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Review article

A review on anti-peptic ulcer activities of medicinal plants used in the formulation of *Enterica, Dyspepsia* and *NPK 500 capsules*

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ABSTRACT

Peptic ulcer disease affects many people globally. With the increasing resistance to some orthodox antibiotics such as Clarithromycin and Metronidazole, it is important that new acceptable, safer and effective therapies are developed to manage this disease. Various herbal medicines have been used traditionally for the remedy of peptic ulcer disease (PUD), however scientific information with regards to their anti-peptic ulcer both in-vivo and in-vitro as well as clinical studies supporting their use is still inadequate. The Centre for Plant Medicine Research, (CPMR) Mampong-Akuapem, Ghana manufactures three herbal Products namely *Enterica, Dyspepsia* and *NPK 500 capsules* which are currently used for the remedy of PUD as a triple therapy at its out-patient clinic with promising effects. The aim of this review is to gather information from literature on the anti-ulcer properties, pharmacological, phytochemical constituents and related activities of herbal plants used at the CPMR for formulation of the triple herbal therapy. This review may, provide some scientific bases for the use of *Enterica, Dyspepsia* and *NPK 500* capsules in the management of Peptic ulcer at the CPMR out-patient clinic.

Methods: Organization for the review involved the on and/or offline search for information from available literature using electronic data and scientific research information resources such as PubMed, Science Direct and Google scholar.

Results: In this review, fifteen ethno-medicinal plants used for the formulation of Enterica, Dyspepsia and NPK capsules have been discussed, presenting the description of the plants, composition and pharmacological activity.

Interpretation: Tables with the summary of reviewed medicinal plants with their anti-ulcer models and inference on possible mechanisms of action were drawn up. The mechanism(s) of action of individual plants and products (*Enterica, Dyspepsia and NPK 500 capsules)* must be further investigated and established experimentally *in-vitro* in addition to *in-vivo* pharmacological and clinical activity studies to confirm their use in the remedy of PUD.

1. Introduction

Peptic ulcer disease (PUD) comprises of esophageal, duodenal and gastric ulcers. The most frequently occurring symptom of PUD is epigastric pain. This pain may occur with dyspepsia, bloating, nausea and/or early satiety. The causes of PUD are mainly two, the first being chronic infection with *Helicobacter pylori* and the second involves abuse of Non-Steroidal Anti-Inflammatory Drugs popularly known as NSAIDs [1]. Therapy is normally focused on the elimination of *H. pylori* from the gut of an infected patient. A standard orthodox triple therapy is normally indicated as first-line therapy which involves combination of Proton Pump Inhibitor, Amoxicillin and Clarithromycin; Omeprazole, Clarithromycin and Amoxicillin; Pantoprazole, Clarithromycin and Amoxicillin among others [2]. Increasing antibiotic resistance of certain

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H. pylori strains particularly to Clarithromycin and Metronidazole is causing a decrease in the efficacy of this combination therapy [3, 4].

Many herbal medicines have been used globally for the treatment of PUD. An assessment by Ardalani and his colleagues identified about 279 plants from 89 families that may be used in the treatment of PUD. In addition, Boakye-Yiadom *et al.* [5] has currently reported 13 plants belonging to 10 different families for the treatment of PUD in Ghana. The relative safety and availability of herbal materials and medicines in addition to cost in comparison to most orthodox drugs give rise to their potential for use in conditions such as PUD [6]. Results from some toxicological studies conducted on some herbal materials have also helped to increase confidence in the use of herbal products [7].

The Centre for Plant Medicine Research (CPMR), Mampong-Akuapem, Ghana established in the year 1975, has a vision of 'Making Herbal medicine a natural choice for all'. CPMR currently produces about 33 herbal medicines which are used in the therapeutic remedy of some diseases at its clinic. The CPMR clinic currently uses a triple herbal therapy to manage gastro-oesophageal disease including peptic –ulcer (PUD) Boakye- Yiadom *et al.* [5]. The three products are branded as *Enterica, Dyspepsia* which are decoctions and *Natural Pain Killer (NPK) 500 capsules.* A combination of different medicinal plant materials is used in the production of *Enterica* and these consists of *Spondias mombin, Momordica charantia, Persea americana, Paullinia pinnata, Psidium guajava, Cnestis ferruginea, Vernonia amygdalina, Trema orientalis Latana carmara, Morinda lucida, Citrus aurantifolia and Bidens Pilosa*. Though *Enterica* is indicated for the treatment of typhoid fever [8], the product has shown great potential in the management of PUD at the CPMR clinic with its anti-ulcer effects probably linked to its antibiotic nature and the likely eradication of *H. pylori.* Though specific anti-*H. pylori* activity has not been conducted on the product, *in-vitro* antimicrobial activity has been reported against *Escherichia coli, Staphylococcus aureus, Staphylococcus saprophyticus, Neisseria gonorrhea, Candida albicans* and some strains of *Salmonella* [9]. *Dyspepsia* is a product of the plants *Maytenus senegalensis, Carapa procera, Trichilia monadelpha* and *Spathodia campunalata. Dyspepsia* is indicated for the remedy of heartburn and nausea which are signs normally related to PUD [10]. *NPK 500* capsules contain *Cassia siebieriana* and is indicated for the remedy of pains occurring from menstruation and stomach ulcer. The product is stable with its shelf-life being determined to be 32.91 months in a previous study conducted by Kumadoh and colleagues [11].

Several *in-vivo* models for the investigation of the anti-peptic ulcer activity of potential products like herbal medicines have been detailed in a paper by Adinortey and colleagues and these include gastric ulcers induced using; histamine, ethanol, water-immersion stress, serotonin, NSAIDs- (indomethacin, aspirin, and ibuprofen), acetic acid, ferrous iron-ascorbic acid and ischemia-reperfussion and reserpine. Other models also include; pylorus-ligated and diethyldithiocarbamate- (DDC)-induced peptic ulcers, methylene blue-induced ulcers, cysteamine and indomethacin-histamine-induced duodenal ulcers and acetic acid-*H. pylori-induced* ulcers [12]. The aim of this article is to put together supporting literature for the use of the products *Enterica, Dyspepsia and NPK 500 capsules* in the management of PUD by reviewing their anti-peptic ulcer and related investigations conducted on the various plant materials used in their preparations.

