

Ethnopharmacological Relevance of Selected Plants used in the Treatment of Peptic Ulcer Disease in Nigeria

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ABSTRACT

Peptic ulcer illness, a prevalent gastrointestinal disorder, is characterized by an imbalance between defensive factors such as mucosal blood flow, prostaglandins, and antioxidants and offensive factors such as excessive gastric acid, *Helicobacter pylori*, and non-steroidal anti-inflammatory drugs (NSAIDs). Medicinal plants like *Carica papaya* (Caricaceae), *Zingiber officinale* (Zingiberaceae), *Musa paradisiaca* (Musaceae), and *Allium sativum* (Amaryllidaceae) have been traditionally used to manage peptic ulcer illness, showcasing their potential gastroprotective properties. These plants are rich in bioactive compounds that may modulate various pathways involved in ulcer pathogenesis. A systematic review of literature on gastroprotective plants was conducted, focusing on phytochemicals and mechanisms of action. Electronic databases (e.g., PubMed, Scopus, and Google Scholar) were searched for relevant studies, and data were extracted and analyzed. Phytochemicals like flavonoids (kaempferol, quercetin), alkaloids (rutaecarpine, rohitukine), and tannins (castalagin, corilagin) exhibited promising anti-ulcer activities, targeting factors like *H. pylori*, COX-1, and oxidative stress. These compounds may exert their effects through various mechanisms, including antioxidant activity, inhibition of gastric acid secretion, and enhancement of mucosal defense. This review highlights the potential of medicinal plants as a source of novel gastroprotective compounds, presenting opportunities for innovative lead treatments for peptic ulcer disease. Further research is needed to isolate and characterize the bioactive compounds and elucidate their mechanisms of action.

Keywords: Peptic Ulcer Disease, medicinal plants, gastric juice, cyclooxygenases, anti-ulcer.

INTRODUCTION

The incidence of Peptic ulcer disease (PUD) complications has remained constant despite a decline in the overall prevalence of PUD in recent decades (Kavitt, 2019). Over 8.09 million cases were reported worldwide in 2019, a 25.82% increase from 1990.

However, in 1990, the age-standardized prevalence rate was 143.47 per 100,000 people; in 2019, it was 99.50 per 100,000 people. Despite this increase in case numbers according to the World Health Organization's mortality database and world life expectancy data, China (37,723 deaths) and India (68,108 deaths) have the highest rates of ulcer-related deaths, followed by several other nations with notable mortality rates. While some countries, such as New Zealand and several African countries, record less than 100 deaths, indicating a minor effect, other regions, such as Australia, Canada, and Europe, exhibit a moderate impact resulting in ulcers, serious side effects such blockage or perforation and disturbance of physiological processes (Al-Garni, Khalifa and Zeyadi, 2021; Malik, Singh and Gnanapandithan, 2023). According to Malfertheiner *et al.* (2023), ulcers are a chronic and recurrent disorder characterized by the sporadic development of sores within the stomach's mucosal membranes. For a long time, gastric ulcers, which are characterized by the formation of open sores in the stomach lining, have been recognized as a serious worldwide health concern (Narayanan, Reddy and Marsicano, 2018). Stress-induced gastric ulcers offer an intriguing area for research, even though ulcers can result from a variety of causes, including *H. pylori* infection, the use of nonsteroidal anti-inflammatory drugs (NSAIDs), and lifestyle decisions like binge drinking. These ulcers are frequently linked to long-term psychological stress and have attracted a lot of study interest because they are still difficult to manage and cure (Malfertheiner *et al.*, 2023).

Proton pump inhibitors (PPIs), histamine-2 receptor antagonists (H₂RAs), antacids and sucralfate are some of the current treatments for PUD that work by neutralizing stomach acid, preventing the production of gastric acid and shielding the gastric mucosa as shown in Figure 1. Furthermore, the prevalence of PUD-related problems like bleeding and perforations has dramatically dropped (Begg *et al.*, 2023; Prayoga *et al.*, 2024). PPIs have significantly expanded over the past ten years due to their remarkable effectiveness in regulating acid production and creating an environment that promotes ulcer repair.

