Capparis species

Description:

- *Capparis* are flowering plants from the family Capparaceae, included in the Brassicaceae, comprising of approximately 251-294 species.
- The taxonomic status of the species is controversial and unsettled. Species within the genus Capparis are highly variable, and interspecific hybrids have been common throughout the evolutionary history of the genus. Zohary (1960) proposed new systematics, which distinguishs two biogeographical groups: the tropical, including *Capparis decidua, C. cartilaginea, C. mucronifolia Boiss.*, and the Mediterranean, including species that have lost their links with the tropical African stock (*C. spinosa, C. sicula Veill., C. leucophylla DC.*).
- *Capparis* plants have been introduced as a specialized culture in some European countries in the last four decades. The economical importance of caper led to a significant increase in both the area under cultivation and production levels during the late 1980s. The main production areas are in harsh environments found in Morocco, the southeastern Iberian Peninsula, Turkey, and the Italian islands of Pantelleria and Salina.
- The plant is best known for the edible flower buds (capers), often used as a seasoning, and the fruit (caper berries), which are usually consumed pickled. Other parts of Capparis plants are used in the manufacture of medicines and cosmetics.
- Out of the many Capparis species, a few are of specific interest for treatment of particular ailments, like tuberculosis, cancer, rheumatism or diabetes, which still requires extensive study.
- *C. spinosa* is one of the several ingredients in Bonnisan, Digyton, Geriforte Aqua, Geriforte, Liv.52 drops, Geriforte Vet, Liv.52 Vet (Companion Care), Liv.52® (Himalayan Co. India) and Liv.52 Vet, Liv.52 DS.

Figure: Photography of C. cartilaginea

Culinary use:

- The fruits of *Capparis* can be dried and pickled in vinegar, or preserved in salt to produce capers for consumption.
- Capers are a common ingredient in Mediterranean cuisine, especially Cypriot, Italian, and Maltese.
- The mature fruit of the caper shrub are prepared similarly and marketed as caper berries. The buds, when ready to pick, are a dark olive green and about the size of a fresh kernel of corn. They are picked, then pickled in salt, or a salt and vinegar solution, and drained. Intense flavor is developed as mustard oil (glucocapparin) is released from each caper bud.This enzymatic reaction leads to the formation of rutin, often seen as crystallized white spots on the surfaces of individual caper buds.
- Capers are a distinctive ingredient in Italian cuisine, especially in Sicilian and southern Italian cooking. They are commonly used in salads, pasta salads, meat dishes, and pasta sauces. Capers are known for being one of the ingredients of tartar sauce. They are often served with cold smoked salmon or cured salmon dishes (especially lox and cream cheese). Capers and caper berries are sometimes substituted for olives to garnish a martini.

History and traditional uses:

- The common caper – *C. spinosa* - was first described by Carolus Linnaeus in 1753 in "*Species Plantarum*".
- Dioscoride (1st century AD) provides instructions on the use of sprouts, roots, leaves and seeds in the treatment of strangury and inflammation.
- The caper was used in ancient Greece as a carminative. In Biblical times, the caper berry was apparently supposed to have aphrodisiac properties.
- Medicinal uses of Capparis are also mentioned in ancient books like Shushrut, Dhanwantri, Nighantu, Kshem Kutulhan and Madanpal.

- In Greek popular medicine, a herbal tea made of caper root and young shoots is considered beneficial against **rheumatism**.
- In tropical Africa leaves are used as a **laxative**. Leaf decoctions and infusions are applied to **eye infections** and root sap to **skin diseases and ulcers.**
- In Pakistan and India, *C. cartilaginea* is used in the treatment of **rheumatism, gout, paralysis** and **tuberculosis**, and as **diuretic, tonic, expectorant, anthelmintic** and **emmenagogue**.
- In Yemen, the leaves of *C. cartilaginea* are used to **treat itching, shortness of breath, for tumors, for wounds ands boils, childbirth, earache, headache, paralysis, snakebite and swelling.** The leaves are boiled for **external application on painful knees.**
- As decoction, it 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.**

Phytochemical analysis of *C. cartilaginea*:

- Phytochemical analysis of Capparis plants showed presence of carbohydrates, saponins, polyphenols, flavonoids, tannins, triterpenes, sterols, amino acids and proteins.
- ***C. cartilaginea*** contents in flavonoid and saponin were 5.1% and 1.8%, respectively.
- Flavonoids: **rutin** (quercetin 3-rutinoside) (~5.6%), **quercetin 7-rutinoside, quercetin 3-glucoside-7-rhamnoside,** kaempferol-3-rutinoside, kaempferol-3-glucoside, and kaempferol-3-rhamnorutinoside.

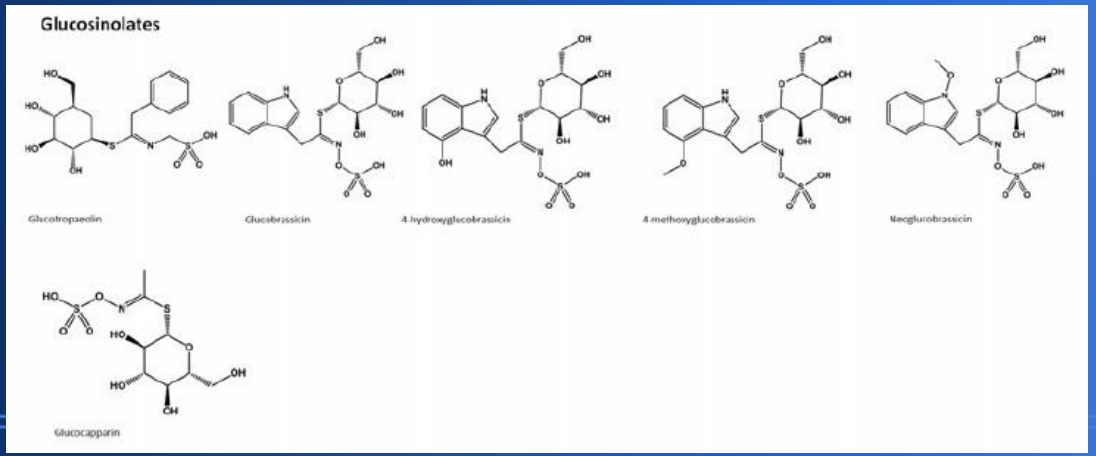
  Capers contains more quercetin per weight than any other plant with 16.72 µg/mg extract for *C. cartilaginea.*
- Isothiocynates: butyl isothiocyanate (65.03%), 6-methyl-sulphonylhexyl isothiocyanate (29.86%), 7-methyl-sulphonylheptyl isothiocyanate (0.066%) and 5-benzyl-sulphonyl-4-pentenyl isothiocyanate (0.914%).
- Glucosinolates: glucoiberin, glucocapparin, sinigrin, glucocleomin, glucobrassicin and glucocapangulin.

