (25.7%), monogalactosyldiglycerides (18.2%), digalactosyldiglycerides (42.4%) and sulfoglucolipids (0.9%) were also identified among others (Talibaev and Glushenkova, 1995).

In a recent study by Yuldasheva *et al.* (2008) powdered seeds of *C. spinosa* were extracted with hydrocarbons for free lipids and with chloroform-methanol for bound lipids using Soxhlet apparatus. Bound lipids were further isolated into neutral lipids, phospholipids and glycolipids by separation with column packed with silica gel. Monogalactosyl diacylglycerides (MGDGs), digalactosyl diacylglycerides (DGDG), sterolglycosides and their esters were identified

as glycolipids while phosphatidylinositols, phosphatidylethanolamines and phosphatidylcholines were confirmed as phospholipids. Fatty acid composition by alkaline hydrolysis was also established.

Glucosinolates, polysaccharides and sugars: Glucosinolates are glucose derivatives, containing nitrogen and sulphur. These compounds are recognized as a natural pesticide (i.e., biopesticides) (Bridges *et al*., 2002) and cancer inhibitors (Hayes *et al*., 2008). Glusinolates are widely distributed in the plants of family Capparidaceae, Brassicaceae and Caricaceae (Rodman *et al*., 1996). *Capparis spinosa* L. plant has also been investigated as a potential candidate for isolation of glucosinolates. Matthaus and Ozcan (2002) reported total contents of glucosinolates in shoots and large flowers buds of *C. spinosa* amounting to levels as high as 6.55 μmol g^{-1}. Among glucosinolates, glucocapperin was found to be the most abundant compound with contribution of 90%. The study concluded that glucosinolates composition may vary with the size of buds (Matthaus and Ozcan, 2002). In another report, indole glucosinolates such as glucobrassicin, neoglucobrassicin and 4-methoxy-glucobrassicin were isolated from roots of *C. spinosa* and identified by HPLC and mass spectrometry (Schraudolf, 1989). Glucosinolates are reported to act as stimulant and appetizer for the digestive process. Other important biological effects exhibited by these compounds include cytotoxic, antibiotic, anti-cancer activities (Montaut and Bleeker, 2013).

Another important group of compounds namely hydrophilic polysaccharides, hemicelluloses and pectin compounds have also been extracted/isolated with water, base and oxalic acid/ammonium oxalate, respectively from the roots of *C. spinosa* and analyzed. The important monosaccharides detected in the roots of *C. spinosa* were xylose, arabinose and galactose (Yili *et al*., 2006).

Phytosterols: Phytosterols, which are derived from vegetable sources, especially, the vegetable oils, are linked with decreasing blood cholesterol level and thus mitigating the risk of heart diseases (Ortega *et al*., 2006). Phytosterols also possess anti-inflammatory, anti-tumor, antibacterial and anti-ulcerative properties (Beveridge *et al*., 2002). *Capparis spinosa* is also a good source of phytosterols. Petroleum ether-extract (oil) from the seeds of *C. spinosa* has notably high amount of total phytosterols (2240.4 mg kg^{-1} of extract). Among these, most abundant phytosterol was β-sitosterol (57.53%) followed by campesterol (17.05%), stigmasterol (11.85%) and 5-avenasterol (6%). Brassicasterol, cholesterol and campestanol were also identified in smaller amounts (Tlili *et al*., 2010a).

Carotenoids, tocopherols and phenolics: Carotenoids are antioxidants that protect cells from oxidative damage, which results in degenerative diseases such as cancer, aging and inflammation (Mayne, 1996; Sies and Stahl, 1995). Leaves, buds and flowers of *C. spinosa* contain an appreciable amount of total carotenoids, 3452.5±1639.4, 1002±518.5 and 342.7±187.9 μg g^{-1}, respectively. Among carotenoids, lutein and violaxanthin had the highest and lowest contents, respectively. The amount of α-tocopherol was found to be 20.19±10 mg 100 g^{-1}, 49.12±17.48 and 28.68±9.13 mg 100 g^{-1} in the leaves, buds and flowers, respectively. There was no γ-tocopherol detected in the leaves but a considerable amount of -tocopherol was present in the buds (48.13±15.08 mg 100 g^{-1}) and leaves (27.8±16.01 mg 100 g^{-1}), respectively (Tlili *et al*., 2009b).

