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Review Article

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PEPTIC ULCER: A REVIEW WITH EMPHASIS ON PLANTS FROM CUCURBETACEAE FAMILY WITH ANTIULCER POTENTIAL

Kaushik Avinash*, Dwivedi Abha, Sharma Ganesh N.
School of pharmaceutical Sciences, Jaipur National University, Jaipur (Raj.), India-302018

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***Corresponding author**
Kaushik Avinash, Student. Email: lavi1191@gmail.com

ABSTRACT
Due to changes in life style and eating habits an increase in frequency to be affected by ulceration in gastric contents can be observed now a day. At the same time a number of semisynthetic and synthetic drugs like proton pump inhibitors, H2 receptor antagonists, mucosal defensive agents along with various antimicrobial agents are available for the treatment of ulcer, but clinical evaluation of these drugs has shown side effects, and drug interactions. Recently a number of approaches have been made for the development of newer ulcer healing or ulcer protective using herbal sources, as they are easily available, of low cost and have no or less side effects. This review aim to compile data on plants from cucurbetaceae family reported for their anti-ulcer or ulcer healing properties.
KEYWORDS: Peptic Ulcer, Cucurbetaceae, *H. pylori*, NSAIDs

INTRODUCTION

Ulcers are sore means open and painful wounds and the peptic ulcers are erosion of lining of stomach (The lining is a wrinkly bag that holds acids to help digest food) or the duodenum.[1] Still, the etiology of peptic ulcer is not clearly known, but it has been well established that peptic ulcer occurrence takes place due to an imbalance between aggressive factors (like acid, pepsin, bile & *H. pylori* infection) and defensive factors (like gastric mucosa, bicarbonate secretion, prostaglandins, nitric oxide and innate resistance of the mucosal cell). In gastric ulcer, acid secretion may be normal or low, while in duodenal ulcer, volume of acid secretion is high in half of patients and may be normal in rest.[2] Mucosal cell death results from increase in H^+ concentration in its immediate environment (decrease pH).[3]

Regulation of Gastric acid Secretion

The terminal enzyme H^+K^+ATPase secretes H^+ ions in the apical canaliculi of parietal cells, and can be activated by histamine, acetylcholine and gastrin acting via their own receptors located on the basolateral membrane of these cells. Histamine directly act through H_2 receptors followed by generation of cAMP formation, along with Ca^{2+} mobilization, while acetylcholine & gastrin acts either may act directly through muscarinic & gastrin receptor respectively or may act indirectly by releasing histamine from "histaminocytes". The muscarinic receptors & gastrin receptors (cholicystokinin receptors) function through IP_3-DAG pathway that mobilizes intracellular Ca^{2+}.

Gastrin is secreted from the antrum in response of antral pH, food constituents & vegal mediated reflexes. Vagus releases acetylcholine which release histamine & gastrin through the acting on histaminocytes & gastrin secreting cells. Prostaglandins produced by gastric mucosa, inhibits acid secretion by opposing cAMP generation & gastrin release. The mechanism of NO is not yet clearly established.[2]

Common Causes of Peptic Ulcerations

H. pylori

The gram negative bacterium Helicobacter pylori (initially named as Campylobacter pyloridis), remains present between the mucous layer and the gastric epithelium, and is strategically designed to live within the aggressive environment of the stomach. Initially, *H. pylori* resides in the antrum but over time, migrates toward the more proximal segments of the stomach. The genome of *H. pylori* has been sequenced and encodes 1500 proteins. Amongst this multitude of proteins there are factors that are essential determinants of *H. pylori*–mediated pathogenesis and colonization such as the outer membrane protein (Hop proteins), urease, and the vacuolating cytotoxin (Vac A). The first step in infection by *H. pylori* is dependent on the bacteria's motility and its ability to produce urease.[4]

Urease produces ammonia & carbondioxide from urea which is secreted from the stomach. This CO_2 interact with environmental water & produce H_2CO_3 in presence of carbonic anhydrase, an essential step in alkalinizing the surrounding pH. This H_2CO_3 converts into the H^+ & HCO_3^- and resulting H^+ ion react with NH_3 to form NH_4^+ which can damage epithelial cells.[2]

Use of Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Prostaglandins are chemicals promoting inflammation i.e. have protective role. The use of NSAIDs is common for the treatment of inflammatory responses; however, they may also inhibit certain prostaglandins causing protection of stomach lining from the corrosive effects of stomach acid. These protective prostaglandins are produced by an enzyme called Cox-1. By blocking the Cox-1 enzyme and disrupting the production of prostaglandins in the stomach, NSAIDs can cause ulcers and bleeding.[5]

