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MEDICINAL PLANTS WITH GASTROPROTECTIVE ACTIVITY FOR TREATMENT OF PEPTIC ULCER DISEASE

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ABSTRACT

Gastric ulcer is the set of symptoms by an imbalance between the acid secreting mechanism of stomach and proximal intestine and the protective mechanism that ensure their safety. Gastric ulcer is the damage in the lining of the stomach corroded by the acid digestive juices which are secreted by the stomach cell. Gastric ulcer is mainly caused by infection with H. pylori and long term use of NSAIDs and is associated with various symptoms. As incidence of the disease is increasing day by day need to find out most effective gastro protective drug which may include the natural plant oriented medicines. In present study we elaborated about the different medicinal plants proved to have gastro protective activity. As present allopathic drugs are having many associated side effects needs to search for the natural drugs which are considered to have less side effects. In India traditionally many natural plants were used for peptic ulcer. Recently many plants were studied for its gastro protective action. Many of these plants used in peptic ulcer were evaluated by different methods like aspirin induced, endomethasone induced etc. The present study elaborates on plants used for peptic ulcer, its extraction, model used etc.

Keywords: Gastroprotecive, Peptic Ulcer, Gastric ulcer, Medicinal Plants.

INTRODUCTION

Gastric ulcer or stomach ulcer is the damage to internal lining of the gastric tract. It is the one of the type of the peptic ulcer disease (PUD). In the gastric ulcer the lining made up of mucus membrane is damaged by excess acid secretion. Gastric ulcer is caused by the imbalance between defensive & aggressive factor. Most of the gastric ulcers are caused due to infection of the bacterium Helicobacter pylori (H. pylori). It is also associated with the long term use of the drugs like Aspirin, Ibuprofen etc. Stomach ulcer is associated with the number of the symptoms it may be dependent on the severity of the peptic ulcer. The commonest symptom of it is burning sensation in the chest region which makes to feel uncomfortable. The annual incidence of the peptic ulcer disease is very less about 0.10 to 0.19% only. The present study revealed decrease in the incidence of peptic ulcer disease. The death rate is approximately one from about one lack of affected cases. [1]

In India traditionally many medical plants were used for the treatment of many diseases as individual plant or may be used in combination as poly-herbal formulations. As these are used since many years these were found to be very effective in many diseases. The natural drugs were preferred because of its less toxicity & are free form many side effects which were commonly observed with many synthetic drugs. As many of the available synthetic drugs are associated with the many side effects there is need to focus on the new plant oriented drugs as alternatives to present drugs. Natural plants are considered to be the basic templates to develop the new molecules. Presently many researchers are focusing on the natural plants for treatment of PUD. [02, 03] The present review highlights some medicinal plants such as *Barleria prionitis L., Prunus persica L, Scrophularia striat, Acanthus ilicifolius* etc. It also highlights the method of extraction, part of plant used & method used to evaluate the activity. Some important medicinal plants for PUD are explained below in table 1.

