ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES Knowledge to Innovation

Vol 7, Issue 1, 2014

ISSN - 0974-2441

Research Article

GASTROPROTECTIVE EFFECT OF *ABRUS PRECATORIUS* ON ETHANOL-INDUCED AND ASPIRIN + PYLORUS LIGATION-INDUCED PEPTIC ULCER IN RATS

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Received: 29 September 2013, Revised and Accepted: 21 October 2013

ABSTRACT

Objective: The present work deals with investigation of Gastroprotective effect of *Abrus precatorius* on ethanol-induced and aspirin + pylorus ligation-induced peptic ulcer in rats. Methods: In ethanol-induced ulcer, after the pretreatment period of one hour, peptic ulcer was induced with absolute ethanol at a dose of 1 ml/200g (p.o.). Whereas, in aspirin + pylorus ligation-induced peptic ulcer, after the pretreatment with aspirin dose of 200mg/kg for 2 days then ulcer also induced by tight ligation of pylorus portion of stomach.
Results: In ethanol-induced and aspirin + pylorus ligation-induced peptic ulcer in rats models, *Abrus precatorius* (AP) has shown significant decrease in ulcer area and significant increase in the mucosal production and also decreased the level of lipid peroxidase (LPO), and increased the levels of superoxide dismutase (SOD), glutathione (GSH) and catalase (CAT).
Conclusion: The present findings elucidate the therapeutic value of ethanolic extract of leaves of AP in the prevention of experimental peptic ulcer by virtue of its antioxidant, antisecretary and cytoprotective mechanisms.

Keywords: *Abrus precatorius*, ethanol induced ulcer, aspirin + pylorus ligation, antioxidant.

INTRODUCTION

Peptic ulcer is the most common gastrointestinal disorder in clinical practice [1]. Peptic ulcer is a conglomerate of heterogeneous disorders, which manifests itself as a break in the lining of the gastrointestinal mucosa bathed by acid and/or pepsin [2]. The pathophysiology of gastric ulcer has generally focused on imbalance between aggressive and protective factors in the stomach [3].

Chronic alcohol consumption, smoking, stress, usage of non-steroidal anti-inflammatory drugs and *H. pylori* infection have been shown to be the causes of gastric ulcer characterized by inflammation and mucosal bleeding in long-term untreated patients. Excess acid secretion and reduced biosynthesis of prostaglandin (PG) E_2 are important in gastric ulcer formation [4]. Pyloric ligation enhances mucosal damage because it interferes with gastric mucosal resistance and modulates the level of cytoprotective PGs, cytokines, membrane lipid peroxidation (TBARS) and endogenous glutathione [5].

The conventional drugs used in the treatment of gastric ulcer include histamine (H_2) receptor antagonists, proton pump inhibitors, antacids and anticholinergics. However, most of these drugs have undesirable side effects and drug interactions. Although few drugs like sucralfate and prostaglandin analogs are being used as antiulcer substances, they may also have the risk of drug interactions, adverse effects and increased incidence of relapse during ulcer therapy [4]. Herbal drugs obtained from the plant sources are relatively less expensive, safe, and possess good tolerability even in higher doses [6]. Plants extracts, are considered as one of the attractive sources some of the attractive sources of new drug and have shown to produce promising results in treatment of gastric ulcers [7].

Flavonoids display several pharmacological properties in the gastroprotective area, acting as anti-secretary, cytoprotective and antioxidant agents [8]. Oral treatment with the fraction of the flavonoid extract demonstrated a good level of gastric protection [9]. The ethanolic extract of AP leaves showed presence of steroids, saponins, alkaloids, flavonoids and glycoside [10].

AP is belongs to family *fabaceae* [11]. The leaves and roots are sweetish and traditionally used to cure fever and stomatitis [10].

Traditionally, AP is used in the treatment of ulcers [12]. The plant possesses antimicrobial [13], antifertility [14], antiimplantation [15], antibacterial, antifungal [16], antitumor, immunopotentiating [17] and anti-inflammatory activities [18].

The aim of this investigation was to assess the gastroprotective activity of the ethanolic extract of AP leaves in ethanol-induced and aspirin + pylorus ligation-induced peptic ulcer in rats.

MATERIAL AND METHODS

Collection and authentication of plant:

Leaves of AP were purchased in November 2011 from local market of Pune, Maharashtra and were authenticated by Botanical survey of India. (Vocher No: BSI/WRC/Tech/2012).