2. Methodology

The organization for this review involved the on line/off line offline search for information from available literature using electronic data and scientific research information resources include: PubMed, Scopus, Scientific Information Database, Springer Link and African Journals on Line, in addition to Google Scholar. Institutional reports, student theses, educational newspaper articles, monographs on medicinal plants, information from labels of products, and reports of the Centre for Plant Medicine Research, Mampong-Akuapem, Ghana, were also consulted. Peptic ulcer disease, herbal products, anti-ulcer activity, *Helicobacter pylori*, *Enterica*, *Dyspepsia*, *Natural Pain killer 500 capsules*, Active and isolated compounds, phytochemical constituents, pharmacological activity and folkloric uses of the medicinal plants were the keywords used in the web search engines. Nevertheless, other phrases reflecting subjects of interest were also used. Throughout the search process, the keywords were used interchangeably including synonyms, different terminologies and related terms. Boolean operators such as "AND", "OR", "-", "NOT" and "+" were used to combine and exclude terms when searching within Google and Google Scholar. Wildcard operators, such as (*), (?), (~) and (!) were used when searching the databases. Examples of medicinal plants explored include: *Spondias mombin, Momordica charantia, Persea americana, Paullinia pinnata, Psidium guajava, Cnestis ferruginea, Vernonia amygdalina, Trema orientalis Latana carmara, Morinda lucida, Citrus aurantifolia and Bidens Pilosa, Maytenus senegalensis, Carapa procera, Trichilia monadelpha* and *Spathodia campunalata* and *Cassia siebieriana*. The search was conducted over an eight-month period and included references published from 1990 up until January 2021. All publications resulting from these searches were screened. Also, both *in vitro* and *in vivo* models for testing anti-peptic ulcer activity of the medicinal plants were included. Investigations conducted on related pharmacological activity which did not fall into the category of the suggested *in-vivo* or *in-vitro* models above were also included. All documents that met the inclusion criteria of the review paper were recovered and assessed by the authors. While the peptic ulcer activities of medicinal plants used in the formulation of *Enterica*, *Dyspepsia*, and *NPK 500 capsules* were the main focus of the review, studies which supported use of the medicinal plants apart from Africa were also included.

3. Results

3.1. Anti- peptic ulcer and related activity of medicinal plants used in the formulation of the three products

Search from available literature reveals no research on the *in-vivo* anti-peptic ulcer activity of the products *Enterica* (FDA Reg. No: FDA/HD.07-7097)*, Dyspepsia (*FDA Reg. No:/HD1. 20-2085*) and NPK capsules* (FDA Reg. No: FDA/HD1.16-1011) as a whole has been conducted. However, these three products have been approved and registered by Food and Drug Authority, Ghana. Some information on the *in-vivo* anti-peptic ulcer activity and related pharmacological activities of the individual medicinal plants used in its formulation was obtained.

3.2. Morinda lucida (L.) Benth

Morinda lucida, also known as Brimstone tree, is found in the tropical West African rain forest and belongs to the family Rubiaceae. At maturity, *Morinda lucida* is a medium sized tree [13, 14]. A distinctive character that distinguishes *Morinda lucida* from other plants of the same genus is its relatively small floral as well as fruiting heads present on long thin peduncles [15]. The leaves, stem bark and roots of the plant are used for the management of diseases such as diabetes, hypertension, leprosy and ulcers in folkloric medicine [16]. Phytochemical constituents discovered from the leaves of *M. lucida* include tannins, saponins, flavonoids, alkaloids, anthraquinones [17, 18] and triterpenes. Isolated compounds found in *M. lucida* include molucidin, a tetracyclic iridoid, rubiadin, purpuroxanthin, lucidin, nordamnacanthal and soranjidol, which are all anthraquinones [19]. Pharmacological activities observed from investigations of the plant include; antihypertensive, analgesic and sedative activities [19]. *Morinda lucida* is valued in the treatment of ulcers [20]. Christophe and his colleagues [15] evaluated aqueous extract of *M. lucida* leaves on indomethacin and acetic acid induced gastric ulcers at quantities of 100, 200 and 400 mg/kg body weight. The result showed marked reduction in the ulcer index. The authors suggest an increase in prostaglandins which play a role as a cytoprotective agent in the stomach in addition to the stimulation of the secretion of mucus and bicarbonate ions which preserves the gastric membrane may be responsible for the

recorded activity [15]. Evaluation of the antiulcer activity of methanol extract of *M. lucida* leaves using acetylsalicylic acid induced gastric ulcer model in rats and intestinal motility in mice has also been conducted. The result showed that leaves extract of *M. lucida* enhanced intestinal motility and gastric emptying time in the tested animal models [21]. The opportunity to conduct more extensive studies using the *in-vivo* models not yet tested exists particularly for the isolated compounds. These tests could also be conducted on all parts of the plant including the stembark and roots. This may help to ascertain and further confirm the use of the medicinal plant in the preparation of *Enterica* as well help to predict the likely mechanism(s) of action of the plant with regard to PUD treatment.

3.3. *Cnestis ferruginea Vahl ex D.C.*

Cnestis ferruginea is a shrub which belongs to the family Connaraceae. It is normally found in western tropical Africa. *Cnestis ferruginea* normally spreads from Senegal to West Cameroons [22]. The whole plant (leaves, roots, stem back) is used in folkloric medicine for remedy of conditions such as fever, gonorrhea, wounds, gum pain, dysmenorrhea, whooping-cough, tuberculosis, headache and arthritis [22]. Phytochemical constituents including alkaloids, tannins, saponins, tannins, reducing sugars, flavonoids, cardiac glycosides, terpenes, phytosterol, oxalate, steroid, cyanogenic glycoside and anthocyanin, have been reported [22, 23]. Stigmasterol-3-O-â-Dglucopyranoside, stigmasterol, oleanolic acid, betulinic and ursolic acid have also been isolated from the methanolic root extract of *C. ferruginea.* These compounds are known to possess some level of anti-peptic ulcer activity by the use of the various testing models though the specific isolates from *C. ferruginea* have not been tested [24, 25, 26]. In addition, isoflavone glycoside afrormosia-7-O-beta-D-galactoside [27] has also been isolated. These isolated compounds may be working in a synergistic manner to demonstrate their anti-peptic ulcer activity. Pharmacological activities investigated on the plant include; anti-inflammatory, antioxidant, antidiabetic [22] antimicrobial, aphrodisiac, hepatoprotective and analgesic effects [28]. Antiulcer activity was reported on *Cnestis ferruginea* root extract using immobilization induced gastric stress models in mice and rats, where at quantities of 300–500 mg/kg body weight, the aqueous root extract of the plant showed significant reduction in stress induced gastric ulcer suggesting a potential for the plant to be used as an anti-ulcer agent, Further *in-vivo* anti-ulcer work is needed to be done on the various parts of the plant such as the stem bark and leaves to confirm its usefulness or otherwise in the treatment of PUD [29].

3.4. *Momordica charantia Linn.*

Momordica charantia is a flowering vine known as bitter gourd which belongs to the family Cucurbitaceae [30, 31] *M. charantia* contains bitter glycosides which are water soluble and ether insoluble, flavonoids, saponins and sterols [33]. Traditionally, the plant is used in wound healing and the management of malignant ulcers. The fruit juice is used in the management of infections, malaria, fevers and parasitic infections [32]. Other chemical constituents obtained from the plant include alkaloids, charantin, momordicilin, momordenol and momordin. These components have not been examined for anti-peptic ulcer activity though it is known that anti-oxidants may contributive to the gastroprotective effects of extracts of *M. charantia*. Pharmacological activities reported on the plant include anticancer, antidiabetic, anti-malarial, hypocholesteromic and immunomodulatory activities [34]. The anti-microbial activity on *E. coli, Salmonella, Shigella, streptococcus, streptobacillus, Staphylococcus, Pseudomonas, H. pylori* and *E. histolytica* has also been reported [34]. Gurbuz and his colleagues [35] reported the gastric cytoprotective effects of fresh fruits extracted with olive oil, dry fruit in honey as well as the ethanolic extract of dry fruits in animal model. Fruits of *Momordica charantia* have been reported to prevent the growth of *H. pylori* as described by Yesilada and his colleagues; and Sathish Kumar and colleagues [16, 36]. Methanolic extract obtained from the fruits of *M. charantia* displayed effectiveness in the management of gastric, duodenal and stress induced ulcers in animal model. It was proposed that its antiulcer activity may be due to the enhanced secretion of mucus, and reduction in production of acid [37]. The extract of the fruit in olive oil also demonstrated similar curative effect in peptic ulcers [38]. In addition, ethanolic and aqueous extracts obtained from the fruits of *M. charantia* used against aspirin, pylorus ligation and stress induced ulcer in rats showed promising results [39]. Tests on the anti-ulcer activity of leaves and other parts of the plant are scarce; this suggests that research may be done on these parts to increase the understanding of the inclusion of the plant material in the preparation of *Enterica*.

