

An Alternative Therapy for Improvement of Efficacy and Safety of Polyherbal Formulation for Treatment of Peptic Ulcer

Dr. Kiran C. Mahajan¹, Soham S. Ghodake², Dr. Shubhrajit Mantry³, Shital Bidkar⁴, Dr. Ganesh Dama⁵

¹Dr. Kiran Mahajan, Shri Gajanan Maharaj Shikshan Prasarak Mandal Sanchalit, Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur) Post Khamundi, Nagar- Kalyan High Way No- 222 Tal- Junnar, Dist- Pune, Maharashtra 410504, India.^{2,3,4,5}Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur) Post Khamundi, Nagar- Kalyan High Way No- 222 Tal- Junnar, Dist- Pune, Maharashtra 410504, India.

Abstract. The main Aim of this study is to Preparing polyherbal formulation is use to cure peptic ulcer. Stress, strain and anxiety have accomplished mankind with many lives style related disorders among which, peptic ulcer is the most common. Psychological stress and faulty food habits are the key factors for initiating and complicating the pathogenesis of peptic ulcer. Thus, peptic ulcer is rapid becoming an alarming social problem in developing countries like India. A number of synthetic drugs are available to treat ulcers. But these drugs are expensive and are likely to produce more side effect s when in compared to herbal medicines. Several Indian medicinal plants have been traditionally and extensively used to prevent different diseases in an Ayurvedic rasayana, which finds mention in ancient Indian texts for treatment of gastric ulcers. Materia medica textbook provides lots of information about ethanol extract of medicinal herbs, this extract are valuable as antiulcer agents and their use experimentally evaluated and proved by many researchers for its suggested that medicinal plant those are evidently reported for its antiulcer activity.

Key Words: Peptic Ulcer, Polyherbal, Asparagus Racemosus, Aegle Marmelos.

Introduction

The most familiar cause of stomach ulcer is a bacterium called *Helicobacter pylori*. Similarly, ulcer can be caused by excessive use of pain killers, such as aspirin and non-steroidal anti-inflammatory such as ibuprofen, naproxen etc. A peptic ulcer is a wound that affects the mucous membrane of the digestive tract. [1] Different names are given to ulcers depending on where they are based (gastric ulcers are located in the lining of the stomach, duodenal ulcers are located in the duodenal). [6] Ayurveda is one of the traditional medicinal methods with an established history of many centuries. Furthermore, known as Ayurvedic Medicine, this ancient Vedic knowledge is considered to be one of the oldest healing sciences and has survived until the present generation over many centuries of tradition. Originated in India thousands of years ago, Ayurveda is known as the “Mother of All Healing” [4] The treatment of peptic ulcer is conducted

against either minimization of the aggressive factors or enhancement of defensive mechanism. The main aims of the treatment of peptic ulcer disease are to relieve pain, heal the ulcer and delay ulcer recurrence. A number of drugs, including proton pump inhibitors and H2 receptor antagonists, are applicable for the treatment of peptic ulcer, but the clinical evaluation of these drugs has shown incidence of loss, side effects and drug interactions. Phytomedicinal All rights reserved agents have traditionally been used by herbalists and indigenous healers for the prevention and treatment of ulcers. Botanical compounds with antiulcer activity include flavonoids, saponins, tannins, gums and mucilage. The natural herbal drugs were found to be the safer alternatives to treat ulcers. In this study the antiulcer activity of a polyherbal formulation is studied. [5]

