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THE CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL EFFECTS OF*CAPPARIS SPINOSA* -AN OVERVIEW

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ABSTRACT

Capparis spinosa contained many biologically active chemical groups including, alkaloids, glycosides, tannins, phenolics, flavonoids, triterpenoids steroids, carbohydrates, saponins and a wide range of minerals and trace elements. It exerted many pharmacological effects including antimicrobial, cytotoxic, antidiabetic, anti-inflammatory, antioxidant, cardiovascular, bronchorelaxant and many other effects. The present review will designed to highlight the chemical constituents and the pharmacological effects of *Capparis spinosa*.

Keywords: *Capparis spinosa*, pharmacology, constituents.

INTRODUCTION

Plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavors, fragrances, colors, biopesticides and food additives. As a result of accumulated experience from the past generations, today, all the world's cultures have an extensive knowledge of herbal medicine.

Capparis spinosa which was commonly used medicinal plant, contained many biologically active chemical groups including, alkaloids, glycosides, tannins, phenolics, flavonoids, triterpenoids steroids, carbohydrates, saponins and a wide range of minerals and trace elements. It exerted many pharmacological effects including antimicrobial, cytotoxic, antidiabetic, anti-inflammatory, antioxidant, cardiovascular, bronchorelaxant and many other effects.

Common names

Arabic:Kabbar, Assef; Berber: Taylulut, Tailoulout, Amserlih, Ouailoulou; English: Caper bush, Caperbush, 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 [1-3].

Family :Capparidaceae

Distribution

It is supposed to be originated in the dry areas of Western or Central Asia. Capers can today be found growing wild all over Mediterranean (especially in France, Spain, Italy and Algeria); furthermore, the plant is found in Iran, Iraq, Cyprus and Greece [3-4].

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, antidiarrheic 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 antidiarrheic 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. As decoction, it

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was used for gastric pain and applied on the body for the treatment of epilepsy. 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 [1,4-11].

Plant description

Capers are the small buds picked very young, even before they have bloomed. If the caper is not picked, it will soon become a flower. This flower produces a fruit called the caperberry. Caperberries are the mature fruits of the caper bush. They are the same size and color as a small green olive, with a delicate fruity flavor [1].

However, *Capparis spinosa*is a perennial spiny bush that bears rounded, fleshy leaves and big white to pinkish-white flowers. The shrubby plant is many-branched, with alternate leaves, thick and shiny, round to ovate in shape. The flowers are complete, sweetly fragrant, showy, with four sepals, and four white to pinkish-white petals, many long violet-colored stamens, and a single stigma usually rising well above the stamens. Herbs or shrubs, erect or climbing, rarely trees. Leaves alternate or rarely opposite, simple or palmately 3-9-foliolate; leaflets usually entire; with or without stipules. Flowers regular or slightly irregular, bisexual or rarely dioeciously. Sepals generally 4, free or connate. Petals usually 4, imbricate hypogynies or sometimes inserted on the disk. Stamens usually 6, sometimes 4 or numerous.Ovary usually stalked, 1-celled; ovules many. Fruit a pod-like capsule or berry or rarely a drupe [2-3,11].

Part used: Capers (flower buds), Caperberries (fruits), leaves, roots and seeds were used medicinally [1].

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% [12].

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 [13-16].

Rutin and quercetin content of the root were 1.02 and 6.3, of the stem were 1.95 and 8.82, of the leaf were 25.82 10.4 and of the floral bud were 11.7 and 9.4 mg/g respectively[17].

The bioactive phytochemicals analysis of *Capparis spinosa subsp. rupestris* (syn. *C. orientalis*) showed that this species represented a very rich source of bioactive and nutraceutical compounds, the oil from 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 [18].

Systematic fractionation of *C. spinosa* L. fruit fractions led to identification of 13 compounds. Major compounds found in the bioactive fraction were flavonoids, indoles, and phenolic acids [8,19].

Khanfar *et al.,* isolated γ -sitosterylglucoside-6'-octadecanoate, 3-methyl-2-butenyl- γ –glucoside from *Capparis spinosa* of Jordanian origin [20].

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-fructofuranosides methyl; uracil; and stachydrine [21].

Ethyl acetate and aqueous fractions of the fruits of *Capparis spinosa* showed greater DPPH scavenging activities compared to the petroleum ether fractions. The antioxidant activity of the isolated antioxidant fractions ranged from 0.011 and 0.350 mM [22].

A new antioxidant cappariside (4-hydroxy-5-methylfuran-3-carboxylic acid), together with many organic acids were isolated from *C. spinosa* [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 *Capparis spinosa* [23].