In another study, the analysis of flower buds of *C. spinosa* demonstrated that they did not contain α-tocopherol but γ-tocopherol and vitamin C were present in small amounts (Tesoriere *et al*., 2007). Tlili *et al.* (2010a) evaluated the antioxidant capacity of methanol extracts of leaves and flower buds of *C. spinosa* by analyzing different bioactives. A high amount of phenolic compounds ca. 3,643 and 2,621 mg 100 g^{-1} fresh weight along with carotenoids ca. 4 and 18 mg 100 g^{-1} was detected in the leaves and flower buds of *C. spinosa*, respectively supporting that the plant could be explored as a potential source of different types of natural antioxidants.

Other components: Some studies demonstrated the occurrence of miscellaneous types of phytochemicals in *C. spinosa*. For example, GC-MS analysis of the fruit of *C. spinosa* showed the presence of sulphides, isothiocyanates and elemental sulphur (S_8). Response of caper to dithiocarbamate test was shown to be positive (Brevard *et al*., 1992). The mature fruit of *C. spinosa* showed the presence of two new glycosides, which were isolated and identified as (6S)-hydroxy-3-oxo-á-ionol glucosides (Calis *et al*., 2002). Al-Said *et al.* (1988) reported the presence of polyprenols (anti-inflammatory agents) such as cappaprenol-12, cappaprenol-13 and cappaprenol-14, containing 12, 13 and 14 isoprenoid units, respectively, in alcoholic extract of *C. spinosa*.

According to a recent report, it was also found that 8.6 g of *C. spinosa* fruit contained considerable amount of rutin (13.76 mg) and isothiocyanates (42.14 μmol). Linoleic acid (18:2 ω 6), γ-linolenic acid (18:3 ω 6), rutin and kaempferol-3-rutinoside were also discovered from buds of *C. spinosa* (Giuffrida *et al*., 2002). Various bioactive components separated and identified from *C. spinosa* are listed in Table 2.

Table 2: Bioactivities separated and identified from different parts of *C. spinosa*