Peptic Ulcer

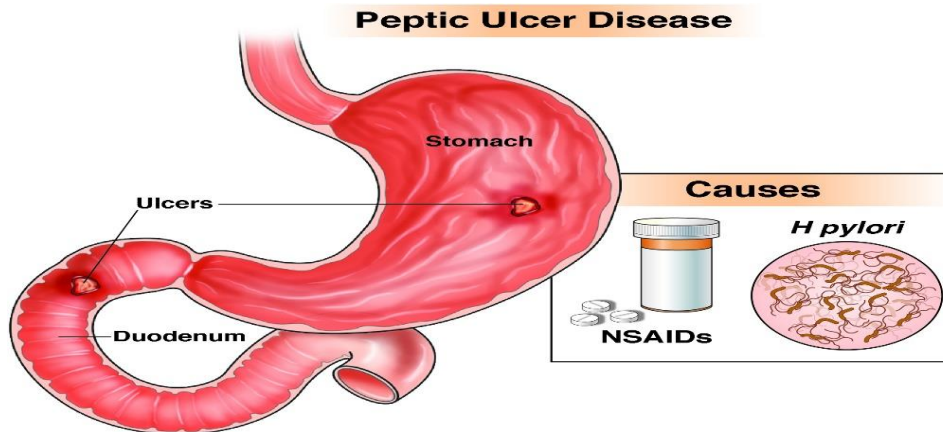


Figure1.Peptic Ulcer

Peptic ulcer disease is a source of significant morbidity and fatality worldwide. A abnormal condition may range from abdominal pain and gastrointestinal bleeding to gastric outlet obstruction and perforation. [2]

H pylori and the use of NSAIDs or aspirin are the main risk factors of both gastric and duodenal ulcers. However, only a few people with *H pylori* infection or taking NSAIDs or aspirin develop peptic ulcer disease, suggesting that individual susceptibility to bacterial virulence and drug toxicity is essential to the initiation of mucosal damage. [1,3]

- **Gastric ulcers** that appear on the inside of the stomach

- **Duodenal ulcers** that appear on the inside of the upper segment of your small intestine (duodenum) [5]

Polyherbal Formulation

(PHF) is the use of more than one herb in a medicinal preparation. The concept is found in Ayurvedic and other traditional medicinal systems where multiple herbs in a particular ratio may be used in the treatment of illness. The Herbal drugs Use to treat the peptic ulcers are as follows [31]

There are some herbal drugs which is given below:

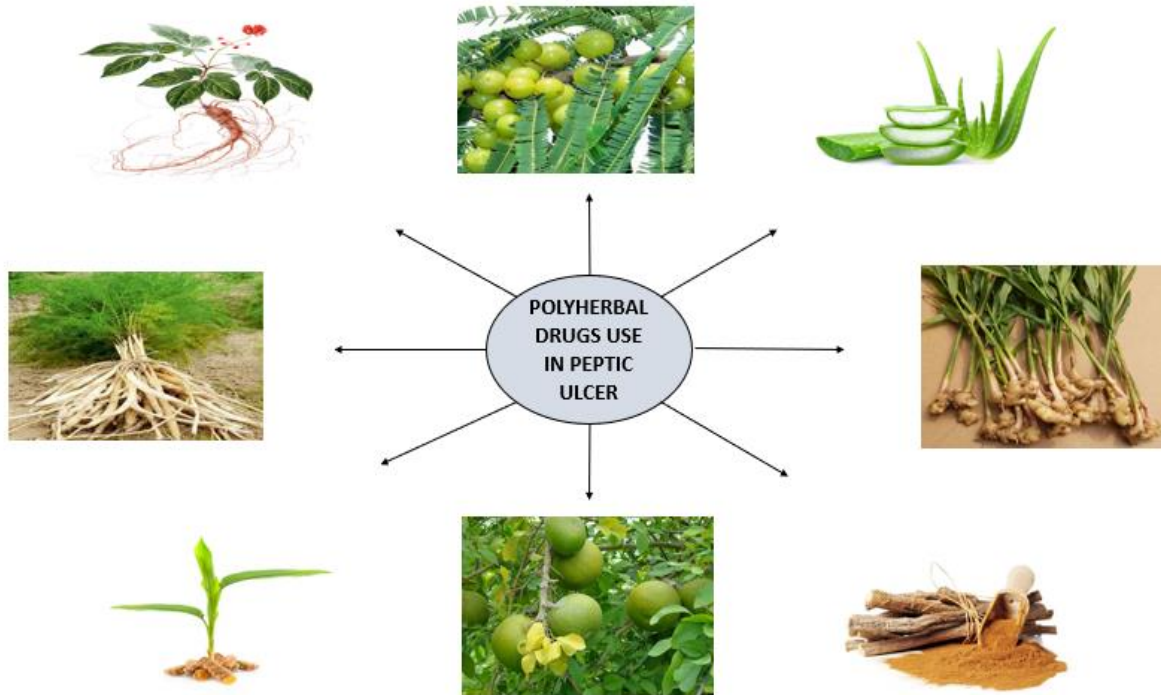


Figure 2. Polyherbal Drugs Use in Peptic Ulcer

Aegle Marmelos

Aegle marmelos, commonly known as Bael (or Bili or bhel), also Bengal quince, golden apple, Japanese bitter orange, stone apple or wood apple, is a rare species of tree native to the Indian subcontinent and Southeast Asia. It is present in India, Bangladesh, Sri Lanka, and Nepal as a naturalized species. The tree is considered to be sacred by Hindus.[7]