The total phenolic contents (mg GA-Eq/g) in the alcoholic crude extract in the root and aerial part were 4.49±1.53 and 14.86±0.62 respectively. The total phenolic contents (mg GA-Eq/g) in the chloroform extract of the root and aerial part were 58.66±2.14 and 25.01±1.64 respectively. The total phenolic contents (mg GA-Eq/g) in the ethyl acetate extract in the root and aerial part were 45.96±5.86 and 87.48±2.04 respectively[24].

Leaves and flowers of *Capparis spinosa* were rich in either polyphenols or flavonoids while roots were the poor [25]. Quercetin was quantitatively determined in different plant parts of *C. spinosa* at the mature fruiting stage. The quercetin contents varied from 1.7 mg/g to 12.8 mg/g among different parts of caper. Flower, floral bud and fruit had higher content of quercetin respectively [26]. On the other hand, leaves had higher rutin contents among all other parts [27]. Besides bitter flavonoid glycosides, rutin, quercetin, quercetin 3-O-glucoside and quercetin 3-O-glucoside-7-O-rhamnoside, quercetin 3-O-[6'''-α-L-rhamnosyl-6''-β-D-glucosyl]-β-D-glucoside, and kaempferol glycosides, *C. spinosa* also contain lipids, glucocapparin (methyl glucosinolate), methyl isothiocynate, isopropyl isothiocyanate, *sec*-butyl isothiocyanate, benzyl-isothiocyanate, β-sitosterylglucoside-6'-octadecanoate, 3-methyl-2-butanyl-β-glucoside, stachydrine (a pyridine alkaloid), and cadabicine (a 24-membered polyamine lactam alkaloid). Furthermore, homologous polypreols namely;

cappaprenol-12, cappaprenol-13, and cappaprenol-14 with 12, 13, and 14 isoprene units were also isolated from the alcoholic extract of *C. spinosa* [28-30].

New (6S)-hydroxy-3-oxo-α-ionolglucosides together with corchoinoside C (6S, 9S)-roseoside, and prenylglucosides, cappariloside 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* . *spinosa* [23].

Capparis spinosa fruits also contained P-hydroxybenzoicacid, 5-(hydroxylmethyl) furfural bis(5-for- mylfurfuryl) ether, daucosterol, α-D-fructofuranosidesmethyl, uracil, and stachydrine [31]. However, Yu *et al.,* isolated eight compounds from the fruit of *Capparis spinosa*by chromatographic methods and their structures were established by spectroscopic methods as β-sitosterol, vanillic acid , p-hydroxybenzoic acid , protocatechuric acid, daucosterol, uracil, butanedioic acid and uridine [32].

Capparis spinosa fruits contained many trace elements included (PPM), Al: 0.48 ± 0.05%, P: 1.15 ± 0.01%, S: 4.00 ± 0.06% , K: 4.54 ± 0.03%, Ca: 1.18 ± 0.01%, Cl: 94.86 ± 25.51, Ti: 55.24 ± 2.30, Mn: 70.04 ± 1.00, Fe: 520.72 ± 4.05, Ni: 24.10 ± 0.05, Cu: 88.27 ± 0.45, Zn: 250.75 ± 0.80, Br: 11.92 ± 0.07, Rb: 79.03 ± 0.19, Sr: 40.20 ± 0.69, Y: 2.48 ± 0.38, Hf: 27.32 ± 0.87 and Pb: 5.34 ± 0.13 [33]. However, on other study, the trace elements isolated from *Capparis spinosa* seeds were included, Al: 361.5±1.7, Ca: 738.4±7.3,Cu: 0.7±0.1, Fe: 63.4±2.3, K: 2421.3±19.4, Mg: 4812.1±24.2, Na: 74.3±1.9, P: 4217.8±23.1 and Zn: 32.4±2.3 mg/kg [12].

The nutritional values of caper berries per 100 g included carbohydrates 5g, fats 0.9g, dietary fibers 3g, sugar 0.4g, protein 2g vitamin C 4 mg. and energy 20 Kcal [34].

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 [35].