Alcohol Consumption

Fermented and nondistilled alcoholic beverages increase gastrin levels and acid secretion. Alcoholic drinks containing succinic and maleic acid also stimulate gastric acid secretion. Low alcohol doses accelerate gastric emptying, whereas high doses delay emptying and slow bowel motility.[6]

Smoking & Tobacco

The relationship between the secretion of pepsin 1 (the most electronegative of the pepsins), and the smoking habits of patients has been investigated. Significantly more cigarette smokers with peptic ulceration secreted pepsin 1 in greater than trace amounts after pentagastrin or histamine than non-smokers with ulceration.[7]

Stress

Studies have well established that susceptibility to gastric as well as duodenal ulceration increases under stress conditions.[8] A no. of preclinical screening methods also based on this approach.

Fasting Condition

Fasting condition causes gastric empty which in some cases cause ulcers.[9]

Radiation

Ulcers are wounds caused by the acute or chronic effects of ionizing radiation. The most common cause of radiation injury is an adverse effect of therapeutic radiation therapy. Other causes are occupational or environmental exposures.[10]

Types and Symptoms of Peptic Ulcers

The two most common types of peptic ulcer are called "gastric ulcers" and "duodenal ulcers". The name refers to the site of ulceration. A person may have both gastric and duodenal ulcers at the same time.

- Gastric ulcers (GU) are located in the stomach, characterized by pain (especially higher in the abdomen) and common in older age group (especially in female). Eating may increase pain rather than relieve pain. Other symptoms may include nausea, vomiting and weight loss. Although patients with gastric ulcers have normal or diminished acid production, yet ulcers may occur even in complete absence of acid.[11]
- Duodenal ulcers (DU) are found at the beginning of small intestine (duodenum) and are characterised by severe pain (in lower abdomen or chest area) with burning sensation in upper abdomen that awakens patients from sleep. Generally, pain occurs when the stomach is empty (about two hours after meal or during the night), and relieve after eating. DU are more common in younger individuals and predominantly affects males. In the duodenum, ulcers may appear on both the anterior and posterior walls i.e. Kissing Ulcers.[12]

In some cases, peptic ulcer can be life threatening with symptoms like; bloody stool (blood may be red, black, or tarry in texture), severe abdominal pain and cramps along with Vomiting blood (resembling coffee grounds).[13]

Diagnosis Peptic ulcerations can be diagnosed by

Barium containing X-ray

A whitish liquid containing barium contents is administered orally, and X-ray film is collected. The ulcer outline can be observed on X-ray film.[14]

Endoscopy

A lighted tube with a special camera on its end is inserted into the stomach or upto initial part of small intestines. The inner lining of organs is observed on monitor. Tissues can be removed during an endoscopy and also used for detection of *H. pylori* presence.[15]

Test for presence of *H. pylori*

Serological tests, breath analysis and stool analysis can be made for the detection of H.pylori, which is a dominant reason for the development of peptic ulcerations.[16]

MANAGEMENT OF PEPTIC ULCER

A number of approaches have been made for the management of peptic ulcers using chemically synthesized drug or product containing herbal ingredients. Some of them are discussed below;

Chemically synthesized antiulcer drugs

1. **For reduction volume of gastric acid**
   a. Antihistamines such as; cimetidine, ranitidine, famotidine, roxatidinen and JB9322[17]
   b. Proton pump inhibitors such as; omeprazole, lansoprazole, pantoprazole, rabeprazole, esomeprazole, dexlansoprazole
   c. Anticholinergics such as; pirenzepine, propantheline, oxyphenonium
   d. Prostaglandin analogue such as; misoprostol
2. **For neutralization of gastric acid**
   a. Systemic such as; sodium bicarbonate, sodium citrate
   b. Nonsystemic such as; hydroxide/ carbonate/ trisilicates containing magnesium, aluminum or calcium
3. **For protection of gastric mucosa:** such as; sucralfate, colloidal bismuth subcitrate
4. **Use of antimicrobial agents for treatment of *H. pylori* infection:** such as; amoxicillin, clarithromycin, metronidazole, tinidazole, tetracycline[2]

Reported Plants from Cucurbetaceae Family with Ulcer Healing Property

Wilbrandia ebracteata

The antiulcer potential of *Wilbrandia ebracteata* leaves was investigated using hydro-methanol extract against ethanol induced ulceration and indomethacin induced gastric damage in mice. The results indicate significant ulcer protective potential in ethanol induced ulceration as the total area of lesions were very less with respect to control group , but was ineffective in indomethacin-induced gastric damage model.[18]

