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An introduction to ethnomedicinal and pharmacological activity of *Capparis sepiaria* L.

Sanila Quadri, Vartika Pant and Vivek Kumar

Abstract
Capparis sepiaria of the Capparidaceae family has a predominant place among the ethnomedicinal plants. The shrub has been known for its therapeutic properties in Ayurveda and Siddha medicinal systems. *C. sepiaria* has a wide variety of pharmacological activities including hepato-protective, antidiabetic and anti-tumor, anti-bacterial, anti-inflammatory, anti-helminthic properties and various others. The plant extracts have exhibited a variety of phytoconstituents such as1, 2, 3, 4-Cyclohexanetetrol; 2-Furanmethanol, 5-ethenyltetrahydro-α, α, 5-trimethyl-, cis-; 2-Methoxy-4-vinylphenol; 3, 7-Cycloundecadien-1-ol, 1, 5, 5, 8-tetramethyl and so on. This article aims to summarize the medicinal potential of *C. sepiaria* concisely.

Keywords: *Capparis sepiaria* L., ethnomedicinal uses, FTIR, GC-MS, pharmacological activity

1. Introduction
The genus *Capparis* dominates the Capparidaceae family. The Capparidaceae family comprises 39 genera and 650 species across the world. Out of 250 species of *Capparis*, 26 are found in India. Shrubs, trees, and woody climbers are the most common among the genus *Capparis* [1].

Capparis sepiaria Linn (synonym: *Capparis affinis* Merr, *Capparis emarginata* C. Presl, *Capparis flexicaulis* Hance, *Capparis glauca* Wall. ex Hook. f. & Thomson, *Capparis incanescens* DC, *Capparis* umbellata R.Br. ex DC. and *Capparis retusella* Thwaites) also known as Wild Caper Bush, is a densely branching hedge plant. The plant is widely distributed throughout tropical and sub-tropical countries [2]. *C. sepiaria* (Kakadamimni, Kanthari, Odeyanakanti, Ippimullu) is found in India, Sri Lanka, Myanmar and Pakistan. In India, it is found all over the brackish ranges of Andhra Pradesh, Maharashtra, and Karnataka also found in Gujarat and Rajasthan [3, 4].

In Gujarat, *C. sepiaria* is distributed in the scrub forests. In addition, plant supports other climbers and twiners present waysides as well as railway lines by its foliage and inflorescence [5]. The plant's presence is also reported near Ognaj village (Ahmedabad District, Gujarat), sparsely in the hedges [4].

2. Classification and Taxonomic Description
Genus - *Capparis*
Kingdom - Plantae
Phylum - Spermatophyta
Sub-Phylum - Angiospermae
Class - Magnoliopsida
Order - Capparales
Family - Capparaceae (or) Capparidaceae

C. sepiaria is a rare indigenous plant in south India and is utilized in many Indian systems of medicine [2]. *C. sepiaria* is a pale green bushy shrub, attaining a height of 5-11 feet. Leaves are oblong, lanceolate to elliptic shaped with entire margin, cuneate base, and obtuse apex. Their thorns are up to 3 cm in length. Flowers are white and occur in corymbose, sub-umbels inflorescence, which blooms between February and April. Fruits are two seeded, globose berries that develop blue color after ripening. The fruiting generally takes place after April. The plant, when crushed, releases a mild chilly odor [2, 6] (Fig. 1).

A B

Fig 1(a-b): *Capparis sepiaria* plant (Source: NIF Database)

