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PHYTOCHEMICALS IN THE MANAGEMENT OF PEPTIC ULCERS: A REVIEW OF PLANT-BASED SUBSTITUTIONS

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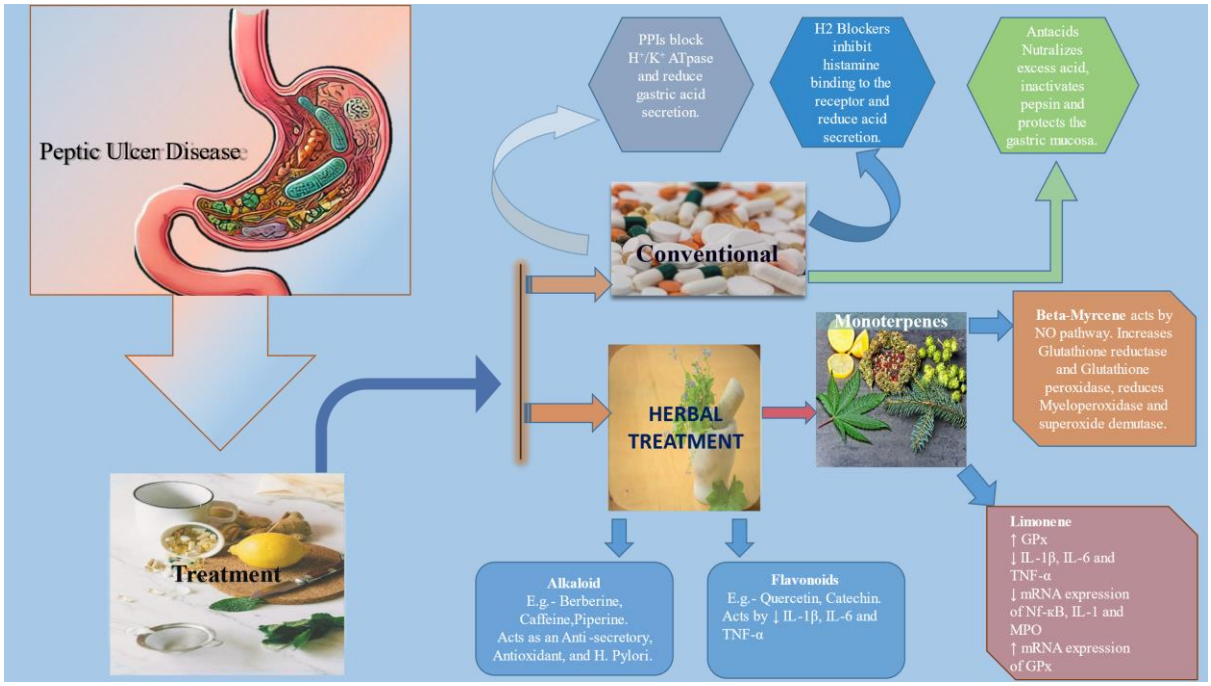
ABSTRACT

Peptic ulcer infection (PUD) is a common gastrointestinal clutter influencing around 10% of the worldwide populace. It is essentially caused by Helicobacter pylori disease and the incessant utilisation of non-steroidal anti-inflammatory drugs (NSAIDs). Routine medicines, such as proton pump inhibitors (PPIs), H2 receptor blockers, and stomach settling agents, offer symptomatic help but are related to side impacts and visit backslides. Later, ponders have appeared that phytochemicals—naturally happening compounds found in plants—hold critical potential in the administration of PUD. These incorporate alkaloids, flavonoids, glycosides, and terpenoids, which have anti-ulcerogenic, anti-inflammatory, and antioxidant properties. This audit examines the pathogenesis of peptic ulcers, centring on the part of H. pylori and NSAIDs, and highlights the helpful guarantee of plant-based medications. Particular phytochemicals like berberine, quercetin, and beta-myrcene have appeared viable in preclinical models by lessening gastric corrosive discharge, upgrading mucosal obstruction, and relieving oxidative push. Conventional plants, utilized in different societies for ulcer treatment, moreover display cost-effective and available options to present-day pharmaceuticals. Future investigations are required to investigate the clinical viability of these phytochemicals, particularly in large-scale trials. Also, the improvement of novel phytomedicines and personalized treatment approaches may lead to more successful and more secure administration of PUD. With anti-microbial resistance on the rise, elective

treatments focusing on H. pylori contamination may also be pivotal in the coming a long time.