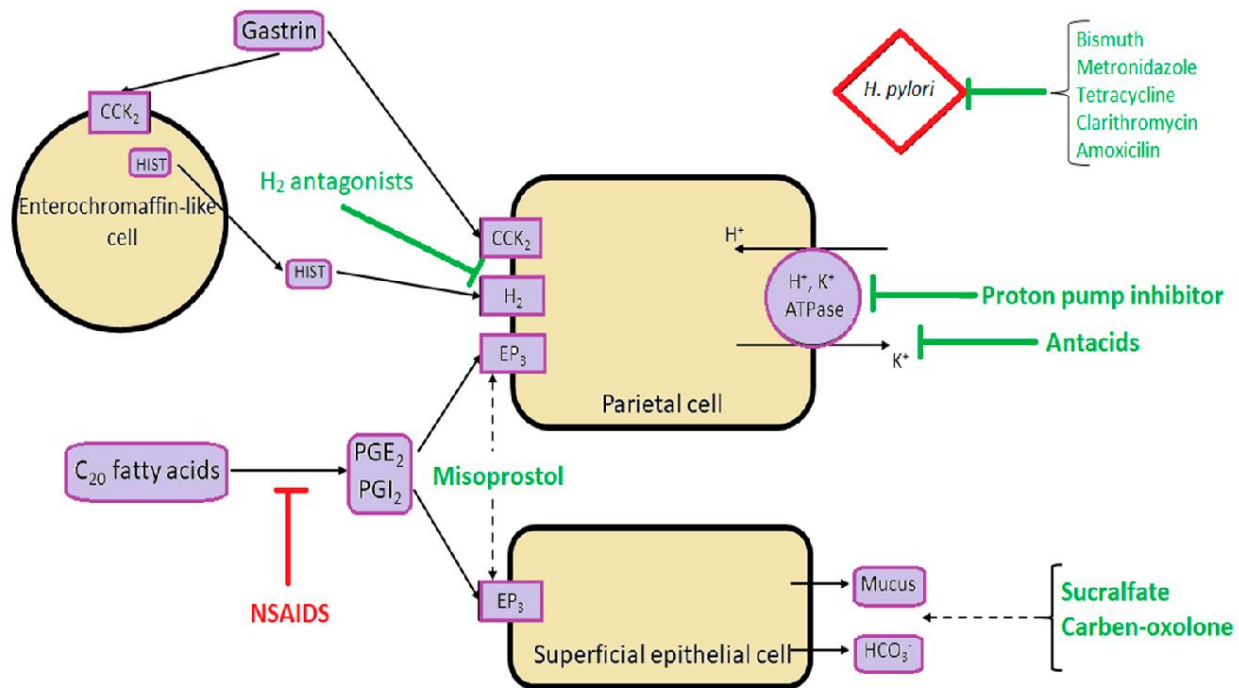


Figure 1: The pharmacological and principal agents responsible for the development of ulcerations (Kuna *et al.*, 2019).

Drivers of Mucosal Injury

About 90% of stomach ulcers are caused by *H. pylori*, which increases the stomach's acidity and prevents the formation of bicarbonate (Malik *et al.*, 2021). The probability of mucosal healing is considerably increased through the use of medications such as potassium chloride, steroids, bisphosphonates and corticosteroids (Malik *et al.*, 2021).

Different molecular and cellular mechanisms generate NSAID-induced lower stomach damage than upper gastrointestinal injury (Whittle, 2004; Wallace, 2012). It damages mucosa and inhibits COX-1, just as it does in the stomach. However, unlike gastric injury, intestinal injury brought on by NSAIDs is patho-physiologized by intestinal flora and bile acid (Otani *et al.*, 2017). NSAIDs and gut flora have a complex and dynamic connection. Through biotransformation into metabolites, the stomach microbiota can directly affect the effectiveness of NSAIDs, or indirectly, it can modify human metabolism (by interfering with hepatic function, for example) (Maseda and Ricciotti, 2020). Conversely, NSAIDs can affect the host's physiological processes, indirectly changing the gut microbiota's composition and function (Maseda and Ricciotti, 2020).

Gram-positive bacteria contribute to the deconjugation of primary bile acids in the intestinal lumen, resulting in the generation of dangerous bile acid secondary products generation of dangerous (Hegyí *et al.*, 2018). The gut microbiota's composition, which is affected by bile acids, controls the type and amount of the bile acid pool (Urdaneta and Casades, 2017; Ticho *et al.*, 2019). Thus, there is interaction between the bacteria and bile acids. After being transported to the duodenum, these bile acid-NSAID complexes are reabsorbed by the enterohepatic circulation and returned to the ileum. In the lumen of the intestine, especially in the colon, gram-positive bacteria are essential for deconjugating conjugated primary bile acids become secondary bile acids,

which are more dangerous (Hegyi *et al.*, 2018). The kind and quantity of the bile acid pool are determined by the gut microbiota's makeup, which is influenced by bile acids (Urdaneta and Casades, 2017; Thicho *et al.*, 2019).

Table 1: The kinds of traditional medications used to treat GUD

Drug class	Characteristics	Examples	References
Antacids	Acid-neutralizing effect, reduction of diarrhea prevent erosion	A combination of calcium and aluminum carbonates,	Saheed <i>et al.</i> , 2018
Gastric muscle stimulants	Accelerates gastric emptying	Domperidone and metoclopramide	Saheed <i>et al.</i> , 2018
Antisecretory medications (anticholinergic agents and H ₂ antagonists)	Inhibits gastric acid secretion and reduces gastric acidity, output, and volume. Histamin H ₂ receptor antagonist functions as a competitor antagonist with gastrin by inhibiting the binding and activity of histamine and reducing gastric acid release	Anticholinergic agents include phentonium, atropine, pyoscyamine, methantheline, and propantheline while H ₂ receptor antagonists include famotidine and cimetidine	Saheed <i>et al.</i> , 2018; Sharifi-Rad <i>et al.</i> , 2018

(Achang *et al.*, 2024).

