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A review on the medical effects of *Capparis spinosa* L.

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ABSTRACT

Background and aims: Plants are a valuable source of wide range of secondary metabolites. Caper (*Capparis spinosa* L.) belongs to the Capparaceae family. It has a lot of medical uses especially in medical fields. The aim of this study is to review the medical uses of this plant in nobel studies.
Methods: In order to conduct this review study, INLM and Google scholar and Science direct databases were searched for English published articles during 2000-2015.
Results: This plant has a lot of traditional and medical use. The whole plant was used for rheumatism. Roots were used as diuretic, astringent, and tonic. Bark root, which has a bitter taste, was used as appetizer, astringent, tonic, ant diarrheic and to treat hemorrhoids and spleen disease. Bark was also used for gout and rheumatism, as expectorant, and for chest diseases. Infusion of stems and root bark were used as anti-diarrheic and febrifuge. Fresh fruits were used in sciatica, and dropsy. Dried and powdered fruit combined with honey was used in colds, rheumatism, gout, sciatica and backache. Seeds were used in feminine sterility and dysmenorrheal and to relieve toothache. Crushed seeds were used for ulcers, scrofula, and ganglions.
Conclusion: The paper reviewed was promising medicinal plant with wide range of pharmacological activities which could be utilized in several medical applications because of its effectiveness and safety.

Keywords: *Capparis spinose* L., INLM, Google scholar**,** Science direct, Medical uses.

Review Article

INTRODUCTION

Today, medicinal plants have an important role in diet of people.[1] With increased resistance resulting from overusing of chemical synthetic antibiotics, finding alternative medicines that have antibacterial properties and have the least side effects on human health appears to be necessary.[2] Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavors, fragrances, colors, bio pesticides and food additives.

Cappari spinosa(C.spinosa) which was commonly used as a medicinal plant contained many biologically active chemical groups including, alkaloids,

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glycosides, tannins, phenolic, flavonoids, triterpenoids steroids, carbohydrates, saponins and a wide range of minerals and trace elements. It exerted many pharmacological effects including antimicrobial, cytotoxic, anti-diabetic, anti-inflammatory, antioxidant effect and many others.

Caper (*Capparis spinose* L.) belongs to the Capparaceae family native to the Mediterranean region. *C.spinosa* is a perennial crop one of the most common aromatic plants that grow along the roadside, on the slopes, rocky and stony area and generally well adapted to dry areas basin.[3-5] Wild species of Capparis are found in countries surrounding the Mediterranean basin extending to the Great Sahara in North Africa and the dry regions of Western and Central Asia.[6] The caper bush requires a semiarid climate. Mean annual temperatures in areas under cultivation are over 14 °C and rainfall varies from 200 mm/year in Spain to 460 in Pantelleria and 680 in Salina. In Pantelleria, it rains only 35 mm from May through August, and 84 mm in Salina. A rainy spring and a hot dry summer are considered advantageous. This drought-tolerant perennial plant has favorable influence on the environment and it is utilized for landscaping and reducing erosion along highways, steep rocky slopes, sand dunes or fragile semiarid ecosystems.

Arabic: Kabbar, Assef; Berber: Taylulut, Tailoulout, Amserlih, Ouailoulou; English: Caper bush, Caper bush, Caper, Caperberry; French: Câprier, Capriercommun,Câpres, Fabagelle, Tapana, Finnish: Kapris; German: Kapper, Kapernstrauch; Gujarati: Kabaree; Hindi: Kiari, Kobra; Hungaria: Kapricserje; Icelandic: Kapers; Italian: Cappero, Capperone (fruit); Kannada: Mullukattari; Maltese: Kappara; Marathi: Kabar; Norwegian: Kapers; Portuguese: Alcaparra; Punjabi: Kabarra; Russian: Kapersy; Sanskrit: Ahimsra, Kanthari, Kantaka, Tiksnagandha; Spanish: Alcaparra, Caparra, Tapana; Alcaparron, Caperberries; Swedish: Kapris; Telugu: Kokilakshmu; Urdu: Kabar.[7-9]