Preparation of extract:

Dried and coarsely powder of AP leaves (500 g) were defatted with petroleum ether and the remaining marc was extracted successively by 95% ethanol in soxhlet extractor. Solvent was evaporated in rotary evaporator under reduced pressure to produce ethanolic extract of AP leaves [10]. The yield obtained was 7.22% w/w.

Chemicals

All chemicals were purchased from HiMedia Lab. Pvt. Ltd., India and Sigma Aldrich, USA.

Experimental animals

The said animals of either sex were purchased from National Toxicology Center, Pune. Wistar albino rats weighing 150-200g were housed in standard cages at room temperature 22 ± 2 °C and 50±5% relative humidity, under a light/dark cycle of 10/12 h, for one week before the study. Animals were provided with standard rodent pellet diet (Amrut, India), and water *ad libitum*. The animals were deprived of food for 24 hrs before experimentation, but had free access to drinking water. All experiments were performed in the morning. Experimental protocols were approved by our Institutional Ethical Committee which follows guidelines of CPCSEA (198/99/ CPCSEA).

Acute toxicity study

Wistar albino rats of either sex weighing 200-250 gm were used in the study. Acute oral toxicity study was performed as per Organisation for Economic Co-operation and Development (OECD) - 423 guideline. The animals were divided in three groups (n=3) and were fasted overnight prior to drug administration.

Experimental Procedure

Induction of peptic Ulcer in Animal Models

Ethanol-induced peptic ulcer

The rats were divided into six groups of six rats in each group. Pantaprazole and ethanolic extract of AP suspension were prepared in 1% w/v sodium carboxy methyl cellulose in distilled water. Group I served as normal control and received 1% w/v sodium carboxy methyl cellulose alone. Group II served as ulcerated control and also received 1% w/v sodium carboxy methyl cellulose. Group III received Pantaprazole (20mg/kg, p.o.) twice a daily for 5 days. Groups IV, V and VI received ethanolic extract of AP 100, 200 and 400 mg/kg, p.o. respectively, twice a daily for 5 days. On 6th day, gastric ulcers was induced by administering ethanol (1ml/200g, p.o.) in 24 hrs fasted rats from group II to VI. Animals were sacrificed after 1 hr of ethanol administration by cervical dislocation. The stomach and liver of each animal was removed and analyzed for parameters such as ulcer index, gastric wall mucus, antioxidant enzyme level [5].

Aspirin+pylorus ligation-induced gastric ulcer

The rats were divided into six groups of six rats in each group. Group I served as control and received 1% w/v sodium carboxy methyl cellulose alone. Group II served as ulcer control and received Aspirin (200mg/kg, p.o.). Groups III served as standard and received Ranitidine (50mg/kg, p.o.) for 7 days. Groups IV, V & VI served as test group and received ethanolic extract of AP at the dose of 100, 200, 400 mg/kg, p.o. respectively for 7 days. From days 5th to 7th day group II- VI received aspirin (200 mg/kg, p.o) 2 hrs after the administration of respective drug treatment. On 8th day, animals were anaesthetized with ketamine hydrochloride (50 mg/kg i.p) and the abdomen of each animal was opened by small midline incision below the xiphoid process and pylorus portion of stomach was slightly lifted out and ligated. Precaution was taken to avoid traction to the pylorus or damage to its blood supply. The stomach was placed carefully in the abdomen and the wound was sutured by interrupted sutures. Nineteen hours after pylorus ligation the rats were sacrificed and the stomach was removed. The gastric content was collected and centrifuged. The volume, pH, and total acidity of gastric fluid were determined. The stomach was then incised along the greater curvature and observed for ulcers. The number of ulcers was counted using a magnifying glass and the diameter of the ulcers was measured using a vernier caliper [19].