Description

Aegle marmelos is a deciduous Plant or small to medium-sized tree, up to 13 metres (43 feet) tall with narrow drooping branches and rather open, uncertain crown. [8]

The bark is pale brown or greyish, smooth or finely expand and flaking, detachment with long linear spines, 1.2–2.5 centimetres ($\frac{1}{2}$ –1 inch) separately or in pairs, often with slimy lattice flowing out from cut parts. The gum is also described as a clear, gummy sap, resembling gum Arabic, which exudes from wounded branches and hangs down in long strands, becoming continuously solid. It is very sweet at first taste and after some time irritating to the throat.

The leaf is trifoliate, alternate, each leaflet 5–14 cm ($2\text{--}5\frac{1}{2}$ in) x 2–6 cm ($\frac{3}{4}\text{--}2\frac{1}{4}$ in), ovate with tapering or pointed tip and rounded base, untoothed or with shallow rounded teeth. Small leaves are pale green or pinkish, finely hairy while well grown leaves are dark green and very smooth. All leaf has 4–12 pairs of side veins which are joined at the centre. The uniqueness of this fruit is it doesn't separate when it is fully ripened it is somewhat pear like shape. The woody shell is smooth and green, Gray until it is properly ripe when it becomes yellow. Inside the fruit there are 8 to 15 or 20 sections filled with aromatic orange pulp, each section with 6 (8) to 10 (15) flattened-oblong seeds each about 1 cm long, demeanour woolly hairs and each enclosed in a sac of adhesive, clear mucilage that thicken on drying. [7]

Gastroprotective effects of bale

It investigated the gastroprotective effects of the unripe fruit extract against different ulcerogenesis (hypothermic restraint stress, absolute theanol and indomethacin) in rats. The report showed that pre-treatment of animals with unripe fruit extract (50 and 100 mg/kg, i.p.) shielded against the theanol-induced gastric ulceration but was useless against the restraint stress or indomethacin. The methanolic extract of the unripe fruit (50, 100 and 200 mg/kg, p.o.) leads a dose dependent decrease in ulcer indicator convinced by theanol, aspirin and cold restraint stress. [7]

Asparagus Racemosus

Asparagus racemosus (satavar, shatavari, or shatamull, shatavari) is a species of asparagus collective throughout India and the Himalayas.[citation needed] and northern Australia. It grows 1–2 m (3 ft 3 in – 6 ft 7 in) tall and selects to take root in gravelly, rocky soils high up in piedmont plains, at 1,300–1,400 m (4,300–4,600 ft) elevation. It was botanically described in 1799. Because of its abundant uses, the demand for Asparagus racemosus is gradually on the rise. Due to increase in destructive harvesting, combined with habitat destruction, and deforestation, it leads the plant is now considered "endangered" in its natural habitat. [9]

Description

Asparagus racemosus (Shatavari) is discussed in Ayurvedic texts for prevention and treatment of gastric ulcers, dyspepsia and as a galactagogue. Generally, the root is engaged in diarrhoea as well as in chronic colic and dysentery problems. Root boiled with some bland oil, is applied in various skin diseases. Root is boiled in milk and the milk is administered to relieve bilious dyspepsia and diarrhoea and to promote appetite; root is also used in rheumatism. Tubers are candied and taken as a sweetmeat. Fresh root juice is given with honey as a demulcent. Boiled leaves smeared with ghee are applied to boils, smallpox, etc., in order to prevent their confluence. Juice of this drug taken with milk is useful in gonorrhoea. [8]

