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Medicinal Plants as Anti-Ulcer Agents

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ABSTRACT

Peptic ulcer disease (PUD) is considered as one of the common diseases in the world. Treatment of peptic ulcer with synthetic drugs such as proton pump inhibitors, H2 receptor antagonists and other non-steroidal anti-inflammatory drugs has shown adverse effects, relapses, drug interactions. Medicinal plants containing active chemical constituents are useful in prevention and treatment of various diseases. Literatures suggest that polyherbal formulations of medicinal plants are considered to be potential source for the treatment of ulcers. Combination of ayurvedic knowledge with modern medicine can produce better antiulcer drugs of natural origin from medicinal plants with fewer side effects. This study has presented the review of commonly used anti-ulcer plants which are used for the treatment or prevention of peptic ulcers and the other reported activities of these plants.

Keywords: Peptic ulcer, Proton pump inhibitors, Medicinal plants, Poly herbal formulations.

1. Introduction

Peptic ulcer is a gastro intestinal disorder due to an imbalance between the aggressive factors like acid, pepsin, *Helicobacter pylori* and defensive factors like bicarbonate secretion, prostaglandins, gastric mucus, innate resistance of the mucosal cell factors [1]. Normally peptic ulcer develops when aggressive factors overcome the defensive factors [2]. The major factors that disrupt the equilibrium between aggressive factors and defensive factors are *Helicobacter pylori*, acid–pepsin hyper secretion, non-steroidal anti-inflammatory drugs, sometimes idiopathic due to usuage of tobacco, psychological stress, rapid gastric emptying and Zollinger-Ellisson syndrome where there is a high and uncontrollable production of acid also leads to ulcer formation [3-5]. Synthetic drugs such as proton pump inhibitors, H_2 receptors, cytoprotectants, demulcents, anti cholinergics, antacids and prostaglandin analogues are used for the treatment of ulceration but these drugs produce several side effects.

So herbal medicines are considered as better alternatives for the treatment of peptic ulcer [6]. For example, proton pump inhibitors (omeprazole, lansoprazole) may cause nausea, abdominal pain, constipation, diarrhoea and H_2 receptor antagonists (cimetidine) may cause gynaecomastia, loss of libido. Due to the occurrence of many side effects by use of synthetic drugs for many diseases, medicinal plants are considered as the main source of new drugs as they have less or no side effects. As herbal medicines are considered as safe for the treatment of ulcers with lesser adverse effects, economical, effective, relatively less toxic, extensive research is carried out in search for potent antiulcer agents of plant origin [7-8]. This article reviews the features of some of the plants reported to possess antiulcer and ulcer healing properties.

1.1 *Allophylus serratus* Kurz

Allophylus serratus Kurz is commonly known as Tippani. It belongs to the family Sapindaceae and used to treat elephantiasis, oedema, and inflammation, fracture of bones, dyspepsia, anorexia and diarrhoea. Phytochemical studies proved the presence of phenacetamide, betasitosterol, quercetin [8]. The mechanism involved in production of antiulcer activity by plant leaf extract is cytoprotective mechanism as well as anti-secretory [8]. The ethanolic leaf extract of the plant proved to possess antibacterial activity [9]. The plant is reported to possess anti osteoporotic activity [10].

1.2 *Aloe vera* (L.) Burm.f.

Aloe vera (L.) Burm.f. is commonly known as Aloe. It belongs to the family Xanthorrhoeaceae. Reported constituents in plant are aminoacids, anthraquinones, enzymes, hormones, lignin, minerals, salicylic acid, saponins, sterols, sugars, vitamins [11]. The anti-ulcer activity of the plant is reported in Indomethacin induced ulcer model. The mechanism involved in production of antiulcer activity of the plant is due to its antioxidant, anti-inflammatory, mucus secreting, cytoprotective or healing activities [12]. Reported pharmacological activities of the plant are hypoglycemic, hypolipidemic, woundhealing, imunomodulatory, antifungal, hepatoprotective [13].

1.3 *Butea frondosa* Roxb.

Butea frondosa Roxb. is commonly known as Flame of the forest .The plant is distributed throughout India and belongs to the family Fabaceae. The leaves of the plant are reported to produce antiulcer activity [14].The seeds and fruits are proved to possess anthelmintic property.

The seed extracts exhibited embryonicidal, ovicidal, larvicidal activity against exogenous stages of *H. contortus* [15]. The plant is also proved to possess aphrodisiac activity [16].

1.4 *Capsicum annuum* L.

