Potential of Phytoconstituents as antiulcer agents

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Author's contribution
Harshitha HNSK Tavva: Gathered articles
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ABSTRACT

In addition to offering a wide variety of pharmaceuticals, nature may also have the solutions to any medical problems. There are still many clinically useful medicines found in nature. Ulcer diseases are a significant and expanding category of health problems. Today, a variety of drugs are used to treat peptic ulcers, but all of them have drawbacks, such as the potential for relapse and drug combinations. Peptic ulcers are a condition that is increasingly being treated with plant-based medications. Pure phytochemicals are difficult to get as ulcer treatments. Both time and money are invested in it. *Mangifera indica, Azadirachta indica, Ocimum sanctum, Annona squamosa, Mimosa pudica, Terminalia chebula, Ficus religiosa, Carica papaya, Aegle marmelos, Moringa oleifera, Psidium guajava,* and other plants are some of the plants that act as antiulcer herbals and are ignored for their beneficial function. Flavonoids can help to decrease free radicals to some extent in combating ulcers. Numerous isolated compounds have significant anti-ulcer activity, such as mangiferin, nimbidin, eugenol, tannic acid, mimosine, gallic acid, chebulinic acid, naringenin, papain, and others. The results of this review paper suggest that the anti-ulcer effect is mediated by a number of medicinal plants and their chemical components. This drives us towards development of novel phytoconstituents with structural modification to act as better antiulcer drug molecules at clinical level.

Keywords: Anti-Ulcer, Peptic Ulcer, Phyto constituents, Structural Modification

Introduction

An open sore on the skin or mucous membrane known as an ulcer is characterized by the expulsion of inflammatory dead tissue (Chan *et al,* 2000). Ulcers can appear almost everywhere, however they most usually affect the lower extremities and the digestive tract. Peptic ulcers are one of many different types of ulcers, which can occur in the vagina, esophagus, or stomach. An erosion of the

duodenal or stomach lining results in peptic ulcers (Debjit *et al,* 2010). According to reports, the agony is growing, intense, and burning. Depending on where an ulcer is placed, the symptoms and indicators can fluctuate. Here are some illustrations of peptic and duodenal ulcer signs and symptoms. Pain can occur anywhere from the breast bone to the belly button. There are times when back ache is experienced, and it might linger for a short while or for several hours. While there is a bleeding ulcer, vomiting, or dark to black stools are present. A duodenal ulcer often hurts more when the stomach is empty and less so briefly after eating. When a person sleeps down or during the night, peptic ulcers often develop worse. Eating meals that improve digestive function is advised for prevention. If there is systemic inflammation and heat, a major focus will be on removing and draining heat from the body. Salads made of bitter greens can be consumed, and seasonings like turmeric and garlic can act as preservatives. Prioritize meals that calm you down, like berries and healthy fats, and steer clear of items that heat you up, like alcohol and extremely hot peppers (Patel *et al,* 2010). The herbals that have proven to be antiulcer along with their phytoconstituents are presented in table (1).

For the treatment of peptic ulcers, there are a number of drugs in the market, but a clinical analysis of those medications reveals they have a high risk of relapse, unfavorable side effects, and drug interactions. For the treatment of peptic ulcers, there are a number of drugs in the market, but a clinical analysis of those medications reveals they have a high risk of relapse, unfavorable side effects, and drug interactions. in the realm of herbs, which is nature's pharmacy. In the development of new therapeutics for a number of ailments, plants have been employed as a rich source of novel molecules and as an alternative strategy. With a few modest chemical modifications, many plants used in traditional medicine could potentially provide new and improved anti-ulcer medications.

Table 1. Anti ulcer Phytoconstituents (Neyres Zinia *et al*, 2012)

Name of the plant	**Phytoconstituents**
Mangifera indica	Mangiferin
Azadirachta indica	Nimbidin
Ocimum sanctum	Eugenol
Annona squamosa	Tannic acid
Mimosa pudica	Mimosine
Terminalia chebula	Tannins, gallic acid, chebulinic acid
Ficus religiosa	Flavanoid- Naringenin
Carica papaya	Chymopapain, papain
Aegel marmelos	Luvangetin
Moringa loeifera	Quercetin, beta setosterol, Bbeta carotene
Psidium guajava	Flavonoids-Quercetin, guaijaverin,
Sesbania grandiflora	Tannins, saponins
Shorea robusta	Ursolic acid, amyrin
Allium sativum	Alliin, allicin
Aloe vera	Barbaloin, isobarbaloin, saponins
Bacopa moniera	Bacoside A
Calendula officinalis	Isorhamnetin
Citrullus lanatus	L-Citrulline

Daucus carota	Chlorogenic acid
Decalepis hamiltonii	Vanillin
Eclipta alba	Wedelolactone
Emblica officinalis	Ellagic acid
Hypericum perforatum	Hyperforin
Silybum marianum	Silibinin

Anti-ulcer activity study of some phyto constituents

Mangiferin

A xanthonoid produced from the *Mangifera indica* plant called mangiferin (MF) has been shown to have anti-secretary and gastro protective activities against a number of gastric ulcer models. The study examined ischemia/reperfusion paradigm affects on various signaling pathways. The vehicle, MF, and omeprazole were administered to the animals (OMP). According to the mechanistic investigation, Nrf2, HO-1, and PPAR- expression were all raised, and this helped MF to some extent in mediating its gastro protective action. Surprisingly, the effect of MF, particularly the high dose, outperformed that mediated by OMP, except in the case of Nrf2. The antioxidant properties of MF were shown by raising glutathione and antioxidant capacity as well as bringing malondialdehyde levels to normal, and the biomarkers that were looked at corroborated the chemical findings.

