Review Article

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A REVIEW ON ACID PEPSIN DISEASES: HISTORY, EPIDEMIOLOGY, ANTACIDS AND PLANT-BASED ALTERNATIVES

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ABSTRACT

Today estimate that about 80% of people in growing nations still believes on traditional medicine based chiefly on species of plants and animals for their basic well-being caution. Herbal medicines are presently in demand and their acceptance is growing day by day. About 500 plants with medicinal use are mentioned in ancient literature and around 800 plants have been used in indigenous systems of medicine. The World Health Assembly (WHA) has acquired several proposals depicting awareness to the aspect that a huge segment of the community in many growing nations still hopes on traditional medicine. Addition of verified traditional medicaments into national drug policies and regulatory measures is proposed. Understanding of their clinical, pharmaceutical and commercial value is still emerging, although this changes extensively between nations. This manuscript aims at a systematic brief review on few herbal drugs/ dietary nutrients and their extracts having potent action (antiulcerogenic, gastroprotective and anti-inflammatory activity) on gastric disorders and their published data on effectiveness of these diseases. Literature (pharmacological investigations) for concerning medicinal plants and their chemical constituents/extracts were compiled from major databases and academic publishers, such as PubMed, Elsevier, etc. Various numbers of medicinal plants and their extracts are reported to have anti-ulcer activity, gastro-protective activity, and antibacterial activity comparable to the existing treatment (antiulcer and antacids drugs) or sometimes even better in potency. Studies and screening of easily available plants with a well-defined strategy may help to develop effective new drugs or treatment giving permanent relief against acid pepsin disorders without side effect.

Keywords: Acid-pepsin disorders, Traditional medicines, *Amlapitta,* Gastro-protective.

INTRODUCTION

Faulty dietary factors, living style and sequel of faulty drug or drug abuse habits lead to the gastric complaints like heartburn, reflux of food taken, abdominal pain , loss of appetite , nausea and vomiting. These gastric complaints mimic the symptoms of *Amlapitta*[1]. It is very difficult to correlate *Amlapitta (~acidity)* with a single disease of modern science. Etiopathology and symptoms of GERD, Gastritis and Non ulcer dyspepsia can be correlated with *Amlapitta*. Gastro Esophageal Reflux Disease (GERD) is a complex disorder caused by the reflux of gastric contents into the esophagus either with or without complications. It negatively affects the quality of life and leads to serious complications like Barret's esophagus, esophageal strictures and adenocarcinoma [2]. GERD is accompanied with increased frequencies of inadequate activity and skipped work, introducing an economic load for both preventive medicine systems and business person alike [3].

Epidemiology & factors responsible for emergence

In the reflux group, irritable bowel syndrome and dyspepsia were the highest functional disorders. In a pan-Indian study on IBS, 37% of 1,301 patients reported heartburn. In a previous study from Mumbai, the prevalence of dyspeptic symptoms was 30%, while among subjects with IBS, the prevalence of dyspepsia was 58% [4].The reason for the increasing prevalence of GERD is not entirely clear, but it appears to be correlated with the increasing prevalence of obesity in many countries and, perhaps, to other dietary factors[5]. Recent studies indicate that its prevalence in India ranges between 8-20% which is comparable to that in the west[6]. This study of India reports inconsistent association with BMI, age, sex, alcohol, smoking and diet. On the other hand, other studies have found female gender[7], large fatty diet[8] shorter dinner-to- bed time[9] and younger age[10] to be significant risk factors. *H.pylori* infection is virtually always associated with a chronic active gastritis. *H. pylori* organisms grow in the mucus secreting cells of the stomach lining and create ulcers or erosions or inflammation in gastric mucosa. Aspirin and other non-steroidal anti-inflammatory drugs like Diclofenac, Ibuprofen etc. inhibits cyclo- oxygenase, decreases prostaglandin E and decreases mucosal blood flow resulting in damage of gastric or duodenal mucosa. Pepsin and hydrochloric acid cause damage to the stomach or duodenum, if the stomach's protective system is altered or damaged [11]. Till now there are no clear findings of involvement of *H.Pylori* infection in Non-ulcer dyspepsia [12].

Historical background

The real references in Ayurveda about this clinical condition seems available, from the period of *Samhithas* itself. *Acharya Charaka* has not mentioned *Amlapitta* as a separate entity, but the treatise is contributing with many scattered references of *Amlapitta* by the name. *Sushruta* has mentioned a condition "*Amlika*" (resulting from excessive use of *Lavana*(~salt) which resembles one of the symptoms of Amlapitta[13]**.** *Kasyapa* explained the variants of *Amlapitta* as per the *doshas*, with the peculiarity in the symptoms in an enhanced manner [14]**.** *Madhava nidana* is the first text available which gives importance to *Amlapitta* and describes its aetio-pathogenesis and symptoms in detail[15].