Anti-ulcerative Potentials of Medicinal Herbs

Herbal products have been utilised as lead compounds to identify several bioactive chemicals throughout history. Given that they are thought to be more secure than manufactured medications, they are frequently utilised in the conventional medical system to provide additional health advantages and to treat a variety of illnesses (Zakaria *et al.*, 2019). Herbal medicines are frequently investigated by researchers as possible substitutes for synthetic ones (Salehi and Sener, 2019; Sharifi-Rad *et al.*, 2019). In recent decades, various preclinical and clinical studies have demonstrated the effectiveness and safety of plant-derived medicines in a variety of pathological conditions as shown in figure 2 (Choi *et al.*, 2016; Quansah and Karikari, 2016). However, a sizable part of the world's population prefers herbal remedies or pharmaceuticals containing herbal components to preserve their health (Khandokar *et al.*, 2021).

Kayode *et al.* (2019), studied the most prevalent plant species used to cure stomach ulcers in South Western and North-Central Nigeria using the use-mention index. Among these are the following species: *Allium sativum* (Amaryllideaceae), *Zingiber officinale* (Zingibireaceae), *Musa parasidiaca* (Musaceae), and *Carica papaya* (Caricaceae),

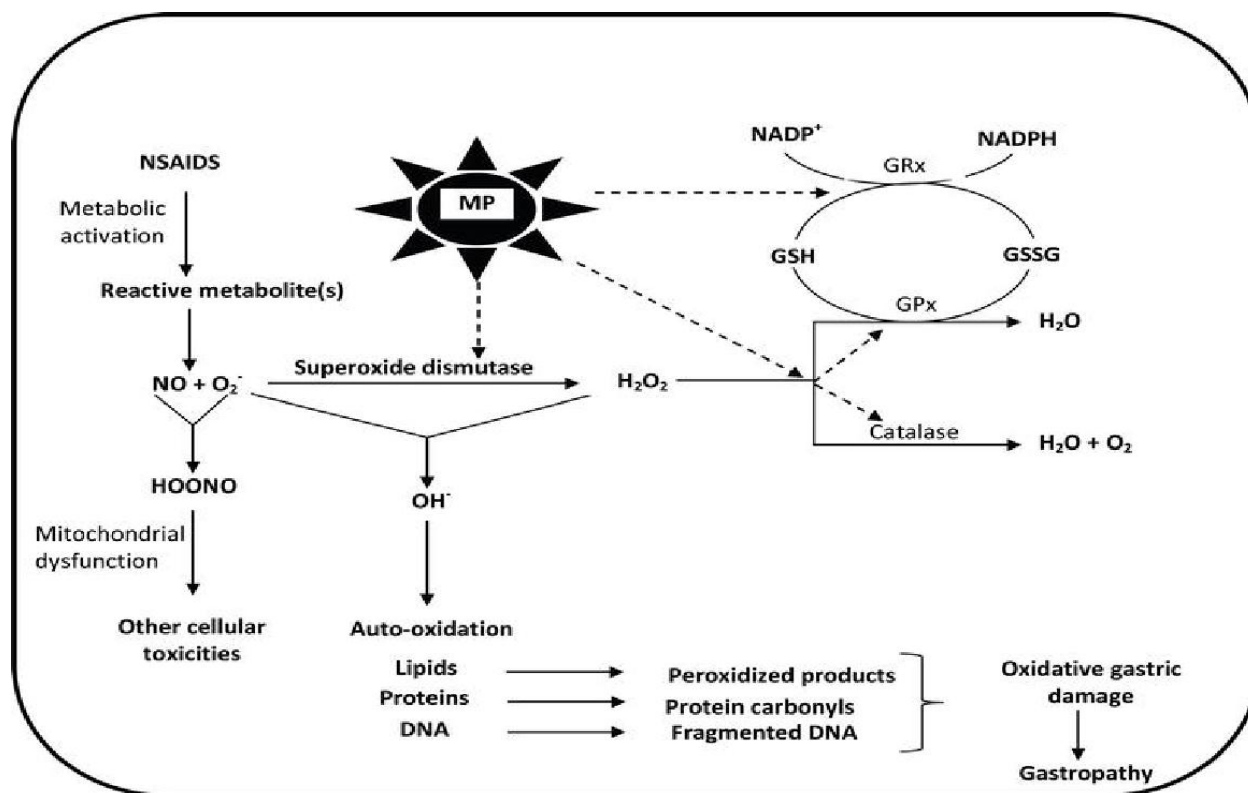


Figure 2: Potential mechanism of medicinal plants' gastroprotective and antioxidant effects (Saheed *et al.*, 2018).

Table 2: Using plant-based bioactive substances to treat gastric ulcer illness (Achang *et al.*, 2024)

Group	Bioactive compound	Source	Dose	Model used	Mode of action	Ref
Alkaloids	Total alkaloids	<i>Phellodendron amurense</i>	30 mg/kg/day	Induction by acetic acid [0.14 mol/L] in rats	Significant increase in serotonin and nor-adrenaline levels, indicating the gastroprotective effect of total alkaloids	Wang <i>et al.</i> , 2017
	Total Alkaloids	Coptis	25 mg/kg/day	Acetic acid induced peptic ulcer in rats	Increases the level of epidermal growth factor (EGF), 5-hydroxytryptamine (5-HT) in the brain and noradrenaline (NE) in the adrenal tissue	Duan, Li and Qin, 2020