3.5. *Vernonia amygdalina Del.*

Vernonia amygdalina belonging to the family Asteraceae is a rapid regenerating tropical shrub growing up to a height of 3 meters. It is also known as bitter leaf. It is found cultivated or wild in the African tropics [38, 39]. Several parts of *V. amygdalina* are employed in the remedy of diseases such as microbial infections, gastrointestinal disturbances and parasitic infections. Phytochemical constituents observed in the plant include flavonoids, alkaloids, saponins, tannins, terpenoid, steroids Cyanogenic glycosides, anthraquinones, coumarins, xanthones, sesquiterpenes, edotides and phenolic compounds [40, 41]. Studies by Yuso and colleagues [42] revealed twenty–three isolated compounds from the dichloromethane extract of *V. amygdalina* leaves including; neophytadiene, triacontane, squalene, heptacosane and phytol which were the five major compounds evaluated. Several compounds have been isolated from leaves of *V. amygdalina* including; luteolin-7-*O*glucuronide, luteolin 7-*O*-glucoside, sesquiterpenes [43, 44], 4,15-dihydrovernodalin, vernodalin, vernolide, 11,13-dihydrovernorodeline, vernomenin [45, 46] 4α-Hydroxy-n-pentadecanoic acid, 11α-Hydroxyurs-5,12-dien-28-oic acid-3α, 25-olide, 1-Hene icosanol-O-β-D-glucopyranoside, 10-Geranilanyl-O-β-D-xyloside, 6β,10β,14β-Trimethyl heptadecan-15α-olyl-15-O-β-D-glucopyranosyl-1,5β-olide, and one new compound; Glucuronolactone [47]. Investigations on the anti-peptic ulcer activity of these isolated compounds have not been reported. Pharmacological activities which have been reported on varying extracts of the plant includes; anticancer, anti-malarial, antidiabetic, antimicrobial, anti-inflammatory, analgesic, anti-pyretic, antioxidant, anthelmintic, chemo and hepatoprotective and hypolipidaemic activities [41]. The antimicrobial property may be useful in *H. Pylori* eradication in the treatment of PUD [39, 48]. *V. amygdalina* leaves extract have shown antacid and carminative properties as reported by Mbatchou and colleagues [39]. Although the methanolic and aqueous leaves extract showed acid neutralizing and carminative characteristics, the aqueous extract produced a higher antacid effect [39]. This characteristic of *V. amygdalina* extract may be beneficial in the remedy of hyper acidity associated with gastric and duodenal ulcers.

Adefisayo and colleagues [49] studied the methanolic leaf extract of *V. amygdalina* for an improved therapeutic outcome in aspirin induced gastric ulcer in rats. A decrease in the gastric content, pepsin activity, malondialdehyde, free and total acidity as well as ulcer index was observed. It is suggested that this was achieved through H_2 receptor antagonism and antioxidation [49].

3.6. *Lantana camara Linn.*

Lantana camara from the family Verbanaceae is also recognized as wild/red sage. *L. camara* is native to tropical and sub-tropical America and grows in temperate, tropical and sub-tropical regions [50]. *L. camara* is traditionally used in the management of malaria, influenza, stomachache [50] fevers, ulcers, epilepsy, chickenpox and eczemas [51, 52]. Phytochemical constituents observed in the plant include saponins [53], tannins, flavonoids, steroids, anthocyanins [54], alkaloids [55], terpenoids [56], glycosides, quinones, cardiac glycosides [57] caumarins, phlobatannins, anthraquinones and phenols [58, 59]. Pharmacological

activities have been reported on varying extracts of the plant including; Anti-diabetic [60], Antiprotozoan [61], anti-inflammatory [62], antioxidant and antimicrobial activity [59]. A study conducted by Sathish and his colleagues [63], revealed the potential of the leaves of *L. camara* against *H. pylori* infection. At quantities of 250 and 500 mg/kg of the methanolic leaf extract of *L. camara*, a significant antiulcer and antioxidant activity against gastric and duodenal ulcers was observed in Wister albino rats. A decreased ulcer index and total acidity in addition to markedly enhanced gastric pH was observed in aspirin, pylorus-ligation and ethanol induced gastric ulcer models [63].

Kazmi and colleagues [63] reported that oleane-12-en-3β-ol-28-oic acid 3β-D-glucopyranoside (OAG), a compound isolated from *L. camara* showed significant gastroprotective activity. This was achieved by the prevention of gastric acid release leading to prevention of gastric membrane destruction. The added improvement in prostaglandin E_2 content also confirms the antiulcer function of OAG from *L. camara* [39]. Another experiment conducted using the cold restraint stress induced ulcer-model as reported by Thamotharan and colleagues [64] showed the methanol extract of leaves exhibiting a dose dependent decrease in ulcer index and significant scavenging of free radicals from the anti-oxidant activity study.

These conducted tests have shown the potential of *L. camara* in the treatment of PUD. More *in-vivo* and clinical studies are needed on formulations made from the various parts of the plant to confirm its use as well as predict likely mechanism of action against PUD.

3.7. Psidium guajava Linn.

Psidium guajava from the Myrtaceae family is used ethno-botanically for the remedy of several stomach diseases including peptic ulcer [65]. Phytochemical constituents observed in the plant include; tannins, phenols, triterpenes, flavonoids, saponins [66] alkaloids, glycosides [67].

Studies by Tachakittirungrod and colleagues [68] reported Isolated compounds obtained in the methanol crude extracts of *Psidium guajava* leaves included; Quercetin, morin morin-3-O-α-L-lyxopyranoside and morin-3-O-α-L arabopyranoside and quercetin-3-*O* glucopyranoside [68, 69] Avicularin (quercetin-3-O-L-arabinofuranoside) and guaijaverin (quercetin-3-O-L arabinopyranoside) [70]. Pedunculagin and (+)-gallocatechin, α-pinene, β-copanene, limonene [71]. Asiatic, Guajavanoic, Guavacoumaric, Jacoumaric, Ursolic, 2α-hydroxyursolic, Maslinic, Isoneriucoumaric and Guavenoic acids isolated from triterpenoids [72], gallocatechin, and 3-sinapoylquinic acid. Quercetin and ursolic acid have been studied and found to possess positive anti-peptic ulcer activity when tested in various models [26, 73, 74, 75, 76].

