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Research Article

EVALUATION OF ANTI-ULCEROGENIC POTENTIAL OF *ABUTILON INDICUM*

Sharma Satish Kumar*[1], Sharma Seshasai Marella[2], Saini Vipin[3], Mohapatra Sharmistha[1]
[1]Sunder Deep Pharmacy College, Ghaziabad, UP, India
[2]MJRP University Jaipur, Rajasthan, India
[3]MM University, Ambala, Haryana, India
Email: sks.pharma55@yahoo.in

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ABSTRACT
The present study was undertaken to evaluate the anti-ulcer properties of *Abutilon indicum* (AI). Ethanolic (AIE) and aqueous extracts (AIA) of AI were studied for their ability to inhibit the gastric lesions in pylorus ligation, aspirin and alcohol induced ulcer models in rats. In addition their effects on pH, wall mucus, total acidity and gastric acid output were recorded. The test drugs in the dose of 200 mg/kg were administered twice daily orally at 10:00 h and 16:00 h respectively for five days for gastro protective studies. Ranitidine was used as reference drug. Ethanolic and aqueous extracts of *Abutilon indicum* significantly inhibited the gastric lesions induced by pylorus ligation, aspirin and alcohol. The gastric volume and total acidity were found to be significantly reduced while the gastric pH and mucus contents were found to be increased as compared to control group. The present findings suggest that the antiulcer properties of *Abutilon indicum* may be due to its effect on both offensive and defensive factors. These results support the ethno medical uses of *Abutilon indicum* in the treatment of ulcer.
Key words: *Abutilon indicum,* Ranitidine, gastric volume, pylorus ligation

INTRODUCTION

Peptic ulcer is a serious gastrointestinal disorder that occurs mainly in the stomach and the proximal duodenum. The peptic ulcers are formed due to imbalance between the various aggressive and defensive factors such as acid-pepsin secretion, parietal cell activation, reduction in mucous secretion, mucosal blood flow, cellular regeneration process and endogenous protective agents(prostaglandins and epidermal growth factors)[1] .Other factors that contribute to ulcers include improper dietary habits, excessive ingestion of non-steroidal anti-inflammatory agents, stress and infection by helicobacter pylori[2].The prevention or cure of peptic ulcer is one of the most important challenges confronting medicine now a days, as it is certainly a major human illness affecting nearly 8 to 10% of the global population. A number of drugs are available for the treatment of gastric ulcer, but clinical evaluation has shown incidence of relapses, side effects and drug interactions. Despite the progress in ulcer therapy from vagotomy to anti-cholinergic drugs, histamine H2 antagonist, antacids, proton pump inhibitors and so forth[3],the search for novel molecules has been extended to herbal drugs that offer better protection and decreased relapse. Before the introduction of potent antiulcerogenic agents,i.e. H2-receptor antagonist, proton pump inhibitors, etc., plant remedies were widely employed for th treatment of various symptoms of peptic ulcer. There has been renewed interest in identifying new antiulcer drugs from natural sources. Abutilon indicum (AI), commonly known as Atibala is a small shrub in the Malvaceae family. In traditional medicine, A. indicum is reported to be used to treat ulcers, headaches, gonorrhea, bladder infection, inflammation and hepatic and pulmonary disorders. In traditional medicine, A. indicum is used as a demulcent, aphrodisiac, laxative, diuretic, pulmonary and sedative (leaves). The bark is astringent and diuretic; laxative, expectorant and demulcent (seeds); anti-inflammatory and anthelmintic (plant); analgesic (fixed oil); diuretic and for leprosy (roots) [4]. The leaves can also be used to treat ulcers, headaches, gonorrhea & bladder infection[5].The plant is very much used in Siddha medicines. In fact, the root, bark, flowers, leaves and seeds are all used for medicinal purposes by Tamils. The leaves are used as adjunct to medicines used for pile complaints. The flowers are used to increase semen in men Dr.J. Raamachandran, "Herbs of Siddha Medicines[6].

A methanol extract of A. indicum had some antimicrobial properties. A chemical compound, β-sitosterol, which has been identified as the active ingredient in many medicinal plants, is present in A. indicum and a petroleum ether extract provided larvicidal properties against the mosquito larvae *Culex quinquefasciatus* [7]. Hence the present study was undertaken to evaluate the therapeutic efficacy of Abutilon indicum in the treatment of peptic ulcer.