Terpenes and Terpenoids

Piperine	<i>Piper nigrum</i>	100 mg/kg bw	Ethanol induced ulcer in rats	Inhibition of ulcer in vitro and in vivo via oxidation by regulating the Nrf2/HO-1 and MAPK signaling pathways	Duan <i>et al.</i> , 2022
(-)-linalool	<i>Dalbergia latifolia</i>	5; 10; 20; 40 mg/kg/day	Acetic acid induced and absolute ethanol-induced peptic ulcer in rats	10 mg/kg/day reduced lipid peroxidation in ethanol induced ulcers and showed strong gastroprotective activity	Da Silva <i>et al.</i> , 2016
Thymoquinone (TQ)	<i>Nigella sativa</i>	20 mg/kg	Acetylsalicylic acid (ASA) induced gastric ulcer in rats	Reduction of TNF- α , ulcer indices, apoptosis, total oxidant status, asymmetric dimethylarginine, nuclear factor kappa-light-chain enhancer of activated B cells (NF- κ B), and inducible nitric oxide synthase (iNOS) expressions Modulation of IL-31 mRNA, protein expression	Zeren <i>et al.</i> , 2016
Apigenin	Celery, parsley, and onions	75 and 150 mg/kg	Atopic dermatitis itch model in mice using compound 48/80	protein expression, and inhibit the phosphorylation activation of Mitogen-activated protein kinase (MAPK) pathway and NF- κ B cells.	Che <i>et al.</i> , 2019

Flavones

Luteolin	Coconut (<i>Cocos nucifera L.</i>)	20 -100 μ g/mL	Indomethacin induced gastric ulcer in human gastric adenocarcinoma epithelial (AGS)	Cytotoxic effect against human gastric adenocarcinoma epithelial	Abiraam i and Uma, 2021
chrysin	Coconut (<i>Cocos nucifera L.</i>)	100 mg/kg and 200 mg/kg	Diclofenac (DIC)-induced gastroduodenal ulcers in rats	Attenuation of gastroduodenal and hepatic damage	Akinrind e <i>et al.</i> , 2022
	Flowers of <i>Passiflora</i>	50 and 100 mg/kg	Indomethacin induced gastric	Activation of peroxisome proliferator activated	George <i>et al.</i> , 2018

			<i>incarnateI</i> and <i>Oroxylum indicum</i>	ulcer model in rats	receptor- γ (PPAR- γ) and downregulation of IL-6. Promote mucus secretion	
	Tangeretin	Citrus peels	100 mg/kg	Ethanol induced acute peptic ulcer in rat model	Exhibited anti-inflammatory functions by decreasing TNF- α , IL-6, and IL-1 β and increasing the IL-10 levels	Susam <i>et al.</i> , 2023
	Nobiletin	Citrus fruits		Coculture of <i>H. pylori</i> in human gastric epithelial (GES)-1 cell line	Nobiletin prevents TNF- α , IL-6, COX-2, Phosphatidylinositol-3 kinase (PI3K), protein kinase B (AKT), and mitogen activated protein kinase molecules	Ouyang, Li and Ling, 2020
	Daidzein	Soybeans	400 mg/kg, ip	Induction of lung inflammation by exposing mice to TNF- α	Inhibition of proinflammatory chemokine Cxcl2 expression in lung tissues	Li <i>et al.</i> , 2014
	Genistein	Soybeans	25 mg/kg orally	Single dose of indomethacin (80 mg/kg) orally	Reduction of the expression of Wnt/ β -catenin and transforming growth factor (TGF- β /SMAD4), and Protein Kinase B (PKB) pathways	Hassan <i>et al.</i> , 2023
	Genistein	Soybeans	16 mg/kg body weight	<i>H. pylori</i> induced ulcer in rat model (10^8 – 10^{10} CFU/mL; 1 mL/rat)	Significant reduction of proinflammatory cells (TNF α and cytokine-induced neutrophil chemoattractant-1 (CINC-1))	Siriviriya kul <i>et al.</i> , 2020
	Glycitein	Soybeans	50 or 100 mg/kg/d	Water immersion restraint (WIR) stress model	Suppression of TNF- α , cytokine-induced neutrophil chemoattractant (CINC-1) levels, and reduction of mucosa injury	Takekawa <i>et al.</i> , 2006
Flavonols	Quercetin	Citrus fruits, grapes, apples, mangoes	50 mg/kg	Ethanol induced gastric ulcer in rat	Upregulation of Nrf2 and HO1 and increased High mobility group box 1 (HMGB1), Toll-like receptor 4 (TLR4), NF- κ B	Shams and Eissa, 2022

Myricetin	Mangoes, berries and red wine	50 mg/kg	Histamine (20 mg/kg)-induced gastric ulcer	Shown inhibitory effects on gastric H ⁺ and K ⁺ -ATPase in a dose-dependent manner	Miyazaki <i>et al.</i> , 2018
Myricetin	Mangoes, berries and red wine	12 mg/kg body weight	Alcohol induced peptic ulcer in rats	Reduction of the level of malondialdehyde (MDA) and NF- κ B) and increased total glutathione (GSSG/GSH), superoxide dismutase (SOD), cyclooxygenase-1 (COX-1) and prostaglandin E ₂ (PGE ₂)	Park <i>et al.</i> , 2021
Kaempferol	Spinach and kale	40, 80, or 160 mg/kg b.w.	Acute ethanol induced lesions in mice mucosa	Reduced ulcer index, myeloperoxidase (MPO) activity and TNF- α , and IL-1 β levels, and improved nitric oxide (NO) levels	Li <i>et al.</i> , 2018