Traditional use: The whole plant was used for rheumatism. Roots were used as diuretic, astringent, and tonic. Bark root, which has a bitter taste, was used as appetizer, astringent, tonic, anti-diarrheic and to treat hemorrhoids and spleen disease. Bark was also used for gout and rheumatism, as expectorant, and for chest diseases. Infusion of stems and root bark were used as anti-diarrheic and febrifuge. Fresh fruits were used in sciatica, and dropsy. Dried and powdered fruit combined with honey was used in colds, rheumatism, gout, sciatica and backache. Seeds were used in feminine sterility and dysmenorrheal and to relieve toothache. Crushed seeds were used for ulcers, scrofula, and ganglions. The crushed leaves were applied in a poultice on the front against headache, on the face against toothache. The plant's decoction is said to clean eyes.[6,10-17]

Medicinal Advantages: In Greek popular medicine, a herbal tea made of caper root and young shoots is considered to be beneficial against rheumatism. Dioscoride (MM 2.204 t) also provides instructions on the use of sprouts, roots, leaves and seeds in the treatment of strangury and inflammation.[18,19]

Different flavonoids were identified in caperbush and capers: rutin (quercetin 3-rutinoside), quercetin 7-rutinoside, quercetin 3-glucoside-7-rhamnoside, kaempferol-3-rutinoside, kaempferol-3-glucoside, and kaempferol-3-rhamnorutinoside. Rutin is a powerful antioxidant bioflavonoid in the body; and is used as a dietary supplement for capillary fragility. Rutin has no known toxicity.[20-22]

Capers contain more quercetin per weight than another plant.[22,23]

Caper root bark and leaves may have some anti-carcinogenic activity. In fact, the

hydrolysis products of indol-3-ylmethyl glucosinolates have anti-carcinogenic effects.[20,24] Although the consumption of capers is low in comparison to intake of other major dietary sources of glucosinolates (white cabbage, broccoli and cauliflower), it may contribute to the daily dose of natural anticarcinogens that reduces cancerrisk. Glucosinolates are also known to possess goitrogenic (anti-thyroid) activity. Also, rutin and quercetin may contribute to cancer prevention.[25] Selenium, present in capers at high concentrations in comparison with other vegetable products, has also been associated with the prevention of some forms of cancer.

Physicochemical properties and chemical constituents: Moisture: 8%, total ash: 9.45%, acid insoluble ash: 2.45%, water soluble ash 5.5%, water soluble extractive value: 13.18%, alcohol soluble extractive value: 6.35% and ether-soluble extract: 17.8±1.1%, Dry matter: 93.6±1.6% and ash: 2.1±0.7%.[26]

Preliminary screening of the alcoholic extract revealed the presence of alkaloids, glycosides, carbohydrates, tannins, phenolics, flavonoids and triterpenoids while the aqueous extract showed the presence of steroids, glycosides, carbohydrates, flavonoids and saponins.[27-30]

The bioactive phytochemicals analysis of *C.spinosa subsp. rupestris* (syn. *C. orientalis*) showed that this species represented a very rich source of bioactive and nutraceutical compounds. The plant seeds oil was rich in unsaturated and rare lipids such as cis-vaccenic acid. The main glucosinolate was glucocapperin. The aerial parts contain edrutin as the dominant flavonoid.[31]

Systematic fractionation of *C. spinose* L. fruit fractions led to identification of 13 compounds. Major compounds found in the bioactive fraction were flavonoids, indoles, and phenolic acids.[32,33]

The chemical constituent of the fraction eluted by ethanol-water (50:50, v/v) showed the presence of seven compounds: P-hydroxy benzoic acid; 5- (hydroxymethyl) furfural; bis (5-formylfurfuryl) ether; daucosterol; α-D-fructofurano sides methyl; uracil; and stachydrine.[34]

A new antioxidant cappariside (4-hydroxy-5-methylfuran-3-carboxylic acid), together with many organic acids was isolated from *C. spinose*.[22] New two (6S)-hydroxy-3-oxo-a-ionol glucosides, together with corchoionoside C ((6S, 9S)-roseoside) and a prenylglucoside were also isolated from mature fruits of *C. spinose*.[35]

C. spinosa fruits also contained P-hydroxybenzoicacid, 5-(hydroxylmethyl) furfural bis (5-for-mylfurfuryl) ether, daucosterol, α-D-fructofuranosidesmethyl, uracil, and stachydrine.[36] However, Yu et al. isolated eight compounds from the fruit of *C. spinosa* by chromatographic methods and their structures were established by spectroscopic methods as β-sitosterol, vanillicacid, p-hydroxybenzoic acid, protocatechuric acid, daucosterol, uracil, butanedioic acid and uridine.[37]