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Plant Name	Family	Parts used	Extraction	Method	Ref
Acanthus ilicifolius	Acanthaceae	Leaves	Methanol extract	Aspirin, indomethacin, stress, ethanol, and pylorus ligation	4
Adhatoda vasica	Acanthaceae	Leaves	Methanol, chloroform	Aspirin, ethanol, and pylorus ligation	5
Aloe barbadensis Mill.	Liliaceae	Leaves	Juice	Ethanol induced	6
Althaea officinalis L.	Malvaceae	Flower	Aqueous extracts	Pyloric Ligation/Indomethacin-Induced	7
Aralia elata	Araliaceae	Roots	Methanolic extract)	HCl, ethanol-induced gastric lesions, and aspirin-induced	8
Barleria prionitis L	Acanthaceae	Leaves	Methanol extract	Ethanol and Indomethacin Induced	9
Biebersteinia multifida	Biebersteiniaceae	Root	Hydro-methanolic extract	Ethanol-induced	10
Cassia singueana	Fabaceae	Leaves	Methanol extract	Ethanol -induced	11
Cyanodon dactylon	Poaceae	Whole plant	Ethanol extracts	Aspirin, ethanol, and pylorus ligation	12
Eremomastax speciosa	Acanthaceae	Leaves	Methanol extract	Pylorus ligation, indomethacin, Ethanol induced	13
Eremurus spectabilis Bieb.	Liliaceae	Leaves	Methanol extract	Indomethacin induced	14
Eruca sativa	Brassicaceae	Leaves	Ethanol extracts	Ethanol-induced	15
Glycyrrhiza glabra	Leguminosae/Fabaceae	Roots, rhizomes	Hydro-alcoholic extract	*Hypothermic restraint stress, HCl, Ethanol Indomethacin*	16
Kalanchoe pinnata	Crassulaceae	Leaves	Ethanol extract	Ethanol and HCl-induced ulcer	17
Malvastrum tricuspidatum	Malvaceae	Leaves	Ethanol extracts	Ethanol-induced	18
Monolluma quadrangula	Apocynaceae.	Plant material	Hydroalcoholic extract	Ethanol-induced	19
Muntingia calabura L.	Muntingiaceae	Leaves	Chloroform-extract	Pylorus ligation, Ethanol-induced	20
Musa Paradisiaca L	Musaceae	Leaves	Ethanol extracts	Indomethacin, ethanol, aspirin	21
Myrcianthes pungens	Myrtaceae	Fruits, leaves	Methonolic extract	Ethanol-induced	22
Oxalis corniculata	Oxalidaceae	Whole plant	Methanol extract	Pylorus ligation and indomethacin	23
Paederia foetida L.	Rubiaceae	Leaves	Methanol extract	Indomethacin-pylorus ligation ethanolWater immersion stress	24
Phyllantus amarus	Phyllanthaceae	Leaves	Aqueous extracts	Ibuprofen-induced	25
Pilosocereus gounellei	Cactaceae	roots	Ethanol extracts	Ethanol, ischemia-reperfusion-induced and cold restraint stress	26
Polygonum chinese	polygonaceae	Leaves	Aqueous extracts	Ethanol-induced	27
Prunus persica L.	Rosaceae	Bark	Ethanol extracts	Pylorus ligation and indomethacin	28
Scrophularia striata	Scrophulariaceae	aerial parts	Aqueous, hydro	Ethanol-induced	29
Struthanthus marginatus	Loranthaceae	Leaves	Aqueous extracts	Ethanol-induced	30

Vitex pubescens	Verbenaceae	Leaves	Ethanol extracts	Ethanol-induced	31
Ziziphus abyssinica	Rhamnaceae	Root	Methanol and hexane extract	Ethanol-induced	32
Zingiber officinalis	Zingiberaceae	Root	Aqueous extracts	Indomethacin induced	33

DETAIL STUDY OF PLANTS EXTRACTS

Acanthus ilicifolius: *Acanthus ilicifolius* belonging to family Acanthacea. It's a mangrove medicinal plant, is widely used by the local inhabitants of the Sundarbans (India) to treat a variety of diseases like rheumatism, snakebite, paralysis, asthma, ulcers, wound healing and it have anti-inflammatory, analgesic, anti-oxidant, hepatoprotective activity. A detailed evaluation of the gastroprotective activity of the methanolic extract of *Acanthus ilicifolius* using different models of gastric ulceration. Methanolic extract of *Acanthus ilicifolius* leaves (MEAL) significantly decreased gastric volume, acidity, and peptic activity. Ulceration induced with ethanol was significantly inhibited with MEAL. A similar pattern of action was also noticed in cold-restraint stress-induced (CRS) ulceration, where MEAL pre-treatment inhibited CRS-induced ulceration, improved the status of antioxidant enzymes, and also reduced the level of lipid peroxides. These results suggest that extracts of the leaves of *Acanthus ilicifolius* may exhibit anti-ulcer activities additional to the anti-inflammatory properties. [4]

Adhatoda vasica*: Adhatoda vasica* belonging to family Acanthaceae. It is found in India, sub Himalayan track and in Maharashtra, specially in Konkan region .The leaves are used for extraction. The effect of Methanolic, Chloroform and Diethyl ether extracts was used for investigation in rats to evaluate the anti ulcer activity by using three models that is Aspirin, alcohol and Pyloric ligation induced gastric ulcer. The parameter taken to assess anti ulcer activity were volume of gastric secretion, pH, free acidity, total acidity, and ulcer index. The result indicate that the alcoholic extract significantly decrease the volume of acid secretion, pH, free acidity, total acidity, and ulcer index. [5]

Aloe barbadensis Mill.: *Aloe barbadensis Mill* belonging to family Liliaceae. It is indigenous to eastern and southern Africa and grown in Cape colony, Zanziber and islands of Socotra. This plant mainly leaves used for extraction. In the present study the anti ulcer activity of aloe vera juice were investigated in the ethanol induced ulcerated rats. The administration of plant juices decreased the offensive factor like ulcer index and acid secretion and also reduced the amount of protein and carbohydrate in the stomach fluid. Further plant juices increased the defensive factor like activity of oxidative enzyme such as superoxide dismutase and reduced glutathione. [6]