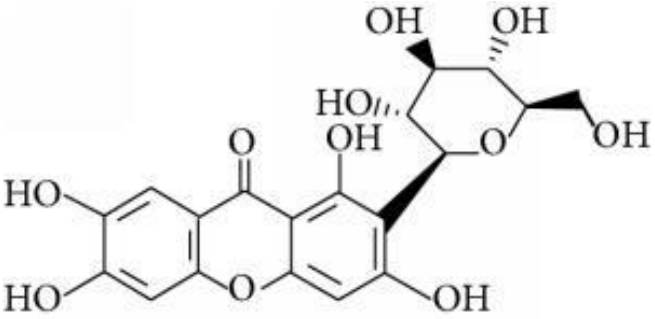

Figure 1. Mangiferin

Additionally, MF inhibited the rise in nitric oxide brought on by I/R more effectively than OMP. While reducing the inducible isoform in serum, MF dose-dependently boosted endothelial nitric oxide synthase. By the result of its anti-inflammatory effects, MF reduced blood levels of myeloperoxidase, a sign of neutrophil infiltration, Interleukins, and SE-selectin. An increase in Bcl-2 and a dose-dependent inhibition in caspase-3 further revealed the anti-apoptotic effects of MF. One of the MF's proposed gastro protective mechanisms is the regulation of inflammation, oxidative stress and apoptosis, perhaps through the Nrf2/HO-1. One of the potential gastro protective actions of MF is the regulation of oxidative stress, inflammation, and apoptosis, probably through the Nrf2/HO-1, PPAR-/NF-B signaling pathways (Mahmoud *et al*, 2015).

Nimbidin

Numerous toxicology tests on mice, rats, dogs were performed on nimbidin, a triterpenoid drug that may be utilised as an antiulcer. Investigation on acute toxicity in both albino rats and mice showed no adverse effects up to oral doses of 2000 mg/kg and intraperitoneal doses of 1000 mg/kg. The LD50 was not determined since it was difficult to administer the medication at high dose levels due to its crude insoluble nature.

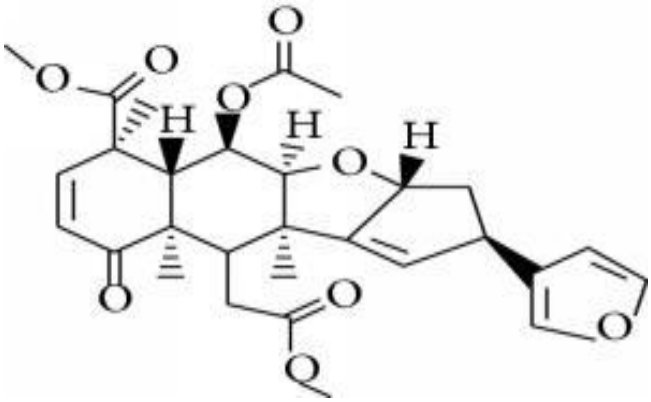

Figure 2. Nimbidin

Studies on subacute toxicology in albino rats were conducted at dosages up to 100 mg/kg per day for six weeks, while investigations in dogs were conducted at doses of 10 – 20 mg/kg per day for four weeks, but no signs of systemic harm were discovered. Furthermore, teratogenic research on rats revealed no signs of toxicity or deformed fetuses (Pillai *et al*, 1984). The activity has been studied by pylorus ligation induced ulcer model in both rats and cats. The results indicated that at 40 mg/kg (i.v). it suppressed histamine and carbachol stimulated gastric acid secretion. The activity was attributed to H2 - receptor antagonism (Pillai NR Iet al,1985).

Eugenol

Clove, a common name for the medicinal herb *Syzygium aromaticum*, is used to cure digestive problems, toothaches, and inflammation. It is possible to create an essential volatile oil from the buds of *S. aromaticum* that is mostly made of eugenol, and a blend of volatile aliphatic, cyclic, and phenylpropanoids. The major objectives of this work were to get the essential volatile oil from the buds of *S. aromaticum*, to recognise and measure its primary component, and to evaluate the essential oil's anti - ulcer effects on various animal models.

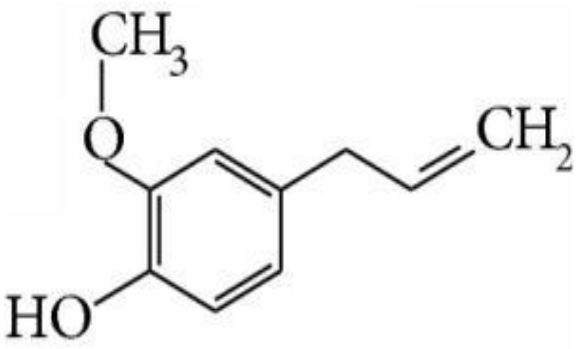

Figure 3. Eugenol

The experiments were carried out on rats utilizing ulcer models generated by indomethacin and ethanol/HCl. In the rat models of indomethacin- as well as ethanol-induced ulcers, eugenol and essential oils of *S. aromaticum* both shown antiulcer effectiveness. Investigations into potential mechanisms of gastro protection used studies to measure gastric secretion using the pylorus-ligated model, identify mucus in gastric content, and examine the functions of nitric oxide (NO) and endogenous sulfhydryl in gastro protection. According to the findings, neither the amount of gastric juice produced nor the overall acidity was considerably influenced. However, the analysis of free gastric mucus revealed that eugenol and clove oil have the ability to dramatically increase mucus

production. The study found no connection between the gastro protective effects of clove oil and eugenol and the effects of endogenous sulfhydryls or nitric oxide. Acute toxicity testing revealed no evidence of damage. The findings of this study demonstrate the antiulcer properties of the essential oil and the primary component of *S. aromaticum*, eugenol. According to the findings, eugenol and essential oils' efficiency is based on their capacity to promote mucus formation, a crucial gastro protective component. More toxicological and pharmacological research is required before being used to treat stomach ulcers (Santin *et al*, 2010).

