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A REVIEW ON THE ANTIULCER POTENTIAL OF VARIOUS HERBAL EXTRACT IN DIFFERENT ANIMAL MODELS

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Abstract

Ulcers, particularly peptic ulcers, remain a significant health issue worldwide, primarily caused by factors like stress, Helicobacter pylori infection, excessive use of nonsteroidal anti-inflammatory drugs (NSAIDs) and imbalances in gastric acid secretion. Although conventional medications like proton pump inhibitors and H_2 antagonists are commonly used to treat ulcers, herbal remedies have garnered considerable attention due to their potential therapeutic benefits and minimal side effects. This review explores the antiulcer activity of various herbal extracts traditionally used in folk medicine. The bioactive compounds present in these herbs, including flavonoids, alkaloids, steroids, glycosides, saponins, tannins, etc. have shown promising effects in promoting gastric mucosal healing, reducing acid secretion and protecting against oxidative stress and inflammation. Herbs like *Aloe vera*, *Zingiber officinale*, *Nerium indicum*, *Carica papaya* and *Prunus persica* have shown strong antiulcerogenic properties by mechanisms such as inhibiting gastric acid secretion, protecting the mucosa and boosting mucin production. Additionally, certain herbs possess antimicrobial activity against H. pylori, a key contributor to ulcer formation. Peptic ulcer disease can affect individuals of all ages, though it is more commonly seen in middle-aged adults and men. The prevalence of peptic ulcers has decreased in many parts of the world due to the use of antibiotics to treat H. pylori infections, though they remain common in certain populations. This review provides a comprehensive overview of various herbal extracts, their pharmacological activities and their potential as effective antiulcer agents, emphasizing the need for further research and clinical trials to validate their efficacy and safety in ulcer treatment.

Keywords: Peptic ulcer, Herbal extract, Antiulcer activity, Animal model, Folk medicine, NSAIDs.

Introduction

Ulcers, which are sores that develop on the lining of the stomach or intestines characterized by inflammation, mucosal bleeding and abdominal pain in patients. Bacterial infections, prolonged use of certain medications, stress, poor dietary habits and chronic alcohol intake are the crucial causes of ulcers. The primary risk factors

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for both gastric and duodenal ulcers include Helicobacter pylori infection and the use of nonsteroidal anti-inflammatory drugs (NSAIDs). These conditions can lead to significant discomfort and if untreated more severe health complications. In ulcers, there is an imbalance that occurs between the gastro-protective (mucus, bicarbonate, prostaglandins) and aggressive (acid, pepsin, bile salts, Helicobacter pylori) factors. The main strategy for treating ulcers involves enhancing gastroprotective factors and counteracting aggressive factors. [1]

It is known that numerous pharmaceutical agents such as proton pump inhibitors, anticholinergics, antacids, antimicrobial agents, H2-receptor antagonists, sucralfate and bismuth are not fully effective and produce numerous adverse effects such as impotence, arrhythmia, hematopoietic alterations, hypersensitivity and gynecomastia. Due to that, investigations of the new pharmacologically active agents through the screening of different plant extracts led to the discovery of effective and safe drugs with gastroprotective activity. Especially, plants with antioxidant capability as the main mechanism are used as the herbal reservoir for the treatment of ulcer disease. Plant extracts and their crude are the most significant sources of new drugs and have been shown to cause promising results in the treatment of gastric ulcers as well.[2]

Treating ulcers can be challenging, but certain herbs with antiulcer properties offer a safer alternative, as they have no known side effects. In contrast, antiulcer medications can cause severe unwanted effects and may be harmful to the body. The primary side effects of anti-ulcer medications include headache, dizziness, fatigue, achlorhydria, constipation and diarrhea. Therefore, the use of herbal medicines for treatment has become increasingly important in recent times. Herbal medicines contain a variety of phytochemical compounds such as alkaloids, glycosides, flavonoids and tannins, which exhibit antioxidant and antibiotic properties with little to no side effects.[3]

Pathophysiology of Ulcer

Peptic ulcer disease (PUD) occurs due to an imbalance between the protective and destructive factors of the gastric mucosa. Key risk factors include:

- Infection with Helicobacter Pylori.
- The use of NSAIDs.
- Having a first-degree relative with a history of peptic ulcer.
- Age.
- Smoking.
- Alcohol.
- Stress.
- Zollinger - Ellison syndrome.