MATERIALS AND METHODS

Animals

Male / Female Albino rats of Wistar strain weighing 120 – 200gm obtained from the Department of Pharmacy, MJRP, were used for the experiment. The animals were housed in cages under standard lab conditions (12:12 hr light / dark cycles at 25±2˚C, RH 55±10%). They had free access to standard pellet diet and water ad libitum. The animals were acclimatized at least one week prior to experiment. All experiments were approved by Institutional Animal Ethics Committee.

Plant Materials and Extracts

The plant *Abutilon indicum* was obtained from Gwalior, India and was authenticated by the Department of Botany, Ambah Post Graduate College, Jiwaji University, Gwalior, India. The authenticated plant materials were shade dried and powered coarsely. The coarsely powdered drugs were extracted separately in soxhlet apparatus in sufficient volume of redistilled water and ethanolfor 18 hrs. The filtrates were collected and evaporated to dryness on rotary evaporator. The solid masses were collected carefully and weighed. Their

yields were calculated and then stored in sealed (air tight) glass bottles at 4˚C for further experimental work.

Treatment protocol

The animals were divided into four groups of six animals each. Group I served as control and received suspension of 1% CMC in distilled water. Group II received the reference drug ranitidine 50 mg/kg. Group III and IV received 200 mg/kg of ethanolic and aqueous extracts of AI. These were administered orally twice daily at 10:00 and 16:00 h respectively for five days for gastro protective studies[8] by oral route (p.o.).The control group received the equal volume of vehicle only. All the test drugs were suspended in1% CMC and were administered in a volume of 5 ml/kg body weight.

Antiulcer Study

Pylorus ligation induced ulcer

The drugs were administered for a period of five days as described above and the animals were kept for 18h fasting. On day six after 18 h fasting, animals were anaesthetized. The abdomen was opened and pylorus ligation was done without causing any damage to its blood supply [9]. The animals were deprived of both food and water during the post operative period [10]. The animals were sacrificed 4 h after ligation and the stomach was then excised and cut along the greater curvature. The gastric juice was collected in a beaker and the pH was measured with pH meter. The lesions were examined in the glandular portion of the stomach under a dissecting microscope. The maximum length of each lesion was determined and the sum of lengths of all lesions in mm for each stomach was expressed as the ulcer index [11-13].

Gastric secretion study

The gastric juice thus collected was centrifuged for 5 min at 2000 rpm. The volume of supernatant is expressed as ml/100gm body weight and the total acid output was determined by titrating with 0.01N NaOH using phenolphthalein as indicator.

Determination of mucin content

The gastric wall mucus was determined in pylorus ligatured induced ulcer models according to the method of Corne et al[14]. The glandular segments from stomachs were removed, weighed and incubated in tubes containing 1% Alcian blue solution (0.16 M sucrose in 0.05M sodium acetate, pH 5.8) for 2 h. The Alcian blue binding extract was centrifuged (100gm) for 10 min and the absorbency of supernatant was measured at 498nm. The quantity of Alcian blue extracted (µg/gm of glandular tissue) was then calculated.

Aspirin induced ulcerogenesis

Aspirin in the dose of 200 mg/kg b.w. was administered to all the animals on the day of the experiment. The gastroprotective effect of AI was investigated on 18 h fasted animals and the water was given ad libitum. After 4 h the animals were sacrificed [15] and the stomach was then excised and cut along the greater curvature. The gastric juice was collected in a beaker and the pH was measured with pH meter. The ulcers were scored carefully as described under PL-induced ulcers.

Table I: Effect of ethanolic and aqueous extracts of Abutilon indicum on gastric volume, pH, total acidity and mucin content in pylorus ligation induced ulcer model

Group	Dose (mg/kg)	Gastric volume (ml)	pH	Total acidity (meq/l)	Mucin (µg/g of wet gland)
Control	-	6.17±0.49	1.96±0.18	104.41±4.97	190.76±6.60
Ranitidine	50	2.76±0.28***	3.98±0.28***	48.13±1.46***	294.47±13.60***
AIE	200	3.90±0.32**	2.86±0.18**	58.35±2.38***	262.38±11.94***
AIA	200	4.66±0.39**	2.71±0.20*	68.65±4.58***	259.96±10.60***

Values are expressed as mean±SEM, n = 6 in each group. *P< 0.05, **P< 0.01, ** *P< 0.001 when compared with control.
AIE: ethanolic extract of *Abutilon indicum*, AIA: aqueous extract of *Abutilon indicum*