Symptoms and diagnosis

Upper abdominal pain which may or may not be related to food, Gastro-oesophageal regurgitation and heartburn, Anorexia, nausea, vomiting, Early repletion or satiety after meals, A sense of abdominal distension or bloating and flatulence[16]. The diagnosis of dyspepsia is challenging because patients often exhibit changing symptoms and because characterization of the symptoms provides little information about the nature of the underlying physiologic abnormality[17]. Diagnosis of acidic disorders is mainly based on the clinical features, histopathology. The initial investigation may include routine hematological (full blood count and ESR) and biochemical (urea and electrolytes, liver function tests, serum calcium, phosphate) tests. Iron deficiency anemia suggests mucosal blood loss, whereas vit.B_{12} deficiency results from small intestinal, gastric or pancreatic disease. Severe vomiting or diarrhea elicits electrolyte disturbances, acid-base abnormalities and elevated blood-urea nitrogen. Luminal contents can be examined for diagnostic clues. Stool samples are cultured for bacterial pathogens or examined for leucocytes or parasites. Gastric Juice Analysis gives the concentration of the acid in gastric juice. Hyperchlorhydria, Hypochlorhydria and Achlorhydria can be easily diagnosed by this test. Duodenal Aspirates can be examined for parasites or cultured for bacterial overgrowth. Oesophageal pH testing is done for refractory symptoms of acid reflux. Urease test, ELISA test, Breath test and stool antigen test are performed for the diagnosis of *H. pylori*. Endoscopy evaluates the oesophagus, stomach and duodenum.

ANTIULCEROUS DRUGS [18] AND THEIR ADVERSE EFFECTS

Description of various treatment groups of acid pepsin diseases is explained in table 1.
Adverse events associated with antacids are dose-related. Large doses of calcium-containing antacids can cause the milk-alkali syndrome, which consists of hypercalcemia, renal insufficiency and metabolic alkalosis. Magnesium-containing antacids can cause diarrhea if administered alone and may lead to hypermagnesemia in patients with renal insufficiency. Aluminum-containing antacids can cause encephalology and osteomalacia in end-stage renal patients and calcium carbonate is the preferred antacid in this population. Although specific interactions with medications are unusual, all antacids can produce drug interactions by changing gastric or urinary pH by altering rates of absorption, bioavailability, renal elimination and drug dissolution, or by reducing gastric acid hydrolysis of drugs [19]. The side effects of most common used treatment proton pump inhibitors are: Headache, Diarrhea, Constipation, Abdominal pain etc. PPIs may increase the risk of *clostridium difficile* infection of the colon. Long-term use may increase the risk of osteoporosis – related fractures of the hip, wrist, or spine. Prolonged use also reduces absorption of vitamin B12 and causes hypomagnesaemia Analysis of patients taking PPIs for long periods of time showed an increased risk of heart attacks[20]**.**

Eradication of *H. pylori* is almost impossible even by administrating 'triple therapy', which is a combination of proton pump inhibitor and antibiotics. One of the major reasons for the *H. pylori* treatment failure is the development of drug resistance. In India, approximately 85% of clinical strains of Kolkata are resistant to 8 mg/l metronidazole. Similarly, 91 and 96% of H. pylori strains from Mumbai and Hyderabad respectively showed resistance to clarithromycin; 73% of Mumbai and 80% strains of Hyderabad are resistant to amoxicillin. Frequent emergence of antibiotic resistance in microbial pathogens encourages the use of natural agents as alternative therapies [21].

Relief offered by present treatment is mainly symptomatic & for short time. Hence, there is a need to search and access the effect of the natural drug materials.

Articles published in different peer reviewed journals were analyzed. Pubmed, Academic journals, Elsevier, Google scholar, Google were searched with specific keywords along with print journals, reports and some textbooks. Ayurveda or plants or herbs or *Shatavari* or *Amalki* or *Shunth*i or *Elaichi* or *Vamshlochan* or *Dalchini* or *Gokshur* or *Patol* or *Kushmand* or *Pippali or Chandan* or *Dhaniya* or *Tejpatra* or *Yashtimadhu* or Traditional medicines or Alternative medicines or GERD or acid pepsin or dyspepsia or gastritis or gastroprotective activity or anti-inflammatory or anti *H.Helicobacter pylori* or anti ulcerous or anti secretagogue or experimental, biochemical and histological study as title, abstract and keywords. There was no restriction in language and publication date. Medicinal plants, Herbs and dietary nutrients and spices that have been evaluated by various researchers to achieve a favorable outcome in gastric diseases have been shown to possess these activities (antiulcer effects, gastro-protective, Anti *H.pylori* activity). (Table 2)