Ulcer score and percentage protection*:* The number of ulcers was counted using a magnifying glass and the diameter of the ulcers was measured using a vernier caliper. Ulcer index was determined by following the scoring method of Suzulki *et al.* (1976) [20]. The ulcer index was expressed as sum of scores given to ulcerative lesions as described below

Score 1: Maximal diameter of 1 mm
Score 2: Maximal diameter of 1-2 mm
Score 3: Maximal diameter of 2-3 mm
Score 4: Maximal diameter of 3-4 mm
Score 5: Maximal diameter of 4-5 mm
Score 10: An ulcer over 5 mm in diameter
Score 25: A perforated ulcer

$$\% \text{ protection} = \frac{\text{UI control} - \text{UI treated}}{\text{UI control}} \times 100$$

Where UI = Ulcer Index

Determination of Gastric Acidity

The junctions between the stomach and the esophagus and the duodenum and pylorus were secured before the stomach was isolated. Then 3 ml of distilled water was introduced into the stomach and the organ was carefully shaken. The gastric juice was then collected and centrifuged for 10 min at 3000 rpm. The supernatant was the taken and diluted 10 times. Following this, a few drops of phenolphthalein was added to the solution. Titration was done using 0.01 M solutions until the color of the test solution changed to light pink, indicating pH 7.0. The volume of sodium hydroxide (NaOH) needed for titration was used in the calculation to derive the hydrogen ion concentration [20]. The total acidity is expressed as mequiv./l using the following formula:

$$n \times 0.01 \times 40 \times 1000$$

Where,

n = volume of NaOH quantified, 40 is the molecular weight of NaOH, 0.01 is normality of NaOH and 1000 is the factor represented in liter.

Volume and pH of gastric juice:

The gastric content of each stomach obtained from the pylorus ligation induced ulcer was drained into a centrifuge tube after an incision with a fine pair of scissors. After the centrifugation of gastric content at 2500 rpm for 20 min at 40^{0}C, the volume of the supernatant (ml) and pH value were measured. The volume was expressed as ml/100g/4hr [21].

Determination of mucin content

The glandular portion was excised and opened down along the lesser curvature of animals from both models. The reverted stomach was soaked for 2 h in 0.1% alcian blue (0.16M sucrose buffered with 0.05M sodium acetate). The uncomplexed dye was removed by two successive washes of 15 and 45 min in 0.25M sucrose solution. The dye complexes with mucus were diluted by immersion in 10 ml of 0.5M magnesium chloride for 2 h. The resulting blue solution was shaken briefly with equal volume of diethyl ether and the optical density of aqueous phase was measured at 605 nm. The mucin content of the sample was determined from the standard curve obtained with different concentrations of mucin [22].

STATISTICAL ANALYSIS

The values expressed as mean ± SEM from six animals. The results were subjected to statistical analysis by using one way ANOVA followed by Dunnett's test to verify the significant difference if any among the groups. $P<0.05$*, $P<0.01$** were considered significant.

RESULTS

Acute toxicity study

No mortality up to seven days after treatment was observed with the ethanolic extract of AP and therefore was found safe up to dose of 2000 mg/kg.

Effect of the ethanolic extract of AP in ethanol induced peptic ulcer

Administration of absolute ethanol (1ml/200g) produced superficial or deep erosions, bleeding and antral ulcers. However, pretreatment with AP extract reduced severity of ethanol-induced peptic ulcer [Figure 1].

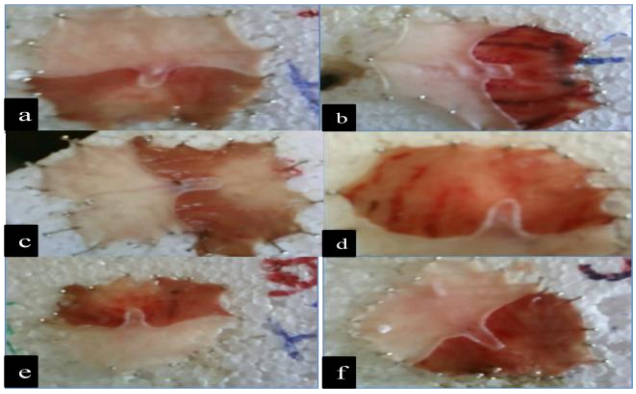

Figure 1: Representative stomachs of rats after ethanol-induced peptic ulcer (a) normal rat (b) ethanol control rat (c) rat pretreated with pantaprazole (20 mg/kg) (d), (e) and (f) Rat pretreated with AP extract (100, 200 and 400 mg/kg respectively).

The gastroprotective effects of 100, 200 and 400 mg/kg doses of AP extract on the ethanol-induced peptic ulcer in various gastric parameters are shown in Table 1. There were remarkable changes in the gastric parameters of AP extract-treated group as compared to ulcerated control. The results indicated that animals treated with the AP extract at the dose of 100mg/kg did not showed any significant decrease in ulcer index and increase in gastric wall mucus as compared to ulcerated control group.