KEYWORDS: Peptic ulcer disease, Diagnosis, Treatment, Beta-myrcene, Monoterpenes.

Graphical abstract



1. INTRODUCTION

A persistent and recurring ailment, ulcers are identified by the sporadic development of lesions in the stomach mucosal membrane.[1] Gastric ulcers, which are characterised by the development of open sores in the stomach lining, have long been acknowledged as a major global wellness risk.[2] Stress is a complicated phenomenon that has a significant impact on many physiological processes in the human body, including the digestive system. Stress can cause modifications to the physiology of the stomach, including increased secretion of gastric acid, and decreased blood flow through the mucosa. These factors all have participated in the development of duodenum pustule. The complicated interaction of variable highlights how difficult it is to treat stomach ulcers brought on by stress.[3] Phytochemicals are naturally occurring molecules found in plants that show great promise in the treatment of stomach ulcers brought on by various factors. The bioactive chemicals having potential therapeutic roles of large amount of phytoconstituents, such as, alkaloid, glycoside, flavonoid, tannins, terpenoids, polysaccharides, and saponins are important for managing ulcers since they have shown remarkable anti-ulcerogenic activities in preclinical and clinical investigation.[4]

'Alkaloids' anti-ulcerogenic qualities have made them appear as viable treatments for stomach ulcers. *Berberine* is a naturally occurring chemical found in many plants, including those in the Berberis species. It has been shown to have a significant ulcer-prevention property. The lowering of stomach acid output and strengthening of the mucosal barrier are the main outcomes of these effects.[5] 'Glycosides' have a broad class of compounds with a variety of biological functions. Studies have revealed that certain glycosides, such as saponins, have the ability to prevent ulcers by regulating stomach acid secretion, encouraging the formation of mucus, and strengthening antioxidant defences.[6] `Flavonoids' have anti-inflammatory and antioxidant qualities that have attracted attention for their ability to have anti-ulcerogenic effects. Certain fruits and vegetables include compounds called *quercetin* and *catechins* that have been shown to reduce inflammation and oxidase stress in the stomach mucosa.[7]

1.1 **PEPTIC ULCER**

Peptic ulcer disease is a prevalent abdominal condition which impacts around 10% of the global population.[8] Oesophageal, gastric, and duodenal ulcers are the components of Peptic Ulcer Disease. The higher symptoms continuously occurring of peptic ulcer is epigastrium which is accompanied by gastroesophageal reflux disease (GERD) and heartburn. The occurring pain may be dyspepsia, bloating, or nausea. Peptic ulcer disease can be caused by some factors, the one is persistent Helicobacter pylori infection and other one is unusual use of Non-Steroidal Anti-Inflammatory Drugs also known as NSAIDs.[9]

Worldwide, a large number of herbal medications have been utilised to treat Peptic ulcer disease (PUD). Approximately 279 plants from 89 families were found in an evaluation by Ardalani and his associates to be potentially useful in the treatment of peptic ulcer.[10] In addition, Boakye-Yiadom et al. have presently documented the use of 13 plants from ten distinct families to treat peptic ulcers in Ghana. The possibilities for the usage of herbal material and medication in illness from ulcers stems from their relative safety, availability and affordability when compared to most traditional herbal drugs.[11] The conventional drugs currently used to treat PUD include antacids, PPIs, H2 antagonists, anticholinergics, mucosal protective agents, and antimicrobials for PUD caused by H. pylori. However, none of these drugs have long-term curative effects, and relapse is common even after extensive treatment. Furthermore, there is a chance that these conventional drugs will have detrimental side effects.[12]

