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Anti-Ulcer Activity Of Capparis Zeylanica Plant Extract

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Abstract:

Capparis zeylanica Linn. (Capparidaceae) has been used as a Rasayan drug in the Ayurvedic system of medicines. *Capparis zeylanica Linn*. Is reported to posses anti oxidant, antipyretic, analgesic, anti-inflammatory, antimicrobial ,anti-ulcer and immunostimulant activity. *Capparis zeylanica Linn*. Is reported to Peptic ulcer is the term which refers to acid peptic injury of the digestive tract, and it results in mucosal break reaching the submucosa. Leaves of *Capparis zeylanica* are used as counterirritant, rubefacient, as a cataplasm in piles, boils and swellings. The objective of the present study was to evaluate the antiulcer activity of C. zeylanica ethanolic extract against chemically induced ulcers. Recently a new compound Eoctadec7en-5-ynoic acid has been reported from root part of this plant. The aim of present study is based on low cost, efficient and eco-friendly way for biological production of nanosized Zinc oxide (ZnO) with *Capparis zeylanica* leaf extract The present study is based on the work done till date regarding the phytoconstituents and pharmacological activity of *Capparis zeylanica Lin.*

Keyword: *Capparis Zeylanica*, Peptic Ulcer,1D and 2D NMR Spectroscopy,Fatty Acid

Introduction:

Capparis zeylanica Linn. (C.horrida Linn., Capparis brevispina DC.) is known as Indian caper belonging to family Capparidaceae. In Sanskrit it is known as Vyakhranakhi, kinkani, tapasapriya, granthila, karambha . It is a rigid, wiry and much branched shrub and is widely distributed in Bangladesh, India, Sri Lanka and Malaysia[1]. *Capparis zeylanica Linn.* (Capparaceae) is a many branched thorny, sub-scandent climbing shrub. Plants are 2-3 m in height, armed with 3-6mm long recurved thorns, branched, leaves are elliptic or broadly lanceolate, base rounded, apex mucronate; flower profuse, pinkish white, later turning pink, berries

are globular or elliposide, 3-4 cm in diameter, and seeds are globase, embedded in white pulp. It is grows in moist habitat. The plant distributed through out the major parts of India, Bangladesh and some parts of Pakistan. *Capparis zeylanica Linn*.

(Capparaceae) commonly known as 'Asadhua' in Oriya & 'Ardanda' in Hindi [2].

A lot of medicinal plants, traditionally used for thousands of years, are present in a group of herbal preparations of the Indian traditional health care system (Ayurveda) named Rasayana proposed for their interesting antioxidant activities[3]. Peptic ulcer treatment involves using a number of chemically produced drugs with aim to reduce the rate of stomach acid secretion, protection of the mucosa thatl ine the stomach and upper portion of the small intestine or to eliminate H. pylori infestation [3]. Gastric ulcer, one of the most widespread, is believed to be due to an imbalance between aggressive and protective factors.[4] Chemistry of caper plants: the flower buds contain a glycoside, *rutic*, which on acid hydrolysis yields *rhamnose*, dextrose and *quercetin*; flower buds also contain about 4% *pentosans* on a dry weight basis, *rutic* acid, pectic acid and *saponin;* caper seeds yield about 35% pale yellow oil containing *palmitic*, stearic, oleic and linoleic acids; the root bark contains rutic acid and a volatile substance with a garlic odour; a series of isomers of the compound *cappaprenols* have been isolated from *Capparis*.[5] . Thus, now a days treatment of peptic ulcer moves keen interest towards use of medicines from natural sources which are safe and cost efficient. Hence main objective of this review article is to summarize and configure the plants having potential for the treatment of peptic ulcers.[6]

Antiulcer medications fall into three main classes:[7]

Antiulcer agents and medications for acid peptic disease are commonly used drugs that rarely cause liver injury. Most agents act by inhibition of gastric acid production, neutralization of acid or protection of the gastrointestinal mucosa from acid injury. These agents are used for both prevention and therapy of duodenal and gastric ulcer disease as well as to alleviate acid reflux, esophagitis and minor upper intestinal discomforts. The antiulcer agents in clinical use that are discussed in the following:

1.Proton pump inhibitors (PPIs): These are more powerful than antacids and H2receptor antagonists. Some common PPIs include:

- Dexlansoprazole
- Esomeprazole
- Lansoprazole
- Omeprazole
- Pantoprazole
- Rabeprazole

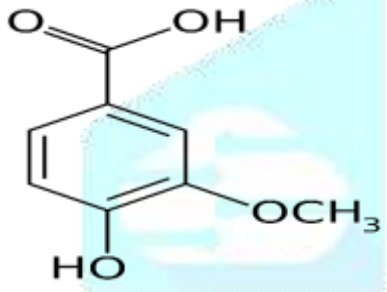
2. Selective histamine type 2 receptor antagonists/blockers: Some examples include:

- Cimetidine
- Famotidine
- Nizatidine
- Ranitidine

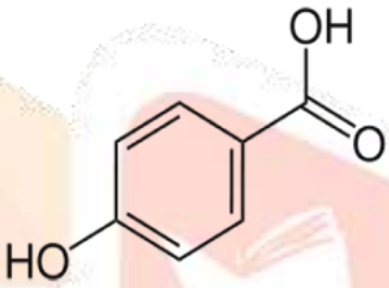
3. Mucosal protectants: These cover and protect gastrointestinal ulcers. An example is sucralfate, which dissociates in the stomach to form a protective barrier

Phytochemistry:

A new fatty acid, E-octadec-7-en-5-ynoic acid, has been isolated from chloroform extract of the roots of *Capparis zeylanica*. The structure of this compound was established primarily by 1D and 2D-NMR spectroscopy. Preliminary phytochemical screening of the extracts showed the presence of alkaloids, flavonoids, saponins glycosides, terpenoids, tannins, proteins and carbohydrates[8]. Whole plant showed the presence of *saponin, p-hydroxybenzoic, syringic, vanillic, ferulic* and *p-coumanic acid*. Leaves & seeds showed presence of *β-carotene, thioglycoside, glycocapparin, n-tricortane, α-amyrin* &fixed oil where as root bark showed presence of an alkaloid, a *phytosterol*, a water soluble acid and a mucilaginous substance[9]. *P-Hydroxy Benzoic Acid, Vanilic Acid, Synergic Acid, Ferulic Acid, Beta-Carotene* presents in the *capparies zeylanica*.[10].



Vanilic Acid



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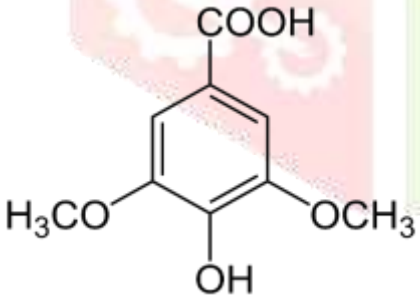
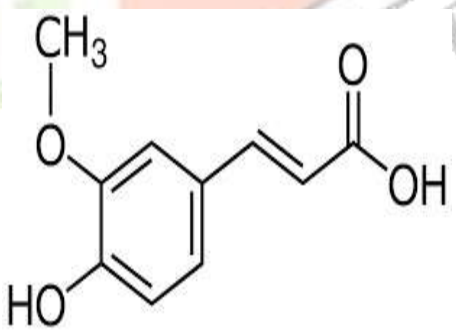
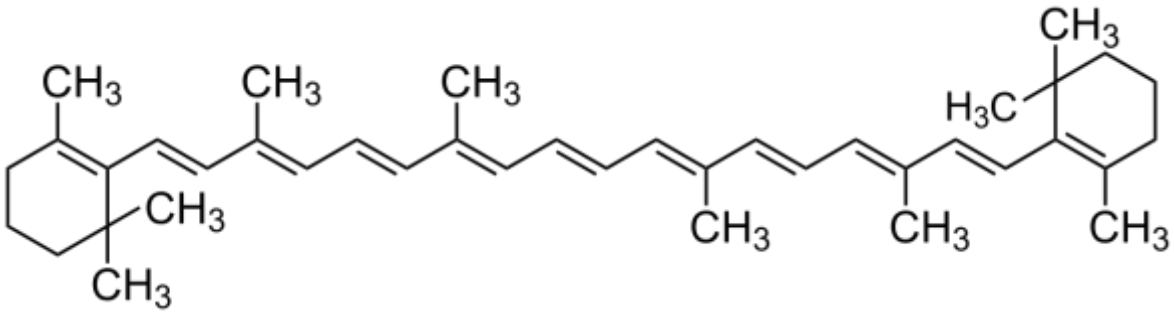