3. Ethno medicinal uses

The use of plants as medicine is as old as human civilization. Ancient civilizations such as Sumerians recognized the therapeutic value of the *Capparis* species and used it for the first time around 2000 BC to treat various ailments. Different Indian ethnomedicinal systems, such as Ayurveda and Siddha, also use roots, flowers, and fruits to treat fever, tumors, inflammation, wound, poisonous bites, oral cancer, and syphilitic ulcer [1, 2, 7, 8]. According to ethnobotanical studies, the plant has a variety of active compounds and is a significant ingredient in traditional medicines, especially in medicinal oils. *C. sepiaria* is known as the most effective remedy for skin problems. It is also used as a blood purifier, boosting liver function, diuretics, hepatic protectors, kidney disinfectants, hepatic stimulants, stomachic, and vermifuges. The plant is also used in the treatment of abscesses, anorexia, arteriosclerosis, asthma, cancers, cold, edema, fever, gastrointestinal issues, muscular problems etc. Further, caper root bark infusions and decoctions have been traditionally used to alleviate dropsy, anaemia, arthritis, and gout. The flowers, leaves, and roots treat cough and toxemia [2, 3, 8]. In Tamil Nadu, the fresh bark, stem, and leaves of *C. sepiaria*, known as "Muruvilikodi" by the Palliyar tribe, treat dandruff, lower body heat, eczema, and some other ailments with this plant [7]. Similarly, in the Dharwad district of Karnataka, the plant leaves are used to treat oral ailments [9, 13]. In addition, the Bhil and Nayaka tribes of North Gujarat smash fresh roots with ginger and asafoetida and use the paste externally to cure mumps [10]. In other countries such as Kenya, Madagascar, Nigeria, South Africa, Tanzania, West Africa, the whole plant, root, root bark, and fruits are used to treat chest pain, lack of sexual desire, toothache, gall bladder related ailments, anthrax, cancer, fever, stomach disorders, wounds and livestock ticks respectively (Table 1) [2]. Additionally, when compared among the plant parts the use of the root is found to be utilized the most for medicinal purposes, followed by its leaves, entire plant, bark, flowers, seeds, and stem bark (Fig. 2).

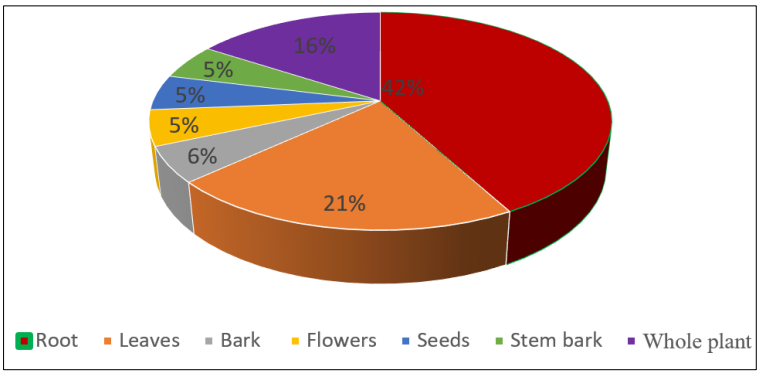


Fig 2: Percent of plant parts used for different types of ethnomedical purposes

Table1: Ethno-medicinal uses of different plant parts of *C. sepiaria*

Disease	Plant parts	Preparation / Use	References
Aphthae	Whole plant	Along with *Oxalis corniculata* and *Ricinus communis* whole plant of *C. sepiaria* is used for the treatment of aphthae	[7]
Aphthae	Leaves	Powder leaves mix with cotton cloth ash and is applied to the affected area to treat aphthae	[10, 11, 12]
Blood purifier	Whole plant	Plant juice is consumed to purify blood	[3]
Cough/Toxaemia	Flowers/Root/ Leaves	Plant juice or paste is taken orally	[3]
Dropsy	Stem bark & Root	Decoction of stem bark along with plant root powder is taken orally	[10, 12]
Gout	Stem bark & Root	Decoction of stem bark along with plant root powder is taken orally	[10, 12]
Earache	Root	Root paste is applied to the affected part	[12]
Eye swelling	Leaves	Root paste with opium is applied to the swelled eye	[7]
Glowing/ Healthy Skin	Leaves	Paste prepared from the leaves is applied over the face.	[10]
Headache	Root	Two or three drops of fresh root juice is instilled into the nostril to reduce the headache	[7]
Mumps	Root	Fresh pastes prepared from root of the plant are smashed along with Ginger and Asafoetida (Hing) and is applied over the mumps.	[10]
Skin disease	Root	Root powder is dusted over the affected area	[1]
Snakebite	Root and Seed	Seed and root paste is applied to the bitten part	[9, 12,14]
Tumour	Whole plant	Plant along with *Cassia fistula* Linn. and *Flacourtia ramontchi* L'Her.	[9, 10]
Skin inflammation	Root	Root powder is dusted over the affected area	[10]
Wound	Bark	Paste is applied to treat the wound	[7]

4. *C. sepiaria* in traditional system of medicine

4.1 Ayurveda

C. sepiaria, called Himsra/Vyaghranakha in Ayurveda, is one of the vital drugs used in many formulations such as Bala taila, Guduchyadi taila, and Kankasava. It is known to reduce flatulence fever, tumors, inflammation, wound, digestive disorders, liver disorders, filariasis, joint swelling and swellings of the testicles. The plant is also used as appetizer, in cardio tonics and as blood purifier [8, 9, 15, 16].