Tannins

The chemical composition of tannins and their capacity to prevent stomach ulcers was well established. Tannins' astringent properties are the main reason they are used in medicine. These traits are the result of interactions between tannins and the tissue proteins they come into contact with. In situations of gastric ulcers, this protein-tannin complex layer protects the stomach from harm or irritation brought on by chemicals and mechanical forces. In numerous experimental models of gastric ulcer, tannins have also been shown to exhibit antioxidant activity, promote tissue repair, be *anti-helicobacter pylori*, and be engaged in gastrointestinal tract anti-inflammatory activities. The presence of tannins in some natural products accounts for their anti-ulcer abilities (De Jesus *et al*, 2012).

Mimosine

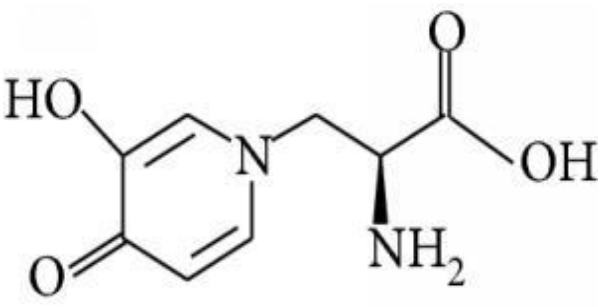

Figure 4. Mimosine

A species of the mimosacea family is called *Mimosa pudica* and the active constituent present in it is mimosine, a non-protein amino acid derived rom tyrosine. This plant, also referred to as touch-me-not, is frequently grown as a weed in topical agricultural area, especially when fields are hand cultivated. The leaf preparations from this species were used as traditional herbal medicine to cure ulcers, fever and burning sensations. Investigating the antiulcer activity of *M. pudica* leaf extract is the primary goal of the current work. The effects of methanolic and aqueous extracts of the plant were investigated in rats using pylorus ligation and indomethacin-induced ulcer models. The ulcer index, total acidity, and pH values were established. The results demonstrated that, when compared to the control, the alcoholic extract significantly (P 0.001) lowered the pH, acid concentration, and ulcer index at a dose of 400 mg/kg (Divya *et al*, 2011).

Gallic acid

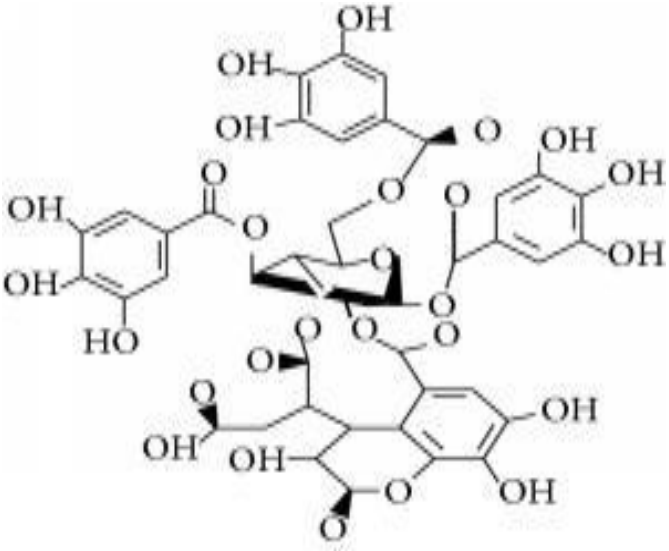

Figure 5. Gallic acid

In Chinese patent medicines like feiyangweiyan pill, gallic acid (3, 4, 5-trihydro benzoic acid, or GA), a phenolic compound, has been used for many years to treat gastrointestinal issues (FY capsule). However, there is not enough support for GA's gastroprotective effects, and the underlying pharmacological mechanisms are still poorly understood. The protective effects of GA against ethanol-induced stomach ulcers in rats and elucidation of the underlying processes was demonstrated.. Male Sprague-Dawley rats were given oral doses of 100% ethanol (5mL/kg), GA (10, 30, and 50 mg/kg), FY tablet (0.4 g/kg), and 30mg/kg lansoprazole to induce stomach ulcers. Lansoprazole and physiological saline were used as a positive and negative control, respectively. Alcohol intoxication in rats resulted in a significantly higher ulcer index, higher serum levels of inflammatory cytokines markers (IL-, IL-6, and TNF), higher levels of TBARS, higher levels of Bax and Capase-3 protein expression, and a significantly lower level of endogenous antioxidant activities or levels (SOD, CAT, and GSH), factors that protect the gastric mucosa from damage (PGE2 and NO), and Bcl-2 protein expression. Pretreatment with GA showed significant improvements over ethanol-treated groups in terms of ulcer index, inflammatory cytokine indicators, TBARS, protein expression of Bax and Capase-3, endogenous antioxidant activity, levels of PGE2 and NO, and protein expression of Bcl-2, Nrf2, and HO-1. This study demonstrated the gastroprotective effects of gallic acid and FY capsules on ethanol-induced stomach ulcers in rats. The underlying mechanism by which GA and FY capsules prevented ethanol-induced gastric ulcer in rats may include the Nrf2/HO-1 anti-oxidative pathway, which ultimately had an anti-apoptotic impact via regulating Bax, Bcl-2, and Caspase-3 (Dan Zhou *et al*, 2020).