Once the protective superficial mucosal layer is damaged, the underlying layers become vulnerable to acidic environments. The mucosal cell's ability to secrete bicarbonate is impaired and H. pylori colonizes the gastric mucosa, leading to inflammation. This further disrupts bicarbonate secretion, promoting increased acidity and the development of gastric metaplasia.[4]

Treatment

Peptic ulcers, particularly duodenal ulcers, are indeed chronic conditions characterized by periods of remission and relapse. The main goals of antiulcer therapy are as follows:

Relief of pain: Medications such as proton pump inhibitors (PPI's), H_2 – receptor antagonists or antacids can reduce acid production and provide relief.

Ulcer healing: Involves acid suppression (via PPI's, H_2 blockers or antacids) and possibly antibiotics if the infection with H. pylori is present.

Prevention of complications: Effective therapy including eradication of H. pylori if present and proper acid suppression, reduces the risk of complications.

Prevention of relapse: Involves ongoing use of PPI's or H_2 blockers and addressing risk factors such as NSAID use, alcohol consumption and smoking.

Drugs for peptic ulcer

1. Gastric acid secretion inhibitors

a) H_2 Antihistamines

Cimetidine, Ranitidine, Famotidine, Roxatidine, Lafutidine

b) Anticholinergics

Pirenzepine, Propantheline, Oxyphenonium

c) Proton pump inhibitors

Omeprazole, Esomeprazole, Pantoprazole, Lansoprazole, Rabeprazole

d) Prostaglandin analogue

Misoprostol

2. Gastric acid neutralizers (Antacids)

a) Systemic

Sodium bicarbonate, Sodium citrate

b) Nonsystemic

Magnesium hydroxide, Magnesium trisilicate, Aluminium hydroxide

3. Ulcer protectives

Sucralfate, Colloidal bismuth subcitrate

4. Anti H. pylori drugs

Amoxicillin, Clarithromycin, Metronidazole, Tinidazole, Tetracycline.[5]

Review of Literature

Terminalia argentea

Claudia Luis Venturi et. al. (2024) conducted a study to evaluate the antiulcer activity of the hydroethanolic extract (HETa) from the leaves of *Terminalia argentea* Mart. In various in vivo and in vitro models. Nonsteroidal anti-inflammatory drugs (NSAIDs) are known to pose a risk of damaging the gastric and duodenal mucosa through several mechanisms. However, species in the *Terminalia* genus, including *Terminalia argentea*, are believed to counteract this damage, likely by inhibiting COX-1 activity and reducing the harm caused by ethanol-induced chronic ulcers. The study showed that the hydroethanolic leaf extract significantly reduced the ulcerated area by over 90% after 7 days of treatment at doses of 2 and 10 mg/kg. The extract's antiulcer effects are attributed to its antioxidant, anti-inflammatory, mucogenic, angiogenesis-promoting and fibroblast proliferating properties. Key active constituents including phenolics, flavonoids and tannins play an essential role in these therapeutic activities.[6]

Tagetes erecta

Amrish Kumar et. al. (2024) conducted a comparative assessment of the antiulcer effects of the hydroethanolic extracts from air-dried ray and disc florets Vs the essential oil of the traditional herb *Tagetes erecta* in Swiss albino rats. Traditionally *Tagetes erecta* has been used to treat various ailments, including ulcers. The study suggests that both the hydroethanolic extract and essential oil may contribute to regulating gastric acid secretion or enhancing the cytoprotective secretion of bicarbonate, mucus and prostaglandin. The observed antiulcer activity is likely attributed to key phytochemicals such as Quercetin- 3- methyl ether, quercetin-7- methyl ether and kaempferol flavonoids in the extract, as well as limonene and terpinolene in the essential oil of the leaves, which supports the traditional use of *Tagetes erecta* for ulcer treatment.[7]