Properties and Action:

Rasa (Taste): Madhura, Katu, Tikta, Kasaya

Guna (Quality): Laghu, Ruksa

Virya (Potency): Usna

Vipaka (Metabolism): Katu

Karma (Impact): Kaphahara, Vatahara, Varnya, ViÀaghna, Kandughna [15].

4.2 Siddha

In the Siddha medicinal system, *C. sepiaria* is known as Sengathari, Karunjoorai, Vinthaiyam, Abanthasam, Amanthalam, and Alanthal and is used in a variety of formulations such as Sengathari ennai, Sarvakulanthaga thylam, Vellarugu chooranam etc. (Table 2) for the treatment of various illnesses [2]

Table 2: List of Siddha formulations

S. No	Medicine	Diseases	Application/Dosage
1	Arathi ennai	Arthritis	Oral administration
2	Echvaramoolich chooranam	Eczema, Odema/Swelling	Oral administration along with hot water
3	Karunkozhi chooranam	Syphilitic ulcer, Arthritis, Carcinoma, Menstrual disorders	Oral administration
4	Mukkottennai	Delirium	Oral administration
5	Notch ennai	Eczema, Infantile Eczema, Itchy Eczema	External application and Oral administration
6	Peisori chooranam	Urticaria, eczema, Syphilitic ulcer	Oral administration
7	Sarvakulanthaga thylam	Tuberculosis, Cough	External application
8	Sengathari ennai	Poison, Toxicity	Oral administration
9	Sengathari ennai	Throat cancer, Tongue cancer, Oral cancer, Fissured tongue, Pale lips, Tongue boils (A type of adenitis)	Oral administration
10	Vellarugu chooranam	Poisonous bites & stings, Eczema, Painful diseases, Syphilitic ulcer	Oral administration along with honey

5. Bioactive compound/Phytochemicals

Bioactive compounds are versatile molecules derived from plant metabolism that contain biochemicals and play various physiological roles [17]. From the root, stem, bark, leaves, flowers, and whole plant of *C. sepiaria*,

bioactive compounds such as alkaloids, amino acids, anthraquinones, botulin, erythrodiol, flavonoids, glycosides-octacosanol, phenols, ßamyrin, ß-sitosterol, sterols, taraxasterol, terpenes, α- and β-amyrin have been reported in methanol, ethanol, acetone, benzene, petroleum ether, chloroform extract (Table 3) [3, 6,7, 9]

Table 3: Phytochemicals present in the plant

Phytochemicals	Aqueous extract	Benzene extract	Chloroform extract	Ethanolic extract	Methanolic extract	Petroleum ether extract
Alkaloids	-	-	-	+	+	-
Anthraquinone	-	-	-	-	-	+
Catechin	-	+	-	-	+	+
Coumarin	-	+	+	-	+	-
Fixed oil	-	+	-	-	-	-
Flavonoids	+	+	-	+	-	-
Glycosides	-	-	+	+	-	-
Gums	+	-	-	+	-	-
Mucilage	+	-	-	+	-	-
Phenol	-	-	-	-	+	+
Proteins	-	-	-	+	-	-
Reducing sugars	+	-	-	+	-	-
Saponins	+	-	-	+	+	-
Starch	+	-	-	+	-	-
Steroids	-	-	-	+	-	+
Sugar	-	+	-	-	+	-
Tannins	-	-	+	+	+	-
Terpenoid	-	-	-	-	+	+
Xanthoprotein	-	-	-	-	+	+

6. Pharmacological action of *C. sepiaria*

6.1 Analgesic activity

Petroleum ether, methanol, and aqueous root extract of *C. sepiaria* were studied for analgesic activity in rats by tail flick response method taking Pentazocin as the reference drug. At a dose of 30 mg/kg at 180 min, the methanol extract showed higher analgesic activity (18.69%) than the reference drug (17. 39%) [18].