Panax Ginseng

Synonyms: Kanji, Hangul Ren Shen, Asiatic ginseng, red ginseng

Morphology

The panax ginseng plant cultivates best in cooler regions of the northern hemisphere and reaches a height of about one foot. The ginseng plant has yellowish-green umbrella shaped flowers that grow in a circle around a straight stem, with its 5 leaflets joined together at one point, it blooms in midsummer. The fruit is a bright crimson berry containing 1-3 wrinkled seeds the size of small peas. [10]

Description

Ginseng shows anti-ulcer action due to the presence of ginsenoside Rb1. Both American ginseng (Panax quinquefolium) and Asian ginseng (Panax ginseng) roots are acquired orally as adaptogens, aphrodisiacs, nourishing stimulants and in the treatment of type II diabetes, as well as for sexual dysfunction in men. The root is most often available in dried form, either whole or sliced. Ginseng leaf, although not as highly prized, is sometimes also used; as with the root, it is most often available in dried form. This ingredient may also be found in some standard energy drinks, often the "tea" varieties; in these products, ginseng is usually present in subclinical

doses and does not have quantifiable medicinal effects. It is also used in cosmetic preparations as well, but does not show that much accurate to have clinically effective results. [11]

Carica Papaya

Synonym: Papaya, Melon tree, Pawpaw, papaya, Tree melon
Family: Caricaceae
Generally, the fruit is melon-like, oval to closely round, somewhat pyriform, or elongated club-shaped, 6 to 20 in (15-50 cm) long and 4 to 8 in (10-20 cm) thick; weighing up to 20 lbs (9 kg). Semi-wild (naturalized) plants bear small-scale fruits 1 to 6 in (2.5-15 cm) long. The skin is waxy and thin but fairly tough. When the fruit is green and hard it is rich in white latex. As it ripens, it becomes light- or deep yellow externally and the thick wall of succulent flesh becomes aromatic, yellow, orange or various shades of salmon or red. It is then juicy, sweetish and somewhat like a cantaloupe in flavour; in some types quite musky. Attached lightly to the wall by soft, white, fibrous tissue, are usually numerous small, black, ovoid, corrugated, peppery seeds about 3/16 in (5 mm) long, each coated with a transparent, gelatinous aril. [12]

Description

Papaya shows good result for digestion problems. This product should not be used for intestinal parasite infections because it may be ineffective. The effects of *Carica papaya* Linn on exogenous ulcer and histamine-induced acid secretion were studied in rats. The latex of the unripen fruit of *C. papaya* was effective in protecting the exogenous ulcer. It significantly lessened the acid secretion induced by intravenous infusion of histamine in chronic gastric fistulated rats. Crystalline papain was also effective in protecting the exogenous ulcer and in decreasing the histamine-induced acid secretion in rats. The conclusion is that papain is the active principle in *C. papaya* that exerts the ulcer-protective effect. [10]

Embilica Officinalis

Synonyms: Indian goobers, Arab. Amlaj; Assam. Amluki; Ayurvedic: Amalaki; Beng. Amia, Amlaki, Amla, Arnloki. Family: Euphorbiaceae
Tree; leaves alternate, bifarious, pinnate, flower -bearing; leaflets numerous, alternate, linear-obtuse, entire; petioles striated, round; calyx 6-parted; flowers in the male very numerous in the axils of the lower leaflets, and round the common petiole below the leaflets; in the female few, solitary, sessile, mixed with some males in the most exterior floriferous axils; stigmas 3; drupe globular, fleshy, smooth, 6-striated; nut obovate triangular, 3-celled; seeds 2 in each cell; flowers small, greenish yellow. Flowers during October.

Description

Indian gooseberry has been used as an admired ingredient of various medicines in India and Middle East from time immemorial. Aperient The green fruits are made into pickles and preserves to stimulate the appetite. Antibacterial, antifungal, antiviral medical studies conducted on Amla fruit suggest that it has antiviral belongings and also functions as an antibacterial and antifungal agent. Antioxidant The use of amla as an antioxidant has been studied by a number of authors. Experiments conducted at the Niwa Institute of Immunology in Japan have proved Amla to be a potent scavenger of free radicals. The studies showed that Amla preparations contained high levels of the free-radical scavenger, superoxide dimutase (SOD), in the experimental subjects. Aphrodisiac Amla is believed to increase ojas, and is considered to be one of the strongest and important rejuvenate herbs in Ayurvedic medicine. It is the primary ingredient used in one of the renowned Ayurvedic herbal formulae, called Chayavanprasha which has great respect as a tonic. [13]