Pharmacological activities reported on varying extracts of the plant include; Anti-diarrheal [77, 78] anti-hypertensive, hepatoprotective, antioxidant [79, 80] anticancer activity [81] anti-microbial [82] Anti-bacterial [80, 83] anti-inflammatory [84, 85] antitumor activity [80].

Studies on the anti-ulcer activity of *P. guajava* done by Livingston and Sundar [66] using aspirin-induced, ethanol-induced and pylorus ligation models in Wistar rats have indicated that the plant may have potential in PUD treatment. Treatment of rats at 100 mg/kg and 200 mg/kg of extract significantly inhibited the gastric ulcers caused by aspirin (70.5%), ethanol (70.4%) and pylorus ligation (65.07%) with potency comparable to omeprazole (74.1%) [66]. Another study using higher doses of the methanol extract of the guava leaves (500 mg/kg and 1000 mg/kg) in Wistar rats in ethanol induced model also demonstrated a significant ulcer protective activity (64.4%) at 1000 mg/kg of extract on the stomach wall when compared to the control which was less than ranitidine (73%) [86]. An analysis of the anti-ulcer potential of the hydroethanolic extract of guava leaves using aspirin induced model showed significant gastroprotective activity with a maximum of 70 % curation in rats who were given 400 mg/kg extract which was found to be higher than lansoprazole (40%) [87]. Furthermore, assessment of the anti-ulcerogenic effect of aqueous extract of the guava leaves using ethanol induced ulcer model demonstrated a dose relative reduction in stomach lesions in rats treated with 500 mg/kg and 1000 mg/kg extract relative to untreated animals. The potency of the aqueous extract was comparable to the standard drug, cimetidine [88]. The anti-peptic ulcer activity demonstrated by the leaves of *P. guajava may* be as a result of phytochemical constituents such as Saponins, flavonoids and volatile oils. No signs of toxicity were observed in investigation of *P. guajava* extracts with doses of extract up to 2 g/kg indicating the relative safety of the extracts [65, 89]. Though all these works have helped to justify the inclusion of the plant material in the preparation of *Enterica* meant for the treatment of PUD, there is a need to also evaluate the various parts of the plant, extracts and formulations using anti-ulcer models that have not yet been tested.

3.8. Trema orientalis Linn.

Trema orientalis is a fast-growing perennial shrub which is widely spread all over the world. *T. orientalis* belongs to the family Ulmaceae. The stem bark, leaves and roots are used in herbal medicine for the remedy of diarrhea, fever [90, 91], asthma, jaundice, malaria, pain, ulcer, hypertension, diabetes mellitus among others [92, 93]. Phytochemical constituents of the leaves and root include; saponins, alkaloids, cardiac glycosides, steroids, terpenoids, tannins, coumarins, flavonoids and phenolics [94]. The stem bark of the plant has been found to contain isolated compounds such as trematol; scopoletin; p-hydroxybenzoic acid; 2α, 3ß-dihydroxyurs-12-en-28-oic acid and methylswertianin [95, 96]. Adesina and colleagues [97] reported compounds isolated from the root bark and trunk of *T. orientalis* including; b-sitosterol; 3, 4-dihydroxybenzoic acid, lupeol, adian-5-en-3-one,2a,3a,23-trihydroxyurs12-en-28-oic acid, scopoletin, 3,4-dihydroxybenzoic acid, 2a,3a,23-trihydroxyurs-12-en-28-oic acid, Hexacosanoic acid, 3-O-s-glucopyranosyl-s-sitosterol and simiarenone. Plant phytosterols have been studied to possess gastroprotective effect with a fraction of an extract containing β sitosterol as major component reported as showing anti-peptic ulcer activity [75, 98, 99]. Pharmacological activities reported on the plant include; antimalarial activity [100], hypoglycemic activity, analgesic, anti-inflammatory activities [101], anti-plasmodial activity [102], diuretic activity [103], laxative effect [104], anti-convulsant activity [105], anti-oxidant and anti-bacterial activity [106, 107]. Investigation of the ethanolic leaves extract of the in Wistar rats using ethanol induced ulcer model showed a significant gastro protective activity comparable to pantoprazole [108]. Uddin and colleagues have also demonstrated a dose relative reduction in ulcer index when the ethanolic leaves extract of the plant at dosage quantities of 100 mg/kg, 150 mg/kg and 200 mg/kg were compared against pantoprazole as well as the controls [109]. Flavonoids are part of cytoprotective materials whose antiulcerogenic efficacy has been considerably confirmed [110, 111]. These active compounds protect the gastro mucosa against numerous ulcerogenic agents via stimulation of the secretion of bicarbonate and prostaglandin, increase mucus production, scavenging of free radicals and antioxidant properties and the inhibition of the growth of *H. pylori* [108, 112]. More research on the anti-ulcer activity of the various parts of the plant and isolates is needed to confirm its effectiveness in PUD as well as establish reasonable dosages for its use.

3.9. Persea americana Mill.

Persea americana from the Lauraceae family, is a native to Central American and Mexico, and later spread to other parts of the world. *P. americana* is mostly cultivated in tropics and subtropics regions and grows up to 15–20 m tall [113]. The common name of the plant is avocado. In traditional medicine, its leaves, fruits and other parts have been recommended for anemia, gastritis, hypercholesterolemia, stomach ache, bronchitis, diarrhea, diabetes, exhaustion, hypertension and peptic ulcers [114]. Phytochemical constituents observed in the plant include alkaloids [115] flavonoids [116, 117], cellulose, polyuronoids [118], saponins, β-galactoside, fatty alcohols, glycosylated abscisic acid, peptone and

polyphenols [119, 120, 121], triterpenoids, tanins and cyanogenic glycoside [122]. Studies by Uzor and colleagues [123] showed that the crude extract of *P. americana* leaf contained bioactive compounds such as Cyclopenol, Cytosporin, Hyperoside (quercetin-3-galactoside), quercetin-3-O-rhamnoside isolated from flavonoids. Aqueous extract of the leaves contained the isolated compound Naamine. Methanol extract of the leaves contained isolated compounds such as hyperoside and Quercetin. The ethyl acetate extract also contained isolated compounds such as hyperin, and hyperoside. The methanol extract also contained Hyperoside. The hexane extract contained isolated compounds such as Cyteo-α-pyrone (Pyrones), quercetin-3-O-rhamnoside, β-Sitoster-ol-3-O-α-pyranoside and pretrichodermamide. These compounds isolated from the leaf extract of the *P. americana* may be potential sources for remedies against peptic ulcer. Quercetin and quercetin-3-rhamnoside have been reported to possess active anti-peptic ulcer active though hyperoside showed weak activity [74, 75]. Pharmacological activities have been reported on varying extracts of the plant including; anti-inflammatory and analgesic [124], antiviral activity [125], antioxidant activity [118], anti-ulcer activity [126] and anti-hepatotoxic activity [118]. Aqueous extract of the leaves investigated in rats by Ukwe and Nwafor demonstrated a dose relative anti-ulcerogenic function in ethanol and indomethacin induced lesions [126]. Investigation of the likely medium of action of the methanolic and aqueous extracts of the leaves of *P. americana* by Oluwole and colleagues reported no relevant change in gastric acid release relative to non-treated rats. Treatment of rats with 200 mg/kg of both extracts caused a marked prevention of histamine-stimulated gastric acid secretion [127]. Although an attempt has been made on leaves extracts of *P. americana* in the treatment of ulcer, further studies should be conducted using the various anti-ulcer models to further evaluate its effectiveness and efficacy in the treatment of PUD.