Gynostemma pentaphyllum

Rujjanawate et al (2003) evaluated butanol fraction (GPB) of G*ynostemma pentaphyllum* for antiulcer activity using indomethacin, ethanol and stress induced ulcer in rat, and the result revealed that the butanol fraction of G*ynostemma pentaphyllum* possess significant gastroprotective potential as the mucous protective effect along with reduction in gastric acid volume was observed.[19]

Cucurbita pepo

Sarkar et al (2008) evaluated aqueous extract of *Cucurbita pepo* fruit pulp for ulcer healing potential against the drug (Aspirin) induced ulcers in albino rats. The result shows that pretreatment of *Cucurbita pepo* fruit pulp extract significantly reduced ulcerative index in animals, and established its antiulcer activity.[20]

Cucumis sativum

Gill et al (2009) evaluated the antiulcer activity of methanolic extract of *Cucumis sativum* seeds against the pyloric ligation and water immersion stress induced ulcer model in rats. The reduction of gastric acid volume, free acidity and total acidity was observed. The antiulcer activity was supposed due to its antioxidant property.[21]

Trichosanthes cucumerina

The antiulcer activity of hot water extract of *Trichosanthes cucumerina* have also been investigated and established. *Arawwawala* et al (2010) evaluated hot water extract of *Trichosanthes cucumerina* for antiulcer potential against indomethacin induced gastric ulcer and alcohol-induced gastric ulcer in wistar rats and observed that the extract possess significant ulcer healing property as compared to standard drug cimetidine. They observed protective effect on gastric mucosa along with acidity of gastric secretion and conclude the remark about its antiulcer potency.[22]

Momordica cymbalaria

Dhasan et al (2010) evaluated different extracts of unripe fruits of *Momordica cymbalaria* for antiulcer activity in animal models, against aspirin, alcohol and pyloric induced ulcerations. The result showed that the methanolic extract of unripe fruits of *Momordica cymbalaria* significantly reduced the volume of gastric acid secretion, free acidity, total acidity and ulcer index, while pH of the gastric medium was found to be increased.[23]

Cholchinchina momordica

Kim et al (2010) evaluated dried ripe seeds of *Cholchinchina momordica* for antiulcer effect in rats using acetic acid induced gastric ulceration model, and found ulcer healing property. The result suggested that the dried ripe seeds of *Cholchinchina momordica* accelerate the healing process by up-regulation of vascular endothelial growth factor (VEGF) and angiogenesis.[24]

Coccinia grandis

The ethanolic and aqueous extract of *Coccinia grandis* leaves were investigated for antiulcer potential against the pylorus ligated ulcer in rats & data revealed that ulcer healing capacity of ethanol extract were nearer to the standard drug omeprazole with respect to reduction in total acidity and mucosal defense.[25]

Benincasa hispida

The petroleum ether and methanol extract of *Benincasa hispida* fruits have been studied for ulcer protective effect in rats against

pylorus ligation induced ulcer and cold restraint stress induced ulceration and the result show significant reduction of ulcer in all models as compared to omeprazole treated group.[26] The similar activity was further confirmed using methanolic extract of seed part.[27]

Citrullus Colosynthis

Methanolic extract of *Citrullus Colosynthis* seeds have also been investigated for antiulcerogenic property in animals against pylorus ligation induced ulcer. It was suggested that the ulcer protective effects may be due to free radical scavenging property within the plant.[28]

Cucumis melo

Gill et al (2011) investigated methanolic extract of *Cucumis melo* seeds for antiulcer property against pyloric ligation, stress & NSAID's induced ulcers in various animal models. The result confirmed significant antiulcer activity of extract as inhibition of gastric volume; free acidity and total acidity were observed. The activity was supposed due to its high antioxidant activity.[29]

Momordica Charantia

Venu et al (2011) evaluated alcoholic & aqueous extract of *Momordica charantia* fruit at the dose of 200 mg/kg b.w. and 400 mg/kg b.w. separately, against pylorus ligation, aspirin and stress induced ulcer in rats. [30]

Lagenaria siceraria

In the same course of study antiulcer activity of methanolic extract of *Lagenaria siceraria* fruits was evaluated and established in animals against pylorus ligation, ethanol induced, NSAID'S induced and cold strain stress induced ulcers.[31]