Aloe Vera

Synonyms: Aloe, Musabber, kumara Family: Liliaceae

Aloe vera is a stemless or very short stemmed moist plant growing to 60–100 cm (24– 39 in) tall, spreading by offsets. The leaves are generous and fleshy, green to grey-green, with some diversities showing white flecks on the upper and lower stem surfaces. The margin of the leaf is serrated and has small white teeth. The flowers are cultivated in summer on a spike up to 90 cm (35 in) tall, each flower pendulous, with a yellow tubular corolla 2– 3 cm (0.8–1.2 in) long. Like other Aloe species, Aloe vera forms arbuscular mycorrhiza, a symbiosis that allows the plant better access to mineral nutrients in soil. [14]

Aloe vera juice is used for consumption and relief of digestive issues such as heartburn and irritable bowel syndrome, although it bears significant potential to be toxic when taken orally, it is common practice for cosmetic companies to add sap or other derivatives. Other uses for extracts of aloe vera include the dilution of semen for the artificial fertilization of sheep, use as fresh food preservative, and use in water conservation in small farms. The supposed therapeutic uses of aloe vera are not exclusive to the species and may be found to a lesser or greater degree in the gels of all aloes, and indeed are shared with large numbers of plants belonging to the family Asphodelaceae. [15]

Curcuma Longa

It is a perennial herb from Zingiberaceae family, distributed native to India and Southeast Asia. Curcumin, an active component of Curcuma, show Santi-

inflammatory and antioxidant properties. On the basis of its antioxidant property, it scavenges reactive oxygen species and regulates MMP activity to exert antiulcer activity [16]. Curcumin (diferuloylmethane), a yellow pigment in turmeric *Curcuma longa*, is used widely as a spice in Indian and Thai cuisine. It exhibits a number of pharmacological effects including anti-inflammatory activity, induced by suppression of PG synthesis [17]. Turmeric root extract has been found to relieve pain from biliary dyskinesia during a double-blinded study [18] and improve endoscopic healing of peptic ulcers as well as symptoms of patients with nonnuclear dyspepsia [19]. And much interest in its potential as a selective COX-2 inhibitory agent [20].

Glycyrrhiza Glabra

Liquorice or licorice is the root of *Glycyrrhiza glabra* from which a somewhat sweet flavour can be extracted. The liquorice plant is a legume (related to beans and peas) that is native to southern Europe and parts of Asia. It is placed under the family Fabaceae. It is an herbaceous perennial, growing to 1 m in height. In north India it is known as "Mulaithi." The root of *G. glabra* is known as licorice used for the treatment of gastric ulcer in Europe. It had been reported that licorice derived compounds elevate the prostaglandin level and promote the mucus secretion from the stomach, increase the life span of surface cell of stomach, and had an antipepsin activity which ultimately leads to ulcer healing [21]. Extracts of licorice have demonstrated the ability to accelerate the healing of gastrointestinal ulceration (especially in the stomach and oesophagus) possibly due to its antioxidant effect. The antiulcer drug carbenoxolone, a succinate derivative of glycyrrhetic acid, was developed in London in the early 1960s and has become the preferred form of licorice used to promote healing of ulcers [22].

The Unripe Plantain Banana

The medicinal properties of plantain banana are part of the tradition of folk medicine. Sanyal et al., [23, 24] for the first time, associated the plantain banana with antiulcer activity of banana against ulcer induced by phenyl butazone prednisolone and restraint stress. [25, 26] Described the antiulcer activity of a variety of preparation of dried unripe plantain banana against aspirin induced ulcer in rats. They showed that only unripe plantain banana was effective both as a prophylactic treatment and also in healing the ulcers already induced by aspirin. Further studies reveal that banana increases the mucosal defence by promoting mucus secretion increasing mucoprotein content of mucosa, decreasing the shedding of cells and leakage of protein in gastric secretion in response to

ulcerogenesis agents, and promotes healing, as shown by the increase in thymidine uptake by gastric mucosal cells and by causing a concentration dependent increase in the eicosanoid stimulation in the incubates of human gastric and colonic mucosa [27, 28].