Capsicum annuum L. is commonly known as Chilli pepper and it is most widely cultivated throughout the world. It belongs to the family Solanaceae. The fruit is proved to possess antiulcer activity [17], antioxidant activity [18]. The methanolic seed extract of the plant reported antiobesity activity in 3T3-L1 adipocyte [19]. The fruit and vegetable peel extracts of the plant exerted radical-scavenging properties [20]. Solasonine present in the plant reported platelet aggregation inhibitory activity [21].

1.5 *Carica papaya* Linn.

Carica papaya Linn. is commonly known as Papaya. It belongs to the family Caricaceae and well known for various medicinal properties. The fruits are reported to possess antiulcer activity [22]. The seeds are reported to exert antimicrobial, anthelmintic, antiamoebic properties. The fruit had shown hepatoprotective activity and also used for pediatrics burns .The seed extracts are proved to exhibit pronounced hyper trophy and hyper plasia of pituitary gonadotrophs. The pollen from flowers of the plant possess histaminergic properties [23].

1.6 *Cissus quadrangularis* L.

Cissus quadrangularis L. is a succulent plant of family Vitaceae. It is commonly known as Asthisamhari and used as a general tonic and analgesic, with specific bone fracture healing properties described in the ancient ayurveda. The dichloromethane and methanolic stem extract of the plant exerted antibacterial activity against *S. aureus, E. coli, and P. aeruginosa* . Ethanol extract of the plant revealed antiosteoporotic activity in ovariectomized rat model of osteoporosis. The ethanolic extract (50%) of aerial parts of the plant proved to possess hypotensive activity and stem extract reported diuretic activity. The methanolic extracts of the plant are proved to possess pharmacological activities such as antioxidant, antiulcer, analgesic, anti-inflammatory [24].

1.7 *Curcuma longa* L.

Curcuma longa L. is commonly known as Turmeric and also a household remedy for biliary disorders, anorexia, cough, diabetic wounds, hepatic disorders, rheumatism and sinusitis which belongs to the family Zingiberaceae. Evaluation of turmeric has been done for gastric and duodenal antiulcer activity in rats [25].Volatile oil of *Curcuma longa* possess anti-inflammatory and anti-arthritic activities [26].

Water and fat soluble extracts of curcumin exhibited strong antioxidant activity comparable to vitamins C and E. Protective effect of curcumin in rat liver injury induced by carbon tetrachloride was reported [27]. Curcumin inhibited cell proliferation and tumor growth in case of prostate cancer. The plant is reported to possess pharmacological activities such as anti-fertility, antibacterial, antifungal [28].

1.8 *Desmostachya bipinnata* (L.) Stapf

Desmostachya bipinnata (L.) Stapf is commonly known as Saved gram belongs to the family Gramineae. Kaempferol, quercetin, quercetin-3-glucoside, trycin and trycin-7-glucoside were isolated from the ethanolic extract of plant. The ethanolic extract of aerial parts of the plant reported anti-ulcer activity [29]. The methanolic extract revealed anti helicobacter activity at MIC value of 40 µg/ml [30]. The alcoholic and aqueous root extracts reported anti-diarrhoeal activity in rats against castor oil induced diarrhoea and charcoal meal test [31]. The methanolic root extract of the plant exerted in *vitro* anticancer activity [32].

1.9 *Excoecaria agallocha* L.

Excoecaria agallocha L. is commonly known as Milky mangrove belonging to the family Euphorbiaceae and useful as anti-microbial, anti tumor, wound healing, anti-oxidant, traditionally used in epilepsy, tooth ache and ulcer treatment .The oil obtained from the plant bark is efficient in treating rheumatism, leprosy and paralysis. The aqueous bark extract of the plant reported anti-ulcer activity on NSAID-induced gastric ulcers in albino rats [33]. The ethanolic stem bark extract of the plant reported anti nociceptive activity [34]. The organic solvent extracts of leaves of the plant proved as potent anti-oxidant and anti-filarial [35].

1.10 *Glycyrrhiza glabra* L.,

Glycyrrhiza glabra L., is a sweet, moist, soothing, flavoring herb commonly known as Liquorice belonging to the family Fabaceae.The plant is widely used as a medicine from the ancient medical history of ayurveda. The glycyrrhetinic acid of Liquorice showed potent *in vitro* activity against *H. pylori* indicating its antiulcer effect on peptic ulcers. The ether, chloroform, acetone root extracts of the plant exerted significant antibacterial activity against *Bacillus subtili, Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa*. The active compound glabridin present in liquorice reported anti-fungal activity against *Arthrinium sacchari M001, Chaetomium funicola M002* and potent antioxidant activity towards LDL oxidation. Reported pharmacological activities of the plant are anti-inflammatory, anti tussive, hepatoprotective, Estrogenic [36].