The hydrolysis products of **indol-3-ylmethyl glucosinolates, as well as lectin** isolated from Capparis may have anticarcinogenic effects.

Glucosinolates are known to possess goitrogenic (anti-thyroid) activity.

Rutin and **quercetin** may contribute to cancer prevention.

Selenium, present in capers at high concentrations in comparison with other vegetable products, has been associated with the prevention of some forms of cancer.



Phytochemical analysis of *C. spinosa*:

- Forty-two compounds were identified in *C. spinosa* including **quercetin, kaempferol** and **isorhamnetin derivatives** in addition to **myricetin, eriodictyol, cirsimaritin** and **gallocatechin derivatives.**
- Phenolic acids, such as **quinicacid, p-coumaroyl quinic acid** and **chlorogenic acid** were also identified in this specie.
- A **dimeric 62-kDa lectin** exhibiting a novel N-terminal amino acid sequence and with antiproliferation properties and antiviral properties against HIV-1 reverse transcriptase was purified from *C. spinosa* seeds.

Table 1: Major chemical constituents of *Capparis spinosa*

Plant part	Chemical constituents
Fruits	Flavonoids, indoles, and phenolic acids Sitosterylglucoside-6′-octadecanoate, 3-methyl-2-butenyl-glucoside P-hydroxybenzoic acid; 5-(hydroxymethyl)furfural; bis(5-formylfurfuryl)ether; daucosterol; α-d-fructofuranosides methyl; uracil, and stachydrine Capparisside(4-hydroxy-5-methylfuran-3-carboxylic acid) (6S)-hydroxy-3-oxo-α-ionolglucosides, corchoinoside C(6S, 9S)-roseoside, prenyl glucosides, capparilosideA, stachydrine, an adenosine nucleoside, hypoxanthine, β-sitosterol, vanillic acid, P-hydroxybenzoic acid, protocatechuic acid, daucosterol, uracil, butanedioic acid, and uridine P-hydroxybenzoic acid, 5-(hydroxymethyl)furfural bis(5-for- mylfurfuryl)ether, daucosterol, α-D-fructofuranosides methyl, uracil, and stachydrine β-sitosterol, vanillic acid, P-hydroxybenzoic acid, protocatechuic acid, daucosterol, uracil, butanedioic acid, and uridine Al, P, S, K, Ca, Cl, Ti, Mn, Fe, Ni, Cu, Zn, Br, Rb, Sr, Y, and Pb Carbohydrates, fats, dietary fibers, sugar, protein, and Vitamin C Isopropyl isothiocyanate, methyl isothiocyanate, butyl isothiocyanate, 3-P-menthene, 2-butenyl isothiocyanate and 3-methylthio-1-hexanol, palmitic, stearic, oleic, linoleic and linolenic acid
Seeds	Lectin HIV-1 reverse transcriptase inhibition potential Al, Ca, Cu, Fe, K, Mg, Na, P, and Zn Cholesterol, brassicasterol, campesterol, campestanol, stigmasterol, B-sitosterol, Δ5 avenasterol, Δ5,24 stigmastadienol, Δ7 stigmastenol, and Δ7 avenasterol

Source: [2] MANIKANDASS, VADIVEL V, BRINDHA P: REVIEW ON ETHNOBOTANICAL STUDIES OF NUTRACEUTICAL PLANT: *CAPPARIS SPINOSA* L. (CAPER). *Asian J Pharm Clin Res,* Vol 9, Issue 3, 2016, 123-126 .

Anticancer activity of different *Capparis* species:

- Root bark extract from *C. spinosa* showed antitumor activity against Ehrlich Ascites carcinoma in albino mice [3][4]. Whole plant was demonstrated to exert activity against hepatoma HepG2 cell lines [3][4] and SGC-7901 gastric cancer cell lines [10][11]. Polyphenol mature fruit extracts were highly active on mitotic index (MI) of HeLa tumor cell line [3][4]. Lectin extracted from *C. spinosa* inhibited proliferation of hepatoma HepG2 and breast cancer MCF-7 cells [7][3][4]. In addition, a polysaccharide (CSPS) extracted from *„C. spionosa“* displayed *in vivo* antitumor activity in H22-bearing mice [8][9].

- One *in vitro* study against A549 human lung cancer cell lines found that beta-sitosterol triacontenate isolated from *C. decidua* showed a dose-dependent cytotoxic activity almost comparable to paclitaxel [5].

- The methanol extract of *C. sepiaria* bark (MECS) exhibited significant antitumor activity in Dalton’s ascites lymphoma (DAL)-bearing swiss albino mice [6].

- Recently, the compound **cappamensin A** (1) (2H-1, 4-benzoxazin-3 (4H)-one, 6-methoxy-2-methyl-4-carbaldehyde) isolated from the roots of *C. sikkimensis* sub sp. Formosana displayed significant *in vitro* antitumor activity in various human cell lines. Furtherware, data suggests that Capparis species roots might contain chemical compounds with anticancer properties, which require standardization [1].

- However, in one study evaluating 26 Yemeni medicinal plants against three human cancer cell lines (A-427, 5637 and MCF-7), *C. cartilaginea* displayed no relevant anticancer activity, whereas IC50 were >50 in all three experiments [12]. No other studies on the possible anticancer activity of *C. cartilaginea* were found. However, the taxonomic status of the species is controversial and unsettled, and despite that the two species belong to two distinct biogeographical groups, *C. spinosa* is sometimes used as a synonym for *C. cartilaginea*. The former has been shown to exert significant antitumor activity *in vitro* and *in vivo* [3][4][7][10][11].