6.2 Anthelmintic activity

The anthelmintic activity of petroleum ether and ethanol extracts of *C. sepiaria* is evaluated on an adult Indian earthworm *Pheretima posthuma* taking Albendazole as a standard drug. The extracts showed a concentration-dependent activity. In the study, the ethanol extract of *C. sepiaria* L. showed significant anthelmintic activity compared to the standard drug Albendazole [19].

6.3 Anti-bacterial activity

The ethanolic leaf and fruit extracts of *C. sepiaria* were tested against *Enterococcus faecalis* bacteria taking Chloramphenicol as the standard drug. The extract showed concentration-dependent anti-bacterial activity. Both the extracts showed maximum activity in the highest concentration of 1000 ppm. In comparison, the fruit extracts showed a higher zone of inhibition against tested bacteria than ethanolic leaf extracts of *C. sepiaria* [20]. In a similar study, antibacterial activity of ethanol bark extract of *C. sepiaria is* carried out against microorganisms *Staphylococcus aureus, Micrococcus luteus, Bacillus subtilis (*Gram-positive bacteria) and *Escherichia coli, Proteus vulgaris* and *Shigella flexneri (*Gram-negative bacteria) by using agar well diffusion method by taking Tetracycline as standard. At 500 µg/mL concentration *B. subtilis* and *E. coli* showed maximum zone of inhibition of 15 mm followed by *S. aureus, M. luteus, P. vulgaris and S. flexneri with* zone of inhibition of 14 mm each [10].

6.4 Anti-diabetic activity

An ethanol leaf extract of *C. sepiaria* (EECS) is tested in streptozotocin-(STZ) induced diabetic rats taking Glibenclamide as standard. At doses of 100, 200, and 300 mg/kg of EECS, respectively, the percentage of blood glucose-lowering potential is observed as 9.40%, 13.57%, and 15.25% compared to the standard Glibenclamide. The results suggested that *C. sepiaria* leaves may be used to supplement traditional formulations and medication treatment for diabetic mellitus control [14].

6.5 Anti-fungal activity

The ethanolic extract of *C. sepiaria* leaf is tested against *Candida albicans* and *Aspergillus* flavans by disc diffusion method by taking Clotrimazole as standard. At 100 mcg C. albicans and A. flavans showed 13- and 18-mm zone of inhibition indicating towards moderate anti-fungal activity of the extract [21].

6.6 Anti-inflammatory activity

The ethanolic leaves extract of *C. sepiaria* is tested in wistar rats for anti-inflammatory activity using Carrageenan, cotton pellet, and cotton oil-induced edema. The findings suggest that *C. sepiaria* extract is a bioactive agent with significant anti-inflammatory activity [2]. Additionally, the crude root extract of *C. sepiaria* is screened using Carrageenan induced rat paw edema method approved by Institutional Animal ethics Committee (CPCSEA Registration no. 448/01/c) in male wistar rats. The study revealed that the mechanism of anti-inflammatory action of the plant is related to inhibition of enzymes responsible for increased vascular permeability, inhibition of degranulation of mast cells and prostaglandin biosynthesis [18].

6.7 Antioxidant activity

The antioxidant potential of ethanolic extract of *C. sepiaria* bark were studied by using DPPH˙ radical scavenging activity, Phosphomolybdenum reduction activity, Ferric (Fe3+) reducing power activity, and Superoxide (O2.-) radical scavenging activity taking Ascorbic Acid as standard. At 120 g/mL concentration, the maximum DPPH radical and superoxide (O2 -) radical scavenging activities of ethanol bark extract of *C. sepiari*a were 48.88±0.16% and 80.85±0.29%, respectively. DPPH radical and superoxide (O2 -) radical scavenging activities had IC50 values of 122.74 g/mL and 65.28 g/mL, respectively. The RC50 values of Mo6+ reduction and Fe3+ reduction were 87.87 g/mL and 67.29 g/mL concentrations, respectively. The maximum Mo6+ and Fe3+ reduction of the ethanol bark extract of *C. sepiaria* were 58.45±0.13% and 76.50±0.25% at 120 g/mL concentration [10].

6.8 Anti-tumor activity

The anti-tumor efficacy of a methanol extract of *C. sepiaria* (MECS) is reported in swiss albino mice carrying Ehrlich ascites carcinoma. At the doses of 200 and 400 mg/kg of MECS significant reduction in tumor volume and tumor cell count is observed with an increase in the life span of mice [3].

