

A REVIEW ON RECENT TREND AND ADVANCEMENT IN NOVEL DRUG DELIVERY SYSTEM USING MEDICINAL PLANT FOR PEPTIC ULCER TREATMENT

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ABSTRACT

Peptic ulcer disease (PUD) is considered as one of the common diseases in the world. Treatment of peptic ulcer with synthetic drugs such as proton pump inhibitors, H₂ receptor antagonists and other non-steroidal anti-inflammatory drugs has shown adverse effects, relapses, drug interactions. Medicinal plants containing active chemical constituents are useful in prevention and treatment of various diseases. Among natural products the alkaloids, biologically active secondary metabolites that can be found in plants, animals or microorganisms stand out. The alkaloids are compounds consisting of a basic nitrogen atom that may or may not be part of a heterocyclic ring. Literatures suggest that polyherbal formulations of medicinal plants are considered to be potential source for the treatment of ulcers. Combination of

ayurvedic knowledge with modern medicine can produce better antiulcer drugs of natural origin from medicinal plants with fewer side effects. This study has presented the review of commonly used anti-ulcer plants which are used for the treatment or prevention of peptic ulcers and the other reported activities of these plants. This study also presented the Recent Advancements in Drug Delivery Systems.

KEYWORDS: Phytoconstituent, peptic ulcer, natural products, Medicinal plants, prevention, treatment, Drug Delivery Systems.

INTRODUCTION

A peptic ulcer happens when the stomach or duodenal lining get Damaged due to certain medicines like NSAIDs stomach acid and peptic, resulting in sores in the intestine.^[1] In the

recent and advancement in novel drug delivery system using alkaloid to treat peptic ulcer, it means understanding how these new treatment are being used, their effectiveness, and any changes in the occurrence and impact of peptic ulcer in populations. Factor contributing to the recent trend and advancement in using alkaloids for treating peptic ulcer include the therapeutically potential of alkaloids, improved drug delivery methods, patient convenience, and reduced side effect, personalized treatments.^[2] the recent and advancement in the treatment of peptic ulcer Phytoconstituent and novel drug delivery system, we find the progress in ulcer treatment more effective.^[3] peptic ulcer are open sores that develop on the inner lining of the stomach, the small intestine, or thresophagus. They can be quite painful and are often caused by factor like heliobacter pylori infection, excessive use of non – steroidal anti- inflammatory (NSAIDs), stress, or alcohol consumption. Drug plays a signification role in the treatment of peptic ulcer. Over the year, there have been several recent trends and advancement in the use novel drug delivery system, including those using medicinal plants, in the treatment of peptic ulcer.^[4] one of the prominent trends in drug delivery is the use of nanotechnology. Scientists have developed tiny particle, known as nanoparticles, to delivery medicinal plant compound to the site of the ulcer. microencapsulation technology involves enclosing medicinal plant compound within microspheres or capsules.^[5] medicinal plant extract often have poor solution in water, which can limit their absorption in body. mucoadhesive drug delivery system are designed to stick to the mucous membranes of the gastrointestinal tract, including the stomach lining.^[6] biodegradable and biocompatible polymer are employed to create drug delivery system that release medicinal plant compound in a controlled manner. The latest trend and advancement in using medicinal plant for creating new way to deliver drug in the treatment of peptic ulcers.^[7]

Pathogenesis of peptic ulcer

Numerous factors, including *H. pylori*, NSAIDs, acid and pepsin, heredity, and smoking, contribute to the pathogenesis of peptic ulcers (Fig. 1). The infection caused by *H. pylori* represents one of the major factors for the pathogenesis and development of peptic ulcers. *H. pylori* has been known to induce significant epithelial cell degeneration and injury due to the inflammatory response with neutrophils, lymphocytes, plasma cells, and macrophages.^[8] Cytokines have been considered as chief mediators of *H. pylori* infection which results in parietal cell secretion. Also, the $H^+ / K^+ ATPase$ -subunit gets directly affected by *H. pylori*. Additionally, *H. pylori* have been reported to inhibit gastrin production.^[8,9] Further, the

cyclooxygenase-1 (COX-1) enzyme has been known to cause prostaglandin synthesis. Moreover, it has been discovered that

