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Review on antiulcerogenic property of Kaidaryadi kashayam - a traditional formulation

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Abstract

A peptic ulcer is a sore on the lining of the stomach or duodenum, the beginning of small intestine. The life time risk for developing peptic ulcer is approximately 10%.Kaidaryadi kashayam is a well known traditional decoction formulation from the text Chikitsamanjari. It can be applied to conditions like diarrhea, peptic ulcer; abdominal pain, indigestion etc .Kaidaryadi kashayam contain 4 drugs i.e.; Zingiber officinale, Murraya koeinigii, Terminalia chebula and Tricosanthes dioica. The four drugs of kaidaryadi kashayam were evaluated for anti ulcerogenic activity based on available research data here in this paper. Zingiber officinale contain active ingredients like gingerols and zingerons are inhibiting proton pump and thereby reducing the gastric secretion. They act as anti oxidants helps in the protection of gastric mucosa. Also acts against H.pylori and other organisms. Murraya koenigii contain carbazole alkaloids which act by cytoprotective and anti microbial properties. It also reduces the acidity of gastric juice.terminalia chebula contain chebulinic acid which is a known anti secretory agent by inhibiting the proton pump. It also acts against H.pylori and reduces the total acidity of the gastric juice. Tricosanthes dioica contain saponins and tannins which reduce pepsin, and acts as a strong cytoprotective factor. So based on the available data we can say kaidaryadi kashayam is an effective formulation against peptic ulcers especially in the initial period of management of PUD.

Keywords: Kaidaryadi kashayam, Zingiber officinale, Murraya koenigii, Terminalia chebula, Tricosanthes dioica

Introduction

Peptic ulcer disease is an imbalance of aggressive gastric luminal factors like acid and pepsin and defensive mucosal barrier function may be environmental and host factors contribute to ulcer formation by increasing gastric acid secretion or weakening the mucosal barrier[1]. Kaidaryadi kashayam is a well known traditional decoction formulation for conditions like ascites diarrhea, peptic ulcer, abdominal pain and indigestion. Kaidaryadi kashayam contain 4 drugs i.e.; Zingiber officinale, Murraya koeinigii, Terminalia chebula and Tricosanthes dioica[2]. For evaluating the properties of the drugs, in vitro and in vivo researches on antiulcerogenic properties are to be conducted. In vitro experiments

usually carried out in wistar albino rats. Pyloric ligation induced gastric ulceration is the common method of inducing ulcers. Ulcer index is the major criteria of evaluation.ie; 10\x where x is the ratio of total area of stomach mucosa and total ulcerated area[3].

Peptic ulcer

A peptic ulcer is a sore on the lining of the stomach or duodenum, the beginning of small intestine. Less commonly, a peptic ulcer may develop just above the stomach in the oesophagus. A peptic ulcer in the stomach is called gastric ulcer. One that occurs in the duodenum is called a duodenal ulcer. People can have both gastric and duodenal ulcers at the same time. They also can develop peptic ulcers more than once in their life time[4].peptic ulcers are very common. Each year in the United States, about half a million people develop approximately a peptic ulcer. The life time risk for developing peptic ulcer is approximately 10%.it had a tremendous effect on morbidity and mortality until the 1st decades of 20th century[5].the annual incidence rates of PUD were 0.10-0.19% for physician diagnosed PUD and 0.0-0.17% hen based on hospitalization data. The 1 year prevalence based on physician diagnosis was 0.12-1.50% and that based on hospitalization data was 0.10-0.19%[6]. The time trends in the epidemiology of peptic ulcer disease (PUD) reflect complex multifactorial etiologies. Peptic ulcers ere rare before the 1800s the prominent form was gastric ulcers in young women. Duodenal ulcers were rare until about 1900 and then became a prevalent condition during the first half of 20th century. However in developed countries the mortality from PUD has dramatically for birth cohorts born after the turn of the 20 Th century[7].