- In addition, the authors of two studies demonstrated the *in vitro* anticancer activity of a Capparis specie named *„C. spionosa“* [8][9] which is not listed in current taxonomy and might identify with *C. spinosa*.

References: see next slide.

References:

References:

[1] Mishra SN, Tomar PC & Lakra N: Medicinal and food value of Capparis—a harsh terrain plant. *Indian Journal of Traditional Knowledge* Vol 6(1)-January 2007 -pp 230-238.
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[4] Al-Snafi AE: THE CHEMICAL CONSTITUENTS AND PHARMACOLOGICAL EFFECTS OF*CAPPARIS SPINOSA* -AN OVERVIEW. *Ind J of Pharm Sci & Res* Vol5|Issue 2| 2015 |93-100.
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[7] AM SK, HAN QF and Tzi Bun NG: Isolation and characterization of a lectin with potentially exploitable activities from caper (*Capparis spinosa*) seeds. *Biosci. Rep.* Volume 29 (5) / P. 293–299.
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[10] JI YB and YU L: *In vitro* analysis of the role of the mitochondrial apoptosis pathway in CSBE therapy against human gastric cancer. *EXPERIMENTAL AND THERAPEUTIC MEDICINE* 10: 2403-2409, 2015.
[11] JI YB and YU L: N-Butanol Extract of *Capparis spinosa* L. Induces Apoptosis Primarily Through a Mitochondrial Pathway Involving mPTP Open, Cytochrome C Release and Caspase Activation. *Asian Pac J Cancer Prev,* 15 (21), 9153-9157.
[12] Mothana R, Lindequist U, Gruenert R and Bednarski PJ: Studies of the *in vitro* anticancer, antimicrobial and antioxidant potentials of selected Yemeni medicinal plants from the island Soqotra. *BMC Complementary and Alternative Medicine* 2009, 9:7.

Other bioactivities from Capparis species:

- *C. spinosa* inhibited HIV-1 reverse transcriptase [3][4][7]. It exhibited antihelminthic activity [3] at high doses [4]. Its stem bark has been found to be effective against paralysis [1]. It exhibited potent antihyperglycemic activity [3][4]. Presence of two glucose containing compounds, **capparilosides A & B & 1H-indol-3 aceto-3 acetonitril glycosides** in mature fruit of *C. spinosa* suggest nutritional richness of the cappers and can be examined for food supplements for diabetic patients [1]. Extracts effectively prevented chemically induced pappillomagenesis in mouse skin [1]. The aqueous extracts reduced carrageen-induced oedema in rats [1][3][4]. Furthermore, this specie exhibited hepatoprotective activities [1][3][4]. *C. spinosa* aerial part extract is being used as constituent of multi herbal formulation used in the treatment of liver disorder. P**-methoxy benzoic acid** (33% w/w) isolated from *C. spinosa* was established to be hepatoprotective against carban-tetrachloride-, paracetamol-, thioacetamide- and galacotosamine induced toxicity in isolated rat hepatocyte [1]. The vasorelaxant effect of aqueous extracts and and bronchorelaxant effects of fruit aqueous extracts were established *in vivo* [4]. When applied topically *C. spinosa* afforded significant protection against UVB light-induced skin erythema in healthy human volunteers [3][4].

- Antibacterial activities from *C. decidua* [1]*, C. cartilaginea [3], C. spinosa* [3][1][4] and *C. tomentosa* [1] have been demonstrated by recent studies. *C. spinosa* [1][4] and *C. decidua* [1] also displayed antifungal activity.

- An alkaloid, **l-stachyhydrin** obtained from seeds, roots bark, flowers, fruits husk and dry fruits of *C. moonii* and *C. tomentosa* exhibited antituberculosis property *in vivo.* The role of this compound was also demonstrated in blood coagulation, thus shortening bleeding time and blood loss [1].

- Recent clinical tests have demonstrated the hypotensive and spasmolytic activities from ethanolic extracts from *C. cartilaginea* [3].

- The ethanol extract from *C. decidua* was demonstrated to reduce carrageen-induced oedema in rats [1].

- Bark and leaf of *C. grandis* were reported to cure swelling eruptions and *C. heyneana* leaves to reduce rheumatic joints pain [1].

- *C. separia* seed and *C. zeylanica* fruit have been considered as antidote to snakebite. Herbal adjuvant to antisnake venom (ASV) can reduce the dose and mitigate the dose demands [1].

References: see previous slide.

Activities of *C. spinosa* (table):