6.9 Hepatoprotective activity

The hepatoprotective effect of the ethanolic extract of the leaves of *C. sepiaria* is studied against liver damage induced by carbon tetrachloride (CCL_4) in Wister rats taking Silymarin drug as standard. At doses 100 and 200 mg/kg, the extract showed a significant hepatoprotective effect, further confirmed by histopathological studies of the liver, showing improved architecture, absence of nuclear pycnosis, hepatocyte congestion, and necrosis when compared with the liver of the toxin group of animals [8]. In a similar study, pretreatment with 100 mg/kg p.o. alcoholic stem extract of *C. sepiaria* for seven days protected the rats from CCl_4-induced hepatotoxicity compared to the reference drug Silymarin [9]. Further, the ethanol and aqueous extracts of the roots of *C. sepiaria* were evaluated for their hepatoprotective potential on carbon tetrachloride (CCl_4)-induced hepatotoxicity in albino Wistar rats. The results indicated that phytosterols present in the ethanol root extract produced better protection from hepatotoxicity than aqueous root extract [16].

6.10 Acute, sub-acute, and chronic toxicity studies

Acute, sub-acute, and chronic oral toxicity of the plant ethanolic extracts of *C. sepiaria* (EECS) is evaluated in Swiss albino mice per the OECD guidelines for one day, one month, and three months respectively. The treated animals showed no toxicity or behavioral abnormalities symptoms from 100 mg/kg/b.w. up to 5000 mg/kg/b.w. in the study [6]. In another study, by OECD guidelines (423), the acute toxicity of aqueous and ethanol root extracts of *C. sepiaria* at the highest dose of 2000 mg/kg on albino Wistar rats of both extracts showed o mortality until the end of the study [16].

7. FTIR (Fourier Transform Infrared Spectrophotometer analysis)

Fourier transform infrared spectroscopy (FTIR) is used to determine the unknown composition's structure and the absorption spectra's intensity related to molecular composition or the content of respective chemical functional groups [22]. *C. sepiaria* is a good source of various functionally active

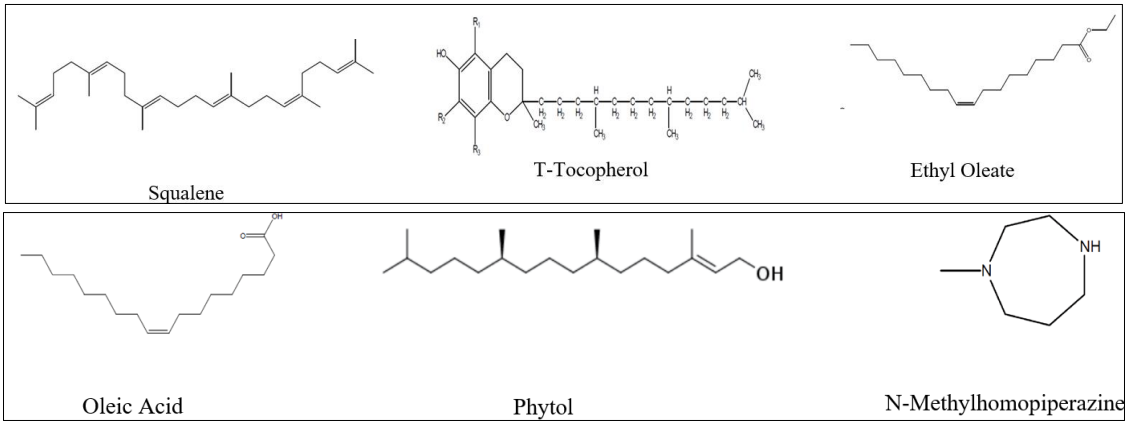
secondary metabolites. The FTIR analysis of the ethanol bark extract of *C. sepiaria* exhibited 18 bands ranging from 655 cm^{-1} to 3369 cm^{-1} such as alcohol, alkanes, alkyls, alkene, alkyl aryl ether, alkynes, amides, anhydride, aromatic amine, aromatic ester, carboxylic acids, halo compounds, sulfate phenols, and sulfone compounds [10].

