

SOME MEDICINAL PLANTS WITH ANTI-ULCER ACTIVITY

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Abstract

Ulcer is a common gastrointestinal disorder which is seen among many people. It is basically an inflamed break in the skin or the mucus membrane lining the alimentary tract. Now a days it's a measure issue due to modern life style. It may be due to the regular usage of drugs, irregular food habits and stress. Ulceration occurs when there is a disturbance of the normal equilibrium caused by either enhanced aggression or diminished mucosal resistance. A number of synthetic drugs are available to treat ulcers. But these drugs are expensive and are likely to produce more side effects when compared to herbal medicines. On the basis of literature and survey of traditional medicinal practitioners, there are many medicinal plants and polyherbal formulations used for the treatment of ulcer. In this review attempts have been made to know about some medicinal plants which may be used in Ayurveda as well as modern science for the treatment or prevention of ulcer.

Key words- *Antiulcer, Ulcer, Gastrointestinal, Polyherbal formulations.*

INTRODUCTION

Ulcer is a common gastrointestinal disorder which is seen among many people. It is basically an inflamed break in the skin or the mucus membrane lining the alimentary tract [Van Zanten et al., 1999].

Now a days it's a measure issue due to modern life style. It may be due to the regular usage of drugs, irregular food habits and stress. Ulceration occurs when there is a disturbance of the normal equilibrium caused by either enhanced aggression or diminished mucosal resistance. A number of synthetic drugs are available to treat ulcers. But these drugs are expensive and are likely to produce more side effects when compared to herbal medicines [Suerbaum et al., 2002].

On the basis of literature and survey of traditional medicinal practitioners, there are many medicinal plants and polyherbal formulations used for the treatment of ulcer [Tytgat et al. 2011]. In this review attempts have been made to know about some medicinal plants which may be used in Ayurveda as well as modern science for the treatment or prevention of ulcer.

It is hoped that in future herbal drugs may be serve as a useful tool for the treatment of ulcer which are safer, potent and cost effective

MATERIALS AND METHODS

An extensive search of existing literature was performed and carefully collected from various scientific journals, original research articles, reviews, short communications, books and reports. All this data collected from worldwide accepted databases such as Scopus, Science Direct, PubMed, Web of Science, Medline, Springer and Google Scholar.

1. *Cynodon dactylon*

Cynodon dactylon (L.) pers. is a creeping grass found in warm climates all over the world (Singh et al., 2009). It belongs to the family Poaceae. It is also known as Durva grass, (Oudhia, 2003). It is the most sacred plant of India next to tulsi.

The plant contains crude proteins, carbohydrates, mineral constituents, and oxides of magnesium, phosphorous, calcium, sodium, potassium, vitamin-c, carotene, hydroquinone, hexadecanoic acid, ethyl ester, linoleic acid, ethyl ester and d-mannose (Shabi et al., 2010).

The plant has been used from ancient days in the traditional medicines to treat various ailments such as cancer, cough, cramps, dysentery, epilepsy, headache, haemorrhage, hypertension, stones, tumours, urogenital disorders, warts and wounds (Chopra et al., 1999, Pal, 2009).

Advanced studies on this plant have been reported that it possess antiulcer, antidiabetic, antidiarrheal, diuretic, antimicrobial, immunomodulatory, antiepileptic, antibacterial, chemoprotective and hepatoprotective activities (Parekh et al., 2005, Singh et al., 2007, Najifi et al., 2008, Surendra et al., 2008, Kumar et al., 2004, Ravindra et al., 2009, Baskar and Ignacimuthu, 2010, Kumar et al., 2010, Santhi and annapoorani, 2010, Garg and paliwal, 2011).

The alcoholic extract of *Cynodon dactylon* inhibited ulceration by inhibiting output volume and total acidity. The ulcer healing activity of the plant extract may be due to antisecretory property associated with an enhancement of the local healing process.

2. *Ocimum sanctum*

Ocimum sanctum, commonly known as Tulsi. It is considered as a sacred plant by the Hindus in India (Singh et al., 2011). It has been extensively used in traditional medicine for a wide range of ailments (Shahedur et al., 2011, Vinod et al., 2011). The whole parts of plant such as leaves, flowers, stem, root, seeds etc. are known to possess a wide range of pharmacological properties and have been used by traditional medical practitioners as a expectorant, analgesic, anticancer, antiasthmatic, antiemetic, diaphoretic, antidiabetic, antifertility, hepatoprotective, hypotensive, hypolipidemic antistress agents (Heinrich, 2009).