3.10. Spondia mombin Linn.

Spondia mombin is an evergreen tree belonging to the family Anacardiaceae and found in Africa and America [128]. *S. mombin* also known as yellow mombin is a fruitful tree grown for its leaves, fruits and oil. In traditional medicine, it is used to cure diseases such as haemorrhoid, stomach ache and discomfort, diarrhea, dysentery, inflammation and others. Phytochemical constituents include; flavonoids, glycosides, saponins, phenolics [129, 130] alkaloid, tannins, [131]. Studies by Almir and colleagues [132] reported isolated compounds from investigation of the ethanolic extract including gallic acid and ellagic acid which have been found to possess antiulcer activity. Other components included chlorogenic acids and isoquercetrin [133]. Gallic acid has gastroprotective activity and ellagic acid is also known to have strong antioxidant properties. Studies also showed gallic acid to possess anti-*H. pylori* activity and a likely synergistic effect with other ethanolic extract consituents resulting from testing using Indomethacin, ethanol and acetic acid induced ulcer models [134, 135]. The ethyl acetate extract of the leaves of *S. mombin* produced compounds such as gallic acid, coumaroyl and quercetin [136], kaempferol, isoquercetin, rutin and anlupeol [137]. β-caryophyllene and γ-cadinene have also been isolated from volatile compositions of fresh and dried leaves of *S. mombin* [138]. Corthout and colleagues [139] evaluated the ethanolic extract of *S. mombin* and isolated phenolic compounds such as geraniin and galloyl geraniin. Also, methanolic extract of the stem bark of the plant showed the present of 3-hydroxy-22-epoxystigmastane and stigmasta-9- en-3, 6, 7-triol [140]. Study by Akanji [141] on n-hexane extract of *S. mombin* leaves revealed the presence of compounds such as; Stigmast-4-en-3-one, Phenol 3-pentadecyl, Phenol 3-methyl-, Phenol 2-methyl-, Gamma-Tocopherol, 2H-1-Benzopyran-6-ol, n-Hexadecanoic acids and Phytol [142]. The anti-peptic ulcer activity of all these compounds when further investigated may help to confirm its use in peptic ulcer disease remedies in addition to providing basis for anti-peptic ulcer synthetic agents. The anti-peptic ulcer activity of the aqueous leaf extract of *S. mombin* using ibuprofen, alcohol and pylorus ligation induced ulcer animal models as well as its acute toxicity has been reported by Oluwatoyin and Deborah [143]. Oral delivery of leaf extract of *S. mombin* at dosage quantities of 50, 100 and 200 mg/kg produced a non-dose dependent antiulcer activity with 200 mg/kg producing the highest percentage protection (90.60%) followed by 50 mg/kg which produced similar percentage protection as misoprostol (81.30% each). Also, studies using the alcohol induced ulcer model showed peak protection of 74.20 % which occurred at a dose of 200 mg/kg. Percentage protection of 45.20 % and 37.10 % were seen at doses of 100 mg/kg and 50 mg/kg respectively with the standard drug, omeprazole showing 67.7% protection. In the pylorus ligation-induced ulcer model, there was a dose – relative antiulcer activity with the highest effect of 64.30 % protection at a dosage quantity of 200 mg/kg, 52.40 % protection at a dosage quantity of 100 mg/kg whiles the extract administered at 50 mg/kg produced the same percentage protection (47.60 %) as that of standard drug (omeprazole). The aqueous leaf extract of yellow mombin showed a marked antisecretory and gastric cytoprotective effects in ibuprofen-, alcohol, and pylorus ligation induced ulcer model respectively. Their study suggested the likely inclusion of nitric oxide synthase and non-protein sulfhydryl pathways in the gastro protective activity of *S. mombin*. Oral acute toxicity test demonstrated no mortality or toxic symptoms up to quantities of 4000 mg/kg. However, lethal dose through the intraperitoneal route was found to be 707.107 mg/kg [143].

The anti-peptic ulcer review on *Spondia mombin* reveals its usefulness in the product *Enterica* meant for PUD treatment. Further in-vivo and clinical studies should be conducted on formulations made from the plant to confirm its use in PUD management.

3.11. Citrus aurantifolia Linn.

C. aurantifolia from the family Rutaceae and domesticated from East Asia. It is now widely distributed to most parts of the world. It is a persistent shrub [144]. Folkloric uses of *C. aurantifolia* include remedy of stomach illnesses, diarrhea, malaria and urinary tract infection [145]. Phytochemical constituents of the aqueous extract of *C. aurantifolia* include; flavonoids, cardiac glycosides, steroids, alkaloids, tannins, saponins and reducing sugars [146, 147]. Studies have reported the presence of isolated compounds in *C. aurantifolia* including: phellopterin; quercetin; 2,4,6-trichloroanisole; β-bisabolene; 6,7- dimethoxycoumarin; 9,10-dimethyl-1,2- benxanthracene; bergamottin; kaempferol; camphene; isopimpinellin; o-cymene; 5-geranoxy-7-methoxy-coumarin; citronellol; rutin; citronellol; 8-geranoxypsoralen; berfapten; terpinolene; monoterpenes; apigenin; b-pinene; sitosterol; furocoumarins; nobiletin; coumarins; terpinolene; lycopene and quercetin [148, 149, 150, 151]. Some of these compounds including quercetin, rutin, sitosterol and kaempferol, have been studied for anti-peptic ulcer activity with positive effects [74, 75] Pharmacological activities investigated include; anticancer/cytotoxic activity [152], antioxidant activity [151, 153] cardiovascular activity [154] and antiobesity activity [155]. The antibacterial activity, antifungal and antiaflatoxigenic activities [156, 157] have also been investigated. Investigation of the antibacterial potential of *C. aurantifolia* leaves extract using *H. pylori* strain P12 has been done. Determination of anti-adhesion was done using *Fluorescein-isothiocyanate* (FITC) labelled *H. pylori*. The results showed that, the extract demonstrated activity with minimum inhibition concentration of 50 mg/ml with a decrease in *H. pylori* bond to the mouse tissue stomach [158]. Also, ethyl acetate extract of *C. aurantifolia* peels was investigated using aspirin induced ulcer model in mice. Results from the studies indicate *C. aurantifolia* peel extract at a dosage of 400 mg/kg body weight significantly reduced ulcer index. Hence, the extract has a gastroprotective effect. Thus, the extract has a potential remedy for management of ulcerogenic disorders [146]. The fruit and essential oil from *C. aurantifolia* at 250 mg/kg, demonstrated cytoprotection of gastric membrane in the ethanol induced ulcer model in experimental animal [147]. Anti-ulcer and antibiotic activity of flavonoids has been reported

[152]. However, further studies should be conducted on the various parts of *C. aurantifolia* using various anti-ulcer models to evaluate their effectiveness in the treatment of PUD.