Chebulinic acid

The gastroprotective characteristics of chebulinic acid, which was extracted from *Terminalia chebula* fruit, was investigated. In stomach ulcers were induced in experimental models using rats, such as pylori ligation, alcohol, aspirin, and cold constraint.

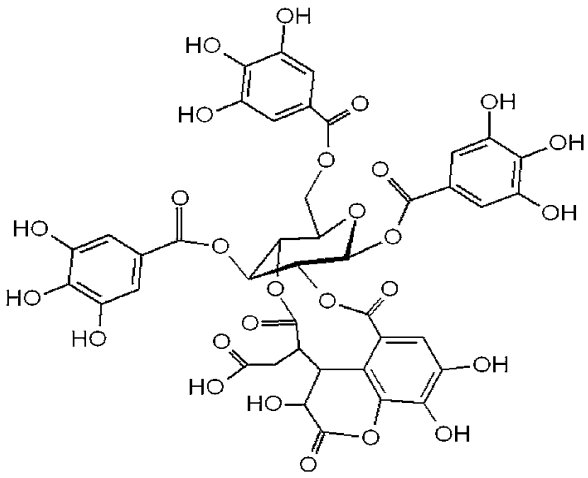

Figure 6. Chebulinic acid

Chebulinic acid, an ellagi tannin may be able to treat ulcers brought on by CRU (62.9%), AS (55.3%), AL (80.67%), and PL (66.63%) ulcer models. Omeprazole (10mg/kg, p.o.) showed 77.73% protective activity against CRU, 55.30% protective activity against AS, and 70.80% protective activity against PL model. Another reference drug, sucralfate (500 mg/kg, p.o.), showed 65.67% protection in an AL-induced ulcer model. Chebulinic acid significantly enhanced total acidity by 38.29%, mucin secretion by 59.75%, and decreased free acidity by 48.82%. Chebulinic acid's significant suppression of H+ K+ ATPase activity in vitro—with an IC50 of 65.01 g/ml compared to omeprazole's (30.24 g/ml)—provided later evidence of its anti-secretory impact (Vaibhav Mishra *et al*, 2013).

Naringenin

Experimentation was conducted to determine whether naringin has gastro protective qualities and whether endogenous postaglandines are responsible for the mucosal damage caused by 100% ethanol. The most effective antiulcer therapy involved oral pretreatment with the greatest dose of naringin, a flavonoid molecule (400 mg/kg), followed by 100% ethanol after 60 minutes.

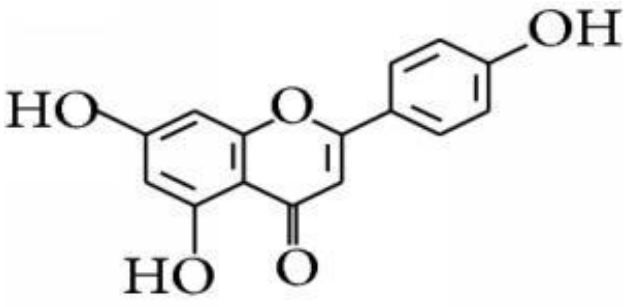

Figure 7. Naringenin

In the rats treated with naringin (400 mg/kg), the subcutaneous administration of indomethacin (10 mg/kg) somewhat reduced the gastrointestinal protection, but the prostaglandin E2 measurement did not reveal an increase in prostanoid levels. Total proteins and the makeup of gastric mucus did not alter appreciably. Hexosamine levels significantly increased in rats receiving naringin therapy; however this increase was less noticeable in animals receiving indomethacin first (Martin *et al*, 1994).

Chymopapain

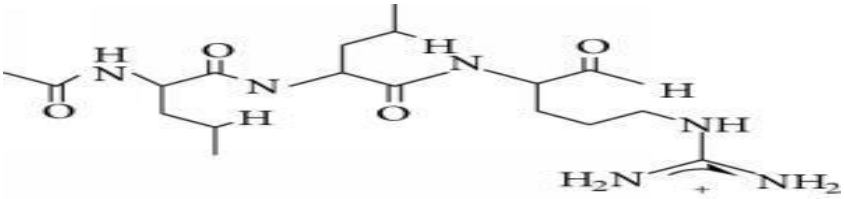

Figure 8. Chymopapain

The anti-ulcer studies of aqueous (AE) and methanolic (ME) extracts from whole unripe *Carica papaya* fruit were investigated using ethanol and indomethacin induced stomach ulcer models in rats. The effects of the extrats on small intestine propulsion were also studied. The extracts significantly (P 0.05) reduced the ulcer index compared to the control group in both experimental models. Unripe *C. papaya* extracts contain chymopapain. Ulcers were more defended by ME against indomethacin model than ethanol-induced ulcers, which were better avoided by AE. The extracts also significantly (P 0.05) decreased intestinal motility, with ME showing the highest level of action. After consuming AE and ME orally in doses up to 5000 mg/kg, mice exhibited no acute toxic effects. (Ezike *et al*, 2009).

Quercetin

Indomethacin 30 mg/kg orogastric gavages were administered to three groups over the course of two days. For 15 days, the rats received 15 mg/kg oral gavage doses of famotidine, 15 mg/kg oral gavage doses of quercetin, or 15 mg/kg oral gavage doses of vehicle alone. The control group was given the vehicle orally throughout a 15-day period in place of indomethacin.