DISCUSSION

Because of the worldwide health problem that gastric diseases represent, it is necessary to invent new drug and advancement that allow better control on gastric disorders. In this review, we have compiled the pharmacological information on fourteen medicinal plants taking account of their properties useful in acid pepsin diseases. The detailed information on the drugs having potent action on gastric disorders has been summarized in Table 2. Amongst the various groups of phytochemical constituents, in majority, the methanol extracts have been found effective gastro protective, antiulcer activity, anti *H.pylori* effect. It is not possible to single out the most effective plant or phytochemical constituent. Use of plant extracts is increasing to treat various diseased states, with somewhat little understanding in respect of their modes of action. Moreover, pharmacological analysis on these medicinal plants and phytochemical component/ingredients may provide practical help for the development of new antitulcerous, gastroprotective drugs. With the help of modern science, the efforts should be made to discover the active ingredients from medicinal plants which still have to be isolated. Multidimensional approach should be followed i.e. searching should be for multiple compounds acting synergistically & those hit multiple targets in different pathways instead of single drug/component. The etiologies of these diseases are not clearly known. It results probably due to imbalance between aggressive (acid, pepsin, bile, & *H. pylori*) and the defensive (gastric mucus and bicarbonate secretion, prostaglandins, nitric oxide, innate resistance of mucosal cells) factors.

The significance of *H. pylori* infection as a supporter to ulcer generation and regression has been identified. Commonly in gastric ulcer, acid release is standard or minimal. In duodenal ulcer, acid release is high in 50% of patients but adequate in rest 50% [44]. Even the standard routine rate of acid secretion may be the basis of ulceration in the ruptured mucosa when some gastro-protective elements are disoriented. The current manner to command on gastric ulceration is to restrict gastric acid secretion, to support gastro-immunity, limit necrobiosis, and trigger epithelial cell multiplication for productive repairing [45].

An interpretation of the process and regulation of gastric acid secretion will clarify/explicate the position of antisecretory drug maneuver -

- The terminal enzyme H^+K^+ATPase (proton pump) which secrets H^+ ion in the apical canaliculi of parietal cells can be

activated by histamines , Ach , and gastrin acting via their own receptors located on the basolateral membrane of these cells.

- Out of the three physiological secretogogues - Histamine (acting through H2 receptors) plays the dominant role, because the other two (Gastrin and Ach) act directly and to the greater extent indirectly by releasing histamine from paracrine entero-chromaffin like cells (histaminocytes) located in oxyntic glands.
- Prostaglandins have been ascribed a "cytoprotective" role in the gastric mucosa by augmenting mucus and bicarbonate secretion, as well as other actions. PGE2, produced by gastric mucosa, inhibits acid secretion by opposing cAMP generation (in parietal cells) and gastrin release (from antral cells)[44].

Aspirin produces direct erythrogenic effect and laminal injury by interrupting with prostaglandin synthesis [46] escalate acid secretion by escalating the H^+ ion shift/ back outflow of H^+ ions [47].

Because of antihistaminic, anticholinergic and antisecretory effects, these extract exhibit gastro-protective action against stress-induced ulceration which may be an indication of its effect on prostaglandin production[48.] Also in experiments performed on extracts of single drugs, there found reduced values of lesion index as compared to the control group suggesting its potent cyto-protective effect which indicates towards gastro-immunity.

After treatment with mixture of Ayurvedic medicines (*Glycyrrhiza glabra, Terminalia chebula, Piper longum,* and *Shanka bhasma*), secretary status of Brunner's glands and β-glucuronidase enzyme activity improved which indicate toward protection against duodenal ulcer[49].

At present, researchers are searching for bioactive compounds to treat bacterial infections due to an increase in drug resistance. Numerous reports have been published on various natural compounds and food supplements that inhibit *H. pylori* growth [50], adhesion [51] or toxin secretion [52] and the aim of these studies was to explore an existing natural compound, which may act against *H. pylori*. For example, results of study on piperine [32] suggest that due to the suppression of the biosynthetic regulator gene *flhA* (integral membrane component of the export apparatus) and flagellar hook gene *flgE* because of piperine treatment may lead to the reduction in motility confirmed by the motility test. Due to decreased motility of *H. pylori*, the organism may be less attracted towards gastric epithelial cells, which results in the less adhesion compared with the untreated bacteria. Daily consumption of black pepper, which is comprised of 5–9% piperine, reduces one's chance of infection and of developing gastric cancer caused by *H. pylori*. Application of antibiotic coupled with antioxidant treatment may be very useful in controlling the pathogen growth and associated inflammation. In study on *Amalaki*, Ethanolic extract of E. officinalis is highly effective in controlling growth of H. pylori in vitro with MIC ranging from 0.91 to 1.87 µg/ µl. The TLC separation followed by detection spray indicates that the bioactive spot is having mixed properties of both phenolics and essential oils. The extract also retained high level of antioxidant properties that makes it suitable for therapeutic use against gastric ulcer[21].

H2 antagonists block histamine induced gastric secretion. The only significant in vivo action of H2blockers is marked inhibition of gastric secretion. All phases (basal, psychic, neurogenic, gastric) of secretion are suppressed more completely. Secretary responses to not only histamine but all other stimuli (Ach, gastrin, insulin, alcohol, food) are attenuated. This reflects the permissive role of histamine in amplifying responses to other secretogogues [53]. Plant extracts are some of the most attractive sources of new drugs and have been shown to produce promising results in the treatment of gastric ulcers [54].