Table 2: Biological activities reported on *Capparis spinosa*

Parts studied	Biological activity
Alcoholic and aqueous extracts of *Capparis spinosa*	Anthelminthic activity
Aqueous extract of flower buds of *Capparis spinosa*	Cytotoxic activity
A novel dimeric 62 kDa lectin from *Capparis spinosa* seeds	
Aqueous extract of leaf of *Capparis spinosa*	
Capparis spinosa seeds	
Capparis spinosa root bark	
Chloroform fractions of *Capparis spinosa*	
Aqueous and methanolic crude extracts and secondary metabolites extracts (polyphenolic, rutin, and alkaloids) of mature fruit of *Capparis spinosa*	
Extract of *Capparis spinosa*	Anti-inflammatory activity
Flavonoids from *Capparis spinosa* fruits	
Aqueous extract of *Capparis spinosa* fruits	
Ethanol and water fractions of *Capparis spinosa* fruits	Antiarthritic activity
Ethyl acetate extract of aerial part and root of *Capparis spinosa*	Antioxidant activity
Methanol and ethyl acetate extracts of *Capparis spinosa*	
Capparis spinosa leaves	
Petroleum ether, water, butanol, methanol and hexane crude extracts of the aerial parts of *Capparis spinosa*	Antibacterial activity
Crude extracts fractions and essential oils of *Capparis spinosa*	
Capparis spinosa extract	
Petroleum ether, methanol, hexane, butanol and aqueous extracts of the whole aerial parts of *Capparis spinosa*	
Ethanolic and petrolium ether extracts of *Capparis spinosa*	
Ethanolic extract of *Capparis spinosa*	Antifungal activity
Methanolic extract of buds of *Capparis spinosa*	Antiviral activity
Aqueous extract of *Capparis spinosa*	Cardiovascular activity
Aqueous extract of roots, leaves, stems, flowers, fruits, and kernels of *Capparis spinosa*	
Leaf and flowers of *Capparis spinosa*	
Aqueous extract of fruits, leaf of *Capparis spinosa*	Respiratory activity
Lyophilized methanolic extract of flowering buds of *Capparis spinosa*	Chondroprotective activity
Capparis spinosa fruit extract	Antidiabetic activity
Aqueous extract of *Capparis spinosa*	Hypolipidemic activity
Lyophilized methanolic extract of flowering bud of *Capparis spinosa*	Antiallergic and antihistaminic activity
Methanolic extract of *Capparis spinosa* buds	Immunomodulatory activity
Essential oil and aqueous infusion of leaf and flower buds of *Capparis spinosa*	Anticarcinogenic activity
P-methoxybenzoic acid from the methanolic soluble fraction of the aqueous extract of *Capprais spinosa*	Antihepatotoxic activity
Ethanolic extract of root bark of *Capparis spinosa*	
Aqueous extract of *Capparis spinosa*	

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

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

Sources: [2] MANIKANDASS, VADIVEL V, BRINDHA P: REVIEW ON ETHNOBOTANICAL STUDIES OF NUTRACEUTICAL PLANT: *CAPPARIS SPINOSA* L. (CAPER). *Asian J Pharm Clin Res,* Vol 9, Issue 3, 2016, 123-126 . [3] Rahnavard R, Razavi N: A review on the medical effects of *Capparis spinosa* L. *Advanced Herbal Medicine*, 2016; 2(1): 44-53.

Cytotoxic activity of n-butanol extract of *C. spinosa* against SGC-7901 cell lines:

- Cytotoxic activity of the n-butanol extract of *C. spinosa* L. (CSBE) was demonstrated *in vitro* against SGC-7901 gastric cancer cells [10][11].
- IC50 of CSBE on SGC-7901 cells was **31.542 µg/ml** [10].
- Inhibition of proliferation and induction of apoptosis were associated with **mitochondrial membrane potential disruption, mPTP Open, cytochrome *c* release into the cytoplasm, and caspase-9 and caspase-3 activation** [10][11].
- CSBE may have induced SGC-7901 cell apoptosis by **upregulating the expression of B-cell lymphoma-2 (BCL-2)-associated X protein, and downregulating the expression of BCL-2** [10].
- Results thereas indicated that n-butanol extracts from *C. spinosa* exerted anticancer activity by **inducing apoptosis via the mitochondrial pathway.**

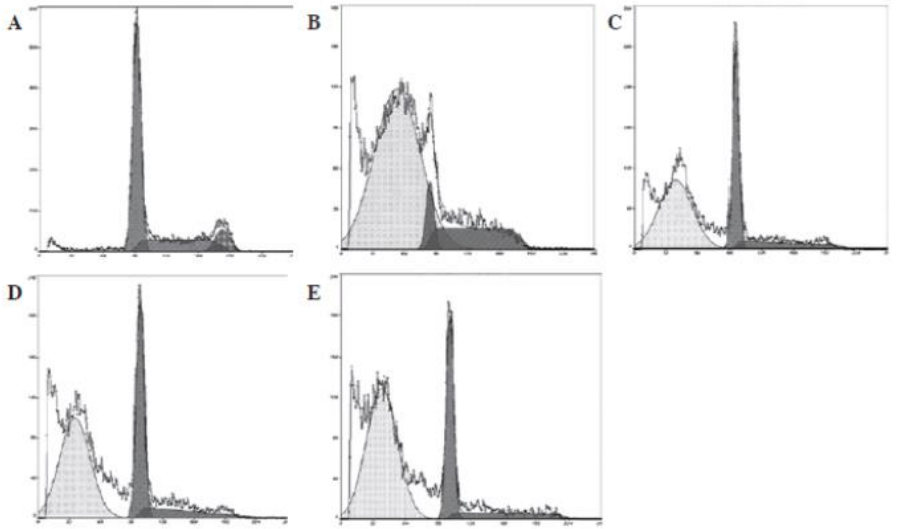

Figure 2. Proportion of SGC-7901 apoptotic cells following inoculation with the n-butanol extract of *Capparis spinosa* L. (CSBE). DNA content data from flow cytometry of SGC-7901 cells cultured with or without CSBE for 48 h, as assayed by propidium iodide incorporation. (A) Control; (B) hydroxycamptothecin treatment (0.2 µg/ml); (C) CSBE treatment (15 µg/ml); (D) CSBE treatment (30 µg/ml); and (E) CSBE treatment (60 µg/ml), at 24 h. CSBE induced DNA synthesis by 48 h, as is evidenced by the formation of an apoptotic peak (sub-G_0/G_1 fraction), corresponding to labeled cells with a decreased DNA content.