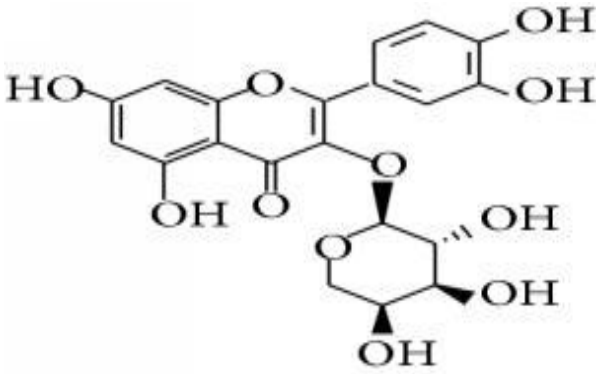

Figure 9. Quercetin

To determine the amount of gastric liquid present, the pH, and the ulcer index, the stomachs were examined using a conventional light microscope. The gastrointestinal mucosal surface of the indomethacin-treated rats suffered considerable damage, and the ulcer index was much higher than in the control group. Significantly higher antioxidant enzyme activity was seen in the groups who received treatments with famotidine and quercetin. The minor inflammatory infiltration did reduce the congestion, degradations, and death, but the treated rats showed no obvious endothelial cell damage. According to the study's findings, quercetin is superior to famotidine at reducing the risk of indomethacin-induced stomach mucosal ulceration (Alkushi *et al*, 2017).

Alliin and allicin

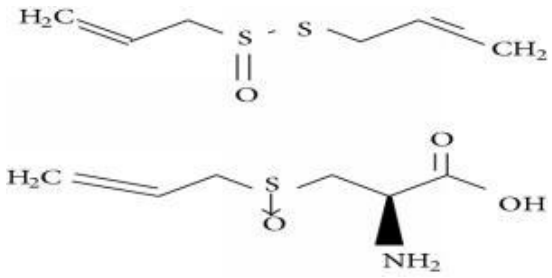

Figure 10. Alliin and allicin

Several gastric ulcer testing techniques and a rat model of a duodenal ulcer caused by cysteamine were used to determine the effects of raw *Allium sativum Linn*. bulb juice on peptic ulcers. Bulb juice from *A. sativum Linn*. was given orally in two doses of 250 mg/kg and 500 mg/kg. Both garlic juice dosages produced antisecretory effects on the stomach in pylorus-ligated rats. They also showed healing effects on chronic acetic acid-induced gastric ulcers and gastric cytoprotective effects on ulcers caused by ethanol and indomethacin. Additionally, the juice significantly reduced the frequency of duodenal and gastric ulcers brought on by stress and cysteamine. The juice was more efficacious at a low dose (250 mg/kg, p.o.) than at a high dose (500 mg/kg, p.o.) which contains alliin and allicin. In conclusion, the juice from *A. sativum* linn bulbs protects rats from experimentally produced stomach and peptic ulcers and promotes gastric ulcer healing (Mohammed *et al*, 2009).

Bacoside A

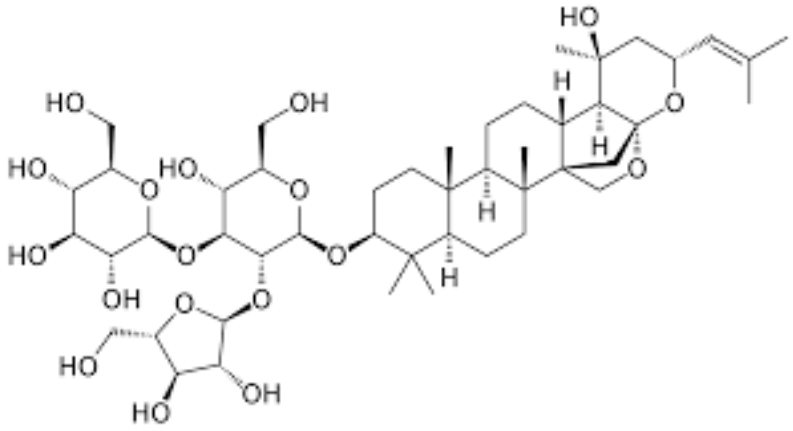

Figure 11. Bacoside A

Gastric ulcer models brought on by ethanol aspirin 2h cold restraint stress and 4h pylorus ligation were utilised to test the anti-ulcerogenic activity of fresh juice from the entire plant of *Bocapa monniera wettst* (bmj) popularly known as brahmi in hindi. *Bocapa monniera* juice (bmj) and doses of sucralfate (sf) of 100 and 300 mg/kg were administered orally twice daily for five days except in the case of ethanol-induced ulcers where 100 mg/kg was not shown to significantly reduce them all experimental stomach ulcer models had a robust antiulcer activity at doses between 100 and 300 mg/kg bmj. 100-300 mgkg had little to no impact on the production of offensive acid-pepsin but it dramatically increased the production of defensive mucosal factors by reducing cell shedding and

mucus secretion in terms of total carbohydrates protein ratio (tcp). Two critical criteria of defensive factors bmj 300 mg/kg and sf both had the capacity to enhance the mucosal glycoproteins in terms of tcp. Despite the fact that the amount of each type of carbohydrate and the overall quantity of carbs were either increased or showed a potential to rise. Therefore rather than offensive components like acid and pepsin the ulcer-preventing effects of bmj may be attributable to its effects on mucosal defence factors such as increased mucin synthesis (mucosal glycoprotein) and decreased cell shedding due to mimosine the chief constituent present in juice (Rao CRV *et al*, 2000).