According to the climatic and geographic conditions, special medicinal plants grow and many of them have unique medicinal properties. Today estimate that about 80% of people in developing countries still rely on traditional medicine based largely on species of plants and animals for their primary health care. About 500 plants with medicinal use are mentioned in ancient literature and around 800 plants have been used in indigenous systems of medicine [55].

The World Health Assembly (WHA) has acquired several proposals depicting awareness to the aspect that a huge segment of the community in many growing nations still hopes on traditional medicine. Addition of verified traditional medicaments into national drug policies and regulatory measures is proposed. Understanding of their clinical, pharmaceutical and commercial value is still emerging, although this changes extensively between nations [56].

TABLE 1: DIFFERENT GROUPS OF ANTIULCEROUS DRUGS AND THEIR DESCRIPTION WITH SUITABLE EXAMPLES

Description	Group	Examples
Neutralization of gastric acids	Antacids	Systemic-.Sodium bicarbonate, Sodium citrate Non-Systemic-.Magnesium hydroxide, Magnesium trisilicate, Aluminium hydroxide gel, Magaldrate
Reduction of gastric acid secretion	Prokinetic agents	Metoclopramide and Domperidone
	H_2 Receptor Antagonists	Cimetidine Ranitidine Famotidine
	Proton Pump Inhibitor (PPI)	Omeprazole Lansoprazole Pantoprazole Rabeprazole
	Anti-Cholinergics	Pirenzipine
	Prostaglandin Analogues	Misoprostol
Anti- *Helicobacter pylori* drugs	Amoxicillin, Metronidazole, Tetracycline, Clarithromycin and Bismuth compounds.	
Ulcer protectives	Sucralfate, colloidal bismuth subcitrate	

TABLE 2: DESCRIPTION OF PLANTS WITH PROVEN PHARMACOLOGICAL ACTION OF THEIR EXTRACTS

Plants	Parts used	Extract / Active principle	Proven pharmacological action
Elettaria cardamomum (*Elaichi*)	Fruit	Methanolic extract	Gastro protective[22]
Bambusa arundinacea (Vamshlochana)	Leaves	Methanol extract	Antiulcer activity, Anti-Inflammatory effect[23]
Cinnamomum Zeylanicum (Dalchini)	Bark	Ethanol methylene chloride extracts	Anti-secretagogue, antiulcer [24] anti-inflammatory & wound Healing properties[25] Inhibitory effect on *Helicobacter pylori* & free urease[26]
Terminalia chebula (*Haritaki)*	Fruit	Water extract, hydroalcoholic extract	Antibacterial activity[27], Anti-ulcerogenic activity[28]
Emblica officinalis (*Amlaki*)	Fruit Pulp	Methanolic extract ethanolic extract	Antiulcerogenic effect[29], Anti-*Helicobacter pylori*[21]
Tribulus terrestris (*Gokshur*)	Fruit	Methanolic extract	Analgesic and anti-inflammatory[30]
Trichosanthes dioica (*Patol*)	Leaves	Methanolic extract	Antiulcer activity[31]
Piper nigrum (Pippali)	Fruit	Piperine	Inhibitory action on *H.pylori* growth and adhesion[32]
Santalum album (*Chandana*)	Stem	hydro-alcoholic extract	Antibacterial activity against *H. pylori*[33], anti-ulcer activity[34]
Coriandrum sativum (Dhaniya)	Seeds	Hydroalcoholic extract	Anti-ulcer activity against stress and aspirin-induced ulcer[35]
Cinnamomum tamala (*Tejpatra*)	Leave	-	Gastroprotective activity[37]
Glycyrrhiza glabra (*Yashtimadhu*)	Root	Aqueous extracts	Antiadhesive effects against *H.Pylori*[38]
Asparagus racemosa	Fresh Roots	Methanolic extract	Gastro-duodenal ulcer protective[39] & anti-ulcer activity[40]
Zingiber officinale (*Sunthi*)	Rhizome	Aqueous extract phenolic acids	*H.pylori* inhibitory activity[41] anti-ulcer[42], gastro protective[43]

CONCLUSION

Acid-pepsin disorders are a burning issue of today's society with palliative cure only. Uses of chemical-based medicine have various local & systemic side effects and on longer use exaggeration of symptom of existing and precipitation of new diseases occurs. Herbal medicines which formed the basis of health care throughout the world since the earliest days of mankind are still widely used and have considerable importance in international trade. Search for natural drug possess easily available, cost effective, high efficacious treatment with minimal side effect and permanent relief of disease.