Table II: Effect of ethanolic and aqueous extracts of Abutilon indicum on ulcer index in pylorus ligation induced ulcer model

Group	Dose (mg/kg)	Ulcer index	% Protection
Control	-	29.53±1.98	-
Ranitidine	50	9.42±0.76***	68.10
AIE	200	15.02±0.78***	49.13
AIA	200	17.05±1.02***	42.26

Values are expressed as mean±SEM, n = 6 in each group. *P< 0.05, **P< 0.01, ** *P< 0.001 when compared with control.
AIE: ethanolic extract of *Abutilon indicum*, AIA: aqueous extract of *Abutilon indicum*

Table III: Effect of ethanolic and aqueous extracts of Abutilon indicum on ph and ulcer index in aspirin induced ulcer model

Group	Dose (mg/kg)	pH	Ulcer index	% Protection
Control	-	2.10±0.08	41.35±2.93	
Ranitidine	50	3.71±0.09***	13.67±0.86***	66.94
AIE	200	2.88±0.09***	20.58 ±1.09***	50.22
AIA	200	2.75±0.10***	27.46±1.60***	33.59

Values are expressed as mean±SEM, n = 6 in each group. *P< 0.05, **P< 0.01, ** *P< 0.001 when compared with control.
AIE: ethanolic extract of Abutilon indicum, AIA: aqueous extract of *Abutilon indicum*

Table IV: Effect of ethanolic and aqueous extracts of Abutilon indicum on ph and ulcer index in alcohol induced ulcer model

Group	Dose (mg/kg)	pH	Ulcer index	% Protection
Control	-	2.00±0.09	32.60±2.33	
Ranitidine	50	3.79±0.09***	11.10±0.77***	65.95
AIE	200	2.70±0.10***	18.93±1.23***	41.93
AIA	200	2.60±0.11**	21.50±1.82***	34.04

Values are expressed as mean±SEM, n = 6 in each group. *P< 0.05, **P< 0.01, ** *P< 0.001 when compared with control.
AIE: ethanolic extract of *Abutilon indicum*, AIA: aqueous extract of *Abutilon indicum*

Ethanol induced ulcers

The gastric ulcers were induced in rats by administering ethanol (1ml/200gm, 1h) [16] and the animals were sacrificed by cervical dislocation and the stomach was then excised and cut along the greater curvature. The gastric juice was collected in a beaker and the pH was measured with pH meter. The ulcers were scored carefully and ulcer index was calculated as above.

Statistical analysis

The results were expressed as mean ± SEM. The statistical analysis of data was done by the Student's *t*-test and one-way Analysis of Variance (ANOVA), followed by Dunnet's test. The results were considered statistically significant at $P < 0.05$.

RESULTS

Pylorus ligation induced ulcers

In the present study an attempt has been made to investigate the anti-secretary, anti-ulcer and cytoprotective properties of ethanolic and aqueous extracts of AI (200mg/kg). Pylorus ligation produced an increase in gastric volume as well as total acidity; and a decrease in gastric pH. As shown in table 1, oral administration of the ethanolic and aqueous extracts of AI significantly (P<0.01) reduced the gastric volume; and highly significantly (P<0.001) suppressed the total acidity as compared to control group. The ranitidine treated group highly significantly (P<0.001) reduced the gastric volume as well as total acidity as compared to control group. Oral administration of 200 mg/kg ethanolic and aqueous extracts of *Abutilon indicum* significantly increased the gastric pH. The ranitidine treated group showed the highest pH. The ethanolic and aqueous extracts of AI highly significantly (P<0.001) prevented the depletion of gastric wall mucus induced by pylorus ligation and these effects were comparable with reference drug ranitidine (P<0.001).

As shown in table 2, the reference drug ranitidine highly significantly (P<0.001) blocked the gastric ulceration caused by pylorus ligation. Ethanolic and aqueous extracts of *Abutilon Indicum* also highly significantly prevented the gastric ulceration caused by pylorus ligation. Pre-treatment with Ranitidine, ethanolic and aqueous extracts of AI produced 68.10%, 49.13% and 42.26% inhibition in ulcer index respectively.