- **Pathogenesis of Peptic Ulcer**

Helicobacter pylori, still one of the most common causes of peptic ulcer illness, is present in about half of the world's population.[13] Developing countries, mainly in Eastern Europe, Africa have higher rates of H. pylori prevalence.[14] H. pylori is a common gastroduodenal mucosa infection, often found in lower socioeconomic countries. It causes an inflammatory reaction in the antrum, resulting in injury and degeneration of epithelium cells. The exact cause remains unclear, but it can be identified by hyperchlorhydria or hypochlorhydria. The primary mediators are cytokines that inhibit parietal cell secretion, H+/K+ ATPase α-subunits, sensory neurones, or gastrin formation.[15]

The systemic suppression of constitutively produced cyclooxygenase-1 (COX-1) is the main mechanism by which NSAIDs cause damage to the gastroduodenal mucosa. This mechanism is associated with mucus and bicarbonate secretion, decreased mucosal blood flow, and suppressed cell proliferation. COX-1 is liable for prostaglandin fusion. The enzymes are reversibly and concentration-dependently inhibited by NSAIDs. When exogenous prostaglandin and COX-2 selective NSAIDs a used together, mucosal damage and ulcer risk are decreased.[16] NSAIDs induce the oxidative phosphorylation in the mitochondria to become uncoupled and disturb mucus phospholipids, which starts the damage to mucosa. NSAIDs become protonated when they are exposed to acidic digestive fluid (ph 2), where they penetrate epithelial cells (pH 7.4) after crossing the lipid membrane, ionise, and release H±. The uncoupling of oxidative phosphorylation, a decrease in mitochondrial energy production, an increase in cellular permeability, and a reduction in cellular integrity result from NSAID's inability to crosses the membrane (lipid) and their subsequent entrapment in epithelium cells. NSAIDs induced ulcers are more common in patients over 65, who take high doses or a mix of NSAIDs, have a history of bleeding or peptic ulcers, and utilise steroids or anticoagulants concurrently.[17]

2. DIAGNOSIS OF PEPTIOC ULCER

Up until the early 1900s, the majority of diagnosis for peptic ulcers were made based on clinical indication and symptoms. A range of flexible endoscopies revolutionized shows a proper visualization of ulcers present in the 1950s. A complete clinical history and physical examination are necessary to create an exhaustive list of all clues and indications for the treatment. It is imperative to record all previous medical history, encompassing the duration of alcohol consumption, NSAID usage, smoking habits, and any potential incidence of peptic

ulcer. The first is to rule out functional dyspepsia as the cause of the symptoms being described, and the second is to identify the precise source of the ulcer.[18]

- **Esophagogastroduodenoscopy**

In this novel method, gastroenterologists observe the stomach and small intestine by inserting a thin pipe consisting camera via oral route to gastric area. During this examination, the doctor could biopsy the stomach wall to check for H. pylori. An investigation of H. pylori infection should be performed on each patient who has a gastric ulcer. After the detections in 1993, the administration has undergone with number of changes. It is commonly recognized that the infection's prevalence increases with age and is gender-neutral. To verify this a variety of tests are carried out for both diagnosis and follow-up after the eradication treatment. To identify H. pylori, both direct and indirect tests are used, depending on whether an endoscopy is required.[19]

- **X-RAY**

This entails making the patient lie down on an inclined examination table and forcing them to consume barium, a white, chalky substance that appears on X-rays. By tilting, the upper digestive tract's barium is evenly disturbed, allowing the X-ray to take pictures from various perspectives. This makes it possible for the physician to find the ulcer and assess its kind and severity.[20]