REFERENCES

1. Vaidya lakshmipati shastri. Yog ratnakar Vidyotini hindi teeka. Chaukhamba prakashan Varansi; 2015. p. 237.
2. Wiklund I. Review of the quality of life and burden of illness in gastroesophageal reflux disease. Dig Dis 2004 Feb [cited 2019 May 20]; 22(2): 108–14. Available from: https://www.researchgate.net/publication/8330748_Review_of_the_Quality_of_Life_and_Burden_of_Illness_in_Gastroesophageal_Reflux_Disease
3. Camilleri M, Dubois D, Coulie B, et al. Prevalence and socioeconomic impact of upper gastrointestinal disorders in the United States: results of the US Upper Gastrointestinal Study. Clin Gastroenterol Hepatol. 2005 Jun [cited 2019 May 20];6(3):543–552. [PubMed])) Available from: https://www.sciencedirect.com/science/article/pii/S1542356505001539
4. Shobna J. Bhatia & D. Nageshwar Reddy & Uday C. Ghoshal & V. Jayanthi et.al., Epidemiology and symptom profile of gastroesophageal reflux in the Indian population : Report of the Indian Society of Gastroenterology Task Force, Indian J Gastroenterol 2011 Jul [cited 2019 May 20]; 30(3):118–127. Available from: https://www.academia.edu/13229292/Epidemiology_and_symptom_profile_of_gastroesophageal_reflux_in_the_Indian_population_Report_of_the_Indian_Society_of_Gastroenterology_Task_Force
5. Worldgastroenterology.org [homepage on internet]. Milwaunkee: World Gastroenterology Organisation, [cited 2019 May 22]. Available from: http://www.worldgastroenterology.org/wgo-foundation/wdhd/wdhd-2015
6. Kumar S, Shivalli S. Prevalence, Perceptions and Profile of Gastroesophageal Reflux Disease in a Rural Population of North Bihar. Natl J Community Med. 2014 Jun [cited 2019 May20]; 5(2):214-218. Available from: http://njcmindia.org/uploads/5-2_214-2181.pdf
7. El-Serag HB, Satia JA, Rabeneck L. Dietary intake and the risk of gastrooesophageal reflux disease: a cross sectional study in volunteers. Gut. 2005 Jan [cited 2019 May 20]; 54(1): 11-17. Available from:
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1774352/
9. Du J, Liu J, Zhang H, Yu CH, Li YM. Risk factors for gastroesophageal reflux disease, reflux esophagitis and nonerosive reflux disease among Chinese patients undergoing upper gastrointestinal endoscopic examination. World J Gastroenterol. 2007 Dec [cited 2019 May 20];13(45):6009–15. Available from: https://www.wjgnet.com/1007-9327/full/v13/i45/6009.htm
10. Fujiwara Y, Machida A, Watanabe Y, et al. Association between dinner-to-bed time and gastro-esophageal reflux disease. Am J Gastroenterol. 2005 Dec [cited May 22];100(12):2633–6. Available from:
11. https://www.researchgate.net/publication/7378731_Association_Between_Dinner-to-Bed_Time_and_Gastro-Esophageal_Reflux_Disease
12. Sushil Kumar et al. Population based study to assess prevalence and risk factors of gastroesophageal reflux disease in a high altitude area. Indian J Gastoenterology. 2011Dec [cited 2019 May 20]; 30(3):135-143. Available from: https://www.academia.edu/10253230/Population_based_stu