Lagenaria siceraria

Vivek Srivastava et. al. (2021) investigated the antiulcer properties of the methanolic extract of *Lagenaria siceraria*, highlighting its anti-secretory, cytoprotective and antioxidant effects. The study found that the fruit extract exhibits antiulcer activity through various mechanisms, including the inhibition of histamine receptors,

modulation of prostaglandins and antioxidant actions. The presence of phytochemical compounds such as flavonoids and triterpenoids may contribute to its antiulcer effects.[1]

Lactuca sativa

B Maheswari et. al. (2020) evaluated the antiulcer activity of the ethanol extract of *Lactuca sativa* leaves in rats. Phytochemical screening of EELS identified the presence of flavonoids, tannins and triterpenoids, which are responsible for its antiulcer activity. This activity is attributed to its anti-secretory, cytoprotective and antioxidant properties. EELS has anti-ulcerogenic potency in Ethanol-induced, pylorus ligation and cold restraint stress-induced ulcers in rats.[8]

Nymphaea alba

Ashish K Paharia et. al. (2020) evaluated the antiulcer activity of the ethanolic extract of *Nymphaea alba* flowers in experimental rats. The phytochemical analysis identified the presence of alkaloids, carbohydrates, tannins, phytosterols, anthraquinone glycosides, saponins, steroids and flavonoids. The study concluded that tannins and flavonoids are likely responsible for the observed antiulcer effects. The ethanolic extract of *Nymphaea alba* demonstrated effectiveness in promoting the healing of gastric ulcers induced by ethanol and pyloric ligation, which was attributed to a reduction in gastric acid secretion and enhanced gastric cytoprotection.[9]

Osyris quadripartita

Mastewal Abebaw et. al. (2017) evaluated the antiulcer activity of the leaf extract of *Osyris quadripartita* in rats, a plant traditionally used in Ethiopia for the treatment of peptic ulcers. Phytochemical analysis revealed the presence of various secondary metabolites, including alkaloids, tannins, glycosides, steroids, terpenoids, flavonoids, saponins and anthraquinones. These compounds are known for their antioxidant, anti-neoplastic, antiulcer, anti-inflammatory and immune-stimulating properties. Flavanoids, in particular, help to increase mucosal prostaglandin levels, reduce histamine release from mast cells, inhibit the growth of Helicobacter pylori, and block proton pumps. Saponins may activate protective factors in the mucus membrane, while terpenoids and alkaloids show potent activity against gastric ulcers. The antiulcer effects of *Osyris quadripartite* are attributed to both its anti-secretory and cytoprotective activities, which are likely due to the synergistic effects of one or more of its identified phytochemicals.[10]