Aspirin induced ulcer

As shown in Table 3, the gastric pH of 2.10 produced by aspirin treated group was highly significantly (P<0.001) increased in reference drug (ranitidine) and ethanolic and aqueous extracts of AI treated groups. Ranitidine increased the gastric pH to 3.71, which is highest among all treated groups. The aspirin induced gastric ulcer was highly significantly (P <0.001) inhibited by the ethanolic and aqueous extracts of AI; and ranitidine. The maximum protection against gastric ulcers was produced by ranitidine (66.94%) followed by AIE (50.22%) and AIA (33.59%).

Ethanol induced ulcer

The gastric pH (2.0) observed in ethanol treated group was highly significantly increased by ethanolic and aqueous extracts of AI; and ranitidine. The reference drug ranitidine was found to be most potent among all treated groups in increasing the gastric pH (3.79).Treatment with ethanol produced the gastric ulceration. As shown in Table 4, the ethanol induced gastric ulceration was highly significantly inhibited by the reference drug ranitidine as well as the ethanolic and aqueous extracts of AI. Ranitidine produced 65.95 % decrease in ulcer index as compared to control group. Ethanolic and aqueous extracts of AI produced 41.93 % and 34.04 % inhibition in ulcer index respectively.

DISCUSSION

Although in most of the cases the etiology of ulcer is unknown, it is generally accepted that ulcer results from an imbalance between aggressive factors and the mucosal defensive mechanism [17-18]. To regain the balance, different therapeutic agents including herbal preparations are used to inhibit the gastric acid secretion or to boost the mucosal defence mechanism by increasing the mucus production.

The results of the ant-ulcer study have demonstrated that the ethanolic and aqueous extracts of AI were found to possess significant antiulcer activity against pylorus ligation, aspirin and ethanol induced ulcers in rats.

Pylorus ligation induced ulcers are due to auto-digestion of the gastric mucosa and breakdown of the gastric mucosal barrier [19]. An increase in acid pepsin accumulation due to pylorus obstruction may cause subsequent mucosal digestion [20]. Ethanolic and aqueous extracts of AI decreased ulcer score and provided protection against ulcers. Protection against pylorus ligation induced ulcers also supports the anti-secretary activity shown by the test drugs. The oral administration of the ethanolic and aqueous extracts of AI significantly (P<0.01) reduced the gastric volume; and highly significantly (P<0.001) suppressed the total acidity as compared to control group. Ethanolic and aqueous extracts of *Abutilon indicum* significantly increased the gastric pH and highly significantly (P<0.001) prevented the depletion of gastric wall mucus induced by pylorus ligation and these effects were comparable with reference drug ranitidine (P<0.001). In order to further prove the effectiveness of AI in preventing the gastric ulcer, it was also tested against aspirin and ethanol induced ulcer models. Ethanol and aspirin-induced gastric ulcer models have been widely used for the evaluation of gastroprotective activity. Acute treatment with ethanol increases oxidative stress, DNA damage, xanthine oxidase activity and malondialdehyde levels; and decreases the total glutathione content in gastric mucosal cells [21]. The ethanol induced gastric ulceration was highly significantly inhibited by the reference drug ranitidine as well as the ethanolic and aqueous extract of AI. Aspirin-induced ulcer is mediated through tissue damaging free radicals which are produced from the conversion of hydroperoxyl to hydroxyl fatty acids, which leads to cell destruction [22]. It has been found that oxygen-derived free radicals are implicated in the mechanism of acute and chronic ulceration in the gastric mucosa and scavenging these free radicals can play an appreciable role in healing the ulcer.

Disruption of prostanoid synthesis is another contributing factor for aspirin induced ulcers. Various physical and psychological stresses cause gastric ulcers in human and experimental animals. Aspirin causes mucosal damage by interfering with prostaglandin synthesis, increasing acid secretion and back diffusion of H^+ ions [23]. In stomach prostaglandins play vital protective role by stimulating secretion of HCO_3^- and mucus, maintaining mucosal blood flow and regulating mucosal cell turnover, and repair. Thus the suppression of prostaglandin synthesis by NSAIDs results in increased susceptibility to mucosal injury and gastro duodenal ulceration. It is also shown that ROS (reactive oxygen species) play an important role in pathogenesis of

mucosal damage caused by aspirin besides inhibition of COX enzymes [24]. The present study has shown that ethanolic and aqueous extracts of AI highly significantly reduced aspirin induced ulcers suggesting possible involvement of prostaglandin and mucus.

The present investigation establishes the ulcer protective effect of Abutilon indicum and the cytoprotective effect could be partially due to the flavonoid content of the drug. These results support the ethnomedical uses of Abutilon indicum in the treatment of peptic ulcer.

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