dy_to_assess_prevalence_and_risk_factors_of_gastroesophageal_reflux_disease_in_a_high_altitude_area
13. Braunwald E, Wilson JD, Kasper DL, Hauser SL, Longo DL,Fauci AS,Jameson JL, Harrison's Principles of Internal Medicine. 16th ed., vol.2. New York: McGraw Hill Publication. p. 1747.
14. S.J.O. Veldhuyzen Van Zanten. The role Helicobacter pylori in non ulcer dyspepsia. Aliment Pharmacol Ther 2003 Oct [cited 2019 may 20];11(suppl. 1),63-69. Available from: https://onlinelibrary.wiley.com/doi/epdf/10.1046/j.1365-2036.11.s1.15.x
15. Acharya Y.T., Sushruta Samhita of Maharshi Sushruta with Nibandha Sangraha teeka of Dalhana Sutrasthana42/9.
16. Vriddhagivaka, Kashyapa Samhita, edi by P.V.Tiwari, KhilaSthana 16/15, Chaukhamba Vishwabhari, Varanasi, 2008, p. no. 336
17. Mahamatishri MadhavakaraaVirachit Madhava Nidanam, "Madhukosha"- Vyakhya, edited by Ayurvedacharya Shriyadhunandanopadhyaya, Part second 51, 12, Varanasi: Chaukhamba Sanskrit Sansthan, 9th edition reprint 2000, page no 667
18. John A.A. Hunter, Nicholas A.Boon, Nicki R. Colledge, Brian R.Walker, Davidson's Principles and Practice of Medicine,20th edition, Churchill Livingstone Elsevier,reprint2006, p.891.
19. Lori M. Dickerson, Pharm.D., and Dana E. King, M.D. Medical University of South Carolina, Charleston, South Carolina. Am Fam Physician. 2004 Jul [cited 2019 May 20]; 70(1):107-114. Available from: https://www.aafp.org/afp/2004/0701/p107.html#afp20040701p107-b22
20. K.D. Tripathi, Essentials of Medical Pharmacology, 6th Edition, Jaypee brothers medical publishers, New Delhi ,reprint 2009, p.628-629.
21. Alex Mejia, Walter K Kraft. Acid peptic diseases: pharmacological approach to treatment, Expert Rev Clin Pharmacol. 2009 May [cited 2019 May 20]; 2(3): 295–314. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3149864/
22. Proton Pump Inhibitors(PPIs) Drug Class, cited at : http://www.medicinenet.com/protonpump_inhibitors/article.htm , on 14 july,2017 at 7: 27 pm
23. Shubhi Mehrotra et.al. Anti-Helicobacter pylori And Antioxidant Properties Of Emblica Officinalis Pulp Extract: A Potential Source For Therapeutic Use Against Gastric Ulcer. J. Med. Plant. Res. 2011 Jun [cited 2019 May 20]; 5(12): 2577-2583. Available from: http://www.academicjournals.org/article/article1380720510_Mehrotra%20et%20al.pdf
24. Jamal A et.al ,Gastroprotective effect of cardamom, Elettaria cardamomum Maton. fruits in rats. J Ethnopharmacol. 2006 Jan [cited 2019 May 20]; 103(2):149-53. Available from: https://www.ncbi.nlm.nih.gov/pubmed/16298093.
25. M Muniappan, T Sundararaj. Anti-inflammatory and antiulcer activites of Bambusa arundinacea. Journal of Ethnopharmacology. 2003 Nov [cited 2019 May20]; 88(2-3):161-7. Available from: https://www.researchgate.net/publication/10576972_Anti-inflammatory_and_antiulcer_activites_of_Bambusa_arundinacea
26. Saleh Alqasoumi. Anti-Secretagogue And Antiulcer Effects Of 'Cinnamon' CinnamomumZeylanicum In Rats. Journal Of Pharmacognosy And Phytotherapy. 2012 Jul [cited 2019 May 20]; Vol. 4(4): 53-61. Available from: http://www.academicjournals.org/article/article1379686358_Alqasoumi.pdf
27. Priyanga Ranasinghe et.al , Medicinal properties of 'true' cinnamon (Cinnamomum zeylanicum): a systematic review, BMC Complementary and Alternative Medicine. 2013 Oct {cited 2019 May20];13:275. cited : https://bmccomplementalternmed.biomedcentral.com/articles/10.1186/1472-6882-13-275