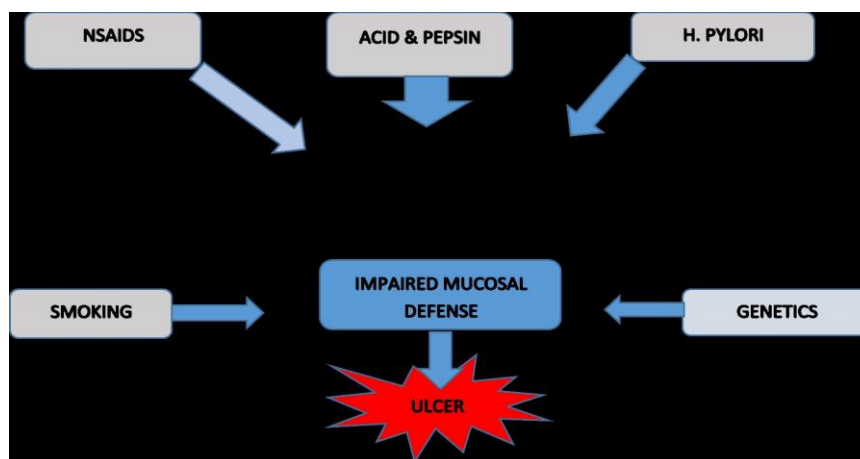


Fig1:- Factors involved in the pathogenesis of peptic ulcer.

COX-1 inhibits cell growth, mucosal blood flow, and bicarbonate secretion.^[9] The systemic inhibition of COX-1 enzyme expression presents the most important route of NSAID-associated damage. The enzyme is inhibited reversibly in a concentration-dependent manner by NSAIDs. The mucosal damage gets initiated by the uncoupling of mitochondrial oxidative phosphorylation, which is a result of mucus phospholipids disruption by NSAIDs.^[10] When NSAIDs are exposed to acidic gastric juice (pH 2), they become protonated. This further causes them to penetrate lipid membranes and enter epithelial cells (pH 7.4), where H⁺ ions are released. Furthermore, in that state, NSAIDs are unable to pass the lipid membrane and become trapped in epithelial cells. This ultimately results in the uncoupling of oxidative phosphorylation, increased cellular permeability, decreased mitochondrial energy production, and reduced cellular integrity.^[11]

This has been well documented that peptic ulcers occur more commonly in smokers when compared to non-smokers.^[12] Smoking-induced peptic ulcers are caused by a number of factors, including an increase in acid secretion and changes in blood flow. Additionally, it has been suggested that factors including bile reflux induction and a decrease in prostaglandin production can result in peptic ulcers in smokers.^[13] According to reports, peptic ulcer development and progression are significantly influenced by genetics.^[14] This has been shown that autosomal dominant inheritance of hyperpepsinogenemia I is seen in patients presenting with duodenal ulcers. Additionally, a variety of uncommon genetic abnormalities,

including familial amyloidosis, gastro cutaneous syndrome, stiff man syndrome, and tremor nystagmus ulcer syndrome, have been linked to peptic ulcer disease.^[15]

Conventional therapy for peptic ulcer

Several conventional treatments, such as PPIs, H₂ receptor antagonists, potassium competitive acid blockers, antacids, and antibiotics, have been documented for the treatment of patients presented with peptic ulcers.^[16,17] The PPIs have been documented to block the gastric hydrogen potassium (H⁺ /K⁺) ATPase, an enzyme that resides on the luminal surface of the parietal cell membrane. The ulcer then heals as a result of the reduction in gastric lining irritation and the inhibition of gastric acid output in the stomach and intestine.^[18] Surprisingly, PPIs have also been reported to treat *H. pylori* infection when used along with antibiotics. In addition, PPIs have also been used to prevent ulcers in the patients exposed to long-term use of NSAIDs.^[19] The main PPIs are omeprazole, lansoprazole, rabeprazole, esomeprazole and pantoprazole. H₂ receptor antagonists, which include cimetidine, famotidine, ranitidine, and nizatidine, are a different class of medications that are frequently used to treat peptic ulcers.^[20] It is known that the histamine type-2 receptors on the basolateral surface of stomach parietal cells bind to H₂ receptor antagonists. This in turn inhibits the binding and activity of histamine, thereby interfering with the gastric acid production pathway, ultimately leading to the inhibition of gastric acid secretion.^[21] This inhibition of gastric acid secretion further reduces irritation to the gastric lining, ultimately helping in the healing of an ulcer. Antacids like aluminum hydroxide, sodium bicarbonate, magnesium hydroxide and calcium carbonate have been known to act by neutralizing the gastric acid in the stomach and intestine.^[22] Antacids have been known to increase the pH inside gastric and intestinal cells, thereby reducing the acid delivery to these sites. In addition, the antacids have been shown to restrain pepsin, a proteolytic enzyme inside gastric and intestinal cells, thus producing potent therapeutic effects.^[23] Another class of drugs that have a place in conventional therapy for the treatment of peptic ulcer is potassium-competitive acid blockers like vonoprazan and revaprazan.^[24] These new medications have been discovered to reversibly bind to K⁺ ions, inhibit H⁺ /K⁺ ATPase enzyme in gastric parietal cells, and ultimately halt the generation of stomach acid.^[25] In addition, this class of drugs possesses dose-dependent effects on gastric acid production, and is known to comprise of fast onset of action.^[26]