Zingiber Officinale

It is widely used as a condiment and therapeutic agent in many countries. In Saudi Arabian traditional medicine, it is used as antiemetic, stomachic, and carminative. In Chinese medicine it is employed in colic and in atonic dyspepsia and is used as a stimulant [29]. Mowery and Clayson found that it is highly effective in motion sickness and significantly reduces gastrointestinal distress in human subjects. It has also marked antiulcer activity [30].

Conclusion

From this study we can conclude that studies with plant sources can result in novel and effective pattern of treatment. In this respect, traditional medicine has introduced good protocols for treatment of various gastrointestinal disorders. All of the remedies presented here had adequate evidence from traditional or scientific source for their efficacy in management of ulcers. Chemical substances derived from plants have been used to treat human diseases since the dawn of medicine. Roughly 50% of new chemical entities introduced during the past two decades are from natural products. Recent technological advances have renewed interest in natural products in drug discovery. Therefore, efforts should be directed towards isolation and characterization of the active principles and elucidation of the relationship between structure and activity. There are various medicinal plants and their extracts (containing active chemical constituents, such as tannins and flavonoids) that have significant antiulcer activity in in vivo experiments on animal models. Ayurveda, the oldest medicinal system in the world, provides leads to find therapeutically useful compounds from plants. The combination of traditional and modern knowledge can produce better drugs for the treatment of peptic ulcer with fewer side effects.

Acknowledgments

The authors are grateful to SGMSPM's Sharadchandra Pawar College of Pharmacy, Savitribai Phule Pune University, Pune, Maharashtra, India.

References

1. Lanas A, Chan FK. Peptic ulcer disease. *The Lancet*. 2017 Aug 5; 390(10094):613-24.
2. Kavitt RT, Lipowska AM, Anyane-Yeboah A, Gralnek IM. Diagnosis and treatment of peptic ulcer disease.