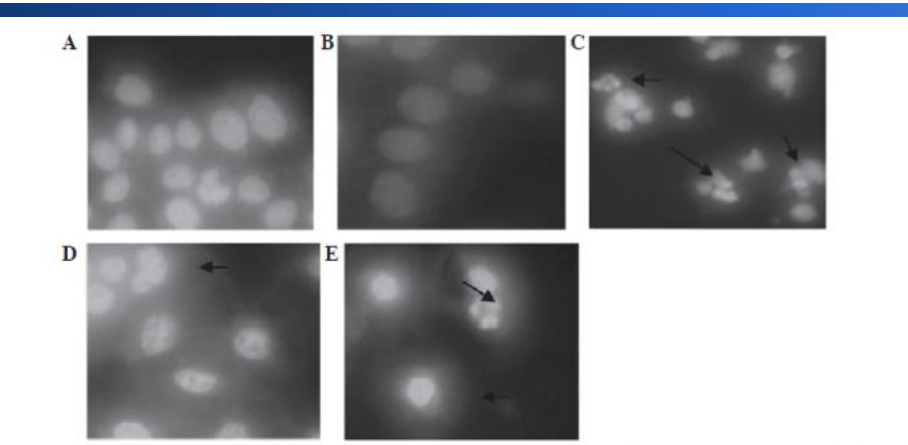

Figure 1. Effects of the n-butanol extract of *Capparis spinosa* L. (CSBE) on the morphology of SGC-7901 human gastric cancer cells. In all groups, cells were stained with Hoechst 33258 and observed by fluorescence microscopy (magnification, x400): (A) Control; (B) hydroxycamptothecin treatment (0.2 µg/ml) at 24 h; (C) CSBE treatment (15 µg/ml) at 24 h; (D) CSBE treatment (30 µg/ml) at 24 h; and (E) CSBE treatment (60 µg/ml) at 24 h. Examples of apoptotic cells, exhibiting condensed, crescentic or "popcorn" nuclear morphology, are highlighted with black arrows.

References:

[10] JI YB and YU L: *In vitro* analysis of the role of the mitochondrial apoptosis pathway in CSBE therapy against human gastric cancer. *EXPERIMENTAL AND THERAPEUTIC MEDICINE* 10: 2403-2409, 2015.

[11] JI YB and YU L: N-Butanol Extract of *Capparis spinosa* L. Induces Apoptosis Primarily Through a Mitochondrial Pathway Involving mPTP Open, Cytochrome C Release and Caspase Activation. *Asian Pac J Cancer Prev,* 15 (21), 9153-9157.

Cytotoxic activity of n-butanol extract of *C. spinosa* against SGC-7901 cell lines:

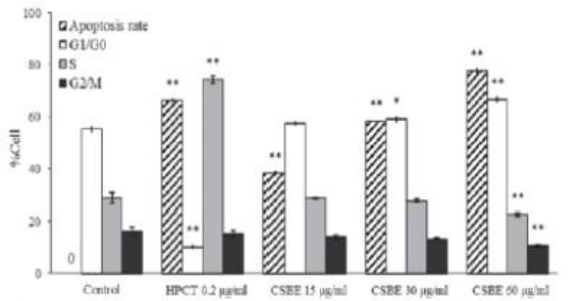

Figure 3. Effect of the n-butanol extract of *Capparis spinosa* L. (CSBE) on the cell cycle distribution of SGC-7901 cells. Cell percentage of apoptosis as determined by flow cytometry. Cells were treated with hydroxycamptothecin (HCPT; 0.2 μg/ml) or 15, 30 or 60 μg/ml CSBE for 48 h. Subsequently, the cells were stained with propidium iodide and analyzed using flow cytometry. *P<0.05, as compared with the control; **P<0.01, compared with the control.

Table 1. Inhibition rate of CSBE on SGC-7901 by SRB Assay

Group	Concentratin (μg·mL⁻¹)	Rate of inhibition %($\bar{x}$±s)	GI_{50} (μg·mL⁻¹)	LC_{50} (μg·mL⁻¹)	TGI (μg·mL⁻¹)
Control	-	0	-	-	-
CSBE	1	8.323±4.998**			
	5	18.047±5.336**			
	25	40.513±5.122**	31.785	40.146	45.864
	50	61.183±2.744**			
	75	82.012±2.824**			
	100	96.588±2.152**			
HCPT	0.01	12.088±0.017**			
	0.1	50.549±0.019**	0.097	5.57	16.11
	1	64.286±0.006**			
	10	70.147±0.006**			

*p<0.05; **p<0.01 *vs* control group

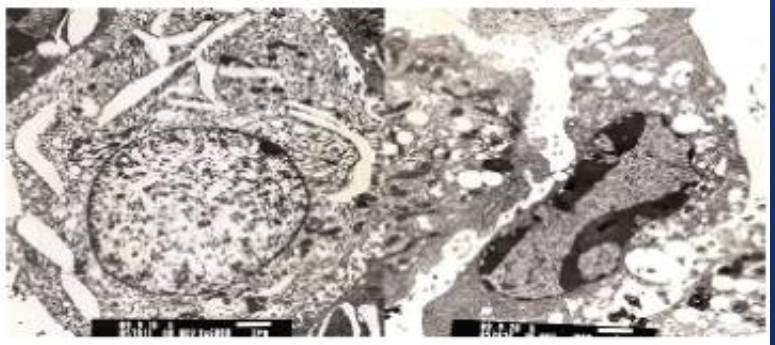

Figure 1. Morphological Appearance of SGC-7901 Cells by Electron Microscope

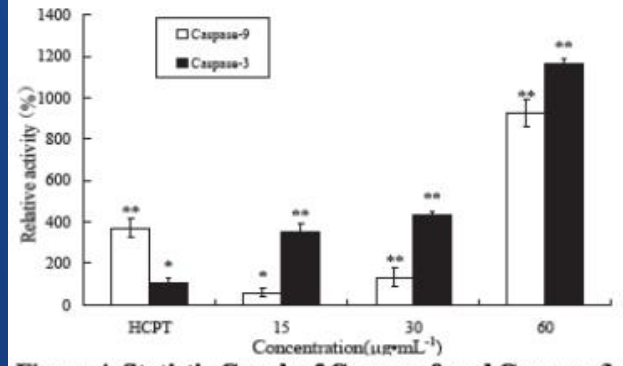

Figure 4. Statistic Graph of Caspase-9 and Caspase-3 activities. *p<0.05; **p<0.01 *vs* Control Group

Reference:

[11] JI YB and YU L: N-Butanol Extract of *Capparis spinosa* L. Induces Apoptosis Primarily Through a Mitochondrial Pathway Involving mPTP Open, Cytochrome C Release and Caspase Activation. *Asian Pac J Cancer Prev,* 15 (21), 9153-9157.