Synergic acid



Ferulic Acid



Beta Carotene

Material and Method

Extraction of C. zeylanica leaves

Fresh leaves of C. zeylanica were collected from the forests of Allahabad in the month of April 2019. It was identifed and authenticated by Dr. Sunil Singh of the respective department. The samples of leaves were deposited in the herbarium of the institute with voucher no.1243. The leaves were dried, grounded and treated with petroleum ether to remove fatty substances. The marc was extracted with ethanol (50%) as solvent using hot perforation method. Vacuum distillation was performed to reduce the volume of extract to 1/10, and remaining solvent was evaporated by boiling on a water bath. The final extracted product was dried in a lyophilized to get it in a powdered form. The yield of the product was 10%, w/w. The powdered extract was packed in an airtight container and used for further studies[11].

Chronic Ulcer Study

Ethanol-induced ulcer

Thirty fasted animals were used in three groups of six animals each. Groups A and B received 5 ml/kg (p.o) of 3% Tween 80 (negative control) and 100 mg/kg p.o. sucralfate (Antepsin) while rats in group C were given 200 mg/kg of MECZ orally (p.o), respectively. After 1 hr all animals received 1 ml/kg of 80% ethanol (Sigma-Aldrich, Germany) oraly. The rats were sacrificed with chloroform (SigmaAldrich, Germany) anaesthesia after 1 hr. The stomachs were isolated, washed gently under clean flowing water and cut open along the greater curvature. The stomachs were then fixed in 10% formalin and craters observed and ulcer scores were recorded [12].

Aspirin-induced ulcer

The wistar albino rats weighing 100-200 g of either sex were divided into three groups, each group consists of 6 animals. All the animals received 200 mg/kg of aspirin once daily for three days. Group1 served as control received 5 ml/kg (p.o) of 3% Tween 80, group 2 treated with 50 mg/kg (p.o) ranitidine as standard and group 3 treated with 200 mg/kg (p.o) methanol extract of C. zeylanica. On the fourth day pylorus part was ligated following 36 hr fasting .Four hrs after the pylorus ligation the animals were sacrificed by decapitation. The stomach was opened and the ulcer index was determined .The gastric contents were titrated against 0.01 N NaOH to determine the free acidity and total acidity [13].

Indomethacin-induced ulcer

Animals (three groups of six rats each) in groups received 5 ml/kg (p.o) of 3% Tween 80, Omeprazole 20 mg/kg (p.o) and 200mg/kg (p.o) of extract, respectively. After 30 min, indomethacin 40 mg/kg (p.o) was administered to each rat. After 8 hr of drug treatment, stomachs were isolated, cut and ulcers counted as before [14].

Acute Ulcer Study

Histamine-induced ulcers

Administration of histamine (300 mg/kg/i.p.) produced ulcers in all treated animals and the mean ulcer area was 10.66±0.13 mm2 and ulcer index (UI)

1.48±0.01 was found in control group animals, indicating the ulcerogenic efect of histamine. Treatment with C. zeylanica extract showed signifcant reduction in the ulcer area (3.2±0.15 mm2) and ulcer index (0.43±0.02) dose dependently in comparison with control group as shown in Table 2. Treatment with standard drug ranitidine (100 mg/kg p.o.) reduced ulcer area (2.7±0.14 mm2) and ulcer index (UI) (0.38±0.03) in all the animals of the group[15].