Althaea officinalis L*.: Althaea officinalis L.*, a member of Malvaceae family, is well-known for its medicinal properties. It is a perennial species indigenous to Europe, Western Asia, North Africa. The aqueous extract of *Althaea officinalis* was demonstrated to be potentially helpful in treating lipemia, inflammation, gastric ulcers, and platelet aggregation with no detected adverse or toxic effects. The pharmacological and anti-oxidant activities of *Althaea officinalis* were attributed to various compounds such as polysaccharides and flavonoids present in the plant. Aqueous extracts of *Althaea offcinalis* used for oral administration. Study inspected that gastro-protective as well as in vitro and in vivo anti-oxidant potential of *Althaea offcinalis* and extracts on pyloric-ligation/indomethacin-induced gastric-ulceration in rats.

Aralia elata*: Aralia elata* belong to family Areliaceae. It is a woody shrub or small tree, widely distributed in China, some parts of Japan, Korea, and Russia. Part of plant used in this experiment is root by methanolic extract by method HCl induced gastric lesions and aspirin induced. This plant has been tested to evaluate their efficacy as drugs to prevent and treat various diseases. It is used to treat cough, rheumatism, diabetes, cancer, neurasthenia, hepatitis, gastric ulcer, and stomach spasms. Several biological activities have been reported from the root bark of A. elata, from properties such as cytotoxic, antiinflammatory, liver-protective, antioxidant, antiviral, and hypolipidemic. Based on findings of investigations of antiulcer effects of A. elata root, Araloside A, as a triterpenoid saponin, was determined as the main substance with antiulcer activity. Its action may be due to its inhibitory property on gastric acid secretion. [8]

Barleria prionitis L: *Barleria prionitis L.* belonging to family Acanthaceae is a medicinal plant found road side in India. Whole plant or its various parts like leaves, root, bark, stem and flowers are used traditionally to treat various disorders like toothache, inflammation, boils, glandular swellings and ulcer. Leaf juice is useful in gastric ulcer. Study was conducted to evaluate the antiulcer activity of methanol extract obtained from the leaves of *Barleria prionitis* Linn. Antiulcer activity was performed using the protocols of ulcer induced by ethanol and indomethacin at two different doses (250 and 500mg/kg) The results provide support for the traditional use of this plant in the treatment of gastric ulcer. [9]

Biebersteinia multifida: This drug belonging to family Biebersteiniaceae. Biebersteinia multifida is one of the native of Irelands its root is used in folk medicine. This study aimed to evaluate the gastro protective effect of hydro methanolic extract in rats with ethanol induced

peptic ulcer. B. multifida possesses gastro protective effect against ethanol induced ulcer model. This effect is at last partially related to plants and anti oxidant and no production accelerating properties [10]

Cassia singueana*: Cassia singueana* belong to family Fabaceae. Found in Tropical countries and Northern Nigeria. The antiulcer effects of the methanolic extract of *Cassia singueana* leaves were investigated using ethanol-induced gastric ulcer model in rats. The methanol extract was prepared by cold maceration of leaves. *Cassia singueana* extract (CSE) exhibited a more gastro-protective effect against ethanol-induced stomach ulcers. Histopathological lesions were observed to deviate from massive severe lesions with marked disorientation of the gastric epithelium in the control to fairly protected mucosa with omeprazole and a better protected mucosa with intact epithelium in CSE (750 mg/kg) treated rats. *C. singueana* extract was found to be significantly protective against ethanol-induced gastric ulcers in the experimental rats. [11]

Eremomastax speciosa: Eremomastax speciosa belong to family Acanthacea. It is native to Tropical Africa, Madagascar. This study investigated the gastroprotective effects of methanol extract of *Eremomastax speciosa* leaf in rats. Cold maceration in 80% methanol extract was prepared. The extract of *E. speciosa* was used on ethanol- and indomethacin-induced gastric ulcer models in rats. Both extract and cimetidine significantly reduced the severity of indomethacin- and ethanol-induced gastric injuries and gastric acid contents in Shay rats. The findings showed that ESE protected the rats against chemical-induced gastric ulcer through anti-cholinergic and antihistaminic mechanisms. [13]