1.11 *Leucas lavandulifolia* Sm.

Leucas lavandulifolia Sm. is commonly known as Gumma belonging to the family Labiatae .The plant is used to alleviate the abdominal discomforts such as stomach ulceration and also to counteract abdominal and liver diseases. The methanolic extract of the plant reported anti-ulcer activity by the significant reduction in

ulcer index as well as gastric acid output in Indomethacin and pylorus ligation induced ulcer models. The plant exhibited ulcer protection in a dose dependent manner [37].

1.12 *Mangifera indica* L.

Mangifera indica L. is commonly known as Mango. It belongs to the family Anacardiaceae. The petroleum ether and ethanol plant leaf extracts reported antiulcer activity [38]. The mangiferin, polyphenolic constituent of the plant reported *in vivo* antioxidant activity in OF1 mice, exerted radioprotective effect against radiation-induced micronuclei formation in cultured human peripheral blood lymphocytes and in DBAxC57BL mice, reported *in vivo* immuno modulatory activity on thioglycollate-elicited mouse macrophages which were stimulated with lipo polysaccharide (LPS) and gamma interferon (IFN-γ) [39]. The ethyl acetate and ethanol root extracts proved to exhibit anti-inflammatory activity [40]. Miscellaneous pharmacological activities reported by the plant are anti-diabetic, anti-viral, ant-helmintic, anti-allergenic, anti-parasitic, anti-bacterial, anti-tumor, anti-spasmodic, anti-pyretic, anti-diarrhoeal, anti-fungal, hepatoprotective, gastroprotective [41].

1.13 *Morus alba* Linn.

Morus alba Linn. is commonly known as White mulberry and belongs to the family Moraceae. The plant leaf extracts reported antiulcer activity in experimentally-induced gastric ulcers in rats [42] and also reported reduction of blood glucose levels by regeneration of β cells [43]. The ethyl acetate soluble fraction of methanol root extracts significantly attenuated the CS-induced perturbations indicating adaptogenic activity [44]. Petroleum ether, chloroform and methanol sequential plant leaf extracts reported anthelmintic activity and also exhibited anti-microbial activity. The methanolic extract of plant leaves proved to possess anti dopaminergic effect and also reported dose dependently increased radical scavenging activity. The mixture of plant leaf extracts along with *Morus nigra* reported anti mutagenic activity. The plant is reported to possess pharmacological activities such as anticancer, immunomodulatory, nephroprotective, hepatoprotective [45].

1.14 *Ocimum sanctum* Linn.

Ocimum sanctum Linn. is commonly known as Holy basil belonging to the family Labiatae and widely used for prevention and cure of many illnesses and everyday ailments. The plant fixed oil reported antiulcer activity due to its lipoxygenase inhibitory, histamine antagonistic and antisecretory effects .The plant is reported for anticancer activity against human fibro sarcoma cells culture. Oral administration of plant leaf extract reported for hypoglycemic effect in normal, glucose fed hyperglycemic and streptozotocin-induced diabetic rats. Reported pharmacological activities of the plant are anti-bacterial, anti-inflammatory,anti hypertensive,cardioprotective,centralnervoussystemdepressant,anti oxidant, chemopreventive, immunomodulatory, analgesic, anti-pyretic, anti-fertility, anti-arthritic, anti-stress, anti-cataract, anticoagulant, hepatoprotective, radioprotective [46].

1.15 *Panax ginseng*

Panax ginseng is commonly known as Ginseng belonging to the family Araliaceae and medicinally used as an adaptogen, restorative tonic. Phyto chemical studies proved the presence of ginsenosides, amino acids, alkaloids, phenols, proteins, polypeptides, vitamins B_1 and B_2. Ginsenosides are reported for antiulcer activity [47]. The plant is reported for anti-sterility activity in an untreated control group by improving sperm count and motility which causes male fertility .Numerous studies reported that ginseng increases physical endurance and causes physiological changes that helps the body in adapting to adverse conditions. The plant is reported to possess pharmacological activities such as anti-inflammatory, anti-diabetic, anti-proliferative [48].