- **Radiology**

Although the endoscopic investigation has largely replaced barium gastroduodenal studies in standard diagnostic protocols, these studies can still be useful in the few individuals who refuse the surgery in circumstances where oesophagal constriction makes endoscopy impossible. The sensitivity and specificity of barium radiology investigations are influenced by the radiologist's experience, the technique employed, the depth of the ulcer, the size of the lesion (less than 0.5 cm in diameter can be difficult to identify), and other factors. A symmetrical mucosal fold with uniform boundaries, a smooth, translucent band collar, an ulcer crater surrounding it that suggests oedema, and an indentation of the opposing wall are radiologic signs that point to a benign nature. Conversely, extensive ulcers, uneven filling, lack of contrast, and irregular mucosal folds are signs of cancer.[21]

- **Computed Tomography**

This is a faster way to detect a suspected penetration and perforation diagnosis related to duodenal ulcers. The purpose of this retrospective study is to evaluate the abdominal computed tomography results in patients suffering from peptic ulcer disease and to correlate them with the patient's clinical history, the results of upper GT series and endoscopic procedures, and any surgery that may have been done.[22]

3. TREATMENT OF PEPTIC ULCER

Both conventional (Table 1) and plant-based treatments (Table 2) play significant roles in managing peptic ulcer disease. While pharmacological treatments provide effective and evidence-based outcomes, plant-based therapies offer complementary options with fewer side effects. Further research is needed to establish standardized dosages and the efficacy of plant-based remedies. An integrated approach combining both modalities may enhance the management of PUD and improve patient outcomes.

Table 1: Mechanism of action and ADR of Conventional Treatment.

Target Areas	Drugs	Mechanism of Action	Adverse Effects	References
Proton Pump Inhibitors (PPIs)	➢ Pantoprazole ➢ Lansoprazole ➢ Rabeprazole ➢ Omeprazole	To pronounce a long-lasting reduction of gastric acid production.	• Diarrhoea • Nausea • Constipation • Abdominal pain • Vomiting	[23,24]
H2 Receptor Blockers	➢ Cimetidine ➢ Famotidine ➢ Nizatidine ➢ Ranitidine	Preventing histamine from binding to H2 receptor on gastric parietal cells.	• Fatigue • Muscle aches • Drowsiness • Thrombocytopenia • Anxiety	[25]
Antacids	➢ Aluminium hydroxide	Raises the pH of the stomach to more than four and stops pepsin's proteolytic action.	• Nausea • Vomiting • Chalky taste • Hypophosphatemia • Abdominal cramping	[26]
Cytoprotective Agents	➢ Misoprostol	Increase blood flow and stimulate formation of mucus in git	• Diarrhoea • Abdominal pain • Headache • Constipation	[27,28]

Table 2: Overview of plants used in the treatment of peptic ulcer disease.

Binomial Name	Family	Part Used	Condition of Plant Used	Method of Preparation	Reference
Aloe gilbertii-Shrub	Asphodelaceae	Leaf	Fresh	Young leaves are pulverized, and filtrate is taken orally.	[29]
Aloe pubescens-Shrub	Aloaceae	Gel	Fresh	Fresh gel is eaten.	[29]
Calpurnia aurea-Shrub	Fabaceae	Leaf	Fresh	Chewing	[30]
Carica papaya-Tree	Caricaceae	Seed	Fresh	Oral	[31]
Casimiroa edulis-Tree	Rutaceae	Fruit	Fresh	Eating	[30]
Dichrostachys cinerea-Tree	Fabaceae	Steam	Dry	Burns stem, make solution from the ash and take it orally.	[32]
Lippia adoensis-Herb	Verbenaceae	Leaf	Fresh	Chewing	[31]
Thymus schimperi-Herb	Lamiaceae	Seed	Dry	Crushed seeds are boiled in water and served as a drink	[33]

4. MONOTERPENES USED IN PEPTIC ULCER DISEASE

Monoterpenes are compounds containing two isoprene units.[34] Monoterpenes can be found as a major compound in plants such as Origanum vulgare L[35], Citrus lemon[36], Citrus aurenticum[37]Humulus lupulus L.[38], etc. Other monoterpenes are listed in table 3. Monoterpenes are volatile and aromatic often found in essential oils, they contribute to plant's fragrance and defence mechanism, and they have several pharmacological properties such as anti-microbial, anti-inflammatory and antioxidant properties.