Isorhamnetin

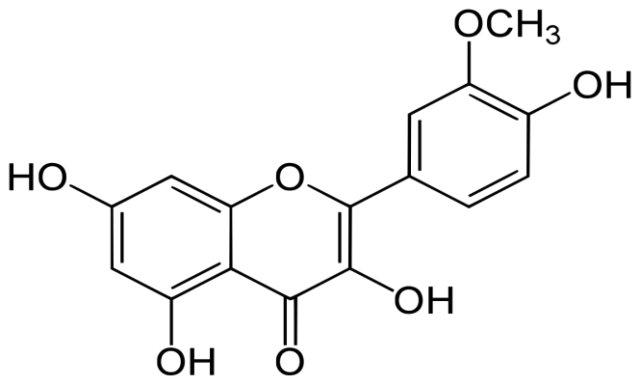

Figure 12. Isorhamnetin

Calendula officinalis has a long history of use in India for blood purification, wound healing, ulcer treatment, herpes, scarring, skin damage, and frostbite. The current study sought to assess the in-vitro antacid and anti-ulcer efficacy of *Calendula officinalis* L extract in experimental rats. *Calendula officinalis* (ECO) ethanolic extract (100 and 200 mg/kg, orally) was tested for anti-secretory and in vivo antacid efficacy in a pyloric ligation-induced ulcer model. The gastro protective effect was investigated using ulcer models induced by 100% ethanol and indomethacin. The amount of gastrointestinal mucus and glutathione was measured to assess the integrity of the gastric mucosa (GSH). The titration method was used to assess the in-vitro antacid capacity. While preserving standards in all ulcer models, ECO significantly reduced the ulcer index. It was discovered that the in-vitro antacid capacity was 20.58 0.08 mEq/g of ECO. In the pylorus ligation model at 200 mg/kg of ECO, the concentrations of total protein and pepsin were determined to be 92.45 1.89 g/ml and 34.67 1.25 moles/ml, respectively. In ulcers brought on by indomethacin, GSH levels were markedly increased by 200 mg/kg of ECO (P 0.01), demonstrating the superiority of complementary medicine (P 0.05). In all three ulcer models, the amount of mucus was increased and was comparable to ranitidine. *C. officinalis*' gastro protective and antisecretory, antiulcer effects on experimental rats resulted due to isorhamnetin. The findings support the traditional use of *C. officinalis* for the treatment of ulcers (Chandra P *et al*, 2015).

L-citrulline

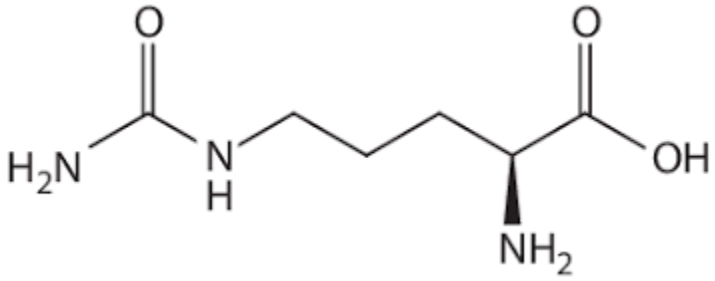

Figure 13. L-citrulline

It is well known that *Citrullus lanatus* has a variety of medicinal benefits. In two separate ulcer models using albino Wistar rats, the anti-ulcerogenic potential of a crude methanolic extract of *C. lanatus* seeds was examined in the current study. The extract exerted a significant effect in the stress-induced ulcer models of pyloric ligation (PL, 4 h ligation) and water immersion (WS, 25 0C for 3 h), showing protection indices of 57.33% and 63.38%, respectively. These values are comparable to those of the standard medications, ranitidine 50 mg/kg and omeperazole (20 mg/kg body weight), which showed protection indices of 64.47% and 70.59%. Additionally, in the case of the pyloric ligation model, the *Citrullus lanatus* considerably reduced the stomach volume (53.55%), free acidity (57.02%), and total acidity (36.53%). In conclusion, *C. lanatus* may have an anti-secretory and cytoprotective mechanism that contributes to its ability to defend against ulcers which is due to citrulline the major phytoconstituent (Alok *et al*, 2012).

Chlorogenic acid

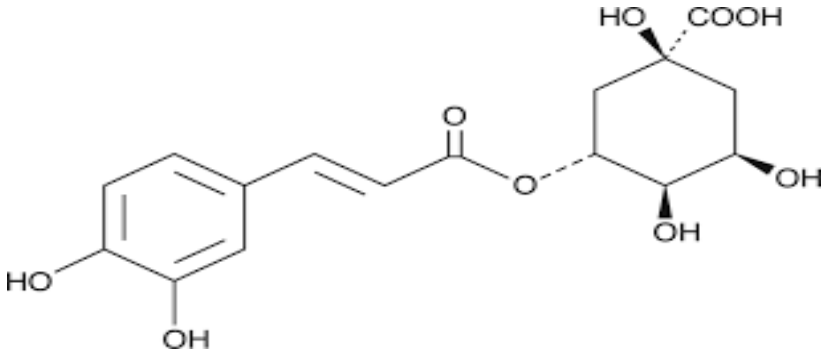

Figure 14. Chlorogenic acid

Chlorogenic acid (CGA), which is found in a wide range of foods like coffee, berries, potatoes, carrots, wine, apples, and many plants, has anti-inflammatory, antidiabetic, and antitumoral characteristics. The CGA is readily absorbed when taken orally, and it has no known effects on stomach ulcers. The current study looked at how oral CGA medication affected male Swiss mice with a stomach ulcer model brought on by ethanol/HCl (Et/HCl) or nonsteroidal anti-inflammatory medicines (NSAIDs). The mice were pretreated with 0.2% carboxymethylcellulose (vehicle, p.o.), 30 mg/kg of omeprazole, 100 mg/kg of carbenoxolone (an antioxidant positive control), or 5, 25, or 50 mg/kg of CGA. The stomach ulcer was produced by administering either piroxicam (100 mg/kg, p.o.) or Et/HCl solution (100 L/10 g body weight; Et 60% + HCl 0.03 M) an hour later. In order to assess the size of the lesion, histological changes, gastric acid secretion, neutrophil migration, oxidative/antioxidative enzymes, markers of lipid peroxidation, or levels of inflammatory mediators, gastric tissues were removed from the Et/HCl- or piroxicam-treated animals after