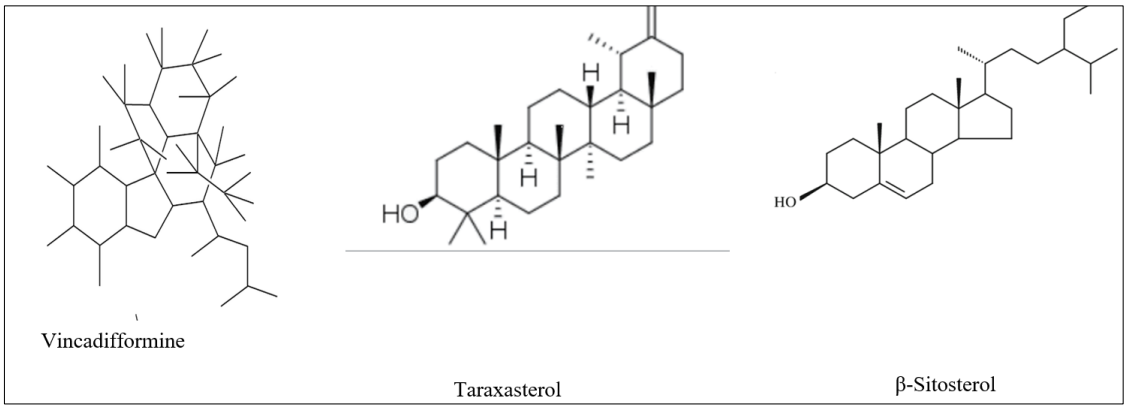
8. Gas chromatography – mass spectroscopy (GC-MS)

GC-MS is a technique to know the bioactive constituents of the plant which plays an important role in phytochemical analysis [23]. The GC-MS analysis of ethanolic extract of *C. sepiaria* showed various chemical (Table 4 and Fig. 3) such as 1, 2, 3, 4-Cyclohexanetetrol; 2-Furanmethanol, 5-ethenyltetrahydro-α,α,5-trimethyl-, cis-; 2-Methoxy-4-vinylphenol; 3, 7-Cycloundecadien-1-ol, 1, 5, 5, 8-tetramethyl; 3-Pyridinecarboxylic acid, 1, 2, 5, 6-tetrahydro-1-methyl-, methyl ester; 3-tert-Butyl-4-hydroxyanisole; 9, 12-Octadecadienoic acid, ethyl ester; Benzofuran, 2, 3-dihydro-; ethyl oleate; Ethyl α-d-glucopyranoside; Hexadecanoic acid, ethyl ester; n-methyl-homopiperazine; Octadecanoic acid, ethyl ester; oleic acid; Pentadecanoic acid 14-methyl-, methyl ester; Phytol; Pyrrolidine, 1-(1-oxobutyl); Squalene; Vincadifformine; τ-tocopherol , Tetradecanoic acid , Benzoic acid, 3, 5-bis(1, 1- dimethylethyl)-4-hydroxy- , 1H-Purine-2, 6-dione, 3, 7-dihydro-7-(4-tert-butylbenzyl)-1, 3-dimethyl-, Phenol, 2, 6-bis (1, 1-dimethylethyl)-4-[(4-hydroxy-3, 5-dimethylphenyl) methyl]-, 8-Carbethoxy-1-methyl-1, 4, 5, 6, 7, 8-hexahydropyrrolo [2, 3-b]azepin-4-one-3-carboxylic acid [10, 6]