Table 3: List of monoterpenes used in peptic ulcer disease.

Compound	Effect	Mechanism	Reference
Linalool	Gastroprotective and healing effect	reduce level of Myeloperoxidase and lipoperoxidase	[39]
Menthol	Gastroprotective effect	reduce acid secretion, myeloperoxidase, tumour necrosis factor and increase mucus, GSH	[40]
α-pinene	Gastroprotective effect	decrease acid secretion and increase mucus secretion	[41]
Thymoquinone	Gastroprotective effect	increase superoxide dismutase & nitric oxide and reduce total oxidation status	[42]
Carvacrol	Gastroprotective and bactericidal effect	increase mucus secretion, sulfhydryl compounds and catalase	[43]
Limonene	Gastroprotective and bactericidal effect	increase mucus secretion, GPx and decrease myeloperoxidase & tumour necrosis factor	[44]
β-myrcene	Gastroprotective and bactericidal against H. pylori.	increase mucus & glutathione reductase and decrease malondialdehyde	[45]

- **Beta-myrcene**

Chemically known as 7-methyl-3-methylene-1,6-octadiene, it is a vital flavouring compound frequently utilized in the food and beverages sector. Additionally, often utilized in products like cosmetics & detergents. It is commercially used as a key ingredient for producing flavours such as geraniol, and linalool.[46]

- **Sources and method of extraction**

β-myrcene can be obtained from various sources like hop-essential oil, cannabis plant, orange, lemongrass and mangoes. Some of the sources and methods of extraction of beta-myrcene are listed in Table 4.

Table 4: Sources and method of extraction of β-myrcene.

Plant	Family	Parts Used	Extraction Method	Assay	Reference
Citrus aurantium L.	Rutaceae	Flower	Hydrodistillation	GC-MS	[37]
Citrus aurantium L.	Rutaceae	Fruit	SPME	GC-O	[47]
Humulus lupulus	Cannabaceae	Cones & Pellets	HS Trap	GC-MS	[38]
Humulus lupulus	Cannabaceae	Essential Oil	SPME	GC-qMS	[48]
Humulus lupulus	Cannabaceae	Cones	HS-SPME	GC	[49]
Cannabis sativa L.	Cannabaceae	Female Flowering Tops	Solvent Extraction	GC-FID-NMR	[50]
Cannabis sativa L.	Cannabaceae	Flowers	Exhaustive SE	GC-MS	[51]
Pistacia lentiscus	Anacardiaceae	Essential Oil	HS-SPME	GC-MS	[52]
Spondias mombin L.	Anacardiaceae	Fruit	SPME	GC-MS	[53]

GC-ms= Gas chromatography and mass spectrometry, GC-O= Gas chromatography olfactometry, GC-FID-NMR= gas chromatography/flame ionization detection- nuclear magnetic resonance, HS-SPME= Headspace solid-phase microextraction, SE= solvent extraction, GC-Qms=gas chromatography-quadrupole mass spectrometry.

4.1 Synthesis of Beta-myrcene

1. Isoprene bromide and Geranyl bromide react with Ethyl acetoacetate to produce β-keto esters via Wetting reaction, they can be transformed to beta-myrcene.[54]

2. It can be obtained from β-pinene (99.2 mol%) by pyrolysis. At a temperature extending from 573K-873K, the inhabitant time was 0.2s. By the end of pyrolysis, it formed β-myrcene, ψ-limonene and limonene by joint biradical reaction intermediates. The medium of adaptation of β-myrcene from β-pinene was closely resembling to the accretive fracture of the cyclobutane ring. Whereas others were formed from biradicals.[55] The synthesis is shown in figure 1.