New (6S)-hydroxy-3-oxo-α-ionolglucosides together with corchoinoside C (6S, 9S)-roseoside, and prenylglucosides, capparilo side A, stachydrine, an adenosine nucleoside, hypoxanthine, β-sitosterol, vanillic acid, p-hydroxybenzoic acid, protocatechuric acid, daucosterrol, uracil, butanedioc acid, and uridine were isolated from the fruits of *C. spinosa*.[35]

The nutritional values of caper berries per 100 g included carbohydrates 5 g, fats 0.9 g, dietary fibers 3g, sugar 0.4 g, protein 2 g vitamin C 4 mg. and energy 20 Kcal.[38]

C. spinosa oil (0.04% pale yellowish oil) was dominated by 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.[39]

The fatty acid composition of *C. spinosa* seeds oils included, palmitic: 10.23%, stearic: 2.61%, oleic: 38.45%, linoleic 23.75% and linolenic 1.17%.[24]

Cholesterol contents ranged from 0.22% (4.54 mg/kg) to 0.83% (18.83 mg/kg), brassicasterol 0.05% (4.54 mg/kg) to 0.33% (18.83 mg/kg), campesterol 15.55% (321.57 mg/kg) to 19.38% (439.81 mg/kg), campestanol 0.13% (2.82 mg/ kg) to 0.33% (7.31 mg/kg), stigma sterol 9.97% (220.87 mg/kg) to 13.92% (315.9 mg/kg), β-sitosterol 50.80% (1180.29 mg/kg) to 62.35% (1381.3 mg/kg) , avenasterol 5.37% (116.53 mg/kg) to 8.11% (179.67 mg/kg), stigmastadienol 0.33% (6.82 mg/kg) to 0.89% (20.68 mg/kg), Stigmastenol 0.07% (1.55 mg/kg) to 0.32% (6.94 mg/kg) and Avenasterol 0.16% (3.47 mg/kg) to 0.74% (16.79 mg/kg).[40]

Pharmacological effects

Antimicrobial effects: The antibacterial activities of petroleum ether, water, butanol, methanol and hexane crude extracts obtained from the aerial parts of *C. spinosa* were examined by agar well diffusion method. Different fractions exhibited good to moderate degrees of activity against most of the tested bacteria. Extracts were most active against *Staphylococcus epidermidis* and *Streptococcus faecalis.*[38]

Crude extract fractions and essential oils obtained from *C. spinosa* L. var. *aravensis* from Jordan were examined for antibacterial activity. Antibacterial activities of extract fractions were evaluated in vitro against a variety of Gram-positive and Gram-negative bacteria by agar well diffusion. The butanol fraction showed the broadest range of antibacterial efficacy, while the hexane fraction showed the narrowest. Antibacterial activity tests of essential oils showed that they were antibacterial, and the highest activities were recorded against *Micrococcus luteus.*[29]

The petroleum ether, methanol, hexane, butanol and aqueous crude extracts of the whole aerial parts of *C. spinosa* exhibited variable degrees of antimicrobial activity. Extracts had low to moderate activity against four bacterial species (*E. coli, S. typhirnurium, B. cereus*, and *Staph. aureus*).[40]

Ethanolic and petrolium ether extracts were used to study the antimicrobial activity of *C. spinosa* against gram positive and gram negative organisms by disc diffusion method. Both extracts shown significant antimicrobial activity against gram positive organisms, *Bacillus cereus* and *Staphylococus auerus*, and gram negative organisms, *Pseudomonas aeruginosa* and *E. coli* compared with standard antibiotics.[41]

A monomeric protein with molecular mass of 38 kDa was purified from *C. spinosa*seeds. It inhibited HIV-1 reverse transcriptase and fungal mycelia growth without having hemoglutinating, ribonuclease, mitogenic or protease inhibitor properties. A novel dimeric 62-kDa lectin was also extracted from caper (*C. spinosa*) seeds; it also inhibited HIV-1 reverse transcriptase and proliferation of both hepatoma HepG2 and breast cancer MCF-7 cells.[42]

Both the alcoholic and aqueous extracts of *C. spinosa* displayed significant anti helminthic properties at high concentrations. Both extracts showed anti helminthic activities in a dose-dependent manner giving short time of paralysis and death with 400 mg/mL concentration. The alcoholic extract induced paralysis of the earthworm Lumbricus terrestris *(L. terrestris)* in 6.16 minutes and death in 9.1 minutes, while the aqueous extract showed paralysis and death in 21.83, and 34.5 minutes respectively. In the meantime, albendazole (20 mg/mL) caused

paralysis of the earth worm in 8.6 minutes and death in 32.23 minutes.[27] Table 1 and 2 generally referred to the pharmacological effects of the plant.