28. Minatabak MinaTabakaRobertArmonbIshakNeeman Cinnamon Extracts' Inhibitory Effect on Helicobacter pylori. Journal Of Ethnopharmacology. 1999 Nov [cited 2019 May20]; 67(3):269-277. cited:http://www.sciencedirect.com/science/article/pii/S0378874199000549?via%3Dihub
29. F Malekzadeh et.al. , Antibacterial activity of black myrobalan (Terminalia chebula Retz) against Helicobacter pylori, International Journal of Antimicrobial Agents. 2001 Jul [cited 2019 May 20]; 18(1):85-88. Available from: http://www.sciencedirect.com/science/article/pii/S0924857901003521
30. Praveen Sharma et al , Antiulcerogenic Activity Of Terminalia Chebula fruit In Experimentally Induced Ulcer In Rats. Journal Pharmaceutical Biology. 2011 Feb [cited 2019 May20]; 49(3): 262-268. Available from: http://www.tandfonline.com/doi/full/10.3109/13880209.2010.503709
31. K. Sairam et.al. Antiulcerogenic Effect Of Methanolic Extract Of Emblica Officinalis: An Experimental Study. Journal Of Ethnopharmacology. 2002 Jan {cited 2019 May 20]; 82(1):1-9. Available from: https://www.researchgate.net/profile/Madhura_Babu/publication/11218340_Antiulcerogenic_effect_of_methanolic_extract_of_Emblica_officinalis_An_experimental_study/links/0f31752faa1f479f61000000.pdf
32. Shafique Ahmad, Javed Akhtar Ansari, Mohd. Jamil, Qamruzzama Qamruzzama. Wound healing potential of methanolic extract of tribulus terrestris l. Fruits. Journal of Drug Delivery & Therapeutics. 2012 Dec [cited 2018 Mar 06]; 2(6):71-74. Available from: http://jddtonline.info/index.php/jddt/article/view/326
33. Devansh Mehta, Anuj Kumar Sharma. Anti-ulcer activity in Trichosanthes Dioica (Roxb.): A Histopathology Report Analysis. Am J of Pharm Tech Res. 2015 Dec [cited 2019 May 20]; 6(1): 178-196. Available from: https://www.trmwriters.com/images/academic-writing-samples/Research%20article%20on%20Histopathology%20report%20analysis%20of%20TD.pdf
34. Nagendran Tharmalingam, Sa-Hyun Kim, Min Park, Hyun Jun Woo, Hyun Woo Kim, Ji Yeong Yang, Ki-Jong Rhee, and Jong Bae Kim. Inhibitory Effect Of Piperine On Helicobacter pylori Growth And Adhesion To Gastric Adenocarcinoma Cells. Infect Agent Cancer. 2014 Dec [cited 2019 May 20]; 9:43. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4290101/
35. Ochi T, Shibata H, Higuti T, Kodama KH, Kusumi T, Takaishi Y. Anti-Helicobacter pylori Compounds From SantalumAlbum. J Nat Prod. 2005 Jun [cited 2019 May 20];68(6):819-24. Available from : https://www.ncbi.nlm.nih.gov/pubmed/15974602
36. NazeerAhmed et al. Anti-Ulcer Activity of Sandalwood (Santalum Album L.) Stem Hydroalcoholic Extract In Three Gastric-Ulceration Models of Wistar Rats. Bol Latinoam Caribe Plant Med Aromat. 2013 Jan [cited 2019 May 20]; 12(1): 81 – 91. Available from: https://www.researchgate.net/publication/270506592_Anti-ulcer_Activity_of_Sandalwood_Santalum_album_L_Stem_Hydroalcoholic_Extract_in_Three_Gastric-Ulceration_Models_of_Wistar_Rats
37. Role Of Coriandrum Sativum In Gastric Ulcer, Lambert Academic Publishing (2012-09-03) , Available from: https://www.lap-publishing.com/catalog/details//store/ru/book/978-3-659-23277-0/role-of-coriandrum-sativum-in-gastric-ulcer
38. I.A.Al-Mofleh, A.A.Alhaider, J.S.Mossa, M.O.Al-Sohaibania, S.Rafatullah, S.Qureshi. Protection Of Gastric