Flavonoids' Function in Peptic Ulcer

Pain alleviation, ulcer healing, and preventing complications and recurrences are the goals of treatment for peptic ulcers. The three mainstays of contemporary peptic ulcer therapy are cytoprotectors, histamine H₂ receptor antagonists, and proton pump inhibitors (PPIs) (sucralfate salts and bismuth) antimicrobials are required when *H. pylori* infection develops (Scally *et al.*, 2018). PPIs represent a significant advance in the management of peptic ulcers. Still, several problems limit the efficacy of pharmacological treatment for peptic ulcers. These include side effects, which are especially problematic for individuals on long-term medication, and *H. pylori*'s increasing resistance to antibiotics (Yu *et al.*, 2017). They also have poor ulcer healing and recurrence rates, which put a heavy financial strain on patients and the public health system. This is primarily because of the side effects, which include bleeding and perforation (Varcus *et al.*, 2018). Several medicinal plants and their constituents have the gastroprotective and antiulcerogenic properties, which aid in the development of supplemental therapies aimed at the seriousness of ulcerative illnesses and avoiding recurrence intervals (Kuna *et al.*, 2019). The significance of medicinal plants as a source of chemicals with therapeutic potential is supported by historical evidence. Moreover, several of its constituents have acted as models or guides for developing new drugs and substances (Barreiro, 2019). Medicinal plants contain a family of secondary metabolites called flavonoids. The pigments that give leaves their colour belong to a vastly diverse class called polyphenolic chemicals, which are commonly found in nature. The phytochemicals of these substances are also crucial for disease and predator resistance, UV radiation defence, and heat tolerance (Mathesius, 2018).

Kaempferol

There are numerous foods that contains such as broccoli and cabbage. It is also found in propolis, *Ginkgo biloba*, and *Moringa oleifera* (Devi *et al.*, 2015). Numerous studies have shown this flavonoid has various pharmacological actions, including antioxidants (Du *et al.*, 2018). By preventing neutrophil build-up, lowering MPO activity and the levels of pro-inflammatory cytokines like TNF- α , IL-1, and IL-6, and increasing gastric mucus and NO levels, kaempferol (40, 80, and 160 mg/kg, p.o.) and the placebo omeprazole (20 mg/kg) protect against ethanol-induced gastric ulcers in mice (Li *et al.*, 2018). Moreover, kaempferol suppresses *H. pylori* growth *in vitro* at a minimum inhibitory concentration (MIC) of 0.05 mmol/L. This function lowers TNF- α levels, which in turn lessens the inflammatory response that this bacterium induces. It involves the production of the genes for cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (Vac A) (Yeon *et al.* 2019).

Quercetin

According to David, Arulmoli and Parasuraman, (2016) demonstrates antiviral, vasodilatory, anti-hypertensive activities when consumed. Numerous researches have examined quercetin's possible *in vivo* gastroprotective benefits (Suzuki, Ishihara and Segami, 1998; Coskun *et al.*, 2004). The gastroprotective properties of 2.5 mg of nano-quercetin in a rat model in a rat model of ulceration caused by ethanol. Based on the available data, it appears that there is a block to oxidative damage, the synthesis and expression of matrix metalloproteinase 9 (MMP-9) and the invasion of inflammatory cells. Quercetin also regulates the activity of nitric oxide synthase, COX, and apoptosis, among other processes (Chakraborty *et al.*, 2012). Research has examined the application of conventional drug mixes containing certain chemicals with demonstrated gastroprotective effects to boost their effectiveness. As examples of these combinations, consider quercetin in conjunction with pantoprazole and famotidine (Abourehab *et al.*, 2017).

Alkaloids' Effect on Peptic Ulcer

Alkaloids and other compounds derived from plants that may have therapeutic value were examined as part of the continuous search for natural plant products with bioactivity. Alkaloids perform various biological functions and serve as therapeutic agents in medicine.

Rutaecarpine

The interplay between both haemorrhagic and non-haemorrhagic lesions in the stomach mucosa is suggested by the fact that this increases the ulcer index and promotes H⁺ back diffusion into the mucosa (Wang *et al.*, 2005). Stress stimulates the sympathetic and parasympathetic nervous systems (SNS and PNS). Sympathetic activation reduces blood flow to the mucosa, causing local hypoxia and ischemia, and also increases levels of ROS, lipid peroxidation, and glutathione depletion. Higher SNP stimulation results in impaired motility of gastrointestinal muscle contractions and increased acid secretion due to mucosal ischemia (Ramsay and Carr, 2011; Morsy *et al.*, 2012). Most capsaicin-sensitive sensory neurons in the gastrointestinal tract contain the neuropeptide calcitonin gene-related peptide (CGRP). The synthesis of CGRP, a neurotransmitter that

may mediate the gastroprotective function of these neurons. Increased mucosal blood flow, reduced stomach acid output, protection against apoptosis, and reduction of oxidative damage are some of the positive effects of CGRP (Luo *et al.*, 2013).