Figure 1: ***Arctocarpus hirsutus***

Figure 2: ***Rheum spiciforme***

Figure 3: ***Rumex tianschanicus Losinsk***

Figure 4: ***Prunus persica***

Figure 5: ***Capparis zeylanica***

Figure 6: ***Ficus thonningii***

Figure 7: ***Croton macrostachyus***

Figure 8: ***Ficus religiosa***

Figure 9: ***Hannoa klaineana***

Figure 10: ***Nerium indicum***

Figure 11: ***Carica papaya***

Figure 12: ***Anvillea garcinii***

Figure 13: ***Spondias mombin***

Figure 14: ***Calpurnia aurea***

Table 1: Antiulcer activity of selected herbal extracts

Botanical Name	Family	Parts used	Solvent used	Chemical Constituents	Animal Used	Screening Method	Reference
Arctocarpus hirsutus [11]	Moraceae	Leaves	Ethanol	Alkaloid, Flavanoids, Proteins, Reducing steroids, Sugar, Tannins	Albino Wistar Rat	1.Ethanol-induced ulcer model 2.Pylorus ligation-induced ulcer model	Chaithra B N et al. 2023
Rheum spiciforme [12]	Polygonaceae	Roots	Aqueous ethanol	Aloe-emodin, Butanol fraction, Emodin	Albino Rat	Ethanol-induced ulcer model	Hafiz Muhammad Irfan et al. 2023
Rumex tianschanicus Losinsk [13]	Polygonaceae	Roots	Ethanol	Anthraquinone, Flavanoids, Tannins	Rat	Indomethacin-induced ulcer	Gulnaz A Seitimova et al. 2023
Calpurnia aurea [14]	Fabaceae	Leaves	Hydromethanol	Flavanoids, Saponins	Rat	1. Acetic acid-induced chronic ulcer 2. Acidified ethanol-induced gastric ulcer 3. Pylorus ligation-induced ulcer model	Yared Andargie et al. 2022
Capparis zeylanica [15]	Capparaceae	Leaves	Ethanol	Flavanoids, Saponins, Tannins	Wistar rat, Swiss albino mice	1. Ethanol-induced ulcer model 2. Histamine-induced ulcer model 3. Naproxen-induced ulcer model	Abhishek Tripathi et al. 2021
Ficus thonningii [16]	Moraceae	Stem bark	Hydromethanol	Alkaloids, Flavanoids, Glycoside, Phenols, Saponins, Tannins, Terpenoids	Female Swiss albino mice	1. Ethanol-induced ulcer model 2. Indomethacin-induced ulcer model	Habtalem Adane et al. 2021
Croton macrostachyus [17]	Euphorbiaceae	Roots	Methanol	Alkaloids, Flavanoids, Phenols, Saponins, Tannins, Terpenoids	Adult Sprague Dawley rats, Swiss albino mice	1. Pylorus ligation model 2. Ethanol/HCL-induced ulcer model	Alefe Norahun Mekonnen et al. 2020
Ficus religiosa [18]	Moraceae	Stem bark	Ethanol Acetone	Alkaloids, Flavanoids, Glycoside, Phenols, Steroids, Tannins	Wistar albino rat	Ethanol induced ulcer model	Marslin Gregory et al. 2020
Hannoa klaineana [19]	Simaroubaceae	Leaves	Methanol	Alkaloids, Flavanoids, Glycoside, Saponins, Steroids, Tannins, Terpenoids	Wistar albino rat	1. Ethanol-induced ulcer model 2. Indomethacin-induced ulcer model	Ibrahim Abubakar et al. 2020

Nerium indicum [20]	Apocynaceae	Stem	Ethanol	Gallic acid, Ellagic acid	Wistar rat	1. Pylorus ligation-induced model 2. Cold restraint induced model 3. Ethanol-induced model 4. Indomethacin-induced model 5. Aspirin-induced model	Shrinivas K Sarje et al. 2020
Carica papaya [21]	Caricaceae	Root	Water	Papain	Wistar rat	Ethanol-induced model	N. Sridhar et al. 2019
Anvillea garcinii [22]	Asteraceae	Leaf	Ethanol	Flavanoid	Sprague Dawley Albino rat	1. Pylorus ligation-induced model 2. Gastric lesions induced by various ulcerogens 3. Gastric lesions induced by indomethacin 4. Ulcers induced by hypothermic restraint stress	Shagufta Perveen et al. 2018
Spondias mombin [23]	Anacardiaceae	Leaf	Ethanol	Gallic acid, Ellagic acid	Wistar rat	Ethanol-induced model	Samara Alves Brito et al. 2018
Prunus persica [24]	Rosaceae	Fruit	Aqueous methanol	Alkaloids, Flavanoids, Glycoside, Phenols, Tannins	Wistar albino rat, Swiss albino mice	1. Ethanol-induced gastric ulcer model 2. Cysteamine-induced duodenal ulcer model	Qaiser Jabeen et al. 2018

Discussion

The review of traditional medicine in the management of peptic ulcers highlights various plant parts with antiulcer properties. The literature indicates that many traditional plants show significant antiulcer activity, primarily due to the presence of diverse chemical constituents. These bioactive constituents exhibit anti-inflammatory effects, antioxidant properties, mucosal protective actions, antibacterial activity, acid-reducing effects and promote tissue regeneration among other benefits. While modern treatment options offer effectiveness, they also present several drawbacks including high costs, patient non-compliance, side effects, antibiotic resistance, rebound acid hypersecretion, overuse, misuse and potential drug interactions. These issues could potentially be addressed through the use of traditional medicine. Traditional remedies offer natural healing, fewer side effects, enhanced overall patient health and greater accessibility. However, further research is necessary to fully understand and promote the widespread use of traditional medicine for peptic ulcer treatment.

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