Table 1: Main pharmacological properties of *C. spinosa*

Pharmacological activity	Animal model	Part of the plant	References
Treatment of rheumatism and inflammatory disorders	Kun Ming mice, wistar rats, human chondrocytes	Fruits, Flower buds	18,23,26,39, 44,45
Antiallergic and antihistaminic	Male guinea-pigs and allergic patients	Flower buds and fruits	6,46,47
Antidiabetic and hypolipidemic	C57BL/6J mice and Type 2 diabetic patients	Fruits	14-16,48,49
Antihepatotoxic	Wistar rats, mice	Aerial parts, roots	6,34
Antimicrobial	Deinococcusradiophilus, Gram-positive and negative bacteria	Whole plant and roots	33,50,51
Antiviral and immunomodulatory	Herpes simplex virus (Type HSV-2)	Flower buds	52,53
Antioxidant	Swiss albino rats	Aerial parts and Fresh buds	54,55
Anti-apoptotic	Human dermal fibroblasts	Fruits	27
Stimulating melanogenesis	B16 murine melanoma cells	Leaves	55
Antimutagenic	In vitro	Flower buds	31
Antiparasitic	Plasmodium falciparum	Aerial parts	55
Diuretic effect	Wistar rats	Fruits	21
Antiproliferative	Human hepatoma HepG2, colon human cancer HT29, human breast cancer MCF-7	Seeds	45
Antifungal activity	Valsamali fungi	Seeds	45
HIV-1 reverse transcriptase inhibitory	DNA molecule	Seeds	45
Hypotensive	Rats and Spotaneously hypertensive rats	Fruits	19,22,55
Anti-Helicobacter pylori	clinical isolates of Helicobacter pylori	Plant crude extracts	55
Anti-complement	In vitro	Fruits	41

Table 2: Elemental analysis values (X ± SD) of *C. spinose* L. using EDXRF system

Mineral	Sample
Al[a]	0.48±0.05
P[a]	1.15±0.01
S[a]	4.00±0.06
K[a]	4.54±0.03
Ca[a]	1.18±0.01
Cl[b]	94.86±25.51
Ti[b]	55.24±2.30
Mn[b]	70.04±1.00
Fe[b]	520.72±4.05
Ni[b]	24.10±0.05
Cu[b]	88.27±0.45
Zn[b]	250.75±0.80
Br[b]	11.92±0.07
Rb[b]	79.03±0.19
Sr[b]	40.20±0.69
Y[b]	2.48±0.38
Hf[b]	27.32±0.87
Pb[b]	5.34±0.13

a: %; b: ppm. Values given are the mean and standard deviation of triplicate measurements.

Cytotoxic effects: Onion bulbs were treated with three different concentrations (10, 20 and 30 g/L) of *C. spinosa* flower buds aqueous extract for 24 h without ethylmethane sulfonate (EMS) treatment.

Growth retardation, significant decrease in mitotic index and chromosome berrations were observed in root-tip cells treated with aqueous extract before and after the (EMS) treatment when compared with the controls in all treatments.

A novel dimeric 62-kDa lectin was also extracted from caper (*C. spinosa*) seeds; it inhibited the proliferation of both hepatoma HepG2 and breast cancer MCF-7 cells.[42]

The effect of the crude aqueous *C. spaniosa* leaf extract in a concentration of used (125, 250, 500 and 1000 µg/ml, for 48-72 hrs exposure time) was studied against two cellular cancer lines, human epidermoid larynx carcinoma Hep-2 and human cervix uteri epitheloid carcinoma Hela.