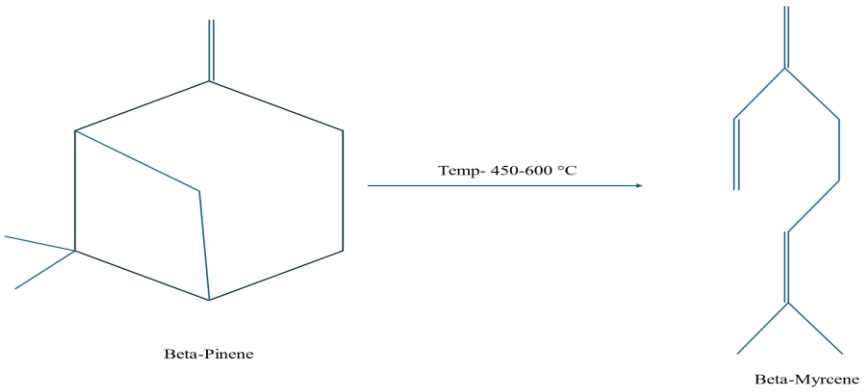


Figure 1: Pyrolysis of pinene to form myrcene.

- **Physical and Chemical properties**

Table 5 Physical and Chemical properties of beta myrcene.

Parameter	Description	References
Appearance	Yellow oily liq./ colourless liq.	[56]
Boiling point (◦C)	167	[57, 58]
Density	0.794 gm/cm^3	[59]
Odour	Woody, herbaceous and balsamic	[60]
Solubility	Water Insoluble, Soluble in alcohol, ether, glacial acetic acid	[61]
Stability	Polymerises at room temp.	[46]

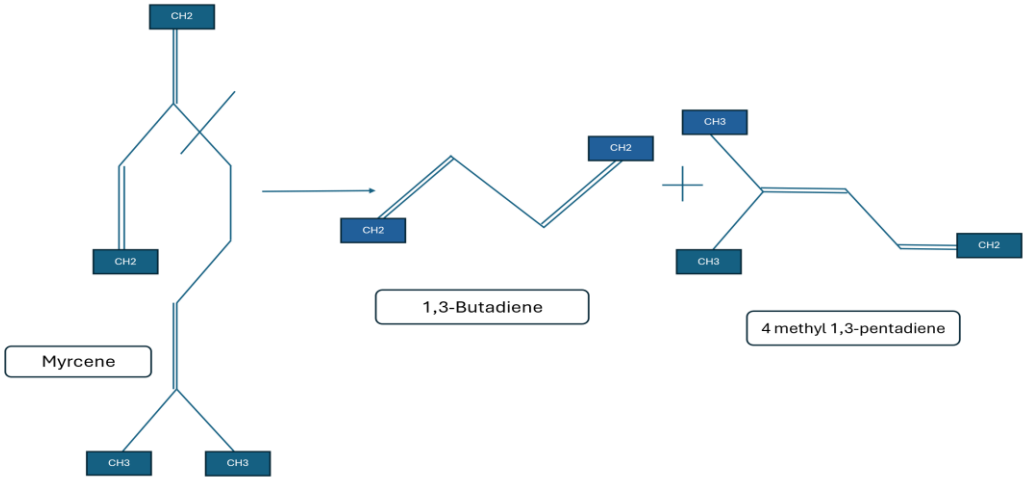


Figure 2: Route of Decomposition.[54]

Myrcene exhibit 2 isomeric forms α & β. β-myrcene is a naturally occurring isomer that has an isopropylidene group. While α-myrcene is not found naturally has an isopropenyl group. Ruziuka et al demonstrated that the naturally occurring form is β-myrcene by ozonolysis experiments. Later confirmed by infrared and NMR.[46]

Decomposition of myrcene forms 1,3-butadiene and 4 methyl-1,3-pentadiene via free radical. This agrees with the universal pyrolysis model by Gwyn.[54] The route is shown in Figure 3.

4.2 Pharmacological Properties of β-myrcene

β-myrcene has a wide range of pharmacological properties. It has sedative and anticonvulsant properties in the neurological system. It also has antioxidant and anti-inflammatory properties. It can also be applied to the control of pain and the treatment of peptic ulcer disease.