1.16 *Piper betel* Linn.,

Piper betel Linn., is commonly known as Betel vine belongs to the family Piperaceae and cultivated in Srilanka, India, Malaysia, Indonesia, Philippine Islands and east Africa. *In vitro* studies reported that the aqueous extract of the plant inflorescence was effective in scavenging H_2O_2, superoxide radical and hydroxyl radical and prevented the hydroxyl radical-induced DNA strand breaks in the PUC18 plasmid [49]. The methanolic leaf extract of plant reported antioxidant activity, analgesic activity, and anti-inflammatory activity [50]. The plant is reported to possess anti-mutagenic effects [51], anti tumor promoting activity [52].

1.17 *Polyalthia longifolia* (Sonn.) Thwaites (PL)

Polyalthia longifolia (Sonn.) Thwaites (PL) is commonly known as *False* Ashoka. It belongs to the family Annonaceae. The plant is widely used in traditional medicine as febrifuge, tonic and useful in fever, skin diseases, diabetes, hypertension, helminthiasis [53]. Phytochemical studies revealed the presence of steroids, alkaloids, terpenoids, phenolics and flavonoids [54]. The ethanolic leaf extracts of the plant reported for antiulcer activity in aspirin, pylorous ligation-induced gastric ulcer in rats, HCl-ethanol-induced ulcer in mice and water immersion stress-induced ulcer in rats at 300 mg/kg body weight p.o. [55]. The ethanolic stem bark extract of the plant was evaluated for its role on reactive oxygen species in tumor initiation and progression [56]. The plant is reported to possess pharmacological activities such as antibacterial, anti-inflammatory, hepatoprotective [57].

1.18 *Rhizophora mangle* L.

Rhizophora mangle L. is a vegetal species belonging to the family Rhizophoraceae. It is commonly known as Red mangrove and distributed in Cuba and other Caribbean countries. The plant is reported for ethno botanical uses such as antiseptic, astringent and haemostatic [58]. Reported phyto constituents of the plant are Epicatechin, catechin, chlorogenic acid, gallic acid, ellagic acid, stigmasterol, betasitosterol, campesterol [59]. The aqueous extract of plant bark is reported for gastroprotective, anti-secretory effects [60]. The plant is reported to possess antioxidant action of polyphenols against gastric damage induced by absolute ethanol and ischemia reperfusion in the rats [61]. The plant is reported to possess anti-inflammatory activity [62], wound healing activity [63] and also in the treatment of experimental TNBS- induced colitis in rats [64].

1.19 *Sapindus trifoliatus* L.

Sapindus trifoliatus L. is commonly known as Soap nut tree belongs to the family sapindaceae. The plant is distributed in south-India and plant seed oil is used in the manufacturing of soaps due to presence of beta sitosterol in seeds. The aqueous extracts of leaves reported potent anti-ulcer activity due to flavonoids, triterpenoids, carbohydrates and sterols present in the extract. The plant reported antagonism on histaminergic activity produced by H_2 receptor blockade. Some other pharmacological activities

reported from the plant are astringent, anti-helmintic, expectorant, in treatment of asthma, cholera, epilepsy, gout, rheumatism and paralysis [65]. The methanolic seed extract of the plant is reported to exhibit anti helmintic activity in earthworms [66].

1.20 *Solanum nigrum* L.

Solanum nigrum L. is a medicinal plant which belongs to the family Solanaceae commonly known as Blacknightshade .Chemical constituents reported are glycoalkaloids, glycoproteins, polysaccharides, gallic acid, catechin, protocatechuic acid, caffeic acid, epicatechin, rutin and naringenin.

The methanolic extract of plant berries are reported to possess antiulcer activity on aspirin induced ulceration in rats with respect to antioxidant status in the gastric mucosa by exerting gastro protective effect by free radical scavenging action. Ethanol, methanol and ethyl acetate extracts of plant leaf, seed and root are reported to possess antifungal activity against various fungal strains. The plant is also reported to possess pharmacological activities such as antiviral, antipyretic, antidiabetic, immunestimulant, cytotoxic, hepatoprotective, cardio protective, analgesic, larvicidal, anti-seizure, anti-inflammatory, anti-cancer [67].

1.21 *Syzygium aromaticum* L.

Syzygium aromaticum L. is commonly known as Clove which belongs to the family Myrtaceae and esteemed as a flavouring agent ,used as a spice for scenting, chewing tobacco, an ingredient of betel chew and to control nausea, vomiting, cough, diarrhoea, dyspepsia, flatulence, stomach distension and gastro intestinal spasm, relieve pain, cause uterine contractions and stimulate the nerves . Dried flower buds of the n-butanol portion of the plant are reported for anti-ulcerogenic and anti-secretory activity in rats [68]. Reported chemical constituents are volatile constituents such as bud oil, leaf oil, stem oil, fruit oil and non-volatile constituents such as tannins, sterols, triterpenes, flavanoids. Reported pharmacological activities of the plant are anti-microbial, anti-viral, anti-oxidant, anti-diabetic, anti-inflammatory, anti-platelet, anti-stress, anti-pyretic, chemo preventive, hepato protective ,anaesthetic, aphrodisiac, insecticidal [69].