Eruca sativa*:* It belongs to family Brassicaceae, native to Britain, Australia, South Africa, Ireland, New Zealand. *Eruca sativa* (Es), known as *jarjeer*, used in traditionally as diuretic, stimulant, and in the treatment of stomach disorders and scurvy. The seeds and the tender leaves possess aphrodisiac activity. They are also used as a carminative and to alleviate abdominal discomfort and to improve digestion. The plant was extracted by 95% of ethanol to evaluate anti-ulcerogenic activity against ethanol induced gastric ulcer. Grossly and histologically, the pre-treated rats with plant extract exhibited a significant protection in dose dependent manner. Further, Es caused elevation of pH of gastric content and mucus production. Therefore, it can be concluded that Es-ethanol leaf extract exhibits an anti-ulcer activity against ethanol-induction model through maintaining the acid base balance of gastric content [15]

Kalanchoe pinnata (Lam.) Pers**:** *Kalanchoe pinnata* (Lam.) Pers. belonging to family Crassulaceae. This species popular in Brazil and other parts of the world. It is widely used to treat diarrhoea, vomiting, earache, gastric ulcers, burns, abscesses and insect bite. Leaves of the plant posses wound healing, anti-inflammatory anti-oxidant, anti-microbial, anti-leishmanial properties. According to study, the hydro-ethanolic extract (HE) and ethyl acetate fraction (EAF) from *Kalanchoe pinnata* leaves against an ethanol/HCl-induced ulcer model in rats shows the gastroprotective effects. This was significantly due to the presence of flavonoids. [17]

Malvastrum tricuspidatum**:** It belongs to family Malvaceae found as a weed distributed worldwide in Argentina, Bolivia, Galapagos Island and also in the Indian subcontinent. *Malvastrum tricuspidatum* is recommended in Ayurveda and Folklore Medicine for the management of gastric ulcers, cough, chest, lung disease. Leaves used for inflamed sores, wounds and flowers given as pectoral and diaphoretic. Traditionally used as antipyretic, smooth muscle relaxant and ulceroprotective. Investigation was done to demonstrate the antiulcer effect of whole plant extract of *Malvastrum tricuspidatum* (MTE) on ethanol (EtOH)-induced, aspirin (ASP)-induced, cold restraint-stress (CRU) and pylorus-ligation (PL)-induced gastric ulcer models in rats. The ethanolic extract showed better ulcer protection than aqueous extract in ethanol induced ulcer model. The ethanolic extract significantly inhibited the gastric lesions induced by EtOH, ASP, CRU and PL. Phytochemical tests revealed presence of antiulcer phytochemical constituents like flavonoids, tannins, terpenes and glycinebetaine in ethanolic extract. It suggests that ethanolic extract (MTEE) of whole plant of *Malvastrum tricuspidatum* is effective against all the four experimentally induced acute gastric ulcers. [18]

Muntingia calabura *L.*: *Muntingia calabura L.* from the family Muntingiaceae, traditionally used to treat gastric ulcer. Gastroprotective activity was determined using ethanol induced the leaves of *M. calabura*, in particular, have been used in Peruvian traditional medicine and Malay folklore medicine. *Muntingia calabura* possesses several medicinal values such as reducing gastric ulcer and swelling of prostate gland, and relieving headache and cold gastric ulcer assay while the mechanisms of gastro protection were determined using the pyloric ligation assay and ethanol induced gastric ulcers. The chloroform-extracted *M. calabura* (CEMC) contains tannins, polyphenolics, triterpenes, and steroids while the chloroform-extracted M. malabathricum (CEMM) contains only triterpenes and steroids exhibits gastroprotective activity. [20]

Musa Paradisiaca: The plant, *Musa paradisiaca L.* is a member of the banana family Musaceae found in Tropical and sub tropical region including Northern India. The ethanol extract was used in indomethacin, ethanol, and aspirin induced gastric ulcers in rats. The phytochemical analysis showed the presence of alkaloids, terpenes, cardiac glycosides, and phlobatannin. The result showed that there was a significant and dose dependent mucosal protection in all the models when compared to the control. Percentage ulcer inhibitions of extract at 1000mg/kg for ethanol, aspirin and indomethacin induced ulcers were 76 %, 85.91% and 60 % respectively. [21]

Phyllanthus amarus: The family is Phyllanthaceae. Distributed throughout India, mainly in tropical and subtropical parts of country. It is used for the treatment of the liver, anti-viral, leaves are used as expectorant, diaphoretic, laxative diuretic. This study investigated the gastroprotective potential of aqueous leave extracts of *Phyllanthus amarus* against ibuprofen, Histopathological assessment of the stomach of experimental rats showed restoration of the mucosal fold suggesting the cytoprotective effect of *P. amarus* as an anti-ulcer agent. This property may be attributed to the combined action of the various antioxidant components of secondary metabolites like alkaloids, phenolic acids, glycosides, flavonoids, saponins and tannins present in the leaves. [25]