The fatty acid composition of *Capparis spinosa* seeds oils included, palmitic: 10.23%, stearic: 2.61%,oleic: 38.45%, linoleic 23.75% and linolenic 1.17%[12]. The*Capparis spinosa* sterols were isolated from seven Tunisian stands. Constituents were differ according to the area. However, 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), stigmasterol 9.97% (220.87 mg/ kg) to 13.92% (315.9 mg/ kg), β-sitosterol 50.80% (1180.29 mg/ kg mg/ kg) to 62.35% (1381.3 mg/ kg) , Δ 5 avenasterol 5.37 % (116.53 mg/ kg) to 8.11% (179.67 mg/ kg) , Δ5,24stigmastadienol 0.33% (6.82 mg/ kg) to 0.89% (20.68 mg/ kg), Δ 7 Stigmastenol 0.07% (1.55 mg/ kg) to 0.32% (6.94 mg/ kg) and Δ 7 Avenasterol 0.16 %(3.47 mg/ kg) to 0.74 % (16.79 mg/ kg) [36].

PHARMACOLOGICAL EFFECTS

Antimicrobial effects

The antibacterial activity of petroleum ether, water, butanol, methanol and hexane crude extracts obtained from the aerial parts of *C. spinosa* was 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* [35].

Crude extract fractions and essential oils obtained from *Capparis 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* [15].

The petroleum ether, methanol, hexane, butanol and aqueous crude extracts of the whole aerial parts of *Capparis spinosa* exhibited variable degrees of antimicrobial activity. Extracts had low to moderate actvity against four bacterial species (*E. coli, S. typhirnurium, B. cereus,* and *Staph . aureus*) [37].

Ethanolic and petrolium ether extracts were used to study the antimicrobial activity of *Capparis spinosa* against Gram positive and Gram negative organisms by disc diffusion method. Both extracts shown significant antimicrobial activity against Gram positive organisms, *Bacillus cerus* and *Staphylococus auerus*, and Gram negative organisms, *Pseudomonas aeruginosa* and *E.coli* compared with standard antibiotics [2].

The antifungal activities of ethanolic extract of (*Capparis spinosa L.*) was investigated *in vitro* against *Alternaria alternata, Fusarium oxysporum, Phoma destructiva, Rhizoctonia solani,* and *Sclerotium rolfsii*at concentrations of 0, 3, 6, and 9% (v/v). It produced concentration dependent fungal growth inhibition [38].

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 hemogglutinating, 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 trans-criptase and proliferation of both hepatoma HepG2 and breast cancer MCF-7 cells [39].

In studying the antiviral and immunomodulatory properties of a methanolic extract of *C. spinosa* buds

(CAP), it was found that CAP treatment interferes with HSV-2 replication in human peripheral blood mononuclear cells (PBMCs), inhibiting the extracellular virus release up-regulating their production of IL-12, IFN-γ and TNF-α. Accordingly, CAP contribute in improving immune surveillance of PBMCs toward virus infection by up-regulating expression of peculiar pro-inflammatory cytokines, the authors postulated that it can be successfully employed for treatment of HSV-2 infections in immune-compromised hosts [40].

Both the alcoholic and aqueous extracts of *C. spinosa* displayed significant antihelminthic properties at high concentrations. Both extracts showed antihelminthic 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 *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 mean time, albendazole (20 mg/ml) caused paralysis of the earthworm in 8.6 minutes and death in 32.23 minutes [13].

Cytotoxic effects

Onion bulbs were treated with three different concentrations (10, 20 and 30g/L) of *Capparis spinosa* flower buds aqueous extract for 24 h without ethyl methane sulfonate (EMS) treatment. Growth retardation, significant decrease in mitotic index and chromosome aberrations were observed in root-tip cells treated with aqueous extract before and after the (EMS) treatment when compared with the controls in all treatments. These effects were concentration-dependent and statistically significant ($p<0.05$). The results suggest that, *Capparis spinosa* buds aqueous extract is non-genotoxic. However, the study reveals that *Capparis spinosa* aqueous extract has antimutagenic potential against EMS induced chromosomal aberrations in *A. cepa*root meristem cells and the antimutagenic potential of *Capparis spinosa* flower buds extract is effective at 30 g/L concentration [41].

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 [39].The effect of the crude aqueous *Capparis spaniosa* leaf extract in a concentration of used (125، 250،500 and1000 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 [42].

Capparis spinosa seeds contain a 38 kDa protein similar to imidazoleglycerol phosphate synthase 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 mM, respectively [43]. 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. *Capparis 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 [39, 44-45].

Chloroform extraction/fractions of *Capparis spinosa* L. also imposed inhibitory effects on SGC-7901 cells, while polar alkaloids showed mitochondrial apoptotic pathway and affected MPTP hole opening, membrane potential losing, cytochrome C releasing and showed IC_{50} value 33.437µg/·ml[46].