1.22 *Terminalia chebula* Retz.

Terminalia chebula Retz. belongs to the family Combretaceae and commonly called as King of medicine and active ingredient of the well-known herbal preparation Triphala. The main phyto constituents reported are tannins such as chebulic acid, chebulinic acid, chebulagic acid, gallic acid, corilagin, ellagic acid and flavonoids, sterols, amino acids, fructose, resin, fixed oils etc., [70]. The methanolic extract of the fruits of the plant are reported for anti-ulcer activity [71].

Reported pharmacological activities of the plant are antibacterial, antifungal, antiviral, antiamoebic, immunomodulatory, antiplasmodial, antidiabetic, retinoprotective, antianaphylactic, adaptogenic, antinociceptive, cardioprotective, hepatoprotective, chemopreventive, hypolipidemic, hypocholesterolemic, antispermatogenic, mollusicidal, anthelmintic, anti-mutagenic, anti-carcinogenic, antioxidant, anti-arthritic, wound healing, cyto protective, anti-aging, radioprotective [72].

1.23 *Triticum aestivum* L.,

Triticum aestivum L., is commonly known as Wheat grass belonging to the family poaceae. Phyto constituents reported are vitamins A, B_1, 2, 3, 5, 6, 8, 12 and C, E, K, enzymes such as protease, amylase, cytochrome oxidase, transhydrogenase, superoxide dismutase, and amino acids. The plant leaf juice is reported for the treatment of active distal ulcerative colitis .The wheat grass juice taken during FAC (5–fluorouracil, doxorubicin, cyclo phospamide) chemotherapy reduced myelotoxicity, dose reduction and need for granulocyte colony stimulating factors support, without diminishing efficacy of chemotherapy reporting anti-cancer activity. The plant is also reported to possess anti arthritic activity, anti-oxidant activity [73].

1.24 *Vinca minor* L.

Vinca minor L. is an ornamental plant which is commonly known as Common periwinkle with lilac-blue flowers and belongs to the family Apocynaceae. The plant is used internally for circulatory disorders, cerebral circulatory impairment and brain's metabolism support [74]. Indole alkaloids such as vincaminorine, vincaminoreine, minovine, minovincine, and vincamine were isolated from the aerial parts of the plant. The alkaloid vincamine, present in the plant leaves shows cerebrovasodilatory and neuroprotective activity. The plant leaves proved for anti-ulcer activity against experimentally induced gastric damage in rats [75].

1.25 *Zingiber officinalis* Roscoe

Zingiber officinalis Roscoe is commonly known as Ginger which is consumed as a flavoring agent, spice belongs to the family Zingiberaceae. The plant extract reported antitumor effects on colon cancer cells by suppressing its growth, striking the G0/G1-phase, reducing DNA synthesis and inducing apoptosis. The aqueous ethanol extract of the plant (200 and 400 mg/kg) reported nephroprotective effect against doxorubicin-induced (15 mg/kg) acute renal damage in rats. The plant root extract reported neuroprotective effect against monosodium glutamate toxicity by the antagonistic action of root extracts on monosodium glutamate. Reported pharmacological activities of the plant are antioxidant, anti migraine, antiemetic, anti inflammatory, anti-microbial, anti thrombotic, anti analgesic, anti proliferative, anti osteoarthritic, hepato protective [76].

2. Conclusion

Peptic ulcer is a gastro intestinal disorder due to an imbalance between the aggressive factors like acid, pepsin, *Helicobacter pylori* and defensive factors like bicarbonate secretion, prostaglandins, gastric mucus, innate resistance of the mucosal cell factors. This article reviews drugs derived from plants such as flavonoids and tannins for the treatment of peptic ulcer and it is evident that plant extracts have significant antiulcer activity in animal models. This article presents a review on medicinal plants with potential anti-ulcer activity. *Allophylus serratus* Kurz, *Butea frondosa* Roxb., *Cissus quadrangularis* L., *Glycyrrhiza glabra* L., *Mangifera indica* L., *Ocimum sanctum* Linn., *Solanum nigrum* L., *Terminalia chebula* Retz., *Zingiber officinalis* Roscoe etc., are popular all over the world as medicinal plants for the treatment of ulcer.

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