another hour or four hours, respectively. CGA therapy showed a gastro protective effect in both models, which reduced the percentage of the lesioned region. CGA therapy had little impact on the secretion of gastric action, but it did prevent neutrophil migration and restore the levels of catalase, superoxide dismutase, glutathione peroxidase, glutathione, and thiobarbituric acid reactive components in mice treated with Et/HCl. Additionally, CGA therapy did not correct the lowered prostaglandin levels, but it did stop the rise in tumour necrosis factor alpha and leukotriene B4 in the NSAID-induced ulcer. According to the information presented here, CGA might be a useful natural remedy for the prevention and treatment of stomach lesions occurring from a variety of etiologies (Rao G *et al*, 2010).

Vanillin

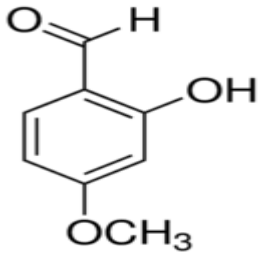

Figure 15. Vanillin

The aqueous extract of the plant *Decalepis hamiltonii* commonly called swallow root, (SRAE) belonging to Asclepiadaceae contain 2-hydroxy-4-methoxy benzaldehyde, an isomer of vanillin. The ulcer index (UI) of 6.0, ±0.01, swim stress-induced ulcers were prevented up to 43% and 72% at 100 and 200 mg/kg b.w. of SRAE, respectively. This is equal to the defense provided by ranitidine (79%) at 30 mg/kg b.w. The extract decreased levels of antioxidant enzymes. The elevated levels of H+-K+-atpase and stomach mucin in ulcerous animals were also rectified by SRAE to values that were 3.1 and 2.4 fold higher than those of unharmed controls, respectively. With an IC50 of 0.17 g/ml gallic acid equivalent, SRAE had lowering power and free radical scavenging ability, similar to BHA (IC50 0.08 g/ml) (GAE). Additionally, DNA preservation of up to 80% was seen at 0.2 g. Rats fed up to 5 g/kg b.w. showed no deadly effects in toxicological tests. Its antiulcer properties have been connected to the actions of SRAE on stomach mucous, antioxidants, and proton pump inhibition (Yogendranaik *et al*, 2007).

Wedelolacetone

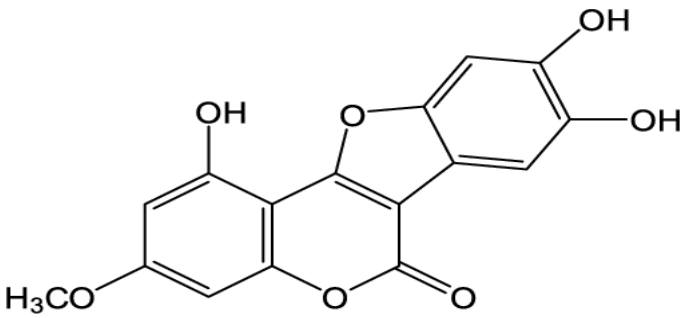

Figure 16. Wedelolactone

Sprague Dawley rats that had not eaten in 36 hours had ulcers caused by aspirin, ethanol, or pylorus ligation combined with aspirin treatment. There were three groups—a normal control, a positive control, and a test—in each induction process. When compared to the control groups, the group receiving oral *E.alba* administration before ulcer induction exhibited a highly significant reduction in the incidence of gastric ulcers and stomach inflammation (after 4 hours of therapy). Additionally, the antiulcer properties of *E.alba* were comparable to those of the proton pump inhibitor rabeprazole (positive control). These findings highlight the necessity of expanding into complementary therapeutic modalities in herbal medicine, where a single readily accessible plant may offer solutions to a number of therapeutic problems, as seen in the anti-ulcer activity of *E. alba* methanol extract which may be attributed to its chief constituent wadelolactone (Banerjee A *et al*, 2005).

Ellagic acid

A polyphenol generated from plants called ellagic acid (EA) possesses anti-inflammatory, gastro protective, and antioxidant effects. Its gastro protective processes as well as its advantages for treating chronic ulcers have not yet been fully defined. Wistar rats were utilised to examine the antiulcer effects of EA utilising models for both acute (ethanol and indomethacin) and chronic (acetic acid) ulcers. In this study, ethanol, indomethacin, and acetic acid use resulted in a marked reduction in the incidence of stomach ulcers after oral administration of EA. In ethanol-induced ulcers, its gastro protective mechanism was partly attributed to increased endogenous nitric oxide production, an antioxidant effect by replacing lost endogenous nonprotein sulfhydryls, and attenuation of tumour necrosis factor-increase, whereas it was partially attributed to a decrease in plasma leukotriene B4 levels in indomethacin-induced ulcers.

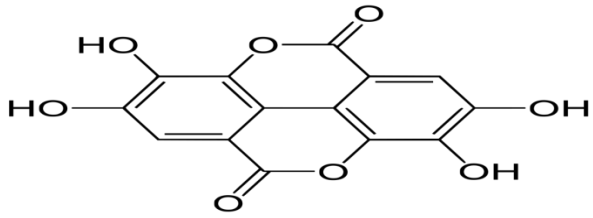

Figure 17. Ellagic acid

The lowering of the inflammatory cytokines TNF-, interferon-, and interleukins-4 and -6, whose greater levels were achieved by the treatment, was partially responsible for the promotion of ulcer-healing effects in acetic acid ulcers. These findings suggest that ellagic acid exerts its antiulcer effect by increasing the preventive factors while lowering the aggravating ones (Sai Ram *et al*, 2002).