- The American journal of medicine. 2019 Apr 1; 132(4):447-56.
3. Huang JQ, Sridhar S, Hunt RH. Role of Helicobacter pylori infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. *The Lancet*. 2002 Jan 5; 359(9300):14-22.
 4. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: Concept of ayurveda. *Pharmacognosy reviews*. 2014 Jul; 8(16):73.
 5. Devaraj VC, Krishna BG. Antiulcer activity of a polyherbal formulation (PHF) from Indian medicinal plants. *Chinese journal of natural medicines*. 2013 Mar 1; 11(2):145-8.
 6. Srivastava S, Lal VK, Pant KK. Polyherbal formulations based on Indian medicinal plants as antidiabetic phytotherapeutics. *Phytopharmacology*. 2012; 2(1):1-5.
 7. Gupta D, John PP, Pankaj K, Kaushik R, Yadav R. Pharmacological review of Aegle marmelos corr. Fruits. *International Journal of Pharmaceutical Sciences and Research*. 2011 Aug 1; 2(8):2031.
 8. Rahman S, Quader MR, Khan MI. Prevention of peptic ulcer by aqueous extract of Aegle marmelos leaf in rats. *IMC Journal of Medical Science*. 2018 Jan 2; 12(1):11-4.
 9. Vimala G, Gricilda Shoba F. A review on antiulcer activity of few Indian medicinal plants. *International journal of microbiology*. 2014 May 25; 2014.
 10. Roy SD, Chakraborty J, Shil D, Das S, Begum N. Herbs Used In Peptic Ulcer: A Review. *International Journal of Pharmaceutical Research & Allied Sciences*. 2013 Apr 1; 2(2).
 11. Sun XB, Matsumoto T, Yamada H. Anti-ulcer activity and mode of action of the polysaccharide fraction from the leaves of Panax ginseng. *Planta Medica*. 1992 Oct; 58(05):432-5.
 12. Pal N, Ghosh D, Molla KI, Dasgupta RK, Roy SD. HERBS USED TO TREAT PEPTIC ULCER: A SYSTEMIC REVIEW.
 13. Roy SD, Chakraborty J, Shil D, Das S, Begum N. Herbs Used In Peptic Ulcer: A Review. *International Journal of Pharmaceutical Research & Allied Sciences*. 2013 Apr 1; 2(2).
 14. http://en.wikipedia.org/wiki/Aloe_vera
 15. http://www.herballegacy.com/Baldwin_Chemical.html
 16. Chatterjee A, Bandyopadhyay SK. Herbal remedy: An alternate therapy of nonsteroidal anti-inflammatory drug induced gastric ulcer healing. *Ulcers*. 2014 May 6; 2014.
 17. Huang MT, Lysz T, Ferraro T, Abidi TF, Laskin JD, Conney AH. Inhibitory effects of curcumin on in vitro lipoxygenase and cyclooxygenase activities in mouse epidermis. *Cancer research*. 1991 Feb 1; 51(3):813-9.
 18. Niederau C, Göpfert E. The effect of chelidonium-and turmeric root extract on upper abdominal pain due to functional disorders of the biliary system. Results from a placebo-controlled double-blind study. *Medizinische Klinik (Munich, Germany)*. 1983. 1999 Aug 1; 94(8):425-30.
 19. Prucksunand C, Indrasukhsri B, Leethochawalit M, Hungspreugs K. Phase II clinical trial on effect of the long turmeric (*Curcuma longa* Linn.) on healing of peptic ulcer. *Southeast Asian journal of tropical medicine and public health*. 2001 Mar 1; 32(1):208-15.
 20. Zhang F, Altorki NK, Mestre JR, Subbaramaiah K, Dannenberg AJ. Curcumin inhibits cyclooxygenase-2 transcription in bile acid-and phorbol ester-treated human gastrointestinal epithelial cells. *Carcinogenesis*. 1999 Mar 1; 20(3):445-51.
 21. Bafna PA, Balaraman R. Anti-ulcer and anti-oxidant activity of pepticare, a herbomineral formulation. *Phytomedicine*. 2005 Apr 20; 12(4):264-70.
 22. Dehpour AR, Zolfaghari ME, Samadian T, Vahedi Y. The protective effect of liquorice components and their derivatives against gastric ulcer induced by aspirin in rats. *Journal of pharmacy and pharmacology*. 1994 Feb; 46(2):148-9.
 23. Sanyal RK, Das PK, Sinha S, Sinha YK. Banana and gastric secretion. *Journal of Pharmacy and Pharmacology*. 1961 Sep; 13(1):318-9.
 24. Sanyal AK, Gupta KK, Chowdhury NK. Banana and experimental peptic ulcer. *Journal of Pharmacy and Pharmacology*. 1963 Sep; 15(1):283-4.
 25. Best R, Lewis DA, Nasser N. The anti-ulcerogenic activity of the unripe plantain banana (*Musa* species). *British journal of pharmacology*. 1984 May; 82(1):107.
 26. Elliott RC, Heward GJ. The influence of a banana supplemented diet on gastric ulcers in mice. *Pharmacological Research Communications*. 1976 Apr 1; 8(2):167-72.
 27. Goel RK, Gupta S, Shankar R, Sanyal AK. Anti-ulcerogenic effect of banana powder (*Musa sapientum* var. *paradisica*) and its effect on mucosal resistance. *Journal of Ethnopharmacology*. 1986 Oct 1; 18(1):33-44.
 28. Goel RK, Tavares IA, Bennett A. Stimulation of gastric and colonic mucosal eicosanoid synthesis by plantain banana. *Journal of pharmacy and pharmacology*. 1989 Nov; 41(11):747-50.
 29. Mowrey D, Clayson D. Motion sickness, ginger, and psychophysics. *The lancet*. 1982 Mar 20; 319(8273):655-7.
 30. Al-Yahya MA, Rafatullah S, Mossa JS, Ageel AM, Parmar NS, Tariq M. Gastroprotective activity of ginger *zingiber officinale* rosc., in albino rats. *Am J Chin Med*. 1989 Jan 1; 17(1-2):51-6.
 31. Parasuraman S, Thing GS, Dhanaraj SA. Polyherbal formulation: Concept of ayurveda. *Pharmacognosy reviews*. 2014 Jul; 8(16):73.