Plant part	Phytochemicals	References
Whole plant	(i). Polyprenols	(i). Al-Said *et al.* (1988)
	(ii). 145 Compounds isolated: methyl-isothiocyanate, benzyl-isothiocyanate, five sesquiterpenes, ten monoterpenes, several aldehydes and esters	(ii). Romeo *et al.* (2007)
	(iii). β-Sitosterylglucoside-6'-octadecanoate and 3- methyl-2-butenyl-β-glucoside	(iii). Khanfar *et al.* (2003)
Aerial parts	(i). Flavonoids	(i). Sharaf *et al.* (1997, 2000)
	(ii). Glucosinolates	(ii). Matthaus and Ozcan (2002)
	(iii). Lipids	(iii). Talibaev and Glushenkova (1995)
Fruit	(i). Two new (6S)-hydroxy-3-oxo-*á*-ionol glucosides	(i). Calis *et al.* (2002)
	(ii). Glucose containing acetonitriles	(ii). Calis *et al.* (1999)
	(iii). Isothiocyanates, n-alkanes, terpenoids, a phenyl propanoid, an aldehyde and a fatty acid	(iii). Afsharypuor *et al.* (1998)
	(iv). Minerals and fatty acids	(iv). Rodrigo *et al.* (1992)
	(v). Sulphur containing compounds	(v). Brevard *et al.* (1992)
	(vi). Tocopherols	(vi). Tesoriere *et al.* (2007)
	(vii). Minerals	(vii). Ozcan and Aydin (2004)
	(viii). Biflavonoids	(viii). Zhou *et al.* (2011)
	(ix). Alkaloids	(ix). Yang *et al.* (2010)
	(x). Rutin	(x). Ramezani *et al.* (2008) and Zhou *et al.* (2010)
	(xi). Fruit oils	(xi). Bai et al. (2007)
	(xii). Thirteen compounds: flavonoids, indoles and phenolic acids	(xii). Fu *et al.* (2007)
Roots	(i). Chemical composition: methyl, isopropyl and sec-butyl isothiocyanates	(i). Afsharypuor *et al.* (1998)
	(Ii). Indole glucosinolates	(ii). Schraudolf (1989)
	(iii). Spermidine alkaloids	(iii). Fu *et al.* (2008)
	(iv). Lipids	(iv). Yili *et al.* (2006)
Seeds	(i). Fatty acids, tocopherols, sterols glucosinolates	(i). Matthaus and Ozcan (2005)
	(ii). Monomeric protein	(ii). Lam and Ng (2009)
	(iii). Lectin	(iii). Lam *et al.* (2009)
	(iv). Seed oil content	(iv). Tlili *et al.* (2009a)
	(v). Total protein and lipid content	(v). Tlili *et al.* (2011)
	(vi). Free and bound lipids	(vi). Yuldasheva *et al.* (2008)
	(vii). Phytosterols	(vii). Tlili *et al.* (2010b)
Flower buds	(i). Glucosinolates	(i). Matthaus and Ozcan (2002)
	(ii). Tocopherols	(ii). Tesoriere *et al.* (2007)
	(iii). Carotenoids and tocopherols	(iii). Tlili *et al.* (2009a)
	(vi). Rutin	(vi). Ramezani *et al.* (2008)
	(v). Essential oils	(v). Kulisic-Bilusic *et al.* (2010)
Buds	(i). Rutin, kaempferol-3-rutinoside, linoleic acid, γ-linolenic acid	(i). Giuffrida *et al.* (2002)
	(ii). Carotenoids and tocopherols	(ii). Tlili *et al.* (2009b)
Leaves	(i). Carotenoids and tocopherols	(i). Tlili *et al.* (2009b)
	(ii). Rutin	(ii). Ramezani *et al.* (2008)
	(iii). Essential oils	(iii). Kulisic-Bilusic *et al.* (2010)

Conclusion and future prospects: *Capparis spinosa* (*C. spinosa*) is mostly popular as a folk remedy for the treatment of hepatitis, tuberculosis, kidney problems, stomach disorders, diabetes and high blood pressure. The plant is also recognized for its anti-inflammatory, antioxidant, cardiovascular, hepatoprotective, antimicrobial, antiviral, hypolipidemic and hypoglycemic activities. Hence, it would be meaningful to isolate and characterize related bioactives from different parts of this species. Further efforts are also needed for the appraisal of clinical and pharmacological applications of novel bio actives in this species using some *in-vitro* and *in vivo* studies.

Various studies have confirmed that *C. spinosa* is a rich source of antioxidants, such as flavonoids and contains rutin and querecitin in considerably high amounts. Therefore, this wildly grown species, which is quite salt and drought tolerant, can be cultivated in saline arid and dry lands as a commercial source of natural antioxidants and preservatives for the functional food and nutraceutical industry. Different anti-inflammatory agents including cappaprenol-13, isoginkgetin and ginkgetin have been separated from different parts of *C. spinosa* to treat arthritis. This supports the future prospects of this species for the discovery of natural drugs. Fruit extract showed anti-hyperglycemic effect in rats; hence, screening of new anti-diabetic compounds in this plant will be helpful in the development of new drugs to treat diabetes. Similarly, the established anti-ulcer attributes of this species provoke the need to isolate and purify the anti-ulcer components and develop natural drug for the treatment of ulcerative disorders.

The plant possesses very good anti-tumor and antimicrobial activities; the related bioactive compounds still need to be isolated in purified form for drug development. Moreover, there is need to isolate potential anti-viral components from this species. The plant seeds also contain a protein that inhibits the multiplication of hepatoma HepG2 cells, colon cancer HT29 cells and breast cancer MCF-7 cells. Other parts of this plant should also be investigated for the isolation of functional bio-peptides and elucidation of their mechanism of biological actions.

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