- **Nervous system (CNS/ANS)**

Cannabis saliva's essential oil (beta-myrcene 22.9%), showed great activity on ANS in healthy humans. They inhaled essential oil for 5 minutes which improved their nerve activity and got relief from stress & anxiety. To the control group, they administered sweet almond oil. This study revealed that those subjects were more energetic and their mood was elevated. Their electroencephalogram reports were similar to those who were doing meditation.[62] Essential oil from *Cinnamosma madgascariensis* (content 8.9%) showed anticonvulsant activity caused by PTZ in Wistar rats. The GABA & glutamate neurotransmission were responsible for the sedative effect due to that beta-myrcene shows anticonvulsant activity.[63]

- **Anti-inflammatory Activity**

Myrcene decreased inflammation in the blood arteries feeding the arthritic knee by reducing leukocyte rolling, an early indicator of inflammation, and adhesion, a more advanced stage of inflammation. The fact that a CB2 antagonist (AM630) prevented this effect but not a CB1 antagonist (AM281) suggests that it was partially mediated by CB2 cannabinoid receptors.[64] In the model of isoproterenol-induced, it prevented cardiac failure via a decrease in MMP-2, TGF-β and NOs.[65] In models of osteoarthritis, it showed anti-inflammatory activity in a dose of 20-50µg/ml. It acts by decreasing the levels of IL-1β, NF-$_k$B, and jun terminal kinase. And promote the maintenance of the differentiated chondrocyte phenotype.[66]

- **Treatment of peptic ulcer disease**

β-myrcene has ulcer healing and antioxidant properties it can be used to manage oxidative stress-induced disease conditions. In the Ethanol-induced ulcer model, β-myrcene inhibited ulcer formation by 60% (dose 7.5 mg/kg) via an increase in glutathione, glutathione reductase and glutathione peroxidase. It also reduced the levels of superoxide dismutase. Also, in the

indomethacin-induced model, β-myrcene reduced ulcers by 74% via a decrease in myeloperoxidase in gastric mucosa. In the ischaemia-reperfusion model, β-myrcene reduced ulcers by 86% through the increase in glutathione level and limiting myeloperoxidase. Pretreating animals with $_{L}$-NAME reversed the ulcer protective effect shown by β-myrcene. It uncovered that the nitric oxide pathway is vital for the component of activity for ulcer protection by β-myrcene. It also increased the level of adhered mucosa by 50% in pylorus-ligated rats. The minimum inhibitory concentration for causing hindrance in the growth of H. pylori was found to be 500 µg/ml via serial dilution.[45]

- **Antinociceptive activity**

β-myrcene possesses central and peripheral palliative effects.[67] In the study, myrcene, one of the active ingredients in Ocimum gratissimum essential oil, had strong antihypernociceptive (pain-reducing) effects. Myrcene decreased mechanical and thermal pain sensitivity in rats with chronic constriction injury (CCI) of the sciatic nerve when given orally at dosages of 5 mg/kg and 10 mg/kg for 14 days. Myrcene did not, however, considerably lower levels of interleukin-1β (IL-1β), a proinflammatory cytokine linked to neuropathic pain, in contrast to eugenol. According to earlier research, myrcene's antinociceptive action is most likely mediated by the stimulation of α2-adrenergic receptors and the release of endogenous opioids. This suggests that rather than directly lowering inflammation, myrcene may work through the opioid and noradrenergic systems.[68]

5. TOXICOLOGICAL STUDIES

A skin irritation test was done by a European multicenter study; out of 1511 dermatitis patients, only a single patient showed a reaction to 3% β-oxidised myrcene (30% myrcene). It indicated that β-myrcene is safe for external use.[69] A study by NTP in 2010 on male &female rodents (F344/N rats & B6C3F mice) was done for 2 years. They administered 0, 250, 500, and 1000 mg/kg with corn oil directly in the stomach by a tube for 5 days a week. All the rodents with a dose of 1000mg/kg died before the end of the study due to renal toxicity. Other male rats showed renal tubular adenoma or carcinoma, and in male mice, hepatocellular adenoma or carcinoma was seen. In any case, no genotoxicity and mutagenicity were seen in strains of *Salmonella typhimurium and E. coli*.[70]

