GASTROPROTECTIVE POTENTIAL OF SOME PLANTS FROM *RUTACEAE* FAMILY: A REVIEW

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Summary

In recent years, a no. of plants has been investigated and reported possessing medicinal values, including plants from r*utaceae* family. Large body of evidence has accumulated to demonstrate promising potential of *rutaceae* plants used in various traditional, complementary and alternative systems. The present review aimed to compile data on promising gastroprotective activity of plants or their parts from *rutaceae* family that have been established against various disease models using modern scientific methodologies and tools.

Keywords: *Rutaceae*, Gastroprotective, Hepatoprotective, Antiulcer, Antiulcer

Introduction

Any anatomical or physiological deviation within gastrointestinal tract (from oesophagus to rectum) is termed as gastric disease. The various essential tasks are being performed within the alimentary canal including administration, swallowing, disintegration or degradation, absorption and elimination of waste products of food, drugs and other materials. Sometimes problems such as; indigestion, constipation, emesis, gastric ulcer and gastroesophageal reflux disease (GERD) may results due to various pathological as well as biochemical factors.

Common gastrointestinal diseases:

- **Ulcerations:** Ulcerations in GI are associated with chronic use of anti-inflammatory medications (NSAIDs; such as aspirin and indomethacin) [1], Smoking [2,3], alcoholism [4], improper diet [5], stress conditions [6,7], and bacterial infections (*H. Pylori*). [8]

- **Gastroesophageal reflux disease:** It is a chronic symptoms or mucosal damage caused by stomach acid coming up from the stomach into the oesophagus. Main cause is changes in the barrier between the stomach and the esophagus, including abnormal relaxation of the lower esophageal sphincter, which normally holds the top of the stomach closed, impaired expulsion of reflux from the esophagus, or a hiatal hernia.[9]

- **Diarrhoea:** Diarrhoea (loose motions) is the passage of 3 or more loose or liquid stools per day, or more frequently than is normal for the individual.Diarrhoea is not itself a disease, but can be a symptom of several diseases and sometimes may be associated with abdominal pain, which may reduce after a stool is passed. Diarrhoea occurs due to the irritation within the lining of small or large intestine, which leads decrease water absorption hence increase in water being passed with stools. Many factors such as food poisoning, infection (bacterial, viral, parasitic), food intolerance, malnutrition, intestinal diseases and sometimes medications can contribute to diarrhoea [10].

- **Vomiting:** Evacuation of gastric contents through oral route is termed as vomiting or emesis. The stomach almost turns itself inside out - forcing itself into the lower portion of the esophagus during a vomiting episode. Vomiting results due to reflex reaching upto the central nervous system that may arise from a bad odour, taste, various illnesses and emotions (such as fear), pain, injury, infection, food irritation, dizziness, motion and other changes in body like; eating disorder (anorexia and bulimia), food poisoning, motion sickness (car sickness seasickness), vertigo, head injuries gallbladder disease or appendicitis, migraine, brain tumour and infection.[11, 12]

Reported gastroprotective activities of various plants from *Rutacae* family:

Rutaceae is a family of dicotyledonous of order Geraniales (Sapindales) having flowering plants, edible fruit and also have values as ornamentals. The *rutaceae* are herbs or shrubs, may be armed/unarmed, sometimes climbing but rarely perennial herbs and trees with glandular punctate**.** From the available literatures it has been well established that the different part of plants from rutaceae family have a no. of therapeutic propertiers, still an approach is made here to compile reported gastroprotective activities of various plants or their parts of rutaceae family. Some members from *rutaceae* family with reported gastroprotective potential are discussed below**;**

Aegle marmelos:

- The oral administration of pyranocoumarin, isolated from *Aegle marmelos* seeds showed significant gastro protective effect against pylorus ligated, aspirin induced and stress-induced ulcerations in rats. The activity was further more confirmed against stress induced ulcerations in guinea pigs. The result suggests that gastro-protective effect was due to the mucosal defensive factor [13] The same activity was again assessed by *Dhuley (2007),* using unripe bael fruit extract against ethanol induced gastric mucosal damage and found to cause significant defense in gastric mucosa [14].