Prunus persica L.: *Prunus persica* L. (Peach) named as *Amygdalus persica* is a perennial and deciduous tree of the family Rosaceae native to Northwest China. The leaves are insecticidal, sedative, diuretic, demulcent, expectorant, vermicidal and are used in leucoderma, and in piles. Leaf paste is used to kill worms in wounds, and fungal infections. The treatment of gastritis, whooping cough, and chronic bronchitis is carried out internally with leaves. The bark is used in leprosy, and jaundice. Leaves of Prunus persica have been investigated for their antioxidant, and anti-inflammatory, Alzheimer's disease. Fruits reported for the hypoglycemic effect for the prevention of Type-2 diabetes,degenerative disorders, hypermenorrhea, and dysmenorrhoea. *Prunus persica* is a rich source for flavonoids and various parts of the plant are used as medicinal agents in traditional medicine. The gastroprotective activity of ethanolic bark extract of *Prunus persica* (EBPP) was determined against Indomethacin plus pylorus ligation induced gastric damage in rats. [28]

***Scrophularia striata*:** *Scrophularia striata*, commonly known as figwort, belongs to family of flowering plants called Scrophulariaceae. It is native to Iran, grows wild. Several chemical components including cinnamic acid, three flavonoids (quercetine, isorhamnetin-3-O-rutinoside and nepitrin) and one phenylpropanoid glycoside (acteoside) have been identified in the aerial parts of *S. striata.* It appears that some compounds isolated from this species have the inhibitory effects on a variety of malignant and inflammatory disorders. Aqueous and etheric extracts which grossly showed significant reduction of ulcer areas and histopathologically showed marked reduction of mucosal necrosis, edema and leukocytes infiltration. Hence, the study reveals the gastroprotective effects of extract of *Scrophularia striata* on ethanol-induced gastric ulcer.

***Struthanthus marginatus*:** *Struthanthus marginatus* from family Loranthaceae, a medicinal herb used in Brazil shows Anti-oxidant, Gastroprotective effects, healing agent, bronchitis, leucorrhoea. The antisecretory activity (basal or stimulated) was determined using the pyloric ligature method. The gastroprotective action of nitric oxide and sulfhydryl groups (–SH groups) were evaluated using ethanol-induced gastric ulcer model. Aqueous extract of *S. marginatus* was used to study gastroprotective activity. The healing ability was evaluated using an acetic acid-induced chronic ulcer. There results showed a significant reduction in gastric secretion, stimulation of mucus production. [30]

Vitex pubescens: *Vitex pubescens* belongs to family Verbenaceae. *Vitex pubescens is* a Malaysian therapeutic plant employed in remedy of disorders like diarrhoea, antipyretic, analgesic, antifungal, antitumour. The purpose of this research is to assess the gastroprotective efficiency of *V. Pubescens* leaves against ethanol-induced gastric hemorrhagic laceration in Rats. Gastric homogenates revealed a remarkable increase in endogenous antioxidant enzyme activities and a decrease in the lipid peroxidation level in animals pre-treated with *V. pubescens e*xtract compared with the ulcer control group. [31]

Ziziphus abyssinica: It is belonging to family Rhamnaceae which has been used by herbalists in northern Nigeria for the treatment of ulcer. The antibacterial, antioxidant and phytochemical screening of the fruit extracts of this plant have been reported. The leaves are applied as poultices and are helpful in liver troubles, asthma and fever. Investigational study was designed to determine the gastro-protective effect of different extracts of *Z. abyssinica* roots with the aim of establishing the most effective gastro-protective extract. *Z. abyssinica* extracts showed significant gastro-protective effect with aqueous extract having the highest gastro-protective effect than Methanol extract whereas ethyl acetate extract is less potent than methanol extract but effective than the hexane. Histological study showed

that pretreatment with aqueous extract resulted in the preservation of the functional cyto-architecture of the entire mucosa with little pathological changes, compared to other extracts. [32].

CONCLUSION

In present review we presented different medicinal plants used for the treatment of peptic ulcer disease. As in India many medicinal plants were preferred because of its less side effects & safety. The present review highlights mainly on presently evaluated gastro protective plants in treatment of PUD. The present review highlights on the different parts of the plants used, method of the extraction & methods used to evaluate the gastro protective activity. The review article may be useful for the researchers working on the gastro protective activity of the plant.

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