Lagenaria vulgaris

Sathaye et al (2011) evaluated *Lagenaria vulgaris* fruit juice for antiulcer potential using NSAID'S induced ulcerations in albino rats. The result data illicit that the fruit juice of *Lagenaria vulgaris* exhibit better ulcer protective along with ulcer healing property as compared to β-carotene.[32]

Lagenaria breviflora

Ethanolic extract of *Lagenaria breviflora* fruit have also been studied for antiulcer activity in different animal models. The results revealed that the ulcer healing property of extract was dose dependent against cold restraint stress induced gastric ulcer. On the other hand the extract also exhibited significant ulcer protective effect in pyloric ligation induced ulcer, aspirin induced ulcer and alcohol induced ulcer models as compared to standard drug.[33]

CONCLUSION

Although the etiology of peptic ulceration is unknown but the various causative agents have been suggested and identified for that. The various approaches have also been established for their treatment using chemical agents, but are not strictly advisable due to their unwanted effects. The herbal products are continuously growing recognition as a safe remedy for treatment of various disorders including peptic ulcers. On behalf of above said studies, plants or herbs from Cucurbitaceae family can be recommended as a major source of drugs with antiulcer potential.

REFERENCES

1. Debjit B, Chiranjib, Tripathi K.K., Pankaj, Sampath Kumar K.P. Recent Trends of Treatment and Medicationpeptic Ulcerative Disorder. International Journal of PharmTech Research 2010; 2(1):970-980.
2. Tripathi K.D. Essentials of medical pharmacology, 6th edition Jaypee Brothers Medical Publishers (P) Ltd., New Delhi 2009 p.p.627-638.
3. Sibel K, Burak S, Ahmet S, Mehmet A, Polat K, Ali A, Hasan D. Effect of subclinical Helicobacter pylori infectionon gastric wall thickness: multislice CT evaluation. Diagnostic & Interventional Radiology 2008; 14:138-142.
4. Kasper DL, Braunwald E, Hauser SL, Jameson JL, Fauci AS, Longo DL. Principles of internal medicine 16th edition, McGraw Hill Medical Publishing Division, USA 2005 p.p.221-222.
5. Vella V. Drug-Induced Peptic Ulcer Disease. The Official Journal of The Malta College Of Pharmacy Practice 2005; 10:15-19.
6. Bujanda L. The Effects Of Alcohol Consumption Upon The Gastrointestinal Tract. The American Journal Of Gastroenterology 2000; 95:3374-82.
7. Walker V, Taylor WH. Cigarette Smoking, Chronic Peptic Ulceration, And Pepsin 1 Secretion. GUT A International Journal of Gastroenterology & Hepatology 1979; 20(11):971-976.
8. Levenstein S, Ackerma S, Kiecolt-Glaser J.K. Stress and Peptic Ulcer Disease. Journal of American Medical Association 1999; 281:10-11
9. Berkowitz N, Schulman L, McGregor C. Gastroparesis After Lung Transplantation : Potential Role In Complications Postoperative Respiratory. CHEST Official Publication Of Amarican College Of Chest 2011; 108:1602-07.
10. Kuwahara M, Hatoko M, Tanaka A, Iioka H, Katsunori N. The Surgical Treatment Of Radiation Induced Ulcers. Journal of Japan Society of Plastic and Reconstructive Surgery 2003; 23(1):21-27.
11. Vyawahare NS, Deshmukh VV, Godkari MR, Kagathara VG. Plants With Anti-Ulcer Activity. Pharmacognosy Review 2009; 3:108-115.
12. Brooks FP. The Pathophysiology Of Peptic Ulcer Disease. Digestive Diseases And Sciences 1985; 30(11):15S-29S.
13. http://www.bettermedicine.com/article/peptic-ulcer-1/symptomsAccessed October 1, 2011.
14. Sizemore AW, Rabbani KZ, Ladd A & Applegate KE. Diagnostic Performance of The Upper Gastrointestinal Series In The Evaluation of Children With Clinically Suspected Malrotation. Pediatr Radiol 2008; 38:518-528.
15. Allez M, Lemann M. Role of Endoscopy In Predicting The Disease Course In Inflammatory Bowel Disease. World Journal of Gastroenterology2010;16(21):2626-2632.