Naproxen-induced ulcers

Naproxen treatment with C. zeylanica extract showed signifcant ($p<0.01$) reduction in the ulcer area(60 and 120 mg/kg) dose dependently. Pretreatment of animals with C. zeylanica extract (30 mg/kg) did not reduce the ulcer area. However, higher dose of C. zeylanica extract, i.e., 120 mg/kg, was efective in protecting against ulcerogenic action of naproxen in comparison with control group. Treatment with C. zeylanica extract (120 mg/kg) reduced area of ulcers(3.622±0.453 mm2) and ulcer index (UI) (0.51±0.01) signifcantly, which was near to standard drug omeprazole. Administration of omeprazole reduced area of ulcer (2.33±0.10 mm2) and ulcer index (UI) (0.32±0.01) signifcantly. Tus, C. zeylanica extract was found efective in ulcerogenic condition[16].

Ethanol –induced ulcer

All animals wewe fasted for 24 h before treatment. Capparis zeylanica extract (30,60 and 120 mg/kg p.o.)was given to three test groups, respectively,as prophylactic dose. Ulcer was induced by administering ethanol (8ml/kg) p.o.after 1 h of C.zeylanica extract pretreatment. Sucralfate (200 mg/kg p.o.) was administered to standard group.The animals wewe killed after 1h of ulcer induction and killed by cervical dislocation. The stomach of all animal was dissected out and observed under microscope[17].

Pharmacological Activities

The roots of C. *zeylanica* were reported to have antibacterial, antioxidant activities; it also found to act as endothelin receptor antagonists. The root bark paste is used on boils and swellings of testicles. The fruit and

root part of *capparis zeylanica* has also been reported to possess anti-allergic, anti-gout, anti-diabetic and astringent property[18].

Antioxidant activity

Antioxidant activity evaluation, ethanol and methanol extracts were of the *Capparis zeylania* L. root were prepared and screened for in vitro antioxidant activities by 1,1-diphenyl-2- picrylhydrazyl (DPPH) free radical scavenging activity and by reducing power assay method. The results of both the methods were compare d with a natural antioxidant ascorbic acid (vitamin C) as a standard. Both the extracts showed strong anti oxidant activity in these methods. Amongst these two extracts, ethanolic extract has shown better antioxi dant activity as compared to methanolic extract[19] .

Immunomodulatory effect

Study was undertaken to explore the immunomodulatory activity of ethanolic and water extracts of *Capparis zeylanica* Linn. leaves on neutrophil adhesion test, humoral response to sheep red blood cells, delayed-type hypersensitivity, phagocytic activity and cyclophosphamide-induced myelosuppression. Oral administration of ethanolic and water extracts of *Capparis zeylanica* leaves, at doses of 150 and 300 mg/kg in mice, dose dependently potentiated the delayedtype hypersensitivity reaction induced by sheep red blood cells[20].

Analgesic, anti-inflammatory and antipyretic effect

The ethanol and water extracts of *Capparis zeylanica* leaves showed dosedependent and significant increases in pain threshold in tail-immersion test. Moreover, both the extracts (100–200 mg/kg) exhibited a dose-dependent inhibition of writhing and also showed a significant inhibition of both phases of the formalin pain test. The water extract (200 mg/kg) significantly reversed yeastinduced fever19. Anti -nflammatory and analgesic activity of *Capparis zeylanica* L. root extract is also documented25. Methanolic extract of *Capparis zeylanica* plant posseses a significant antipyretic effect in yeast induced elevation of body temperature in experimental rats. It was revealed that the extract showed dose dependent antipyretic activity. At a dose of 200mg/kg it showed significant antipyretic activity. Presence of flavonoids in the methanolic extract of *Capparis zeylanica* plant may be contributory to its antipyretic activity[21,22,23].

Anti-ulcer activity

Three models (ethanol, aspirin, and indomethacin) with effective induction of ulcer experimentally in rats were employed to evaluate the anti-ulcer activity of the methanolic extract of C.*zeylanica.* All the rats used were fasted for 18 hr hours but were given water ad libitum till the start of the experiment[24].

Antimicrobial activity

Antimicrobial activities were evaluated by agar well diffusion method using ethyl acetate leaf extract of C. *zeylanica.* The pathogens such as Staphylococcus *epidermidis* MICC 2639, *Enterococcus faecalis* MTCC 439, *Salmonella paratyphi* MTCC 735, *Shigella dysenteriae* (Lab isolate from stool), Mycobacterium tuberculosis (H 379) and *Candida albicans* (MTCC 227)) were obtained from MTCC (Microbial type culture collection), Chandigarh, India through *Eumic*

Analytical Lab and Research Institute, Trichy, India. The plates were incubated at 37° ± 2 °C at 24–48 h for bacteria and 27° ± 2 °C at 72–96 h for fungi respectively. The experiment was conducted in triplicate. The zones of inhibitions were measured for their diameter (mm) around each test organism[25].