Animals treated with the AP extract at the dose of 200mg/kg showed significant increase in gastric wall mucus and did not show any significant decrease in ulcer index as compared to ulcerated control group.

AP extract at the dose of 400mg/kg treated group showed significant decrease in ulcer index and increase in gastric wall mucus as compared to ulcerated control group. AP extract showed a dose-dependent ulcer inhibition against ethanol-induced ulcers in rats. Maximum inhibition was observed in the pantaprazole-treated group [Table 1].

Table 1: Effect of AP extract on various gastric parameters in ethanol induced peptic ulcers

Groups (n= 6)	Ulcer index	Ulcer percentage protection	Gastric wall mucus (µg Alcian blue/ gm tissue)
Group- I (NC)	1.25 ± 2.22	98.62%	91 ±2.76
Group- II (UC)	91.00 ± 2.55#	-	65.15 ± 2.59#
Group- III (Standard)	9.33 ± 2.10**	89.74%	94.64 ± 2.55**
Group- IV (AP 100)	85.88 ± 2.00	5.63%	76.48 ± 1.98
Group- V (AP 200)	53.22 ± 1.99	41.51%	81.22 ± 3.25*
Group- VI (AP 400)	43.90 ± 1.54**	52.17%	92.17 ± 1.19**

NC- Normal control, UC- Ulcerated control; AP- *Abrus precatorius*

Data was expressed as mean ± SEM, compared with normal control by unpaired t-test (#p< 0.05) and ulcerated control by one-way ANOVA followed by Dunnett's test where Group III, IV, V, VI compared with Group II. (*p<0.05, **p<0.01)

AP extract at the dose of 100mg/kg and 200mg/kg treated group did not showed any significant increase in catalase, glutathione, superoxide dismutase levels and significant decrease in lipid peroxidation level in comparison to ulcerated control group.

AP extract at the dose of 400mg/kg showed significant increase in catalase, glutathione, superoxide dismutase levels and decrease in lipid peroxidation level as compared to ulcerated control group [Table 2].

Table 2: Effect of AP extract on Antioxidant enzyme levels in stomach in ethanol induced peptic ulcers.

Groups (n= 6)	LPO (nmoles MDA/g tissue)	SOD (Units/g tissue)	GSH (µmoles/g tissue)	Catalase (µmoles H_2O_2consumed / g tissue)
Group- I (NC)	9.27 ± 1.90	12.02 ± 0.88	6.65 ± 1.811	6.76 ± 1.00
Group- II (UC)	3.33± 0.66#	5.42 ± 0.12#	20.63 ± 0.74#	1.98± 0.77#
Group- III (Standard)	8.09 ± 1.01**	10.98 ± 0.48**	9.94 ± 0.62**	6.38 ± 1.03**
Group- IV (AP 100)	4.55 ± 0.76	5.41 ± 0.34	17.61 ± 0.41	4.62 ± 0.62
Group- V (AP 200)	5.44 ± 1.60	7.99 ± 0.19	15.30 ± 0.64	5.92 ± 0.60
Group- VI (AP 400)	7.20 ± 1.66*	11.12 ± 0.66**	7.66 ± 0.92*	6.20 ± 1.04*

NC- Normal control, UC- Ulcerated Control; AP- *Abrus precatorius.* GSH- reduced glutathione; LPO- lipid peroxidation; MDA- malonaldehyde; SOD- superoxide dismutase. Data was expressed as mean ± SEM, compared with normal control by unpaired t-test (#p< 0.05) and ulcerated control by one-way ANOVA followed by Dunnett's test where Group III, IV, V, VI compared with Group II. (*p<0.05, **p<0.01)

Effect of AP extract on aspirin + pylorus ligation-induced gastric ulcer in rats

Due to administration of aspirin and pylorus ligation of the stomach for 19 hours resulted in the over secretion and accumulation of gastric acid which in turn leads to autodigestion of gastric mucosa and formation of pointed gastric lesions [Figure 2].