There are different causes for peptic ulcers among which Helicobacter pylori infection is the major one constitutes about 48%.inappropriate use of non steroidal anti inflammatory drugs (NSAIDS) is the second major cause constitutes 24%.also varieties of infections like cytomegalo virus, tuberculosis, crohn's disease, hepatic cirrhosis, chronic renal failure etc may also cause ulcers. Smoking increases the risk of ulcer recurrence and slows healing[8.] H.pylori is present in the gastro duodenal mucosa in most patients with duodenal ulcers, only a minority 10-15% of patients with H.pylori infection develops peptic ulcer disease .H.pylori bacteria adhere to the gastric mucosa. The presence of an outer inflammatory protein and a functional cyto toxin –associated gene island in the bacterial chromosome increases virulence and probably ulcerogenic potential[9].H.pylori infected patients have increased resting and meal stimulated gastrin levels and decreased gastric mucus production and duodenal mucosal bicarbonate secretion, all of which favors ulcer formation[10].NSAIDS are the most common cause of peptic ulcer in patients without H.pylori infection. Topical effects of NSAIDS cause sub mucosal erosions. In addition by inhibiting cyclooxygenase, NSAIDS inhibit the formation of prostaglandins and their protective cyclooxygenase 2 mediated effects[11].

Clinical features of PUD includes burning epigastric pain i.e.; occurs 2-5 hrs after meals or on an empty stomach. Nocturnal pain relieved by food intake and antacids, indigestion, vomiting, loss of appetite, heart burn etc[12].

Management of PUD in Modern pharmacology is based on some principles i.e.; eradication of H.pylori and administration of H2 blocker or proton pump inhibitor which provide acid suppression, healing rates and symptom relief. Mucosal protective drugs also play a key role in the management of PUD. Proton pump inhibitors constitute the promising group of medicines for ulcer therapy in modern pharmacology[13].

Kaidaryadi kashayam

Kaidaryadi kashayam is a well known traditional decoction formulation from the text Chikitsamanjari, a precious gift to the vaidyas in Kerala by an unknown author. The formulation is explained in the context of mahodara (ascites). Ascites is a condition caused by the vitiation of Agni (digestive power).so it can be applied to similar conditions like diarrhea, peptic ulcer, abdominal pain and indigestion. Kaidaryadi kashayam contain 4 drugs i.e.; Zingiber officinale, Murraya koeinigii, Terminalia chebula and Tricosanthes dioica in the ratio of 1:3:4:4[14].

1. Zingiber officinale

Fig. 1: Zingiber officinale.

Zingiber officinale belonging to the family zingiberaceae has been used as a traditional source against gastric disturbances from time immemorial. The ulcer-preventive property of aqueous extract of ginger rhizome is reported. It consists of gingerol group of structurally related poly phenolic compounds known to be the active constituent. It is proved that gingerols inhibit the growth of H.pylori and E.coli. The phenolic compounds gingerol and zingerone play a major role in inhibiting parietal cell H+, K+ ATPase, thereby acting as proton pump inhibitors. Gastric mucin damage was recovered up to 77% and 74% in swim stress and ethanol stress, respectively after ginger rhizome treatment. It also inhibited the growth of *H. pylori* and also possessed reducing power, free radical scavenging ability. DNA protection up to 90% at 0.4 μg was also observed. Compositional analysis favored by determination of the efficacy of individual phenolic acids towards their potential ulcer-preventive ability revealed that between cinnamic (50%) and gallic (46%) phenolic acids, cinnamic acid appear to contribute to better H^+, K^+-ATPase and *Helicobacter pylori* inhibitory activity, while gallic acid contributes significantly to anti-oxidant activity. It is clearly demonstrated that aqueous extract of ginger was able to protect the gastric mucosa from stress-induced mucosal lesions and inhibits gastric acid secretion probably by blocking H^+, K^+-ATPase action, inhibiting growth of *H. pylori* and offering anti-oxidant protection against oxidative stress-induced gastric damage. Phenol fraction is constituted by syringic (38%), gallic (18%) and cinnamic (14%) acids and water extract constituted by cinnamic (48%), p-coumaric (34%) and caffeic (6%) acids as major phenolic acids. Both fractions further exhibited free radical scavenging, inhibition of lipid peroxidation, DNA protection (80% at 4 microgram) and reducing power abilities indicating strong antioxidative properties[15-17].

2. Murraya koenigii

Fig. 2: Murraya koenigii.

Three extracts of Murraya koenigii (L.) Spreng leaves (Rutaceae) exhibited anti ulcer property by cyto protective and anti microbial effect. Phytochemically, leaves of this plant were found to contain various biomolecules such as carbazole alkaloid, volatile oil, glycozoline, xanthotoxin, and sesquiterpine that are effective against various diseases and disorders. All parts of this plant including root, stem, leaves and fruits yielded carbazole alkaloids. Carbazole alkaloids such as mahanimbine, girinimbine, murrayanine, murrayafoline-A, and 3-methlcarbazole were isolated and identified from stem bark and roots of *M. koenigii*. A flucoumarins and a triterpene were isolated from stem bark and roots of *M. koenigii*. Several copolin-a-glucoside and free glucose were also presented in *M. koenigii*. Doses of Murraya Koenigii extract showed significant reduction in ulcer index, free acidity, total acidity and gastric volume but raised PH of gastric Juice as compared to the control groups. It was showing protection index 47.06% and 58.82% at a dose of 200 and 400 mg/kg respectively [18-20].