Hyperforin

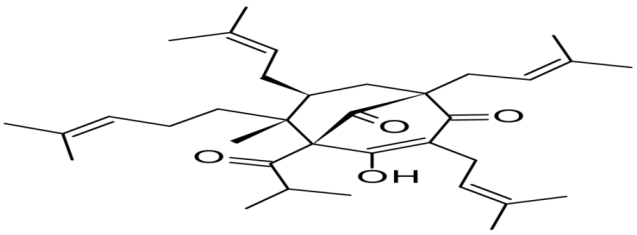

Figure 18. Hyperforin

The plant *Hypericum perforatum* (HP) is indigenous to Asia and Europe. Burns, depression, and anxiety are just a few of the illnesses it has been proved to be effective in treating. In rats with ethanol-induced gastric ulcers, this study looked at the gastro-protective effects of esomeprazole and *H.perforatum* leaf extract (the drug of choice for stomach ulcers). The mechanism of action was carried out using the Auto Dock Vina approach. Ethanol consumption up-regulates the inflammatory response by raising the stomach's pro inflammatory TNF- and lowering its pro inflammatory IL-1 levels. On the other hand, HP's phytochemical study revealed that it included alkaloids, flavonoids, tannins, phenols, steroids, and saponins. The stomach mucosa of the ulcer control rat group shows significant damages, in contrast to the esomeprazole group, which shows modest gastric mucosa injuries. Amentoflavone and quercitrin have the best interactions and highest affinities with the active site of the H+/K+ ATPase, according to *in silico* results. This study shows that HP is approximately as effective in preventing ethanol-induced gastric ulcers as esomeprazole at binding to stomach proton pumps due to its chief component hyperforin (Sargul *et al*, 2020).

Silibinin

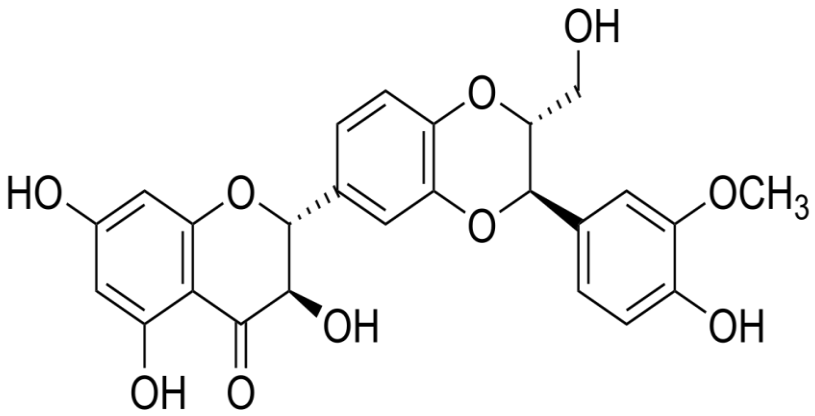

Figure 19. Silibinin

When rats' stomachs were damaged by ischemia-reperfusion, researchers looked at silymarin's effects on mucosal myeloperoxidase activity, a marker of polymorph nuclear leukocyte infiltration, and its antiulcer properties. Silymarin is a hepatoprotective compound discovered in the plant *Silybum marianum* L. These outcomes were contrasted with those from rats that had previously received an injection of dexamethasone and methotrexate to make them neutropenic, as well as with outcomes from rats that had previously received the xanthine oxidase inhibitor allopurinol. Pretreatment with silymarin prevented post-ischemic mucosal damage. In comparison to control rats, rats given 25, 50, and 100 mg of silymarin/kg body weight had significantly lower mean ulcer indices (U.I.) (4.79 0.75, 4.50 0.81, and 3.63 0.74, respectively) (p 0.05, 0.05, and p 0.005). The estimated U.I. for allopurinol was 2.33 0.45, p 0.001, significantly lower than that for silymarin. A reduction in neutrophils in the stomach mucosa was specifically blamed for these protective effects. Lower levels of circulating neutrophils in rats receiving methotrexate (MPO level of 7.2 10-2 0.56 10-2U/mg wt) and dexamethasone (MPO level of 6.97 10- 0.68 10-2U/mg wt) significantly decreased their sensitivity to the harm brought on by ischemia-reperfusion to the stomach. These findings imply that neutrophils are necessary for the malfunctioning of the gastric mucosa brought on by ischemia-reperfusion. These findings further

suggest that silymarin's ability to decrease neutrophil function may have a substantial impact on its gastro protective properties (Alarcon *et al*, 1995).

Conclusion

This study suggests that investigation into plant origins can result in the creation of distinctive and effective treatment plans. Due to contemporary medicine's present inability to effectively cure a variety of disorders, traditional medicine is being investigated more and more. This study suggests that investigation into plant origins can result in the creation of distinctive and effective treatment plans. Due to contemporary medicine's present inability to effectively cure a variety of disorders, traditional medicine is being investigated more and more.Due to contemporary medicine's present inability to effectively cure a variety of disorders, traditional medicine is being investigated more and more. Pharmacologists, pharmaceutical chemists, and pharmacognosists must therefore take a more active interest in assessing the potential antiulcer activity and standardising such medications in order for herbal medicines to be clinically effective and globally competitive.

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Conflict of interest

None

Funding source

None

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