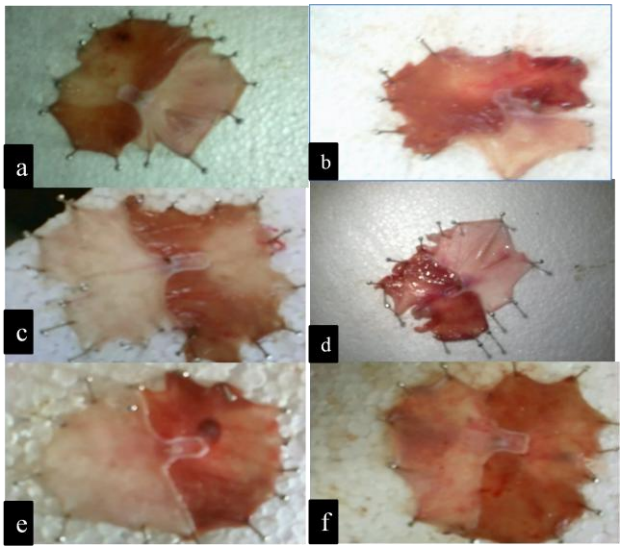

Figure 2: Representative stomachs of rats after aspirin + pylorus ligation-induced peptic ulcer (a) Normal rat (b) Pylorus ligated control rat (c) Rat pretreated with ranitidine (50 mg/kg) (d), (e) and (f) Rat pretreated with AP extract at the dose 100, 200 and 400 mg/kg respectively.

Discernable changes were found in the gastric parameters of AP extract-treated group as compared with the ulcerated control animals [Table 3].

Table 3: Effect of AP extract on basal gastric secretion in aspirin +pylorus-ligated rats

Groups (n= 6)	Ulcer index	Ulcer percentage protection
Group- I (NC)	2.65 ± 0.76	95.45%
Group- II (UC)	58.25 ± 1.17#	-
Group- III (Standard)	17.50 ± 0.99**	69.95%
Group- IV (AP 100)	57.35 ± 1.61	1.54%
Group- V (AP 200)	52.49 ± 1.90*	9.88%
Group- VI (AP 400)	28.05 ± 1.77**	51.85%

NC- Normal control, UC- Ulcerated Control; AP- *Abrus precatorius*

Data was expressed as mean ± SEM, compared with normal control by unpaired t-test (#p< 0.05) and ulcerated control by one-way ANOVA followed by Dunnett's test where Group III, IV, V, VI compared with Group II. (*p<0.05, **p<0.01)

Animals treated with AP extract at the dose of 100mg/kg did not show significant decrease in ulcer index, gastric volume and total acidity as compared to ulcerated control. AP extract at the dose of 100mg/kg as significantly increased pH of gastric juice when compared to ulcerated control group.

Animals treated with AP extract at the dose of 200mg/kg showed significant decrease in ulcer index, gastric volume and total acidity as compared to ulcerated control. Animals treated with AP extract at the dose of 200mg/kg showed significant increase in pH as compared to ulcerated control.

Animals treated with AP extract at the dose of 400mg/kg showed significant increase in pH and showed significant decrease in gastric volume, ulcer index and total acidity as compared to ulcerated control. AP extract showed a dose-dependent ulcer inhibition against ethanol-induced ulcers in rats. Maximum inhibition was observed in the ranitidine-treated group [Table 3].

Animals treated with AP extract at the dose of 100mg/kg did not show significant decrease in peptic activity and increase gastric wall mucus in comparison to ulcerated control group.

AP extract at the dose of 200mg/kg treated group showed significant decrease in peptic activity and significant increase in gastric wall mucus in comparison to ulcerated control group.

AP extract at the dose of 400mg/kg treated group showed significant increases gastric wall mucus and significant decrease in peptic activity in comparison to ulcerated control group [Table 4].

Table 4: Effect of AP extract on various gastric parameters in aspirin +pylorus ligated rats

Groups (n=6)	Gastric wall mucus (µg Alcian blue / gm tissue)	Peptic activity (µmoles Tyrosine / ml)
Group- I (NC)	81.22 ± 1.98	9.98 ± 1.32
Group- II (UC)	70.05 ± 2.44#	21.33 ± 1.63#
Group- III (Standard)	83.12 ± 1.70**	7.175 ± 1.115**
Group- IV (AP 100)	71.24 ± 2.58	19.02 ±1.45
Group- V (AP 200)	77.63 ± 1.65*	15.25 ± 1.16*
Group- VI (AP 400)	80.22 ± 1.52**	10.40 ± 1.5627**

NC- Normal control, UC- Ulcerated Control; AP- *Abrus precatorius*

Data was expressed as mean ± SEM, compared with normal control by unpaired t-test (#p< 0.05) and ulcerated control by one-way ANOVA followed by Dunnett's test where Group III, IV, V, VI compared with Group II. (*p<0.05, **p<0.01)

Animals treated with the ethanolic extract of AP at the dose of 100mg/kg and 200mg/kg did not showed any significant decrease in lipid peroxidation and increase in catalase, glutathione and superoxide dismutase levels as compared to ulcerated control group.