Medicinal Plant and there phytoconstituent used for GIT treatment

medicinal plant containing alkaloid and their phytoconstituent have been traditionally used and studied for their potential gastrointestinal (GIT) treatment benefits.^[27] these compound can have a wide range of action on the digestive system, including anti-inflammatory, antispasmodic, antimicrobial, and other therapeutic effect.^[28,29]

Ginger (*Zingiberofficinale*) Phytoconstituent:- Ginger contains **gingerol**, a compound with anti-inflammatory and antiemetic (anti-nausea) properties. It is often used to alleviate symptoms of indigestion, nausea, and motion sickness.^[30]

Peppermint (*Mentha × piperita*): Phytoconstituent:- Peppermint contains **menthol**, which has antispasmodic effects and can help relax the muscles of the gastrointestinal tract. It is used to relieve symptoms of irritable bowel syndrome (IBS) and indigestion.^[31]

Turmeric (*Curcuma longa*): Phytoconstituent:- **Curcumin**, the active compound in turmeric, has anti-inflammatory and antioxidant properties. It is used to reduce inflammation in the gut and may benefit conditions like inflammatory bowel disease (IBD).^[32]

Dandelion (*Taraxacumofficinale*) Phytoconstituent: Dandelion contains bitter compounds that stimulate digestion. It is used to support liver and gallbladder health, which can have indirect benefits for digestion.^[33]

Clove (*Syzygiumaromaticum*) Phytoconstituent:- Clove contains **eugenol**, which has antimicrobial and analgesic properties. Clove oil can be used to relieve dental pain and has been used for stomach-related discomfort.^[34]

Cinnamon (*Cinnamomumverum*) Phytoconstituent:- Cinnamon contains **cinnamaldehyde**, which has been studied for its potential to help regulate blood sugar levels and improve insulin sensitivity, which can be relevant for GIT conditions like diabetes.^[35]

Aloe Vera (*Aloe barbadensis miller*) Phytoconstituent:- Aloe Vera contains compounds like **aloin** and **aloe-emodin**, which have been investigated for their potential anti-inflammatory and soothing effects on the gut. Aloe Vera is used to relieve symptoms of gastritis and indigestion.^[36]

Licorice (Glycyrrhizaglabra): Phytoconstituent:- Licorice contains **glycyrrhizin**, which can protect the stomach lining and reduce inflammation. It is used for managing symptoms of gastritis and ulcers.^[37]

Fennel (Foeniculumvulgare) Phytoconstituent:- Fennel contains **anethole**, which has antispasmodic properties and can help relieve symptoms of indigestion and bloating.^[38]

Chamomile (Matricariachamomilla) Phytoconstituent:- Chamomile contains **apigenin**, which has anti-inflammatory and calming effects. Chamomile tea is often used to soothe the digestive tract and reduce symptoms of indigestion.^[39]

Medicinal Plant there phytocontituents and there GIT treatment Benefit.

Table No. 1: Alkaloids and there phytoconstiteud or GIT treatment.

Medicinal Plant	Alkaloid & phytocontituents	GIT Treatment Benefit
Ginger (Zingiber Officinale)	Phytoconstituent: gingerol	Anti-inflammatory properties antiemetic effect (reduce nausea) alleviates symptoms of indigestion used in motion sickness. ^[30]
Peppermint (Mentha piperita)	Phytoconstituent: menthol	Antispasmodic properties muscle relaxant for the gastrointestinal tract alleviates symptoms of irritable bowel syndrome (IBS) helps with indigestion. ^[31]
Turmeric (Curcumin Longa)	Phytoconstituent: Curcumin	Anti-inflammatory properties antioxidant effect reduced inflammation in the gut. ^[32]
Dandelion (Taraxacum Officinale)	Phytoconstituent: bitter compound	Stimulates digestion supports liver and gallbladder health indirect benefit for digestion by aiding liver function. ^[33]
Clove (Syzygium aromaticum)	Phytoconstituent: eugenol	Antimicrobial properties analgesic effect(pain relief) used to alleviate dental pain and related discomfort potential benefits for stomach-related issues. ^[34]
Cinnamon (Cinnamomum verum)	Phytoconstituent: cinnamaldehyde	Potential blood sugar regulation improved insulin sensitivity relevant for GIT conditions associated with diabetes. ^[35]
Aloe Vera (Aloe barbadensis miller)	Phytoconstituent:-aloin, aloe-emodin	Soothes the digestive tract may have anti-inflammatory effect on the gut used to relieve symptoms of gastritis and indigestion. ^[36]
Licorice (Glycyrrhiza glabra)	Phytoconstituent: Glycyrrhizin	Supports the stomach lining