Mucosal Damage By CoriandrumSativum L. Pretreatment In Wistar Albino Rats. Environmental Toxicology And Pharmacology. 2006 Jul [cited 2019 May 22, 2019]; 22(1): 64-69 , Available from: http://www.sciencedirect.com/science/article/pii/S1382668905002085

39. M. Bavanieswaran, S.Surendran, M.Vijayakumar, S.K.Ojha, A.K.S.Rawat, Ch.V.Rao. Gastroprotective Activity of CinnamomumTamala Leaves On Experimental Gastric Ulcers In Rats. Journal Of Ethnopharmacology , 128(2), 24 2010 Mar [cited 2019 May 22]; 128(2): 537-540 , Available from:http://www.sciencedirect.com/science/article/pii/S037887411000053X
40. Nicole Wittschier et al. Aqueous Extracts And Polysaccharides From Liquorice Roots (Glycyrrhiza Glabra L.) Inhibit Adhesion Of Helicobacter pylori To Human Gastric Mucosa. Journal Of Ethnopharmacology. 2009 July [cited 2019 May 22]; 125(2): 218-223. Available from: https://www.researchgate.net/ profile/Andreas_Hensel/publication/26675737_Aqueous_extracts_and_polysaccharides_from_Liquorice_roots_Glycyrrhiza_glabra_L_inhibit_adhesion_of_Helicobacter_pylori_to_human_gastric_mucosa/links/5693a30308aee91f69a8400d.pdf
41. K sairam, S Priyambada, N.CAryya, R. K goel. Gastroduodenal Ulcer Protective Activity Of Asparagus Racemosus: An Experimental, Biochemical And Histological Study. Journal of Ethnopharmacology. 2003 May [cited 2019 May 22]; 86(1):1-10. Available from: http://www.sciencedirect.com/science/article/pii/S0378874102003422
42. Kasif Ahammed Anti-Ulcerative Efficacy Of Methanolic Root Extract Of Asparagus Racemosus (Mear) On Gastric Ulcer Has Similar Effect In Albino Rats When Compared With Ranitidine Hydrochloride, A H2-Receptor Antagonist. Int J Pharm Bio Sci. 2015 Apr-Jun [cited 2019 May22]; 5(2): 3019-313. Available from: http://ijpbs.com/ijpbsadmin/upload/ijpbs_55abc7fe97755.pdf
43. Siddaraju M. Nanjundaiah, Harish Nayaka Mysore Annaiah, and Shylaja M. Dharmesh. Gastroprotective Effect Of Ginger Rhizome (Zingiber Officinale) Extract: Role Of Gallic Acid And Cinnamic Acid In H+, K+-ATPase/Helicobacter pylori Inhibition And Anti-Oxidative Mechanism. Evidence-Based Complementary And Alternative Medicine. 2009 May [cited 2019 May 22]; 2011:13. Available from: https://www.hindawi.com/journals/ecam/2011/249487/.
44. M. Yoshikawa, S. Yamaguchi, K. Kunimi, Matsuda H, Okuno Y, Yamahara J, Murakami N. Stomachic Principles In Ginger. III. An Anti-Ulcer Principle, 6- Gingesulfonic Acid, And Three Monoacyldigalactosylglycerols, Gingerglycolipids A, B, And C, from Zingiberis Rhizoma originating In Taiwan. Chem Pharm Bull. 1994 Jun [cited 2019 May 22]; 42(6):1226–1230. Available from: https://www.ncbi.nlm.nih.gov/pubmed/8069973
45. M. A. Al-Yahya, S. Rafatullah, J. S. Mossa, A. M. Ageel, N. S. Parmar, And M. Tariq, "Gastroprotective Activity Of Ginger Zingiber officinale Rosc., In Albino Rats," Am J Chin Medicine. 1989 [cited 2019 May 22]; 17(1-2):51–56. Available from: https://www.ncbi.nlm.nih.gov/pubmed/2589236
46. K.D. Tripathi, Essentials of Medical Pharmacology, 6th Edition, Jaypee brothers medical publishers, New Delhi ,reprint 2009, p.627
47. 45. Walt RP. () Misoprostol for the treatment of peptic ulcer and anti-inflammatory-drug-induced gastroduodenal ulceration. N Engl J Med. 1992 Nov [cited 2019 May 20];327:1575–1580. Available from: https://www.nejm.org/doi/full/10.1056/NEJM199211263272207
48. Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin like drugs. Nat New Biol. 1971 May [cited 2019 May 22]; 231:232–235. https://www.nature.com/articles/newbio231232a0#article-info
49. Rao Ch V, Sairam K, Goel RK. Experimental evaluation of Bacopa monniera on rat gastric ulceration and secretion. Indian J Physiol Pharmacol. 2000 [cited 2019 May 22]; 44(4):435–441. https://www.ijpp.com/IJPP%20archives/2000_44_4/435-441.pdf
50. Hollannder D, Taranawski A, Gergely H, Zipsere KD. Sucralfate protection of the gastric mucosa against alcohol-induced injury: A prostaglandin-mediated process. Scand J Gastroenterol. 1984 Jan [cited 2019 May 22]; 101:97–102. Available from: https://europepmc.org/abstract/med/6599542
51. Nadar TS, Pillai MM. Effect of Ayurvedic medicines on beta-glucuronidase activity of Brunner's glands during recovery from cysteamine induced duodenal ulcers in rats. Indian J Exp Biol. 1989 Nov [cited 2019 May 22]; 27:959–962. https://europepmc.org/abstract/med/2620935
52. Ali SM, Khan AA, Ahmed I, Musaddiq M, Ahmed KS, Polasa H, Rao LV, Habibullah CM, Sechi LA, Ahmed N. Antimicrobial activities of eugenol and cinnamaldehyde against the human gastric pathogen Helicobacter pylori. Ann Clin Microbiol Antimicrob. 2005 Dec [cited 2019 May 22]; 4:20. Available from: https://ann-clinmicrob.biomedcentral.com/articles/10.1186/1476-0711-4-20
53. Burger O, Weiss E, Sharon N, Tabak M, Neeman I, Ofek I. Inhibition of Helicobacter pylori adhesion to human gastric mucus by a high-molecular-weight constituent of cranberry juice. Crit Rev Food Sci Nutr. 2008 May [cited 2019 May 22]; 42(S3):279–284. Available from: https://www.tandfonline.com/doi/abs/10.1080/10408390209351916
54. Kim SH, Park M, Woo H, Tharmalingam N, Lee G, Rhee KJ, Eom YB, Han SI, Seo WD, Kim JB. Inhibitory effects of anthocyanins on secretion of Helicobacter pylori CagA and VacA toxins. Int J Med Sci. 2012 Nov [cited 2019 May 22]; 9(10):838–842. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3498748/]
55. K.D. Tripathi, Essentials of Medical Pharmacology, 6th Edition, Jaypee brothers medical publishers,New Delhi ,reprint 2009, p.629
56. Jainu M, Devi CSS. Antiulcerogenic and ulcer healing effects of Solanum nigrum (L.) on experimental ulcer models: Possible mechanism for the inhibition of acid formation. J Ethnopharmacol. 2006 Mar [cited 2019 May 22]; 104(1-2):156–163. https://www.sciencedirect.com/science/article/pii/S0378874105005945
57. S.A. Nirmal Et.al , Scope of Drug Discovery From Indian Traditional Medicine, THE PHARMA REVIEW (NOVEMBER - DECEMBER 2011), KONGPOSH Publications Pvt. Ltd., cited : file:///D:/Scope%20of%20Drug%20Discovery%20From%20Indian%20Traditional%20Medicine.html
58. Regulatory Situation of Herbal Medicines A worldwide Review , The WHO Traditional Medicine Programme. WHO/TRM/98.1, page 2, http://apps.who.int/medicinedocs/pdf/whozip57e/whozip57e.pdf

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