The ethanolic extract of AP at the dose of 400mg/kg treated group showed significant increase glutathione and superoxide dismutase level and significant decrease in Lipid peroxidation level as compared to ulcerated control group. The ethanolic extract of AP at the dose of 400mg/ kg did not show any significant increase in catalase levels as showed in table 5.

Table 5: Effect of the AP extract on Antioxidant enzyme levels in stomach in aspirin + pylorus ligated rats

Groups (n= 6)	LPO (nmoles MDA/g tissue)	SOD (Units/g tissue)	GSH (µmoles/g tissue)	Catalase (µmoles H_2O_2consumed / g tissue)
Group- I (NC)	6.72 ± 1.22	9.05 ± 0.88	5.76 ±1.21	11.27 ± 0.90
Group- II (UC)	17.78 ±1.44#	5.29 ± 0.15#	1.82 ± 1.11#	7.58 ± 0.52#
Group- III (Standard)	7.78 ± 2.2*	8.56 ± 0.72*	5.22 ± 1.04*	10.24 ± 0.29**
Group- IV	17.01 ± 2.18	6.78 ± 0.70	1.94 ± 0.60	8.68 ± 0.66

(AP 100)				
Group- V (AP 200)	15.33 ± 1.08	6.39 ± 0.61	1.99 ± 0.55	8.90 ± 0.61
Group- VI (AP 400)	9.18 ± 2.42*	7.21 ± 0.42*	4.28 ± 0.88*	9.22 ± 0.23

NC- Normal control, UC- Ulcerated Control; AP- *Abrus precatorius.* GSH- reduced glutathione; LPO- lipid peroxidation; MDA- malonaldehyde; SOD- superoxide dismutase. Data was expressed as mean ± SEM, compared with normal control by unpaired t-test (#p< 0.05) and ulcerated control by one-way ANOVA followed by Dunnett's test where Group III, IV, V, VI compared with Group II. (*p<0.05, **p<0.01)

DISCUSSION

Peptic ulcer is a multifactorial disease associated with inflammation, acid induced necrosis, oxidative damage, apoptosis and loss of gastroprotection [23]. The genesis of ethanol-induced gastric lesion is of multifactorial origin with the decrease in gastric mucus amount also it is associated with significant production of free radicals leading to increased lipid peroxidation which inturn causes damage to cell and cell membranes [24]. Ethanol induced gastric lesion formation may be due to stasis in gastric blood flow which contributes to the development of the haemorrhage and necrotic aspects of tissue injury. Thus, due to gastric acid over secretion increases ulcer index [25].

In present study, observed that the AP extract significantly reduced ulcer index. The AP extract showed protection against characteristic lesions produced by ulcer due to ethanol administration. This gastroprotective effect of AP extract may be due to both reductions in gastric acid secretion and gastric cytoprotection which may further contribute in the treatment of peptic ulcers.

Ethanol produces necrotic lesions in the gastric mucosa by reducing the secretion of bicarbonate and production of mucus, increasing vascular permeability and decreasing non-protein sulfhydryl groups of gastric mucosa [26]. Alcohol rapidly penetrates the gastric mucosa apparently causing cell and plasma membrane damage leading to increased intracellular membrane permeability to sodium and water and thus causing gastric mucosa damage [27]. Suppression of prostaglandins synthesis by ethanol results in increase susceptibility of the stomach to mucosal injury and gastro duodenal ulceration [25].

AP extract offered protection against damage of gastric mucosal layer induced by the ethanol may be due to the reinforcement of resistance of the mucosal barrier by a protective coating, decrease in intracellular membrane permeability to sodium and water [22] and also by protecting the mucosa from acid effect by selectively inhibiting prostaglandins synthesis [28].This may further contribute in the treatment of peptic ulcers by providing gastro protection.