The extracts induced significant inhibitory effect ($P<0.001$) on the cancer lines growth, Hep-2 and Hela with low concentration. The cellular Hep-2 density was (0.340%), whereas the density in Hela was (0.6545%) at the lowest concentration 125 µg/ml. The highest inhibitory effect of the extract was recorded at 1000 µg/ml. The effect appeared time dependent.[43]

C. spinosa seeds contain a 38 kDa protein similar to imidazoleglycerol-phosphate dehydratase syntheses that inhibited proliferation of hepatoma HepG2 cells, colon cancer HT29 cells and breast cancer MCF-7 cells with an IC_{50} of about 1, 40 and 60 m, respectively.[45]

On the other hand, Stachydrine was potent anti-metastatic agent, it markedly inhibit the malignancy and invasive capacity of malignant cancer cells. It inhibited the expression of chemokine receptors (CXCR3 and CXCR 4) in cancer cells. *C. spinosa* root bark extract also showed antitumor activity against Ehrlich Ascites carcinoma in albino mice. It significantly decreased the tumor volume, packed cell volume, and viable cell count and it prolonged the life span of EAC tumor-bearing mice.[42,45,46]

The cytotoxic effects of aqueous, methanolic crude extracts and secondary metabolites extracts (polyphenolic, rutin, and alkaloids) of mature fruit of *C. spinosa* was on human larynx carcinoma (Hep-2) and human cervix adenocarcinoma (HeLa) tumor cell lines in vitro have been studied.[47]

Antidiabetic effects: The antidiabetic hypolipidemic effect of *C. spinosa* fruit extract was studied in diabetic rats (200 mg/kg and 400 mg/kg bw) for 28 days, these doses cause none significantly decreased the glucose level at 60 and 120 min. However, *C. spinosa* extract exerted lipid lowering effects with the same extract.[48] Histological assessments showed a significant increase in the number of β cells, diameter of islets, and amount of insulin in groups treated with hydroalcoholic

extract of *C. spinose* compared to the diabetic control group.[39,49]

Anti-inflammatory effects: The anti-inflammatory effects of the flavonoids from caper fruits were evaluated by secreted placental alkaline phosphatase (SPAP) reporter assay, which was designed to measure nuclear factor-kappa B (NF-κB) activation. Isoginkgetin and ginkgetin showed inhibitory effects in initial screen at 20 μM, while the effect of ginkgetin was much greater than that of isoginkgetin. In a dose-response experiment, the IC_{50} value of ginkgetin was estimated at 7.5 μM, suggesting it could be a strong NF-κBinhibitor.[50]

The anti-inflammatory activities of *C. spinosa* L. fruit (CSF) aqueous extract was studied mice. The CSF aqueous extract were separated into three fractions (CSF1-CSF3) by macroporous adsorption resins. The fractions CSF2 and CSF3 effectively inhibited the carrageenan induced paw edema in mice.[14]

The extracts of *C. spinose* were found to possess marked anti-inflammatory activity but devoid of analgesic activity in animal models, cappaprenol-13 isolated from *C. spinosa* showed significant anti-inflammatory activity.[51]

Antioxidant effects: *C. spinosa* aerial part and root extracts were extracted with solvents of varying polarity. Ethylacetate extract of the aerial part contains the highest concentration of phenolic compounds and flavonoids followed by the chloroform extract of roots. The antioxidant activity of different extracts of *C. sspinosa* was evaluated by DPPH radical scavenging method. The antioxidant activity (IC_{50} μg/ml) of methanol and ethyl acetate extracts were 94.4±4.5 and57.75±2.3 respectively.[52]

Other effects: Ethanolic root bark extract of *C. spinose* (100, 200 and 400 mg/kg) afford significant dose-dependent protection against CCl4 induced hepato cellular injury. Blood samples from the animals treated with ethanolic root bark extracts showed significant decrease in the levels of serum markers, indicating the protection of hepatic cells.[53]

When *C. spinosa* applied topically it afforded significant in vivo protection against UVB light-induced skinerythema in healthy human volunteers.[54]

Treatment of the paracetamol-induced liver damage in rats with aqueous extract of *C. spinose* (25, 50, 100, 200 mg/kg of body weight) for 7, 14, 21 days decreased alanine amino transferase, aspartate amino transferase activity, total bilirubin and creatinine levels in comparison with non-treated group, as well as improving the damaged liver tissues with dose dependent manner.[55]

CONCLUSION

The paper reviewed *C. spinosa* was promising medicinal plant with wide range of pharmacological activities which could be utilized in several medical applications because of its effectiveness and safety.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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