Other pharmacological activities

C. *zeylanica* constitutes flavonoids have been known to possess, anti-neoplastic, anti-ulcer activities. Anti-allergic, gout, astringent, diabetic (kidney disinfection) are found in fruits and roots of the C. *zeylanica* was reported[26].

Traditional Uses

Traditionaly *Capparis zeylania* L. was first time reported used as vegetable . Root bark is ground with water, boiled and taken orally to treat indigestion. Traditionally it is use as Antidote to snake bite, to cure swelling of testicle, small pox, boils, cholera, colic, hemiplagia, neuralgia, sores, pneumonic & pleurisy.[27] Leaf juice of CZ taken orally with cup of fresh gout milk for curing cough and cold. For the treatment of diabetes ripe fruits are consumed twice for fortnight and during ingestion, stem bark extract is administered thrice daily[28]. In Northern India, the leaves are widely used as counter-irritant, febrifuge and as a cataplasm in swellings, boils and piles . Leaf and stem parts are as spasmolyte . Root bark preparation is used as a sedative. Leaves extract of *Capparis zeylania* L with black pepper powder is taken towice daily for the treatment of dysentery . Leaves juice of *Capparis zeylania* L taken orally with cup of fresh gout milk for curing cough and cold[29]. In Ayurveda called *Vyakhranakhi*; the root bark of C.*zeylanica* is used for cooling, cholagogue and as a bitter. It removes ‘Kapha’. The root bark of C.*zeylanica* is used traditionally as stomachic, sedative, antihydrotic and also in cholera, neuralgia, hemiplegia and rheumatism. The fruits are used to remove ‘Tridosha’, bitter removes ‘Kapha’ and ‘Vata’. The seeds and fruits are used in urinary purulent discharges and dysentery In Northern India, the leaves are used as a rubefacient , counterirritant and as a cataplasm in boils, swellings and piles[30].

Discussion

The anti-ulcer activity of the methanol extract of C.*zeylanica* against ethanol, aspirin and indomethacin-induced ulcers was established in this study. Results of acute toxicity of this plant as flavonoids have been reported to possess anti-ulcer activity in various experimental models of ulcers[5]**.**In the present investigation, the various groups of animals were treated prophylactically with the C. *zeylanica* extract to determine its ulcer protective potential. Naproxen was used as the ulcerogenic tool to produce acute gastric lesions, and it is due to non-selective inhibition of cyclooxygenase I and II, leading to reduced PGE2 synthesis and decreased mucus secretion [31]. Results showed that C. *zeylanica* extract has mild ulcer protective activity against naproxen-induced ulcer at a dose of 120 mg/kg p.o. Our results are in accordance with the observations of Halter et al. [32]. Many studies have been performed to identify antioxidant compounds with pharmacologically activity and a limited toxicity. In this context, ethno pharmacology represents the most important way possible of finding interesting and therapeutically helpful molecules[33].

Conclusion

The present study suggests that the C. *zeylanica* extract possesses potent antiulcer activity against chemicals induced ulcer with signifcant antimicrobial activity. The extract showed efectivity in both acute and chronic ulcers by reducing area of ulcers. *Capparis zeylanica* extract signifcantly restored the morphology of ulcerated stomach to normal one. The extracts inhibited both phases of the formalin-induced pain with a more potent effect on the second than the first phase. The formalin pain test is very useful for evaluating the mechanism of pain and analgesia. Drugs which act mainly centrally, such as narcotic analgesics, inhibits both phases of pain in this model while peripherally acting drugs, such as acetylsalicylic acid or indomethacin, only inhibit the late phase. Thus, ethanolic extract of C. *zeylanica* leaves may be considered as a potential therapeutic candidate in gastric ulcers infected with H. pylori. It can be developed into suitable formulation after clinical trials.

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