A study on Sprague-Dawley rats was done by Bastaki et al. in 2018, which showed no renal adverse effects in both male and female rats. The histopathological examination revealed no damage or neoplastic lesions. Mild nephropathy in some rats was age-related rather than

myrcene exposure. Earlier, the study by NTP showed kidney tumours in rats and liver tumors in mice at high doses. However, they were strain-specific spontaneous pathologies. The NOAEL was established at 115.2mg/kg/day for male and 135.9mg/kg/day for female rats.[71]

7. CONCLUSION

Peptic ulcer disease (PUD) is still a major global health concern, and its development is mostly caused by Helicobacter pylori infection and long-term use of non-steroidal anti-inflammatory medicines (NSAIDs). Although antacids, proton pump inhibitors, and H2 receptor blockers are examples of traditional therapy methods that offer excellent relief, it is clear that these alternatives have drawbacks, including long-term dependency, side effects, and recurrence. On the other hand, plant-based solutions offer a more affordable, easily available, and frequently less disruptive alternative. Particularly, plants with bioactive chemicals like β-myrcene have a lot of promise for their ulcer-healing, antioxidant, and anti-inflammatory qualities. One promising approach to enhancing patient care is the use of phytochemicals in the treatment of PUD. Nevertheless, more thorough research is required to completely comprehend the pharmacological processes and therapeutic effectiveness of plant-based treatments for PUD. With its capacity to lower oxidative stress, shield the stomach mucosa, and prevent ulcer development, β-myrcene in particular has shown promise and may prove to be a useful supplement to traditional treatments. Although traditional treatments continue to be the mainstay of managing PUD, plant-based medicines should be investigated further due to their complementing roles in offering sustainable, affordable, and safe alternatives. Future studies could benefit from concentrating on the complementary effects of phytochemicals, investigating personalised medicine strategies based on each patient's unique genetic profile, and developing diagnostic methods to enhance ulcer monitoring and identification. Furthermore, the ongoing development of PUD management will depend heavily on reducing the adverse effects of traditional treatments by using natural alternatives and fighting antibiotic resistance in H. pylori.

8. FUTURE ASPECTS

The treatment of peptic ulcer disease (PUD) continues to evolve, and future research could focus on several promising directions to improve patient outcomes and reduce recurrence rates.

- **Advanced Phytochemical Research**: Synergistic preclinical studies have demonstrated the potential of phytochemicals, including terpenoids, in enhancing safety profiles, indicating their potential in developing effective plant-based therapies.

- **Personalized Medicine for PUD**: Personalized medicine utilizes genetic information to develop therapeutic herbal treatments for PUD, enhancing therapeutic outcomes by tailoring treatments to individual patient's unique needs

- **Novel Diagnostic Techniques**: Continued advancements in non-invasive diagnostic methods, including advanced imaging and biomarker identification, are paving the way for real-time monitoring and improved early detection of ulcers.

- **Combating Antibiotic Resistance in H. pylori**: Antimicrobial treatments are increasingly being explored to combat antibiotic resistance, with phytochemicals potentially acting as standalone or combined treatments to combat resistant strains.

- **Minimizing Side Effects of Conventional Treatments**: Receptor blockers, drugs used in treatment, have side effects that can be mitigated by incorporating natural products into the regimen.

In conclusion, the future of PUD management lies in a multidisciplinary approach that integrates traditional medicinal knowledge with modern therapeutic advances. By leveraging the benefits of phytochemicals, personalised treatments, and innovative diagnostic tools, the treatment landscape for peptic ulcer disease may become more effective and patient-centred.

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