The chemical composition of *Ocimum sanctum* is highly complex, containing many nutrients and other biologically active chemically compounds. Eugenol is the principle constituent of tulsi, has been found to be largely responsible for the management of various types of diseases (Lalit et al., 2011). Tulsi has specific aromatic odour because of presence of essential or volatile oil, mainly concentrated in the leaf.

The leaf contains eugenol, eugenic acid, urosolic acid, estragol while the seed volatile oil have fatty acids and sitosterol. The stem and leaves contains number of constituents including saponins, flavonoids, triterpenoids and tannins (Shishoda et al., 2003). In addition it contains phenolic compounds which exhibit antioxidant and anti-inflammatory activities (Dhar et al., 1968). It also contains two water soluble flavanoids orientin and vicianin shows protection against radiation induced chromosomal damage in human blood lymphocytes (Uma et al., 2000).

Advanced studies on this plant have been reported that it possess antiulcer activity, insecticidal activity, antiemetic activity, antistress activity, analgesic activity, antioxidant activity, heart tonic activity, antidiabetic activity, antitubercular activity, immunomodulator activity and antifertility effect (Rajeswari, 1952, Sen, 1993, Singh, 1995, Hussain et al., 2001, Prakash and Gupta, 2005, Glolade and lockwood, 2008, Shankar et al., 2009, Khan et al., 2010, Tabassum et al., 2010, Vinod et al., 2011).

The fixed oil shows antiulcer activity due to its lipoxygenase inhibitory, histamine antagonistic and anti-secretory effects (Singh and Majumdar et al., 1999).

3. *Glycyrrhiza glabra*

Glycyrrhiza glabra is most commonly used in herbal medicine and has been used in the management of various diseases for more than 4000 years. It is from the leguminosae family. The root of *Glycyrrhiza glabra* contains the chief constituent known as glycyrrhizin which is 60 times sweeter than sugar. In traditional siddha system of medicine, it is also used in the treatment of acute respiratory problems, gastric ulcers, gastritis, inflammatory conditions in general and adrenal exhaustion (Fukai et al., 2002) Components of *Glycyrrhiza* root have both estrogenic and anti-estrogenic activity. So it is therefore an important herb in the management of hormone related female disorders.

Glycyrrhiza glabra exhibit wide spectrum of activities like antiulcer-activity, antioxidant-activity, and immunostimulatory effects, antihyperglycemic, anticonvulsant, antiinflammatory, antimicrobial, anticarcinogenic effects (Segal et al., 1985, Demizu et al., 1988, Chopra and Simon, 2000, Ambawade et al., 2002, Taro et al., 2002, Krausse et al., 2004, Shirazi et al., 2007, Panneerselvam et al., 2009).

Bennett demonstrated deglycyrrhizinated licorice using a rat model of Aspirin-induced gastric mucosal damage (Bennett et al., 1980). He suggested that several components exist in the extract which promote gastric healing, although in consistencies are apparent between these studies. *Glycyrrhiza glabra* reduces stomach secretion produces thick protective mucus which covers the lining of stomach and therefore protects from peptic ulcers and other inflammatory diseases. Further it has been reported to raising the local concentration of prostaglandins which promotes mucous secretion and cell proliferation in the stomach (Khare, 2004).

Presence of such a wide range of chemical compounds indicates that the plant could serve as a “lead” for the development of novel agents having good efficacy in various disorders.

4. Ficus religiosa

Ficus religiosa, commonly known as peepal tree is one of the foremost plants utilized from antiquity till to date (Ghani, 1998). It belongs to family moraceae (Hamed, 2011). The bark of *Ficus religiosa* is reputed to have a number of chemical constituents. It contains tannins, saponins, flavonoids, steroids, terpenoids and cardiac glycosides (Ruby et al., 2000). The bark has also been reported to contain bergapton, bergapton, lanosterol, β - sitosterol, stigmasterol, lupen-3-one, phytosterol, vitamin K1, lupeol, lupeol acetate, α -amyryn acetate (Joseph and Justin, 2010).