Phenylquinoline

Galipea longiflora bark contains an alkaloid called 2-phenylquinoline, which Zanatta *et al.* (2009) and Campos-Buzzi *et al.* (2010) have isolated. Zanatta *et al.* (2009) assessed the gastroprotective qualities of 2-phenylquinoline extracted from *G. longiflora* bark. They started with the whole alkaloids fraction, eluted it with ethyl acetate to yield 2-phenylquinoline, and then chromatographed it on a silica gel column. By adopting the HCl/ethanol-induced ulcer model in pharmacological research, 50 mg/kg of 2-phenylquinoline was found to be effective against ulcers. According to this hypothesis, ethanol breaks down the mucus-bicarbonate-phospholipid layer, which causes H⁺ ions to be released. This process activates mast cells and damages epithelial cells, which attracts neutrophils that produce reactive oxygen species, exacerbating cellular damage and inducing tissue necrosis.

Rohitukine

Rohitukine is another term for it. The chromane alkaloid is found in the plants *Amoora rohituka* and *Dysoxylum binectariferum*, both of which belong to the Meliaceae family (Naik *et al.*, 1988; Yang *et al.*, 2004). According to Naik *et al.* (1988) and Singh *et al.* (2012), this alkaloid effects anti-inflammatory, immunomodulatory, and gastroprotective qualities. In the pylorus ligation ulcer model, researchers examined rohitukine at 20 mg/kg to assess mucin levels, peptic activity, and gastric juice. To assess rohitukine's anti-ulcer qualities, they also tested it at 10 mg/kg in an ulcer model caused by ethanol. Additionally, they measured intracellular calcium ions, gastrin levels, and H⁺/K⁺ ATPase activity, investigating the latter two in vitro (Singh *et al.*, 2012).

In relation to the control group, rohitukine decreased the ulcerative lesion index in the ulcer models generated by stress and ethanol. Furthermore, by raising the levels of prostaglandin E₂ (PGE₂) and mucin, rohitukine improved the protective mechanisms of the gastric mucosa (Singh *et al.*, 2012). Parietal cells produce gastric secretion (Ramsay and Carr, 2011), which helps transform pepsinogen into pepsin, an enzyme necessary for protein breakdown. It also promotes the absorption of iron and vitamin B₁₂ and inhibits the growth of germs and potential infections (Schubert, 2009).

Some Selected Nigerian Plants in the Treatment of PUD



Figure 3: *Zingiber officinale* (Khanpara and Mavani, 2022).

Zingiber officinale as shown in figure 3 is a common ingredient both as a spice in Indian food and in conventional medicine. Researchers have discovered that volatile oils, comprising 1-4% of ginger's proximate chemical makeup, contribute to its medicinal properties (Yoshikawa, Yamaguchi and Kunim, 1994). Gingerol and zingerone make up most of the phenols in solvent-extracted ginger. It was observed that phenolic acids significantly suppress the ulcer. *H. pylori*, inhibit $H^+ K^+$ -ATPase in parietal cells, and demonstrate antioxidative properties *in vitro* (Siddaraju and Dharmesh, 2007).

Zingiber officinale Roscoe, a naturally occurring dietary rhizome in the Zingiberaceae family, possesses various biological qualities and actions. Compounds such as gingerols, shogaols, paradols, and zingerones are believed to be responsible for its therapeutic properties. Gingerols exhibit antibacterial activity against *H. pylori*, causative bacteria causing PUD and dyspepsia. Ginger has proven effective against peptic ulcer diseases (Mahady *et al.*, 2005). One of the key active chemicals in ginger is called shogaol (Roli *et al.*, 2020). The benefits of ginger extract have been investigated in studies on ulcer prevention in ethanol- and stress-induced ulcer model in mice. Ginger extract has anti-inflammatory and free radical-scavenging qualities that help treat and prevent ulcers and *H. pylori* infection (Nanjundaiah *et al.*, 2011).

Allium sativum



Figure 4: *Allium sativum* (Khanpara and Mavani, 2022).

Garlic (*Allium sativum*, family: Amaryllidaceae) as shown in figure 4 has been employed medicinally and as a spice since ancient times to treat different number of ailments such as stomach discomfort, asthma and hypertension (Sadacharam *et al.*, 2013). Keiss *et al.* (2003) suggest that Garlic Powder Extract's (GPE) anti-ulcer activities result from its ability to regulate pro-inflammatory cytokine levels, including interleukins and tumour necrosis factor-alpha. Mice in the treatment group had a lower ulcer score than animals in the control group after pre-treatment with an *A. sativum* methanolic extract, suggesting its anti-ulcer potential. Because they can lessen stomach perforations in male Wistar rats administered with indomethacin, *Allium sativum*, *Brassica oleracea*, and *Aloe barbadensis* have potential application in the treatment of ulcers (Adeniyi *et al.*, 2006; Tope *et al.*, 2014; Akinbo and Eze, 2016).

Curcuma longa



Figure 5: Pictures of the botanical sources of turmeric (Basnet and Skalko-Basnet, 2011).