Table 4: Chemical compounds present in plant

S. No.	RT	Name of the compound	Chemical formula	Molecular weight	Peak area	Application	References
1	29.76	Squalene	$C_{30}H_{50}$	410	3.63	Lowering cholesterol, in cancer, as a detoxifier, for skin hydrating	[24]
2	34.70	T-Tocopherol	$C_{28}H_{48}O_2$	416	1.02	Reduce inflammation, anti-cancer, anti-aging Anti-oxidant properties.	[25]
3	19.64	Ethyl Oleate	$C_{20}H_{38}O_2$	310	5.23	Used as a solvent for pharmaceutical drug preparations, food additive	[26, 27]
4	19.39	Oleic Acid	$C2_0H_{34}O_2$	282	6.49	preventing heart disease, cancer, reducing cholesterol, wound healing, blood pressure	[28]
5	18.96	Phytol	$C_{18}H_{40}O_2$	296	3.86	antinociceptive, anti-inflammatory, anti-allergic, antimicrobial	[29]
6	2.94	N-Methylhomopiperazine	$C_6H_{14}N_2$	114	0.72	Antifungal, antibacterial, antimalarial, antidepressant anti-tumor	[30]
7	14.26	Vincadifformine	$C_{21}H_{26}N_2O_2$	338	0.51	An antiplasmodial drug	[31]
8	-	Taraxasterol	$C_{30}H_{50}O$	426.7	-	anti-allergic, anti-oxidant, anti-inflammatory, Alzheimer's and Parkinsonism disorders, antivenom	[32]
9	-	β-Sitosterol	$C_{29}H_{50}O$	414.71	-	lower cholesterol levels, reduce the risk of some cancers	[33]
10	-	Betulin	$C_{30}H_{50}O_2$	442.72	-	antimalarial, anti-inflammatory, antiulcer antifungal activity, anti- HIV	[34]





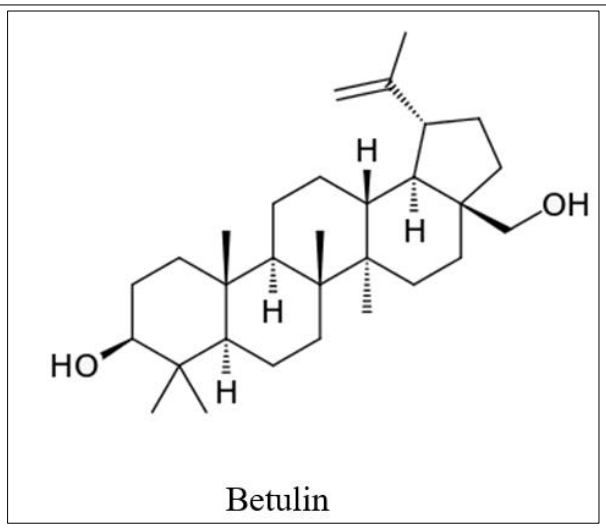


Fig 3: Phytoconstituents reported in the *C. sepiaria* using Gas Chromatography-Mass Spectrometry

9. Patents on *C. sepiaria*

For thousands of years, medicinal plant formulations have been used in traditional medicines. Plant-based medicine continues to be a major source of potential drug leads, and herbal treatments are massively lucrative in the international market [35]. While conducting a patent search, certain patents are found having *C. sepiaria* either as a single ingredient or main ingredient or in combination with other plants in the formulation (Table 5).

Table 5: Patents on *C. sepiaria*

S. No.	Title of patent	Application number	Application status	Plant use as single ingredient/or in combination
1.	Herbal compositions and medicaments thereof for treatment of arthritis	429/KOL/2011	Application refused, U/S 15	In combination with other plants
2.	Herbal formulation for the prevention and treatment of bloat in animals	202/MUM/2007	Application Granted, Patent no.- 375514	In combination with other plants
3.	Herbal medicaments	436/KOL/2011	Application Granted, Patent no.- 298858	As single ingredient
4.	A novel synergistic herbal composition for use in treating head and body aches	482/KOL/2011	Application Granted, Patent no.- 349481	In combination with other plants
5.	Herbal composition for the treatment of enteritis and process for making the same	999/CHE/2014	Application Granted, Patent no.- 362840	In combination with other plants

10. Conclusion

C. sepiaria is an ethnomedicinal plant as it has many therapeutic properties against various ailments. The shrub has its potent use in Ayurveda and Siddha medicinal systems, which could be attributed to its varied pharmacological activities like anti-tumor, anti-diabetic, hepatoprotective, anti-inflammatory, antibacterial, anthelmintic, and antioxidant activity. *C. sepiaria* is a good source of various functionally active secondary metabolites. The plant exhibits the presence of various chemical compounds such as 1, 2, 3, 4-Cyclohexanetetrol; 2-Furanmethanol, 5-ethenyltetrahydro-α, α, 5-trimethyl-, cis-; 2-Methoxy-4-vinyl phenol; 3, 7-Cycloundecadien-1-ol, 1, 5, 5, 8-tetramethyl and so on. The review may help understand the ethnomedicinal profile, identify the role of bioactive present in the plant, and ultimately develop an herbal medicament from *C. sepiaria*.

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12. Conflict of interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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