3.12. Bidens pilosa L.

B. pilosa is an upright herb from the family Asteraceae which grows in the tropics and temperate regions of West Africa. It originates from South America and is now distributed to all parts of the world [159, 160]. In traditional medicine, the whole plant is used for the management of gastrointestinal disorders, ulcers, hypertension, bleeding and cardiovascular diseases. Phytochemical evaluation of the extracts of *B. Pilosa* indicates it contains Polyenes, flavonoids, phenylpropanoids, fatty acids, and phenolics [161]. Owoyemi and colleagues [162] also detected flavonoids, cardiac glycosides, saponins, tannins, alkaloids and steroids in the aqueous extracts of the plant which could account for its anti-ulcerative activity. Some compounds have been isolated from the group of polyacetylenes and flavonoids from *B. pilosa.* For instance, 1-phenylhepta-1,3,5-triyne which is a polyacetylene has been observed in the root oil and aerial parts of the plant in addition to aurones and chalcones which are flavonoids [163, 164]. Studies also revealed the presence of terpenoids [165, 166], hydrocarbons and sterols [167, 168] and phenylpropanoids [169, 170]. The flavonoid 2,4-dihydroxychalcone has been reported to have gastric cytoprotective activity [171]. Chalcones have been suggested to have anti-ulcer activity [172]. These compounds may contribute to the overall anti-peptic ulcer activities of the plant [162]. Other Pharmacological activity of the plant reported include; antimalarial [173], anticancer, anti-inflammatory [160, 174], antioxidant [159], anti-diabetic [175, 176] and anti-influenza activity [177].

Investigation of anti-ulcer activity of ethanolic leaves extract of *B. pilosa* in indomethacin and pylorus-ligated animal model has indicated a significant reduction in gastric lesions, gastric juice volume, acid secretion, as well as pepsin secretion in pylorus-ligated rats leading to an increased cytoprotective activity. The function may be due to the presence of flavonoids, of which quercetin has been identified by high performance liquid chromatography [178]. In a similar study by Alvarez and colleagues [179] in pylorus-ligated rats, the ethanolic leaves extract dose-dependently caused a reduction in gastric juice volume, pepsin and acid secretion. Ethanol and indomethacin induced gastric lesions were significantly inhibited ethanol at a dose of 2 g/kg being more potent relative to sucralfate (400 mg/kg). Tan and colleagues [180] also screened the methanol, cyclohexane and methylene chloride extracts of the plant for their anti-ulcer activity. The methylene chloride extract was observed to have the highest activity [180]. In vivo tests of toxicity (acute) indicated the aqueous leaves extract to be relatively non-toxic (L_D50 = 12.30 g/kg) [181]. The conducted works supports the use of the plant in formulations meant for PUD treatment. However, more studies using models that have not yet been tested will help to fully understand its usefulness in PUD management.

3.13. Carapa procera D.C.

C. procera is an evergreen tree plant from the Meliaceae family. It is the commonest species cultivated in West Africa. It grows up to approximately 25–35 m tall. *C. pocera* is prominent for its therapeutic and economic benefits. The folk medicinal uses of the plant include; management of gastrointestinal disorders, paralysis, epilepsy, external anti-inflammation, anthelmintic, treatment of fever [182, 183]. Phytochemical constituents of the ethanolic extract of the stem bark of *C. procera* include; alkaloids, saponins, flavonoids, coumarins, tannins [184], astringents, anthocyanins, phenolic acid [185], glycosides, triterpenoids [186] reducing sugars, steroids [187]. Flavonoids have been extensively studied for its anti–peptic ulcer activities [188]. Studies by Adjé and colleagues [185] revealed the presence of some isolated compounds in the aqueous leaf extract of *C. procera* including; 2 anthocyanins (cyanidin 3-O-glucoside and cyanidin 3-O-rutinoside), 5 phenolic acids (protocatechuic, the three ca eoylquinic isomers, and coumaroylquinic acid), and 5 flavonols (quercetin 3-O-rutinoside, quercetin 3-O-galactoside, quercetin 3-O-glucoside, quercetin aglycone, and kaempferol 3-O-rutinoside). The anti-peptic ulcer activity of some of these flavanols have been investigated with positive results [74, 75]. Pharmacological activities obtained from investigation of the leaf extract of the plant include; antibacterial, antioxidant, anti-inflammatory [189], anti-carcinogenic, antibacterial [187], antiplasmodial activity [190]. Literature survey showed that this plant has not been evaluated for anti-ulcerative properties or anti – *H. pyloric* activity. Ngbolua and colleagues [191] evaluated the radical scavenging activities of the methanolic extracts from *C. procera* stem bark using DPPH assay with promising results (ED50 = 1.698 ± 0.079 μg/mL). The anti-ulcer effect of this plant can be attributed to its anti-oxidant mechanism of action [192]. The opportunity to conduct extensive anti-PUD studies using *in-vivo* anti-ulcer models exists. This will help to confirm the usefulness of the plant in the preparation of *Dyspepsia* as well help to predict the likely mechanism(s) of action of the plant with regard to PUD treatment.

3.14. Maytenus senegalensis (Lam.)

Maytenus senegalensis from the Celastraceae family is a perennial shrub commonly found in Africa. *M. senegalensis* grows normally up to 7–9 m tall. Studies have showed that *M. senegalensis* has several folk medicinal uses including; helminths infection, cough, asthma, diarrhea [193, 194], malaria, inflammatory diseases, healing of chronic wounds, rheumatism, snakebites and dyspepsia [195, 196]. Phytochemical constituents present in *M. senegalensis* includes; alkaloids [197], flavonoids [198], triterpenes, saponins, phenol, tannins and glycosides [199, 200]. Jigam and colleagues [201] investigated leaf extract of *Maytenus senegalensis* and reported bioactive compounds such as 3,5,7-tetraen-carboxylic acid-methylester, 3-hydroxy-20-lupen-28-ol, 20α)-3-hydroxy-2-oxo-24-nor-friedela-1, phytol and 2(4H)-Benzofuranone, 5,6,7,7a-tetrahydro. The isolated compounds from the leaf extract of *Maytenus senegalensis* may exhibit promising antiulcer activity and other pharmacological properties. *Maytenus senegalensis* chloroform root extract has been investigated by Khalid and colleagues [202]. The results from their studies showed the presences of isolated compounds including; (20α)-3-hydroxy-2-oxo-24-nor-friedela-1, 3,5,7-tetraen-carboxylicacid-methylester (pristimerin). Several studies have reported the chemical compounds isolated from the phytochemical constituents (phenolic compounds, triterpenes and alkaloids) includes; *epi*catechin (4*β*→8) *epi*catechin, (−)-*epi*catechin (4*β*→8) (−)-4′-methyl*epi*gallocatechin, (−)-4′-methyl*epi* gallocatechin, 5-*O*-*β*- Glucopyranoside, phloroglucinol 1-*O*-*β*-Dglucopy ranoside [203], 3-*O*-acetyloleanol acids, pristimerin, *β*-sitosterol [204, 205], *β*-sitosterol xyloside [205], triacontano, norephedrine and ephedrine [204]. Some of the bioactive compounds isolated from *M. senegalensis* such as epicatechin and the phytosterols contain many contribute to the beneficial anti-ulcer activity [74, 75, 206]. Pharmacological activities obtained from investigation of the plant include; anti-inflammatory and antioxidant properties [201, 207] antiplasmodial and analgesic activity [207]. The antimicrobial activity has also been evaluated [208, 209].