The cytotoxic effects of aqueous, methanolic crude extracts and secondary metabolites extracts (polyphenolic, rutin, and alkaloids) of mature fruit of *C. spinosa* was studied on human larynx carcinoma (Hep-2) and human cervix adenocarcinoma (HeLa) tumor cell lines *in vitro*. The study also included the investigation of the effect of polyphenol mature fruit extracts on mitotic index (MI) of HeLa tumor cell line. The effect of (aqueous and methanol) crude extracts and secondary metabolites extracts (polyphenol, rutin, and alkaloids) of mature fruits of *C. spinosa* on Hep-2 and HeLa tumor cell lines have been showed highly significant difference ($P\leq 0.0001$) or ($P \leq 0.01$) among all types of extracts, and among all concentrations for each extract in two periods 24 and 48 hrs of the treatment. However, the study revealed that the effective extracts against the proliferation of tested cell line were polyphenol extracts with concentration of 10000 µg/ml in Hep-2 cells after 24 and 48 hrs, and with concentrations of 10000 and 5000 µg/ml in HeLa cell line after 48 hrs. The cytotoxic concentration 50% (CC50%) of polyphenolic extract was 6400 and 6800 µg/ml on Hep-2 tumor cell line after 24 and 48 hrs of treatment, respectively. The CC50% against HeLa cells was 7100µg/ml after 48 hrs. Other extracts, aqueous, methanolic crude extracts and secondary metabolites extracts (rutin and alkaloids) of mature fruit of *C. spinosa* caused less inhibition activity on the growth of Hep-2 and HeLa tumor cell lines. The CC50% for all these extracts were more than 10000 µg/ml [47].

Antidiabetic effects

The antidiabetichypolipidemic effect of *Capparis spinosa* fruit extract was studied in diabetic rats (200mg/kg and 400mg/kg bw) for 28 days, these doses caused non significantly decreases in the glucose level at 60 and 120 min. However, *Capparis spinosa* extract exerted lipid lowering effects with the same extract [48].The effects of *Capparis spinosa* fruit on

histomorphological changes in pancreas in streptozotocin induced diabetes in male rats were studied . 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 *Caparis spinosa* compared to the diabetic control group [34,49].

Anti-inflammatory effects

The anti-inflammatory effects of the flavonoids from caper fruits were evaluated by secreted placental alkaline phosphatase (SEAP) 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-κB inhibitor [19].

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 [8].

The extracts of *C. spinosa* 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 [29].

The anti- arthritic active fractions of *Capparis spinosa* fruits was evaluated by adjuvant arthritic rat model. The fraction eluted by ethanol-water(50:50v/v) had the most significant anti- arthritic activity. The chemical constituents of this fraction showed that it contained seven known compounds: P-hydroxybenzoicacid, 5-(hydroxymethyl)furfura,lbis(5-for- mylfurfuryl) ether, daucosterol, α-D-fructofuranosidesmethyl, uracil, and stachydrine. Ethanol and ethanol-water extracts of *Capparis spinosa* fruits showed anti-arthritic effects due to the presence of an important chemical constituents such as P-hydroxy benzoic acid, 5-(hydroxymethyl) furfural, bis (5-formylfurfuryl) ether, daucosterol, α-D-fructofuranosides methyl, uracil and stachydrine [21,50].

Antioxidant effects

Capparis spinosa aerial part and root extracts were extracted with solvents of varying polarity. Ethyl acetate extract of the aerial part contains the highest concentration of phenolic compounds and flavonoids followed by the chloroform extract of roots. In DPPH test, the radical scavenging activity for the root and aerial part extracts decreased in the following order chloroform extract > ethyl acetate extract > crude extract and ethyl acetate extract > crude extract > chloroform extract. In general the aerial part extracts had an antioxidant activity greater than that of root part as estimated by ß-carotene-linoleate model system and ferric reducing ability [24].

Total phenolic compounds (GAE.100/gDW) were 37.01±0.03, ferric reducing antioxidant power (μmol Trolox.100/g DW) was 145.07 ± 0.04 and DPPH radical scavenging activity (SC50: mg/.ml) was 0.32 ± 0.26 [33].

The antioxidant activity of different extracts of*Capparis spinosa* 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 and 57.75±2.3 respectively [51].