In vitro anticancer activity of a lectin isolated from *C. spinosa:*

- A dimeric lectin (62 kDa) was isolated from *C. spinosa* that exhibited a novel N-terminal sequence. It was evaluated for its anticancer activity *in vitro* [7].
- The lectin inhibited proliferation of HepG2 and MCF-7 tumour cells with an IC50 of approx. 2 µM.
- Apoptosis was observed in treated HepG2 and MCF-7 tumour cells (see figure). The level of apoptosis was increased by 34% when the cells were incubated with 30 µM lectin for 24 h.

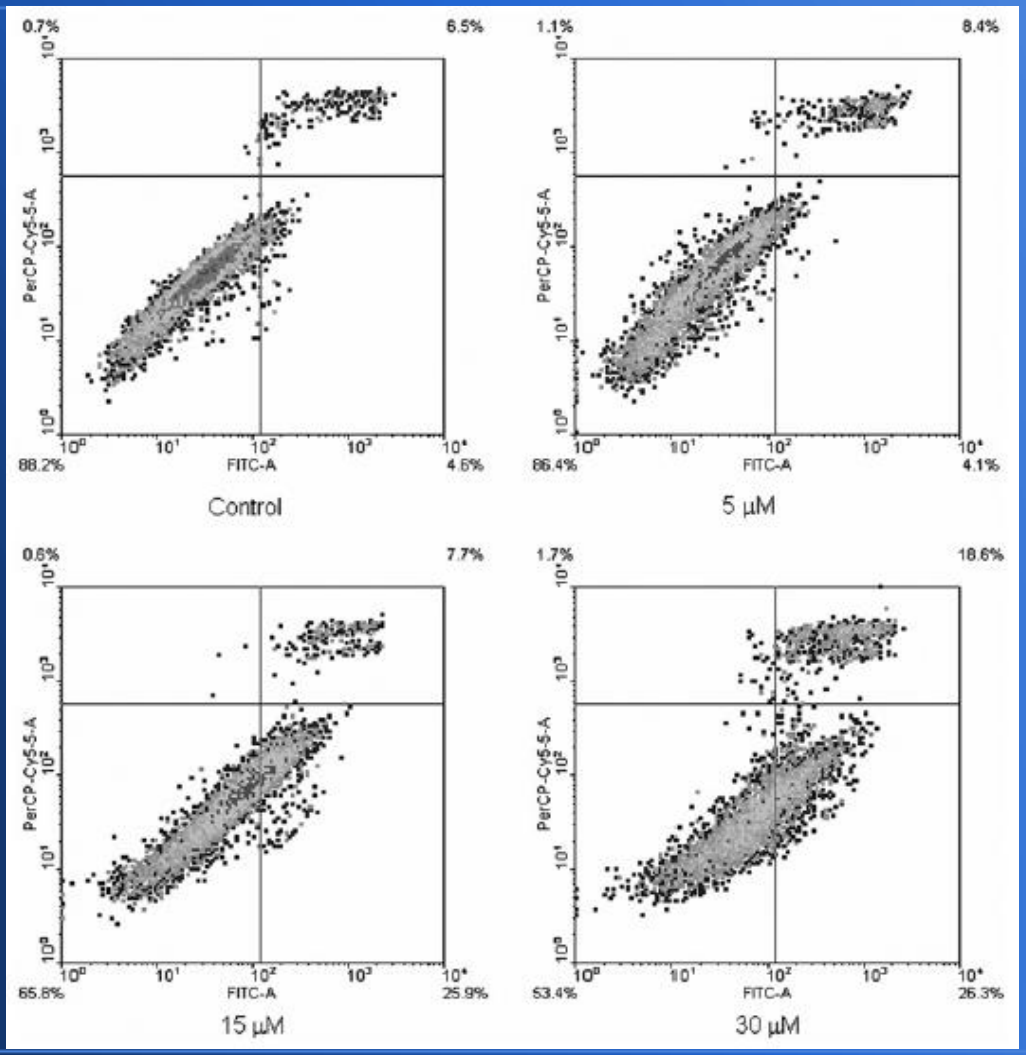

Figure: Induction of apoptosis of MCF-7 cells by *C. spinosa* lectin
MCF-7 cells were incubated with lectin on a 6-well culture plate for 24 h. After washing the lectin-treated/untreated MCF-7 cells with PBS, they were stained with annexin V/propidium iodide and then analysed by flow cytometry. The lower left quadrant shows healthy cells. The upper and lower right quadrants of each plot show annexin V/propidium iodide double-positive cells (i.e. cells undergoing late apoptosis) and annexin V single-positive cells (i.e. Cells undergoing early apoptosis) respectively. Results are expressed as the means for triplicate experiments. The level of apoptosis was increased by 34% (i.e. 18.6+26.3−6.5−4.6%) when the cells were incubated with 30 µM lectin for 24 h.

Reference:
[7] AM SK, HAN QF and Tzi Bun NG: Isolation and characterization of a lectin with potentially exploitable activities from caper (*Capparis spinosa*) seeds. *Biosci. Rep.* Volume 29 (5) / P. 293–299.

In vitro cytotoxicity of beta-sitosterol triacontenate isolated from *C. decidua:*

- One *in vitro* study against A549 human lung cancer cell lines found that beta-sitosterol triacontenate isolated from *C. decidua* showed a dose-dependent cytotoxic activity almost comparable to paclitaxel at concentrations of 5 µM and 10 µM [5].
- ICD50 value was 1 µM.
- However, its molecular mechanism of action remains elusive.