Ethanol decreases the CAT, GSH and SOD levels resulting in an accumulation of free radicals causing deleterious effects in the integrity and function of the membrane. Absolute ethanol promoted the depletion of the non-protein sulfhydryl groups and the decrease of the CAT activity in the gastric mucosa. The release of superoxide anion and hydroperoxy free radicals during metabolism of ethanol as oxygen derived free radicals has been found to be involved in the mechanism of acute and chronic ulceration in the gastric mucosa [25].

In stomach homogenate, AP extract showed significant restoration i.e. increased the level of SOD, GSH, and CAT and significantly reduced the lipid peroxidation.

The etiology behind aspirin + pylorus ligation induced ulcer includes increase in the acid secretion, which in turn cause increase in gastric volume, low pH, and increase in free and total acidity resulting into increase in ulcer index. In pyloric ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for induction of ulceration [29].

The AP extract significantly increased the pH of gastric juice and decreased the gastric volume and total acidity when compared with ulcerated control group. The weak basic pH of AP extract, elevate the gastric pH by decreasing acidity and volume of gastric fluid collected from AP extract received rats may be due to down regulating the activity of acid secreting cell. AP extract has also offered protection against ulcer as it decreased the ulcer index significantly. AP extract was able to suppress the gastric damage induced by aggressive factors. Thus, AP extract may provide antisecretary action by giving gastroprotective effect which may further contribute in peptic ulcer.

Aspirin is known to induce gastric damage by suppression of prostaglandins. Oxy radicals may play important role in the aspirin induced erosive gastritis. After an initial hydrophobic intermolecular interaction, the free carboxyl group presents in all NSAIDs forms a strong electrostatic bond with the positively charged head group of zwitter ionic phospholipids of mucus layer and increase the phospholipids solubility and neutralize its surface activity. Thus, NSAIDs topically act on tissue to disrupt the hydrophobic protective lining of the mucus gel layer [25]. Pylorus ligation-induced ulcers are due to accumulation of gastric acid and pepsin which lead to autodigestion of gastric mucosa and breakdown of gastric mucosal barrier. Leakage of plasma proteins into the gastric juice is increases with weakening of the mucosal resistance/barrier of the gastric mucosa which occur by over secretion of gastric acid due to aspirin [26].

In present study, prior administration of AP extract to the group of rats treated with aspirin showed significant increase gastric wall mucus in comparison to ulcerated control group. This may be due to decrease in leakage of protein content into the gastric juice which further strengthening the mucosal barrier and increase in its resistance to the damaging effect of aspirin. Due to increase in gastric acid, pepsin secretion by aspirin and their accumulation in stomach due to pylorus ligation, increases peptic activity. It was observed that AP extract pretreatment has reversed the increased peptic activity by decreasing gastric acid and pepsin secretion associated with aspirin which may further contribute in the treatment of peptic ulcers.

Aspirin+ pylorus ligation induced ulcer is mediated through tissue damaging free radicals, which are produced from the conversion of hydroperoxyl to hydroxy fatty acids, which leads to cell destruction. The hydroperoxyl fatty acids are generated from the degeneration of mast cells and generalized lipid peroxidation accompanying cell damage. Reactive oxygen species are also involved in the pathogenesis of pylorus ligation ulcer [20].

In stomach homogenate, AP extract significantly restored the level of SOD, GSH, and decreased lipid peroxidation. But, it could not restore the decreased catalase level significantly in comparison to ulcerated control [29].

AP extract during preliminary phytochemical investigation showed the presence of flavonoids, alkaloids, tannins and saponins. The antioxidant activity of flavonoids is efficient in trapping superoxide anion, hydroxyl, peroxyl and alcohoxyl radicals [30]. Thus, the presence of flavonoids, tannins, alkaloids and saponins may contribute in gastroprotective effect of AP extract against peptic ulcer induced by ethanol and aspirin + pylorus ligation.

CONCLUSION

The results obtained in the present investigation concluded that the ethanolic extract of AP has shown gastroprotective effect and thus may be used in treatment of peptic ulcer. The gastroprotective effect may be due to its antisecretary, cytoprotective antioxidant activities

and also by the presence of flavonoids, saponins, alkaloids and tannins.

ACKNOWLEDGEMENT

Authors are grateful to Dr. Sohan S. Chitlange, Principal of Pad. Dr. D. Y. Patil Institute of Pharmaceutical Sciences and Research, Pimpri, Pune, M.H., India, for providing laboratory facilities.

CONFLICT-OF-INTEREST

The authors declare that they have no conflict of interest.

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