	acid	reduces inflammation in the gut used to manage symptoms of gastritis and ulcer. ^[37]
Fennel (<i>Foeniculum vulgare</i>)	Phytoconstituent: anethole	Antispasmodic properties -help relieve symptoms of indigestion and bloating. ^[38]
Chamomile(<i>Matricaria chamomilla</i>)	Phytoconstituent: apigenin	Used as a natural remedy for various gastrointestinal issues, such as indigestion, bloating, and irritable bowel syndrome. ^[39]

Recent Advancements in Drug Delivery Systems

Nanoparticle

Nanoparticle are tiny structure made of synthetic or semi-synthetic polymer, typically ranging in size from 10 to 1000 nanometer s. they are like small capsules that can safty transport drug to the right place in the body. Peptic ulcers are a broad term that includes ulcers of digestive tract in the stomach or the duodenum.^[40] The formation of peptic ulcers depends on the presence of acid and peptic activity in gastric juice plus a breakdown in mucosal defenses. A number of synthetic drugs are available to treat ulcers. But these drugs are expensive and are likely to produce more side effects when compared to herbal medicines. The literature revealed that many medicinal plants and polyherbal Formulations are used for the treatment of ulcer by various ayurvedic doctors and traditional medicinal practitioners. The ideal aims of treatment of peptic ulcer disease are to relieve pain, heal the ulcer, and delay ulcer recurrence. In this review attempts have been made to know about some medicinal plants which may be used in ayurvedic as well as modern science for the treatment or prevention of peptic ulcer. Now treatment of ulcer mainly targets the potentiation of the defensive system along with lowering of acid secretion. 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).^[41]

Dendrimers

That characterized by their branched nanostructures, possess a high drug loading capacity and controlled release properties, rendering them well-suited for the sustained delivery of alkaloids to the site of the ulcer. Recent research has explored the use of dendrimers for delivery of various Phytoconstituent in peptic ulcer treatment: Berberine-loaded dendrimers: Studies have shown that berberine-loaded dendrimers exhibit improved anti-inflammatory and ulcer healing properties compared to free berberine. Capsaicin-conjugated dendrimers: These dendrimers specifically deliver capsaicin to the ulcer site, reducing gastric acid secretion and promoting healing with minimal systemic sideeffects. Matrine-encapsulated dendrimers: These dendrimers enhance the bioavailability and efficacy of matrine, providing sustained protection against gastric ulcers. Curcumin-loaded dendrimers: These dendrimers offer improved delivery of Curcumin to the ulcer site, enhancing its anti-inflammatory and antioxidant effects for faster healing.^[42]

Micelles

A drug delivery system Micelles as a drug delivery system. Micelles are self-assembled amphiphilic molecules with a hydrophobic core and hydrophilic shell. The hydrophobic core can accommodate poorly water-soluble drugs, while the hydrophilic shell helps the micelle stay dispersed in the aqueous environment. Nanostructured delivery systems, including micelles, show great potential in addressing these constraints and enhancing the therapeutic effectiveness of Phytoconstituent in treating peptic ulcers. Micelles, composed of amphiphilic molecules, spontaneously form self-assembled structures characterized by a hydrophobic core and a hydrophilic shell. This unique architecture enables them to encapsulate alkaloids, shielding them from degradation within the harsh gastrointestinal environment. Moreover, the design of micelles allows for a sustained and controlled release of their cargo, ensuring an extended therapeutic impact at the intended target site.^[43]

Microparticals & polymeric

Micro particulate carriers like polymeric micro particles are found to have lots of applications in ulcerative colitis patients. Advances in the understanding of pathogenesis of ulcerative colitis and mechanism of action of drug brought novel ideas for drug targeting to specific site of action. There are various conventional and unconventional therapies used for the treatment of ulcerative colitis include amino salicylates, glucocorticoids, immune modulators, etc. These therapies need to be administered frequently to patients, which

reduces patient compliance and can cause systemic side-effects. Thus, Microparticles are found to be a promising approach for controlled and site specific drug delivery, which minimize dose- age frequency and improve patient compliance.^[40,41,43]