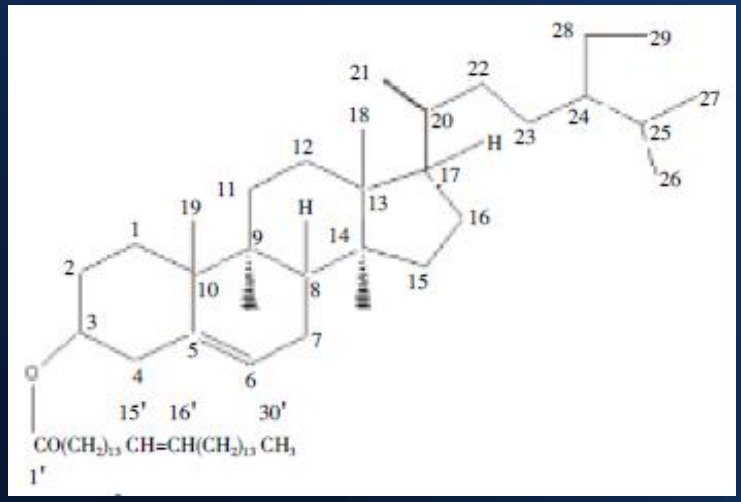

Figure: beta-sitosterol triacontenate

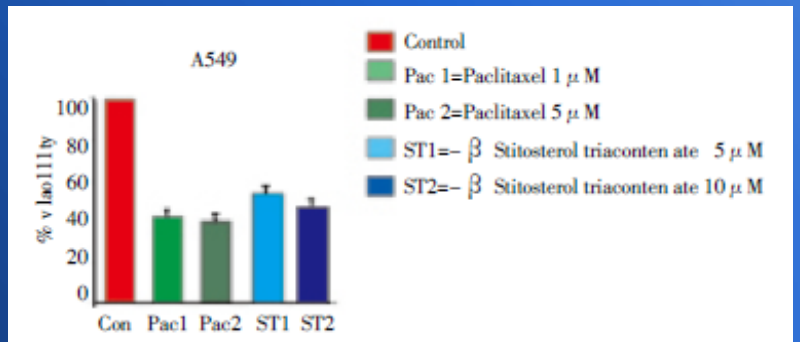

Figure 7. *In–vitro* cytotoxic activity was evaluated by MTT assay. Cells were treated with 5 µ M and 10 µ M of β –Sitosterol triacontenate and positive control (Paclitaxel–1 µ M and 5 µ M) for 48 h, thereafter cultures were evaluated as described in text. Percentage cell viability of isolated compound on lung cancer cell lines was calculated. Con: Control; Pac: Paclitaxel; ST: β – Sitosterol triacontenate.

Reference:

[5] Rathee P, Rathee D, Rathee D, Rathee S: In-vitro cytotoxic activity of 球-Sitosterol triacontenate isolated from Capparis decidua (Forsk.) Edgew. *Asian Pacific Journal of Tropical Medicine* (2012)225-230.

Antitumor activity of *C. sepiaria in* DAL-bearing mice:

- The methanol extract of *C. sepiaria* bark (MECS) exhibited significant antitumor activity in Dalton's ascites lymphoma (DAL)-bearing swiss albino mice [6].
- MECS caused significant decrease in tumor volume after 14 days of treatment, which attained 4.7 ml at 400mg/dose, compared to 18 ml in the control group and 4.8 ml for paclitaxel; it decreased tumor packed cell volume and viable cell count; it prolonged the life span of DAL-tumor bearing mice to 22.5 days at 400mg/dose, compared to 13.5 days in the control group and 25.6 days in the paclitaxel-treated group.
- Hematological profile converted to more or less normal levels in extract-treated mice.

Table 5: Effect of *Capparis sepiaria* on solid tumor growth

	Solid tumor volume in ml			
Groups	15th day	20th day	25th day	30th day
DAL control	0.086±0.01	2.0±0.3	3.9±0.7	6.4±1.19
MEDP 400	0.20±.007	0.15.±0.16	0.08.±0.09**	0.03±0.22***

Data are expressed as the mean of results in 4 mice ± SEM. $^{**}P<0.01$, $^{***}P<0.001$, MEDP 400 Vs DAL Group

Table 2: Effect of methanol extract of *Capparis sepiaria* on hematological parameters

Parameters	Control	DAL	DAL + MEDP 200 mg/kg	DAL+ MEDP 400 mg/kg	DAL +5-FU 20 mg/kg
Hemoglobin (%)	14.52±0.46	6.7±1.22[a]	7.98±0.49[e]	10.54±0.69[e]	9.86±0.99[e]
RBC (x10^{6}cell/mm^3)	13.14±0.56	7.5±0.5[a]	8.4±0.5[e]	9.52±0.39[e]	11.3±0.60[e]
PCV (%)	29.74±4.13	43.26±3.61[c]	35.5±3.45[d]	24.98±1.32[d]	22.62±1.57[d]
WBC (x10^{4}cells/mm^3)	0.625±0.13	5.74±0.7[c]	2.48±0.23[d]	1.7±0.19[d]	1.51±0.17[d]
Neutrophils (%)	37.6±1.74	53.8±7.01[b]	52.1±1.88	40.6±0.7[e]	38.4±1.69[e]
Lymphocytes (%)	60.4±2.33	46±5.07[a]	39.6±1.28	46.2±1.06	45.2±2.43
Eosinophils (%)	3.3±1.03	1.6±0.4	2.5±0.67	3.4±5..0	4.4±1.03
Monocytes (%)	1.8±0.37	0.2±0.2	0.2±0.2	0.2±0.2	0.8±0.37

Data are expressed as the mean ± SEM, n=5. $^aP<0.05$, $^bP<0.01$, $^cP<0.001$, Control Vs DAL. $^dP<0.05$, $^eP<0.01$ and $^fP<0.001$, DAL Vs extract treated groups

Table 1: Effect of methanol extract of *Capparis sepiaria* on tumor growth parameters:

Parameters	DAL	DAL + MEDP 200 mg/kg	DAL+ MEDP 400 mg/kg	DAL + 5-FU 20 mg/kg
Mean survival time (days)	13.5±0.96	19.2±0.58	22.5±2.24*	25.6±2.06**
Increased life span (%)	---	31	46*	61*
Tumor volume (ml)	18±2.4	11.4±2.08**	4.7±0.91***	4.8±1.29***
Tumor packed cell volume (ml)	51.12±2.9	33.61±2.9**	36.7±1.7**	31.6±1.7**
Viable cell count (x10^{7}cells/ml)	18.63±0.96	17.91±0.83*	12.48±0.7**	12.65±0.68**
Nonviable cell count (x10^{7}cells/ml)	0.17±0.017	0.25±0.02*	0.52±0.04**	0.71±0.06**

Data are expressed as the mean ± SEM. n= 5. $^*P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$, extract-treated groups compared with the DAL Group

Reference:

[6] Sreenivas SA, Gopal VY, Ravindranath A, Kalpana G and Rajkapoor B: Antitumor and Antioxidant Activity of *Capparis sepiaria* Against Dalton's Ascites Lymphoma in Rodents. Academic Journal of Cancer Research 5 (2): 46-52, 2012.