Antioxidant activity (%) of*Capparis spinosa L*eaves collected from nine different sites from three valleys in trans-Himalayan region of Ladakh (India) were measured using DPPH, ABTS and FRAP assay. Maximum DPPH and ABTS radical scavenging activity was observed in the leaves samples collected from Skuru and least from Tirchey site. FRAP assay revealed that plant from Skuru site possessed maximum antioxidant content as compared to the samples collected from any other location. IC_{50} of ABTS were quite reasonably correlated with FRAP assay (R 2=0.517) while, DPPH IC_{50} was poorly correlated with both ABTS (R2=0.100) and FRAP assay (R2=0.223). The highest and lowest phenolic and flavonoid contents were recorded in Skuru and Tirchey sites respectively. Total phenolics (27.62-21.42 mg GAE/g DW) and flavonoid content (6.96-2.69 mg quercetin equivalent/g DW) were found reasonably correlated with IC_{50} of ABTS (R2=0.741 and 0.703, respectively) and FRAP (R2=0.605 and 0.649, respectively) but poorly correlated with DPPH IC_{50} (R2=0.303 and 0.408, respectively) [52].

Cardiovascular effects

The vaso relaxant effect of *Capparis spinosa* aqueous extract (CSAE) at a dose of 10 mg/ ml was studied on the isolated aortic rings of normal rats. Adding of CSAE during the plateau phase of contraction, induced by noradrenaline and KCl, produced a rapid relaxation. Incubation of aortic ring with CSAE during 30 min shifted the noradrenaline induced dose response curve ($p<0.001$), the maximum response ($p<0.001$) was attenuated which indicating that antagonistic effect of the α1- adrenoreceptors was non-competitive. However, endothelium remove significantly reduced the vaso relaxant effect of CSAE ($p<0.01$). Furthermore, nitric oxide inhibition reduced the vaso relaxant effect of CSAE. However, cyclo-oxygenase inhibition did not affect the vaso relaxant effect of CSAE ($p<0.05$). Inhibition of L-type voltage dependent Ca^{2+} channels did not reduce the observed CSAE vaso relaxant effect ($p<0.05$). Accordingly the authors suggested that vasorelaxant effect of (CSAE) may by mediated via an α1-adrenoreceptors antagonism and/or modulation of nitric oxide synthesis [53].

The *in vitro* vasomotor effect ts of aqueous extract of different parts of *Capparis spinosa*(roots, leaves, stems, flowers, fruits and kernels) were evaluated on the rings of thoracic aorta and windpipe of rat. The addition of *Capparis spinosa* extracts with different concentrations

during the stage of contraction led by the phenylephrin for the thoracic arteries showed a light vasodilatation. Another protocol, by incubation 30 min with extracts at different concentrations showed a significant vasodilator effect for fruits and kernels, and vasoconstrictor effect for leaves [54].

Leaves and flowers of *Capparis spinosa* were rich in either polyphenols or flavonoids, while roots are the poor ones. All extracts have anti lipid peroxidation and antioxidant effects with a dominance of flowers and leaves especially in the methanolic extracts (82.78 ± 2.64 and 80.94 ±1.57 respectively). Seeds exerted the acceptable effects followed by bud than roots [25].

Respiratory effects

The bronchorelaxant effects of *Capparis spinosa* was studied on the rings of windpipes of rat. The addition of *Capparis spinosa* extracts (0.1, 1 and 10 mg/ml) during the step of contraction by acetylcholine showed various effects on trachea. Incubation of the windpipe for 30 min with extracts proves to be so efficient. The dose of 10 mg/ml from fruits and seeds extracts showed a significant relaxant effect. The results showed a potent relaxant effect of the fruit aqueous extract of *Capparis spinosa*, on rat trachea, with a dose dependant manner. However, the leaf aqueous extract has a contractive effect. A muscarinic receptor blockade / stimulation was suggested for *Capparis spinosa* leaf extracts [55].

Other effects

Plant extracts extracted with solvents of varying polarity were effective either in inhibiting the activity of xanthine oxidase or Cyt C. The IC_{50} ranges from 0.0226 ± 0.00019 to 4.32 ± 0.15g/l [24].

When stachydrine was given to dogs, rabbits and rats, it quickened the coagulation of blood [56]. When *Capparis spinosa* applied topically it afforded significant *in vivo* protection against UVB light-induced skin erythema in healthy human volunteers [57]. Ethanolic root bark extract of *C. spinosa* (100, 200 and 400 mg/kg) afford significant dose-dependent protection against CCl_4 induced hepatocellular 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 [58].

Treatment of the paracetamol-induced liver damage in rats with aqueous extract of *Capparis spinosa* (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 [59].

Adverse effects and toxicity

There was no report regarding acute, subacute and chronic toxicity of *C. spinosa*, the popular use of the plant in traditional medicine and its prolong usage as a flavouring agent and by food industry documented its safety. Allergic contact dermatitis caused by *C. spinosa*was reported previously [60].

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.

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