Ficus religiosa has been extensively used in traditional medicine for the management of various types of diseases like diarrhoea, asthma, cough, toothache, migraine, in gastric problems, haematuria, diabetes, diarrhoea, leucorrhoea, anxiety, cardiac tonic, vomiting (Pandit et al., 2010, Khan et al., 2011). *Ficus religiosa* possess a wide range of pharmacological activities like anti-ulcer activity, anti-inflammatory activity, anti-microbial activity, anti-anthelmentic activity, anti-asthmatic and (Malhotra et al., 1960, Viswanathan et al., 1990, Hemaiswarya et al., 2009, Kaur et al., 2010, Khan et al., 2011, Patil et al., 2011, Sawarkar et al., 2011).

The alcoholic extract of *Ficus religiosa* was screened for antiulcer activity in swiss albino rats against pylorus ligation induced ulcers, ethanol induced ulcers and aspirin-induced ulcers at dose level of 250 mg/kg and 560 mg/kg. The alcoholic extract of *Ficus religiosa* inhibited ulceration by significantly decreasing the gastric volume, total acidity, free acidity and ulcer index (Saha and Goswami, 2010).

The ethanolic extract of stem bark of *Ficus religiosa* also exhibited potential antiulcer activity exhibited potential antiulcer activity. The antiulcer activity of *Ficus religiosa* was evaluated in vivo against cold restrained stress and indomethacin-induced gastric ulcers and pylorus ligation assay. The extract significantly reduced the ulcer index in all assay used (Khan et al., 2011). Since *Ficus religiosa* is a nontoxic, highly promising natural crude drug having a wide spectrum of biological functions. It is expected that it may find application as a novel drug in the near future to control various diseases.

5. Cordia dichotoma

Cordia dichotoma commonly known as Bhokar which is used Ayurveda Medicine. The methanol fraction of the crude methanol extract of *Cordia dichotoma* bark (500 mg/kg) showed a protective role against acid acetic-induced ulcerative colitis in Swiss mice through anti-inflammatory and antioxidant mechanisms [Ganjare et al., 2011]

6. Moringa oleifera

Moringa oleifera L. is known as drumstick tree. It is used for medicinal and nutritional purposes. The ethanolic root-bark extracts of *Moringa oleifera* (150, 350 and 500 mg/kg) were tested as antiulcer agent in albino Wistar rats with ethanol-induced and pylorus ligation-induced gastric ulceration models, being stated prominent antiulcer, anti-secretory and cytoprotective abilities [Choudhary et al., 2013].

The hydroalcoholic extract (50, 100 and 200 mg/kg) and its chloroform fraction (100 and 200 mg/kg) from *Moringa oleifera* seeds showed therapeutic effects in Wistar rats with acetic acid-induced colitis, even causing a significant reduction of ulcer severity, area and index as well as on mucosal inflammation severity and extent, crypt damage, invasion involvement, total colitis index and myeloperoxidase activity [Minaiyan et al., 2014].

The aqueous leaf extract (50–500 mg/kg) of this plant was also able to prevent gastric ulceration in Holtzman strain albino rat'sulcered using aspirin through potentiation of serotonin release [Debnath et al.,2011]

7. Capparis zeylanica

Capparis zeylanica L. is widely recognized in traditional Ayurvedic Medicine. The methanol extract from its leaves (200 mg/kg) exhibited a stomach-protective effect against ethanol necrotic damage in a study performed using three different models such as ethanol, aspirin and indomethacin of induced ulcers in albino rats [Sini et al.,2011]. The authors reported that ulcer protection might be attributed to the phytochemicals present in *Capparis zeylanica* leaves, among them flavonoids, tannins and saponins.

8. Morinda citrifolia

Morinda citrifolia L. is known as noni. It is commonly used in popular medicine in all over the World. The health benefits of fruit aqueous extract (0.63 to 2.50 g/kg). Its isolated compound such as scopoletin, were evaluated in models of gastro-esophageal inflammation in rats. The studied extract was able to inhibit acid reflux esophagitis, reduced gastric lesions formation induced by alcohol and serotonin and accelerated gastric ulcers healing induced by acetic acid. Isolated scopoletin also produced similar effects, though it's anti-secretory and prokinetic activities included an inhibitory activity on serotonin, free radicals and cytokine-mediated inflammation [Mahattanadul et al., 2011].