3. Terminalia chebula

Fig. 3: Terminalia chebula.

Terminalia chebula from family combretaceae is the constituent of triphala which is considered as king of medicine because of its traditional value. Chemical constituents in terminalia chebula are tannins, chebulic acid, glycosides, sugar, triterpenoids, steroids and small quantity of phosphoric acid. Chebulinic acid significantly reduced free acidity (48.82%), total acidity (38.29%) and upregulated mucin secretion by 59.75% respectively. Further, chebulinic acid significantly inhibited H (+) K (+)-ATPase activity in vitro confirming its anti-secretory activity. The methanolic extract of the fruits of terminalia chebula has been reported with potential anti ulcer activity. It acts by boosting up the mucosal defence mechanism and by inhibiting the gastric acid secretion. Water extracts of the black myrobalan at a concentration of 1-2.5 mg/ml inhibited urease activity of H. pylori. The results show that black myrobalan extracts contain a heat stable agent(s) with possible therapeutic potential. Other bacterial species were also inhibited by black myrobalan water extracts[21-23].

4. Tricosanthes dioica

Fig. 4: Tricosanthes dioica.

Phytochemical evaluations of Aqueous and Ethanolic extracts of *Trichosanthes dioica* from the family cucurbitaceae have showed the presence of saponins, triterpenoids, flavanoids &tannins. Early chemical study reveals that in addition to a number of tetra & pentacyclic triterpenes, the toxic bitter principles cucurbitacins may be considered as a taxonomic character of Cucurbitaceae

.Pointed gourd is rich in vitamins and contains magnesium, sodium, potassium, and copper. The seeds of *Trichosanthes dioica* contain a large amount of peptides. The seed extract of *T. dioica* contains 7-oxidihydrokarounidol-3-benzoate as the most predominant component. Two main phytosterols present in *T. dioica* are namely, 24α- ethylcholest-7-enol & 24β-ethylcholest-7-enol 14. The extract significantly increased the pH of gastric acid while at the same time reduced the volume of gastric juice, free and total acidities. Also it showed significant reduction in pepsin activity. Thus *T. dioica* extract significantly reduced the ulcer index in all the models used. The Ethanol/HCl induced ulcer model was used to screen drugs for possible cytoprotective activity and the ability of *T. dioica* extract at dose of 500 mg/kg to reduce Ethanol/HCl induced gastric ulcer partly suggested the involvement of local and nonspecific mechanism called cytoprotection. Cytoprotection may occur due to the capacity of some compounds to induce prostaglandin production, which in turn stimulates mucus and bicarbonate synthesis .Thus, the protection afforded by *T.dioica* extract at dose of 500 mg/kg in Ethanol/HCl model can be linked to decrease in vascular permeability and, in so doing, preventing damage to the capillary endothelium. The ability of *T. dioica* extract (500 mg/kg) to reduce Ethanol/HCl-induced gastric ulcer is further suggested to be attributed to its previously reported anti-inflammatory and antioxidant effects[24-27].

Conclusion

After evaluating the anti ulcerogenic pharmacology of drugs of Kaidaryadi kashayam, it is evident that each drug acts through specific pharmacology. Zingiber officinale contain active ingredients like gingerols and zingerons are inhibiting proton pump and thereby reducing the gastric secretion. They act as anti oxidants helps in the protection of gastric mucosa. Also acts against H.pylori and other organisms. Murraya koenigii contains carbazole alkaloids which acts by cytoprotective and anti microbial properties. It also reduces the acidity of gastric juice. Terminalia chebula contain chebulinic acid which is a known anti secretory agent by inhibiting the proton pump. It also act against H.pylori and reduces the total acidity of the gastric juice. Tricosanthes dioica contain saponins and tannins which reduce pepsin, and act as a strong cytoprotective factor. Surprisingly all these drugs possess hypoglycemic and hepato protective activities which are associated with ulcer pathogenesis.ie; type 2 diabetes mellitus patients are in a risk to develop H.ylori infection. Also hepatic insulin resistance and type 2 DM are inter related[28].so based on the available data we can say Kaidaryadi kashayam is an effective formulation against peptic ulcers especially in the initial period of management of PUD.

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