Solid Lipid Nanoparticles

Novel drug delivery systems utilizing Phytoconstituent for the treatment of peptic ulcers with a focus on solid lipid nanoparticles peptic ulcers are a prevalent gastrointestinal condition impacting millions globally. Traditional approaches to treatment have primarily centered on suppressing gastric acid and eradicating helicobacter pylori infection. However, recent developments in pharmaceutical research have explored innovative drug delivery systems employing alkaloids, natural compounds found in medicinal plants, to enhance the effectiveness and precision of peptic ulcer therapy. Notably, solid lipid nanoparticles have garnered significant attention for their distinctive attributes and potential to enhance the bioavailability and therapeutic outcomes of alkaloids in the treatment of peptic ulcers.^[44,45]

Liposome

Novel Drug Delivery Systems Utilizing Phytoconstituent for the Treatment of Peptic Ulcers liposomes Peptic ulcers, a common gastrointestinal affliction, have been historically treated through conventional methods such as acid suppression and the eradication of *Helicobacter pylori* infection. However, recent strides in pharmaceutical research have ushered in a new era of drug delivery systems that aim to enhance the effectiveness and precision of peptic ulcer therapy.^[46] One such innovative approach involves the utilization of liposomes as a drug delivery system. Using liposomes for alkaloid delivery offer a promising approach to the treatment of peptic ulcers. Liposomes offer improved drug bioavailability, targeted delivery, controlled release, and protection for alkaloids.^[47] Ongoing research and clinical trials will further determine the clinical applicability of these innovative approaches for managing peptic ulcers. Liposomes are small, spherical vesicles made from a phospholipid bilayer membrane. They are biocompatible and biodegradable, making them promising candidates for drug delivery systems. Liposomes can encapsulate a variety of drugs, including alkaloids, and protect them from degradation in the harsh environment of the gastrointestinal tract.^[48]

Gastro retentive system

Today, a large amount of work is being carried out in an extensive area and shows an extremely huge potential for miraculous works in the fields of medicine and biotechnology Today, a large amount of work is being carried out in an extensive area and shows an

extremely huge potential for miraculous works in the fields of medicine and biotechnology, Due to these unique characteristics of the Nano fibers, they can serve as wonderful gastro-retentive system, which seems to be a better alternative to the available gastro-retentive.^[49]

Future Perspectives and Challenges

Recent trends in the novel drug delivery system for peptic ulcer treatment involving Phytoconstituent have witnessed significant advancements, promising improved efficacy and reduced side effects. Researchers are increasingly exploring the encapsulation of alkaloids in nanoparticles to enhance drug delivery to the targeted sites within the gastrointestinal tract. Future perspectives in this field involve refining existing technologies and exploring synergistic combinations of alkaloids to enhance therapeutic outcomes. The integration of smart technologies that allow real-time monitoring of drug release and response could revolutionize treatment strategies for peptic ulcers.

CONCLUSION

From this current review, it can be concluded that majority of the products discussed above are from the natural sources. Moreover, during the past two decades, approximately 50% of new chemical moieties introduced as bioactive agents are from natural products. It also revealed that acid secretion is not the only cause of ulcer formation; there are also other causes such as less mucus secretion which is associated with the defense system of our body. That is why nowadays treatment of ulcer targets potentiating of the defensive system and also lowering of acid secretion. Different active constituents present in nature which play the role to increase in defensive mechanisms of our body against ulcer. The combination of herbal products/alkaloids and standard anti-gastric ulcer drugs might present a synergistic effect against *H. pylori* and gastric ulcer disease and improve the outcome for patients with gastric ulcer. With only a few human studies, it is suggested to conduct further clinical studies with larger sample sizes on the efficacy and safety of medicinal plants with antiulcer activity. Also, it would be beneficial to design studies to investigate and further elucidate the mechanisms of action of medicinal plants used for the treatment or prevention of peptic ulcer. Finally, herbal products used for medicinal purposes require licensing in order to ameliorate their safety and quality, and ensure that randomized controlled investigations validate demands of its possible efficacy. With increased reports of herb–drug interactions, there is still a problem of deficient research in this field, with no measures taken to address this problem. Hence, pharmacists and doctors should be aware especially of the risks associated

with the usage of herbal preparations, whether on their own or in combination with other herbal or standard conventional therapy.

Authors' Contributions

Carried out the review & drafted the manuscript. Selection of content, & supervised it throughout the work.

Conflict of Interest

The authors do not have interests or struggle to share. The authors assert that they have no known conflicting financial interests or personal connections that may have been used to support the arguments made in this paper.

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