Curcumin, the primary naturally occurring polyphenol in the rhizome of *Curcuma longa* as shown in figure 6, a member of the Zingiberaceae family used in the different of several ailments. Researchers have used various animal models, including those induced by indomethacin and reserpine examining curcumin's anti-ulcer properties in several preclinical investigations. The extract formulation offers significant protection against chemicals that cause cyst destructive changes. The gastro protective effects in rats are believed to be caused by a noteworthy rise in stomach wall mucus, as well as the restoration of GSH levels and non-protein sulfhydryl content (Akbik *et al.*, 2014). Turmeric's anti-inflammatory effects are thought to arise from suppressing the COX enzyme and reducing inflammatory mediator levels (Koosirirat *et al.*, 2010; Hosseini and Hosseinzadeh, 2018).

Carica papaya



Figure 6: *Carica papaya* (Khanpara and Mavani, 2022).

Carica papaya as shown in figure 7, an herbaceous succulent plant in the Caricaceae family, is indigenous to tropical and subtropical regions across the globe. Papaya is used to cure a variety of illnesses because of its potent antibacterial and numerous properties (Vij and Prashar, 2015; Anjana *et al.*, 2018). Researchers evaluated the anti-ulcerogenic efficacy of *C. papaya* methanolic extracts using a range of ulcer models, including pyloric ligation. Through a marked reduction in stomach acidity as well as an increase in mucus production and GSH levels, they were able to demonstrate the gastroprotective benefits of the aqueous and methanolic extracts (Pinto *et al.*, 2015). Furthermore, they observed no toxicological symptoms following extract therapy (Ezike *et al.*, 2009). In another investigation, researchers used rats with ethanol-induced ulcers to test the anti-ulcer effects of *C. papaya* seed aqueous extract. In contrast to the group under control, they observed that the treatment groups had noteworthy decreases in acidity, total stomach volume, and ulcer index. This suggests that *C. papaya* seed aqueous extract could be a potentially effective medicinal substance for the course of treatment of ulcers (Okewumi and Oyeyemi, 2012).