9. Cyperus rotundus

Cyperus rotundus L. a widely used plant against gastric ailments in traditional Indian Medicine, especially in Ayurveda. The oral administration of methanol extract from rhizomes of *Cyperus rotundus* (250 and 500 mg/kg) inhibited aspirin-induced ulceration in Wistar rats in a dose-dependent manner, being even comparable with standard drug ranitidine (50 mg/kg) [Thomas et al.2015]. Also, the same study showed that this extract inhibited oxidative damage in gastric mucosa through increasing antioxidant enzymes activity (SOD, GSH and GPx) [Thomas et al., 2015]. It is reported that this plant exhibited anti-inflammatory and antiulcer activities at doses of 300 and 500 mg/kg [Ahmad et al., 2014].

10. Tectona grandis

Verbascoside, a phenolic glycoside isolated from *Tectona grandis* L. evidenced a prominent ability to mediate gastric protection in experimental animals via inhibiting proton pump (H⁺/K⁺ -ATPase) activity with a corresponding decrease in plasma gastrin level [Singh, et al., 2010].

11. Terminalia catappa

Terminalia catappa L. is a plant widely used to treat gastritis. The aqueous extract from leaves (25 mg/kg) showed preventive and curative effects on acute and chronic induced gastric ulcers on rats and an important inhibitory profile against *H. pylori* [Silva et al., 2012]. The authors reported that the mechanisms involved on *Terminalia catappa* gastroprotective effects are related to nitric oxide pathway, increasing endogenous prostaglandins levels and mucus production and inhibiting MMP-9 and MMP-2 activities [Silva et al., 2012].

12. Terminalia arjuna

Terminalia arjuna (Roxb.) Wight & Arn. bark contains antioxidant polyphenols and flavonoids and has been reported to have antibacterial activity [Devi et al. 2008]. The methanol extract of bark of *Terminalia arjuna* (100, 200 and 400 mg/kg) showed marked antiulcer and ulcer healing activities against ethanol, diclofenac sodium and dexamethasone induced ulcer rat models [Devi et al.,2007]. Also, methanol bark extract (100, 200, 300 and 400 mg/kg) showed anti-secretory activity in *H. pylori* lipopolysaccharide-induced gastric ulcer in rats [Devi et al., 2008]. The authors reported that the antiulcer effect of *Terminalia arjuna* extract reflects its ability against gastric mucosa damage and its mucosal protective factors [Devi et al., 2008 and Devi et al., 2007].

13. Terminalia belerica

Terminalia belerica Roxb. is a plant used in traditional Ayurvedic medicine. The fruits of *Terminalia belerica* being one of the three constituents of the important Indian Ayurvedic preparation that is Triphala." The antiulcer activity of 70% methanol extract from *Terminalia belerica* fruits (100, 250,

500, 1000 mg/kg) was evaluated on wistar rats by employing ethanol, aspirin, cold restraint stress and pylorus ligation ulcer models [Jawanjalet al., 2012]. This extract was able to suppress ethanol-induced peptic ulcer, at dose of 500 mg/kg, reduced gastric volume, free acidity, total acidity, ulcer index and protein and peptide contents, while increased mucus content in pylorus ligated rats. [Jawanjal et al., 2012]

Also, the extract of *Terminalia belerica* provided protection against aspirin-induced ulcers but not in cold stress restraint model. Hence, the authors reported that the possible mechanism of gastric mucosal protection conferred by Molecules from *Terminalia belericamethanol* extract may be due to reinforcement of the mucosal barrier resistance through protective coating [Jawanjal et al., 2012].

14. Terminalia chebula

The fruit of *Terminalia chebulais* one of the three constituents of the important Indian Ayurvedic preparations such as Triphala. Aspirin, ethanol and cold restraint stress-induced ulcer methods were used in Sprague Dawley rats to assess the antiulcer effects of the hydroalcoholic (70%) extract from *Terminalia chebula* fruits (200 and 500 mg/kg) [89].