Evaluation of the peptic ulcer activity using the ethanol induced model was investigated by Haule and colleagues [195] with a polyherbal extract including *M. senegalensis* in animal model. The level of gastric mucosal lesions was decreased comparable to pantoprazole. The mechanism of reducing ulceration could be due to increase in gastric mucus secretion and stabilization of the mucosal lining in addition to reduction of acid distribution, gastric mucosal absorption [195]. However, some species of *Maytenus* such as *Maytenus ilicifolia, Maytenus robusta, Maytenus obtusifolia, Maytenus aquifolium and Maytenus truncate* [210, 211] in literature have anti-ulcer activity. The result of Haule and colleagues [195] is similar to the hydro-alcoholic extract of *Maytenus robusta* reducing ulceration at doses of 500 mg/kg body weight comparable to 30 mg/kg body weight omeprazole at almost same levels of gastro

protection. Toxicity studies in animal model indicated the aqueous oral extract was relatively safe [212]. This review has shown the opportunity for more anti-ulcer activity work to be conducted on *M. senegalensis* to justify its inclusion in the preparation of *Dyspepsia* for treatment of PUD.

3.15. Trichilia monadelpha (Thonn.) JJ De Wilde

Trichilia monadelpha is a deciduous plant from Central Africa and subsequently spreading to other parts of the world. *T. Monadelpha* is from the family, Meliaceae. The local names in Ghana are *Otanduro* in (Twi) and *Tenuba* in (Nzema). It can be found in river banks, deciduous and evergreen semi-deciduous forest and grows up to 12–20m tall. In traditional medicine the plant is used for managing diseases such as epilepsy, inflammation, healing of chronic wounds, diabetics, pains, cough, gonorrhea, syphilis [213, 214]. Phytochemicals present in the stem bark of *T. monadelpha* include; alkaloids [215], flavonoids [216], glycosides, saponins, sterols, tannins, terpenoids [217], anthraquinones and reducing sugars [218]. A study by Nangmoa and colleagues of the root and leaf extracts of *T. monadelpha* revealed the presence of some compounds including; scopoletin, stigmasterol, protocatechuic acid, β-sistoterol coixol and ellagic acid. Sisquiterpenes; trichins A and B and limonoid derivatives; monadelphins A and B were newly discovered [110]. β-Caryophyllene was isolated as a major component of the essential oil obtained from the leaves which subsequently investigated for antimicrobial properties and showed moderate inhibition against the tested microorganisms. No activity against *H. pylori* has been reported. A lower antioxidant activity of the essential oil was recorded relative to that of ascorbic acid and BHA. However, a relatively higher antioxidant activity was reported compared with tocopherol [219]. Isolated compounds such as stigmasterol and ellagic have been studied to possess anti-peptic ulcer activity [74, 75]. Pharmacological activities observed from investigation of the plant include; antioxidant activity [218], antiplas-modial activities [220] anti-inflammatory [219], antimicrobial and anti-cancer activities [221, 222]. A study by Avande [223] aimed at investigating the effectiveness of *T. monadelpha* stem bark extracts on surface ulcers, ulcerative colitis and the degree to which it could remove colonic microflora in animal model has been conducted. In the indomethacin-induced ulcerative colitis, colons of animals treated with the ethanolic extract of the stem bark at doses of 100 mg/kg and 300 mg/kg showed a decrease in ulceration of the colon whilst there was persistent mucosal ulceration in the disease control group. A significant restoration of the mucosal strength was observed when aqueous stem bark extract of 100 mg/kg and 300 mg/kg dose treated groups was used and compared to the ulcerated and edematous mucosae of 30 mg/kg treated group. This shows an increasing response to treatment in a dose dependent manner. Similar dose dependent activity was also seen on colonic microflora in colitis rats. *T. monadelpha* was found to be detrimental to colonic microflora [223]. This review has been undertaken to ascertain the anti-ulcer activities and various anti-peptic ulcer models works done on the plant. The need for more research into anti-peptic ulcer activity using the different anti-ulcer models still exists.

3.16. Cassia siebieriana D. C.

Cassia sieberiana is an erected shrub from the Fabaceae family and generally distributed in the savanna zones of South and West Africa. It arrays from 10-20 m in height [224, 225]. *C. sieberiana is* extensively used in traditional medicine for the remedy of dysmenorrhea, gastric ulcer, pains, fever [226], diabetes mellitus, gonorrhea, malaria, leprosy, dropsy and dysentery [227, 228]. *C. siebieriana* has a high content of calcium oxalate crystals in addition to other phytochemicals like quercitrin, isoquercitrin and rhein [229, 230], anthraquinones, flavonoid, saponins, steroid, terpenoids [231, 232], tannins and cardiac glycoside [233], reducing sugars [225]. Studies by Jibril and colleagues showed that ethyl acetate extract of *C. sieberiana* contained isolated compounds such as quercetin, piceatannol, dihydrokaempferol, kaempferol, emodin, islandicin, physcion and chrysophanol [234], epiafzelechin [235] stigmasterol and β-sitosterol [236]. The anti-peptic ulcer activity of some of these compounds have been studied and shown to have positive effects [74,75]. Pharmacological activity reported on the plant include; anti-parasitic [237], anti-microbial [238], anti-oxidants, anti-inflammatory and anti-nociceptive activity [239]. The pharmacological activity (analgesic and anti-inflammatory) of the *C. siebieriana* used in the preparation of *NPK 500* were evaluated in animal model using the acetic acid induced and carrageenan-induced oedema models. Aqueous extract from the root of *C. siebieriana* showed comparable analgesic and anti-inflammatory activity relative to the acetylsalicylic acid standard [240]. A study conducted on the anti-ulcer potential of the *C. siebieriana* produced significant and dose dependent anti-ulcer activity [240]. In another anti-ulcer study in rat model, the extract remarkably prevented the ethanol induced reduction in function levels of some enzymes like superoxide dismutase, catalase and glutathione peroxidase. Inhibition of ethanol-induced reduction in serum total anti-oxidant capacity was also observed. Build-up in ethanol-induced lipid hydroperoxides quantity and myeloperoxidase function was also prevented [232]. Though it can be inferred that the plant may act mainly by the pain-relieving mechanism in PUD, further studies including *in-vivo* and clinical, should be conducted on the plant using different anti-ulcer models to confirm the efficacy and usefulness of the plant in the treatment of PUD.