In vivo cytotoxic activity of a polysaccharide extracted from *C. spionosa:*

- A polysaccharide (CSPS) extracted from C. spionosa was demonstrated to possess antitumor activity *in vivo*, whereas it increased the survival life-spans of H22-bearing mice in a dose-dependent manner. The survival time in control group mice was significantly extremely lower than that of the mid-dose and high-dose CSPS groups ($p < 0.01$, see table) [8].

- Synthesis of seleno-C. spionosa L. polysaccharide (Se-CSPS) could be optimized by response surface methodology and Se-CSPS was shown to inhibit the proliferation of human gastric cancer SGC-7901 cells more efficiently than CSPS in a dose- and time-dependent manner.

- The maximum inhibition rate of Se-CSPS at 24, 48, 72 h attained to **32.12%, 47.22% and 69.49%, respectively; IC50 = 111.90 μg/mL.**

- Procedure: Different ratios of Na2SeO3 and CSPS were dissolved by HNO3 (100 mL, 0.05%) in erlenmeyer flasks. $HSeO_3^-$ was thus introduced into CSPS and substituted 6'-OH, p-orbital of oxygen and Se=O bond formed the p–π conjugated system in which the electron cloud of C–O transferred to Se=O. This caused that C–O bond energy in Se-CSPS was lower than that of CSPS and C–O bond in Se-CSPS could be broken more easily. It implied that absorption and utilization of Se-CSPS were better than that of CSPS in vivo and in vitro at the same dose.

Figure 4. Selenylation mechanism of seleno-polysaccharide.

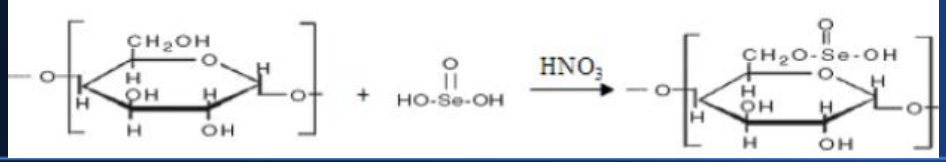

Table 5. Effects of CSPS on survival time of tumor H_{22} bearing mice.

Groups	Number	Dose (mg/kg)	Survival time (d)	Prolonging rate (%)
Control	12	Normal saline	10.24 ± 2.97	—
Low-CSPS	12	50	12.66 ± 2.53 *	23.63
Mid-CSPS	12	100	15.48 ± 3.15 **	51.17
High-CSPS	12	200	16.72 ± 2.31 **	63.28
APS	12	100	14.89 ± 2.35 **	45.41

Compared with control group, * $p < 0.05$ and ** $p < 0.01$. Data were expressed as means ± standard deviations (n = 10).

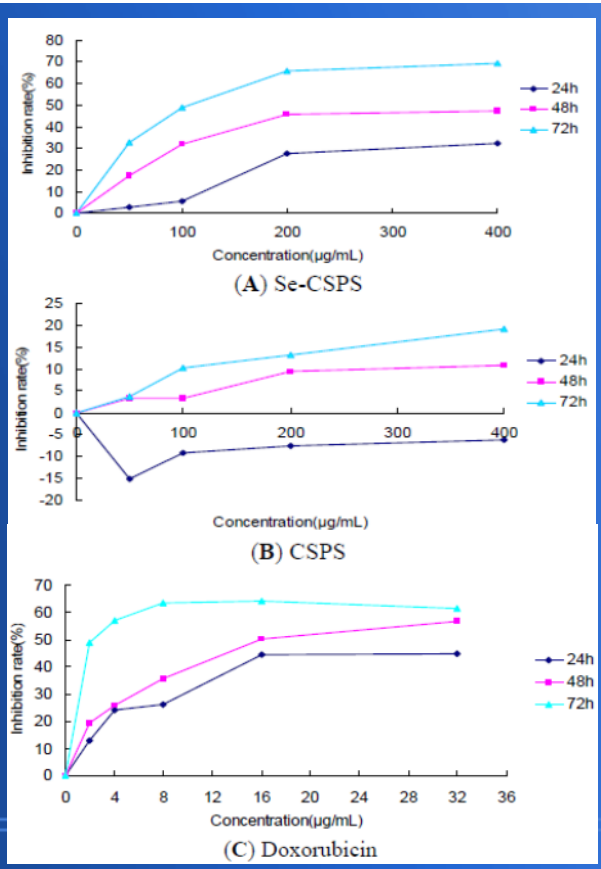

Figure:. Inhibition effect of (**A**) Se-CSPS; (**B**) CSPS and (**C**) doxorubicin on SGC-7901.

References:

[8] Ji YB, Dong F, Ma DB, Miao J, Jin LN, Liu ZF and Zhang LW: Optimizing the Extraction of Anti-tumor Polysaccharides from the Fruit of *Capparis spionosa* L. by Response Surface Methodology. *Molecules* 2012, *17*, 7323-7335.

[9] Ji YB, Dong F, Lang L, Zhang LW, Miao J, Liu ZF, Jin LN and Hao Y: Optimization of Synthesis, Characterization and Cytotoxic Activity of Seleno-*Capparis spionosa* L. Polysaccharide. *Int. J. Mol. Sci.* 2012, *13*, 17275-17289.

Toxicity:

- There was no report regarding acute, subacute and chronic toxicity of C. Spinosa. Furthermore, the popular use of the plant in traditional medicine and its prolong usage as a flavouring agent and by food industry documented its safety.

Conclusions:

- *C. spinosa* appears to be a promising medicinal plant with a wide range of pharmacological activities including anticancer effects, which could be utilized in several medical applications because of its effectiveness and safety.
- Litterature survey suggested that the chemical compounds isolated from *Capparis* species have not been systematically examined for their biological properties.
- Furthermore, reported antitumor properties of some Capparis extracts may provide new prospects in cancer treatment without any side effects.