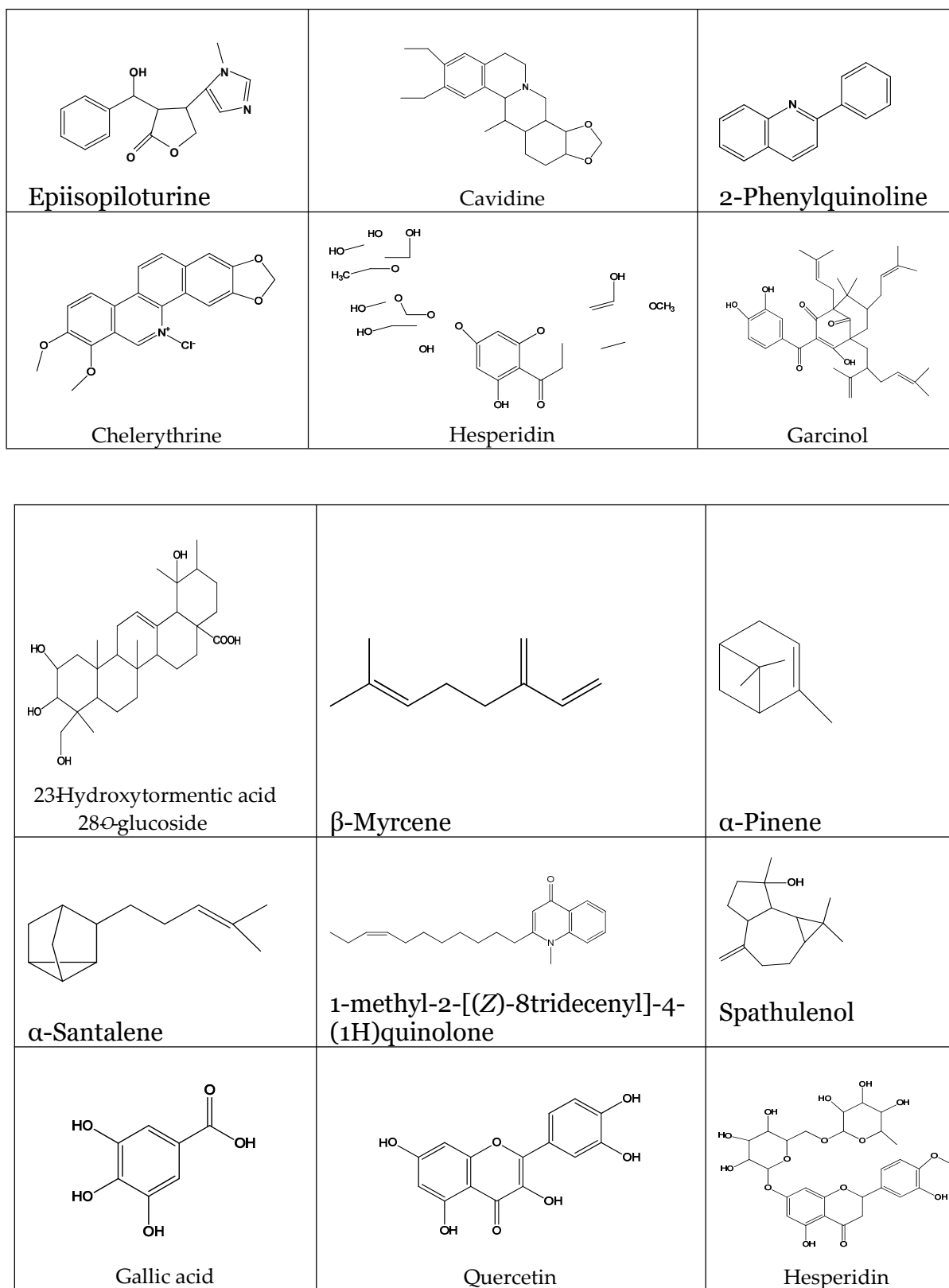


Figure 7: The structural analysis of certain phytochemicals as potential antiulcer agents (Sharifi-Ras *et al.*, 2018)

Antioxidant Capacity of Plant Based Bioactive Compounds

Oxidative stress is a key component of the pathophysiology of peptic ulcers, causing damage to mucosal tissue and hindering healing. Tissue damage and cellular dysfunction can result from the oxidative destruction of macromolecules, including proteins, DNA, and lipids, caused by free radicals and reactive oxygen species (ROS) generated during oxidative stress. Oxidative stress in the gastrointestinal tract disrupts the delicate balance between mucosal defense systems and harmful substances, increasing the mucosa's susceptibility to ulcer development and delaying healing (Gündoğdu, Özbayer and Kar, 2023).

Plant-based antioxidants, including flavonoids, phenolic acids, and carotenoids, are crucial for halting oxidative stress and hastening ulcer repair. These bioactive compounds can prevent oxidative damage to biological components by scavenging free radicals and reactive oxygen species. They also fortify cellular antioxidant systems by boosting the activity of naturally occurring antioxidant enzymes such as glutathione peroxidase, catalase, and superoxide dismutase (SOD) (Silvan *et al.*, 2021).

Flavonoids are potent antioxidants that scavenge free radicals and prevent oxidative stress-induced cell damage. They are found in large quantities in various fruits, vegetables, and drinks like tea and red wine. These substances use various methods to produce their antioxidant effects, such as metal chelation, direct radical scavenging, and altering the activity of antioxidant enzymes (Silvan *et al.*, 2021).

Foods like berries, nuts, and whole grains contain phenolic acids, which are also powerful antioxidants. They efficiently combat free radicals and prevent lipid peroxidation, which damages mucous membranes and leads to ulcer development. Furthermore, phenolic acids strengthen the body's defenses against oxidative stress by increasing the activity of endogenous antioxidant enzymes (Geetha and Anitha, 2022; Alimi *et al.*, 2023).

By scavenging free radicals and singlet oxygen species, carotenoid pigments found in vibrant fruits and vegetables act as potent antioxidants. By preventing lipid peroxidation and maintaining cellular integrity, these substances aid in repairing ulcers and shielding the stomach mucosa from oxidative damage (Pol *et al.*, 2023).

Plant-derived antioxidants protect the stomach mucosa from oxidative damage and speed ulcer healing by scavenging free radicals and enhancing cellular antioxidant defenses. In terms of prevention and treatment, their capacity to combat oxidative stress offers a promising therapeutic approach for the management of gastric ulcers. For people with peptic ulcers, including foods or supplements high in antioxidants in the diet may help lower oxidative stress and encourage mucosal repair (Gündoğdu, Özbayer and Kar, 2023).

Efficiency of Herbal Products in Gastric Ulcer Management

It is a long-standing tradition to employ plants to cure illnesses as medicines (Qadir and Raja, 2021). Plant-based medications are frequently utilized since they are generally safer, more readily available, and less expensive than synthetic ones (Khursheed *et al.*,

2022). Scientific research has demonstrated that some of these medicinal herbs have gastric protecting and anti-ulcer properties (Kayode *et al.*, 2015). However, because GUD receives less attention in this region than other diseases, not many studies often consider this; the prognosis for individuals with gastric ulcers may be improved by combining traditional anti-gastric ulcer drugs and herbal therapies, which may work in concert to combat *H. pylori* and gastric ulcer illness.

To ascertain the safety and effectiveness of medicinal plants with anti-ulcer action, further clinical research with higher sample numbers is required because there are so few human trials currently available. Designing methods to examine and determine would also be advantageous in deciphering the role of herbs used in medicine to prevent and cure gastric ulcers (Sonnenberg, 2013).

CONCLUSION

It is clear that a large number of plant species have been recognized, assessed, and formally acknowledged by science for their gastro-protective as well as anti-ulcer qualities in suitable animal models. The search is now on for substitutes in medicinal plants, which are utilized extensively in traditional medical systems and offer a possible source of anti-ulcerogenic medications due to the important functions that their phytonutrients play. In the end, this will present stimulating, lucrative, and globally competitive chances for the development of novel lead medications for PUD and other associated illnesses.

AUTHORS CONTRIBUTION

All authors made fascinating contributions in the development of this research paper.

CONFLICT OF INTEREST

The authors affirm that there is no conflict of interest associated with this work's publication.

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