4. Discussion

In this review, fifteen ethno-medicinal plants belonging to thirteen different families including Asteraceae and Meliaceae used for the formulation of *Enterica, Dyspepsia* and *NPK capsules* have been discussed. The parts of the plant most often used for the preparations were the leaves (44 %), followed by stem bark (22 %) and roots (19 %), the fruit (11 %), and the whole plant (4 %). Several compounds were isolated from the various plants. *Oleane*-12-en-3β-ol-28-oic acid 3β-D-glucopyranoside (OAG), a compound isolated from *L. camara* had been investigated specifically for anti-peptic ulcer activity showing significant gastroprotective activity. Gallic acid and ellagic acid from *S. mombin* had also been investigated for gastroprotective effects with positive results. Isolated compounds such as quercetin and sitosterol obtained from more than one plant had also been investigated for anti-peptic ulcer activity. Literature search on *in-vivo* and *in-vitro* works done on the medicinal plants revealed seven (7) different anti-ulcer models, with respect to their possible mechanisms of actions. The most obtained *in-vivo* and *in-vitro* anti-ulcer model was ethanol induced (28.57 %), followed by aspirin induced and pylorus ligation anti-ulcer models (both having same percentages of 14.28 %), the indomethacin induced and acetic acid induced anti-ulcer models (both having same percentages of 17.14 %), the stress induced anti-ulcer model (5.71 %), and the NSAID (ibuprofen) induced anti-ulcer model (2.85 %).Screening of potential antiulcer activities on plants used for management of peptic ulcer is very important in confirming the therapeutic effects of the plants. A summary of the plants and tested anti-peptic ulcer activities with reference to models used and some isolated compounds that may contribute to the anti-peptic ulcer activity has been presented in Table 1: Medicinal plants, parts used, anti-peptic ulcer models tested, inference on possible mechanism (s) of action and some active compounds contributing to activity. Positive effects were observed in all tests.

From the Table 1, it can be seen that each plant material may possess more than one category of anti-ulcer effect with the exception of *Cnestis ferruginea, Trema orientalis* and *Maytenus senegalensis*. This may be similar or otherwise when the products are tested using the various *in-vivo* anti-ulcer test models available. The composition of each plant material per product may determine the eventual outcome of its pharmacological or

Table 1. Medicinal plants, parts used, anti-peptic ulcer models tested, inference on possible mechanism (s) of action and some active compounds contributing to activity.

Product	Medicinal plants/Family	Plant part in usage	Tested anti- peptic ulcer models.	Inference on possible mechanisms of action deduced from anti-peptic ulcer models	Some Compounds tested for anti-peptic ulcer activity
Enterica FDA Reg. No:FDA/ HD.07-7097	*Morinda lucida (L.)Benth* ***Rubiaceae***	Leaves. Roots and stem bark	1A [15] and 2A [21]	1D and 2B	NC
	Cnestis ferruginea Vahl ex D.C. ***Cannaraceae***	Leaves, roots and stem bark	3A [29]	3B	Oleanolic acid, betulinic and ursolic acids [24, 25, 26]
	Momordica charantia Linn. *Cucurbitaceae*	Leaves and fruit	1C, 3A and 5A, [33]	1D, 3B and 5B	NC
	Vernonia amygdalina Del. ***Asteraceae***	Leaves	1C [49] and 4A [39]	1D and 4B	NC
	Lantana camara Linn. ***Verbanaceae***	Leaves	1C, 4A and 5A [63]	1D, 4B and 5B	*Oleane*-12-en-3β-ol-28-oic acid 3β-D-glucopyranoside (OAG) [63]
	Psidium guajava Linn. ***Myrtaceae***	Leaves	1C [65, 88] 4A [65, 87, 89] and 5A [65]	1 D, 4B and 5B	Quercetin stigmasterol and ursolic acid [26, 74, 76]
	Trema orientalis Linn. ***Ulmaceae***	Stem bark, Leaves and roots	4A [108, 109]	4B	β sitosterol [75]
	Persea americana Mill. ***Lauraceae***	Leaves and fruits	1A and 4A [126]	1D and 4B	Quercetin and quercetin-3-o-rhamnoside [74, 75]
	Citrus aurantifolia Linn. ***Rutaceae***	Leaves	1C [146], 2A [158] and 4A [147]	1D, 2B and 4B	Rutin, quercetin, kaempferol, stigmasterol and β sitosterol [74, 75]
	Spondias mombin Linn. ***Anacardiaceae***	Leaves and fruits	1A, 2A [134, 135] 1B, 4A and 5A [143]	1D, 2B, 4B and 5B	Gallic and ellagic acid [134, 135]
	Bidens pilosa L. ***Asteraceae***	Whole plants	1A, 4A [179, 180] and 5A [179]	1D, 4B and 5B	2,4-dihydroychalcone [171]
Dyspepsia FDA Reg. No:/ HD1. 20-2085	*Carapa procera* ***Meliaceae***	Leaves and stem bark	NR	NR	Quercetin and derivatives, kaempferol and derivatives [74,75]
	Maytenus senegalensis (Lam.) ***Celastraceae***	Leaves and roots	4A [195]	4B	Epicatechin and β sitosterol [74, 75]
	Trichilia monadelpha (Thonn.) JJ De Wilde ***Meliaceae***	Stem bark	1A and 2A [223]	1D and 2B	Stigmasterol, β sitosterol [74, 75] and ellagic acid [134, 135]
NPK 500 Capsules FDA Reg. No:FDA/ HD1.16-1011	*Cassia siebieriana* D.C ***Fabaceae***	Roots, stem bark	2A [231] and 4A [232]	2B and 4B	Quercitrin, quercetin, kaempferol, stigmasterol and β sitosterol [74, 75]

1.Indomethacin-induced **(1A)**, NSAID (Ibuprofen) induced **(1B)** and Aspirin-induced **(1C)** Models: Enhancement of prostaglandins cyclooxygenase pathway, ensuring the secretion of bicarbonate and mucus and decreased production of reactive oxygen species **(1D).**
2.Acetic acid induced **(2A)**: Ensuring anti-secretive and cyto-protective effects **(2B)**.
3.Stress-induced **(3A)**: Reduced release of histamine and production of acid in the stomach **(3B)**.
4.Ethanol-induced **(4A)**: Inhibition of alcohol penetration (diffusion) through gastric mucosa and prevention of destructive wounds in the gastric mucosa **(4B)**.
5.Pylorus ligation **(5A)**: Reduced ligation of the gastric acid accumulation **(5B).**
NR: Not recorded; NC: Not confirmed.

clinical effect. This cannot be assumed or predicted unless these tests are conducted.

5. Conclusion

The medicinal plants used in the formulation of the three herbal products (*Enterica, Dyspepsia* and *NPK 500* capsules) at CPMR has been discussed. The review showed that *in-vivo* and *in-vitro* works on the medicinal plants with respect to their anti-peptic ulcer and antiulcer models have been presented. Folkloric uses, phytochemical constituents, pharmacological properties have also been set forth. However, it can be seen that anti-*H. pylori* activity/*H. pylori* eradication activity studies are lacking on most of the plants reviewed. The opportunity to conduct such studies is available to help ascertain if these plants have any anti-*H. pylori* activity or otherwise. The mechanism(s) of action of individual products must be further investigated and established experimentally *in-vitro* in addition to *in-vivo* pharmacological and clinical activity studies to confirm their use in the remedy of PUD. This review may, provide some scientific bases for the use of *Enterica, Dyspepsia* and *NPK 500* capsules in the management of gastro-oesophageal disease including peptic –ulcer at the CPMR out-patient clinic.

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