16. Yuan Y, Padol IT & Hunt RH. Peptic Ulcer Disease Today. Nature Clinical Practice Gastroenterology & Hepatology 2006; 3(2):80-89.
17. Palacios B, Montero J, Sevilla A & Roman LS. JB-9322, A New Selective Histamine H2-Receptor Antagonist With Potent Gastric Mucosal Protective Properties. Wish Journal of Pharmacology 1995; 115:57-66.
18. Gonzalez FG, Di Stasi LC. Anti-Ulcerogenic And Analgesic Activities Of The Leaves Of *Wilbrandia Ebracteata* In Mice. International Journal of Phytotherapy & phytopharmacology 2002; 9(2):125-134.
19. Rujjanawate C, Kanjanapothi D, Amornlerdpison D. The Anti-Gastric Ulcer Effect Of *Gynostemma Pentaphyllum* Makino. International Journal Of Phytotherapy & Phytopharmacology 2004; 11(5):431-435.
20. Sarkar S, Guha D. Effect Of Ripe Fruit Pulp Extract Of Cucurbita Pepo Linn. In Aspirin Induced Gastric And Duodenal Ulcer In Rat. Indian Journal Of Experimental Biology 2008; 46:639-645.
21. Gill NS, Garg M, Bansal R, Sood S, Muthuraman A, Bali M, Sharma PD. Evaluation Of Antioxidant and Antiulcer Potential of *Cucumis sativum L* Seeds Extract in Rats. Asian Journal Of Clinical Nutrition 2008;1(3):131-138.
22. Arawwawala LDAM, Thabrew MI, Arambewela LSR. Gastroprotective Activity Of *Trichosanthes Cucumerina* in Rats. Journal of Ethnopharmacology 2010; 127(3):750-754.
23. Dhasan PB, Jagadeesan M. Gastro Protective Activity Of *Momordica Cymbalaria* Fruits Against Experimentally Induced Gastric Ulcer in Rats. International Journal of Phytomedicine 2010, 2:385-391,
24. Kang mook jung, kim nayoung, kim bongcheol, kim joo-yun, lee bong-yong, park hyun jee, lee kyoung mi, lee seung hye, kim sang joon, jung chae hyun and song sung In. Enhancement Of Gastric Ulcer Healing And Angiogenesis By Cholchinchina Momordica Seeds Extract In Rats. Journal Of Korean Medical Sciences 2010; 25:875-881.
25. Manoharan P, Johnz S, Gollaz U, Dr.Thangathirupathi. Antiulcer Effect Of *Coccinia Grandis* On Pylorus Ligated (Albino) Rats. International Journal Of Pharma. Research And Development 2011, 2(5):001.
26. Rachchh AM, Jain SM. Gastroprotective Effect Of *Banincasa Hispida* Fruit Extract. Indian Journal Of Pharmacology 2011; 40(6):271-275.
27. Gill N, Bajwa J, Sharma P, Dhiman K, Sood S, Sharma PD, Singh B and Bali B. Evaluation Of Antioxidant And Antiulcer Activity Of Traditionally Consumed *Cucumis Melo* Seeds. Research Journal of Medicinal Plant 2011; 5(5):596-604.
28. Gill NS, Kaur S, Arora R and Bali B. Screening Of Antioxidant & Antiulcer Potential Of *Citrullus Colocynthis* Methanolic Seed Extract. Research Journal of Phytochemistry 2011; 5(2):98-106.
29. Gill NS, Bajwa J, Sharma P, Dhiman K, Sood S, Sharma PD, Singh B and Bali B. Evaluation Of Antioxidant And Antiulcer Activity Of Traditionally Consumed *Cucumis Melo* Seeds. Journal of Pharmacology And Toxicology 2011; 1-8.
30. Rao NV, Venu K, Sowmya U, Reddy GJ, Anirudha k. Evaluation Of Anti -Ulcer Activity Of *Momordica Charantia* in Rats. International Journal of Pharmacy and Biological Sciences 2011; 1(1):1-16.
31. Dr.Rao CV, Pandey A, Yadav V. Antiulcer Activity Of Methanolic Fruit Extract *Lagenaria Siceraria*(Mol.). International Journal Of Pharma. Research And Development 2011; 3(7):187-192.
32. Sathaya S, Mehta BV, Mohd SF, Amin DP. Preventive And Curative Effect Of *Lagenaria Vulgaris* in Nsaid's Induced Ulcer. International Journal Of Research In Pharmaceutical Sciences 2011; 2(1):88-91.
33. Onasanwo SA, Singh N, Saba AB, Oyagbemi AA, Oridupa OA, Palit G. Anti-Ulcerogenic And In Vitro Antioxidant Activities Of *Lagenaria Breviflora* (LB) Whole Fruit Ethanolic Extract In Laboratory Animals. Pharmacognosy Journal A Rapid Publication Journal 2011; 3(1):2-8 .