The results of this study confirmed the antiulcerogenic potential of the extract, reducing lesion index, total affected area and lesions percentage in aspirin, ethanol and cold restraint stress-induced ulcer models.

The extract of *Terminalia chebula* showed anti-secretory activity in pylorus ligated model, which lead to a reduction in the gastric juice volume, free acidity, total acidity and increased gastric pH [89]. Chebulinic acid was isolated from *Terminalia chebula* fruits and showed anti-secretory and cytoprotective effects on gastric ulcers through the inhibition of H⁺/K⁺ -ATPase activity and antioxidant mechanisms [Mishra et al., 2013].

15. Argemone mexicana

Argemone mexicana L. is a plant that contains numerous alkaloids and is widely used in traditional medicine. A study carried out to assess the effects of methanol and aqueous extracts from this plant (500–3000 mg/kg), in Wistar rats with duodenal ulceration. From this study it is concluded that both extracts produced significant activity in cysteamine-induced duodenal ulceration [Das, et al., 2011].

16. Piper betle

Piper betle L leaves are widely consumed as a mouth freshener. The ethanol extract from leaves (200 mg/kg) exhibited protective effects against indomethacin-induced gastric lesions through increasing the antioxidant machinery (SOD and CAT) [Majumdaret al., 2002].

Same results were also obtained using ethanol extract at 150 mg/kg after NSAID-induced peptic ulcer in albino rats [94]. Further studies evaluated the role of the major antioxidant constituent present in *Piper betle* is allylpyrocatechol, which act as a gastroprotective agent [Bhattacharya et al. 2007, Yadav et al., 2009, and Yadav et al., 2013]. This compound healed indomethacin-induced stomach ulceration in Sprague-Dawley rats by its antioxidant action and ability to form mucus, involving free radical scavenging that protects the gastric mucosa from oxidative damage [Bhattacharya et al., 2007].

17. Ficus religiosa

Ficus religiosa L. is a plant species belonging to the Moraceae family that has been recently studied. *Ficus religiosa* contains phytochemicals which act as a potential H₂ receptor antagonist using molecular docking approach and lanosterol and α -amyrin acetate were found to have higher stability during simulation studies. So, these compounds may be suitable therapeutic agents on peptic ulcer treatment, acting as H₂ receptor antagonist [Chaudhary et al., 2017].

18. Ziziphus jujuba

Ziziphus jujuba Miller is a plant species belonging to Rhamnaceae family, commonly used in Persian folk medicine for the treatment of gastrointestinal diseases, such as ulcers [Hamediet al., 2015]. Fruits and stem of *Ziziphus jujuba* are employed to treat digestive disorders. Fruits possess antitussive, laxative and hypotensive properties, while the stem bark and leaves could cure wounds and peptic ulcer.

Bark of *Ziziphus jujuba*, has been traditionally employed by Iranian healers to treat digestive disorders and gastric ulcers. The effect of the aqueous extract from *Ziziphus jujuba* stem bark (100,

200 and 400 mg/kg) against acidified ethanol-induced gastric ulcers in albino Wistar rats, as well as its anti-**H. pylori** activity was tested by disc diffusion assay [Hamed et al., 2015].

From this study it is concluded that, the extract exhibited antiulcer potential through protecting gastric mucosa and anti-**H. pylori** activity. The authors proposed that the flavonoids present in the stem bark extract may be responsible from the observed effects due to increased gastric wall mucus. Also it is suggested that, the mechanism of gastric mucosal protection may be due to the enforcement of mucosal barrier through a protective coating, in addition to the antioxidant activity [Hamed et al., 2015].

CONCLUSIONS

In this review article, there are enlisted medicinal plants for which showing anti-ulcer activity. From this review we can conclude that number of medicinal plants and their active chemical constituent are responsible for treatment of ulcer.

This study shows that there are many phytochemicals which result in novel and effective pattern of treatment. From this review, we find out the drug which possesses antiulcer activity in different gastric ulcer models. Here several researches have confirmed that, the efficacy of medicinal plants for the treatment of various types of ulcer diseases.

Analysis of literature data indicated that phytochemicals are natural, safe and effective resources that can be used in the prevention and even treatment of ulcers. Hence there is urgent need to validate the large number of preclinical data and forming herbal drugs for treatment of various types of ulcer.

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