Later on, *Verma et al. (2010)* established the earlier work done on *Aegle marmelos* using ethanol extract of root part in different animal models. The ethanol extract administered orally, twice daily for 5 consecutive days at the doses of 200 mg/kg b.w. and 400mg/kg body weight, showed dose dependent ulcer healing potential. The extract produced significant decrease in ulcer index, lipid peroxidation, superoxide dismutase along with increased in catalase activity. [15]

- The antioxidant properties along with hepatoprotective potential of *Aegle marmelos* have also been established. The oral administration of alcoholic extract of *Aegle marmelos* showed significant protection of hepatic cells against CCl_4 induced toxicity. The protective effect was concluded due to free radical scavenging activity of the extracts [16] In the same course of study, the hepatoprotective of the plant was confirmed using ethanolic and aqueous extracts of leaf in mice against carbon tetrachloride induced liver damage using silymarin as control. The inhibition of serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) and alkaline phosphatase (ALP) level indicates hepatoprotective potential. [17] Subsequently the same activity was confirmed evaluating TBARS (thiobarbituric acid reactive substances), glutathione, glutathione peroxidise, SOD level, vitamin E and C level. [18]

- The antidiarrheal potential have also been proved in dried unripe fruit pulp of *Aegle marmelos*. The aqueous extract (decoction) significantly was found to reduce bacterial adherence and invasion of HEp-2 cells along with reduction in binding of both labile toxin and cholera toxin to ganglioside monosialic acid but had no effect on stable toxin. [19]

***Bergamot orange (Citrus aurantium)*:**

- The essential oil extract of *Bergamot orange* have been investigated for its hepatoprotective effect on carbon tetrachloride-induced hepatotoxicity in rats. A significantly reduction in serum ALT level was observed, but AST level was unaffected. The histopathological examination also revealed weak hepatoprotection [20]. Later on, the activity was confirmed against absolute ethanol and NSAID induced toxicity in rats. The results indicate that gastro protective activity of the pant extract was due to increase in gastric mucus production by conversing the basal PGE_2 level.[21]

***Chloroxylon swietenia*:**

- Hepatoprotective action of ethanol extract of *Chloroxylon swietenia* have been proved in rats against acetaminophen induced hepatic injury. Conclusion was made due to elevation in serum glutamate pyruvate transaminase (ALT), serum glutamate oxaloacetate transaminase (AST), serum alkaline phosphatase (SALP) and total bilirubin level. [22]

Citrus aurantifolia:

- Hepatoprotective activity of the *Citrus aurantifolia* has also been proved against paracetamol induced hepatic damage.[23]

***Citrus karna*:**

- The ethyl acetate extract of *Citrus karna* peel have been evaluated for anti-ulcerogenic property against water immersion and hypothermic restraint stress model at different doses (200, 300 and 400 mg/kg, b.w) in Wistar rats. The collected data established significant ulcer protective activity of the said plant as ulcerative index and thiobarbituric acid reactive species level in blood and gastric tissue was found to be decreased than normal.[24]

***Citrus lemon*:**

- The phytochemical analysis of *Citrus lemon* (CL) fruit bark essential oil indicate presence of limonene (LIM) and β-pinene (PIN). The gastroprotective mechanism activity along with mechanism of action of CL, LIM and PIN in ethanol and indomethacin-induced gastric ulceration was evaluated along with its *in vitro* anti-*Helicobacter pylori* activity. In ethanol model, CL and LIM demonstrated 100% of gastroprotection, while PIN did not exert effective gastroprotection. Similar results were found against indomethacin model. During in vitro studies, the minimum inhibitory concentrations were 125 μg/ml, 75 μg/ml and 500 μg/ml for CL, LIM and PIN respectively. The gastroprotective effect of CL and LIM was involved with increasing in mucus secretion, HSP-70 and VIP, but not with GSH, NO or SH compounds. CL gastroprotective mechanism was found to be involved with PGE_2 synthesis. PIN did not present any gastroprotective activity. [25]

Citrus microcarpa:

- The fruit peel extract of *Citrus microcarpa* have been investigated for hepatoprotective activity in rats, evaluating changes in liver morphology and serum liver enzyme levels such as; bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (AP). A decrease in ALT, AST and AP levels proved hepatoprotective potential in *Citrus microcarpa* fruit. [26]

Clausena dentate

- Another plant of *rutaceae* family is *Clausena dentata,* whose hepatoprotective capacity also have been established against acetaminophen induced hepatotoxicity in rats. The *Clausena dentata* ethanol extract was found to normalize; level of biochemical parameters, which were altered due to administration of acetaminophen [27]

Clausena lansium:

- The hepatoprotective action of some isolated compounds of *Clausena lansium* leaves have been well established. They were find effective against CCl_4, thioacetamide and acetaminophen induced toxicity in mice, as the serum transaminase level was found to diminish in animals treated with these isolated compound. Along with this inhibition in lipid peroxidation was also observed. [28]

***Feronia elephantum*:**

- Ulcer healing property of ethanolic extract of *Feronia elephantum* fruit pulp also have been proved in albino rats. The extract was found to inhibit gastric acid secretion along with increase in pH in indomethacin induced gastric ulceration model [29].

Galipea longiflora:

- The bark extract of *Galipea longiflora* have also been evaluated for the gastroprotective activity in mice against NSAID, ethanol and stress-induced ulcer. The effects of the extract on gastric content volume, pH and total acidity were also evaluated, using pylorus ligated model. *Galipea* longiflora alkaloid extract at the three doses (50, 125 and 250 mg/kg b.w.) significantly diminished the lesion index, total lesion area, and percentage of lesion, in comparison with the negative control groups in all the models evaluated. Regarding the model of gastric secretion, a reduction in volume of gastric juice and total acidity was observed, as well as an increase in gastric pH. [30]

Glycosmis pentaphylla:

- The methanolic extract of *Glycosmis pentaphylla* also have been reported with hepatoprotective activity against paracetamol induced toxicity in rats. Later on, the activity was confirmed using ethyl acetate and methanolic extracts against carbon tetrachloride induced hepatotoxicity.[31]

Limonia acidissima:

- The alcoholic and aqueous extract of *Limonia acidissima* bark was found to create inhibition of gastrointestinal motility, and also causing antidiarrhoeal effect in rats. Beside these reduction in mean weight of faeces was also observed. [32]

Murraya koenigii:

- Three carbazole alkaloid viz. kurryam, koenimbine and koenine were isolated from *Murraya koenigii* seed extract, and were found to possess antidiarrhoeal property against castor oil-induced diarrhoea and PGE_2-induced enteropooling in rats.[33]

- In another study, *Murraya koenigii* was found to containing antiulcer potency. The aqueous extract was evaluated against NSAIDs and pylorus ligation induced ulcer model in albino rats. The study data revealed that the extract at doses of 200 mg/kg b.w. and 400 mg/kg produced significant inhibition of gastric lesions in both the screening models, at the same time marked reduction in gastric volume, free and total acidity and rise pH of gastric juice was observed in pylorus ligated rats. [34]

Toddalia asiatica:

- Investigation of alcoholic and aqueous extracts of *Toddalia asiatica* roots antioxidant property was made, against CCl_4 induced oxidative stress in rats. A significantly increase in reduced glutathione, proteins, antioxidant enzymes was observed along with decreased lipid peroxidation. This shows that the free radical scavenging/antioxidant activity of *T. asiatica* roots may be responsible for its therapeutic effect on tissue damage. [35]

Zanthoxylum armatum:

- The administration of 500 mg/kg b.w. of ethanolic extract *Zanthoxylum armatum* of leaves against CCl_4-induced hepatotoxicity in rats, was found to decrease serum glutamyl oxalacetic acid transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT), alkaline phosphatase (ALKP), and serum bilurubin (SBLN) level alongwith liver inflammation, exhibiting hepatoprotective activity.[36]

Zanthoxylum hyemale:

- Beside all over the mentioned gastroprotective profile of plants or their parts from *rutaceae* family, hydroalcoholic extract of *Ruta chalepensis* leave[37] and ethanolic extract of *Zanthoxylum hyemale* stem bark[38] have been reported to possess antispasmodic activity.

Conclusion

Occurrence of gastric problems or disorders is common in society, and have many factors like dietary habits, life style and sometimes environmental also. The various approaches have also been established for their treatment using chemical agents, but are not strictly advisable due to their unwanted effects. The herbal products are continuously growing recognition as a safe remedy for their management. On behalf of above said studies, plants or herbs from *rutaceae* family can be recommended as a major source of natural drugs with capability to restore gastric disorders.

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