



ANTI-ULCER ACTIVITY OF JIVAN MIXTURE

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ABSTRACT

The cause of ulceration in patients is mainly due to hyper secretion of gastric juice and many also due to hyper secretion of pepsin. In traditional system of medicine a number of herbal preparations have been used for the treatment of peptic ulcers. Jivan mixture has been used for the treatment of gastrointestinal disorders. Study was performed by using two methods, pyloric ligation and ethanol induced ulcers in rats pretreated with the doses of 1ml/kg (Absolute ethanol), 1mg/kg (Test drug – Jivan mixture), 27mg/kg (Ranitidine -Standard reference drug). Jivan-mixture maintains the integrity of gastric mucosa by virtue of its effect on offensive and defensive gastric mucosal factors. Jivan-mixture significantly ($P < 0.05$) decreased free-acidity, total-acidity, ulcer index and gastric volume and significantly ($P < 0.05$) increased the pH in pylorus ligated model whereas ulcer index significantly ($P < 0.05$) decreased in ethanol induced model. Cyto-protective action is the major mechanism responsible for the present study which cause the generation of prostaglandins promoting inhibition of ulcer, also presence of tannins which having the anti-ulcer property. Our study shows that Jivan mixture has the potential to be used as an anti-ulcer. This further point out the action of Jivan mixture was found to be effective against both the models.

Keywords: Peptic ulcer, Pyloric ligation, Herbal treatment for peptic ulcer, Ethanol induced ulcer, Antiulcer Drugs.

INTRODUCTION

According to the old hypothesis, acid secretion was thought to be the sole cause of ulcer formation and reduction in acid secretion was thought to be the major approach towards therapy. However, in the light of recent evidences this concept has changed. Now, treatment of ulcer mainly targets the potentiation of the defensive system along with lowering of acid secretion.¹

Peptic ulcer disease (PUD) encompassing gastric and duodenal ulcer is the most prevalent gastrointestinal disorder. The pathophysiology of peptic ulcer disease (PUD) involves an imbalance between offensive (acid, pepsin, and *H. pylori*) and defensive factors (mucin, prostaglandin, bicarbonate, nitric oxide and growth factors). An estimated 15,000 deaths occur each year as a consequence of PUD. In India, PUD is common. In the Indian Pharmaceutical industry, antacids and antiulcer drugs share 6.2 billion rupees and occupy 4.3% of the market share.² Today there are two main approaches for treating peptic ulcer. The first deals with reducing the production of gastric acid and the second with re-enforcing gastric mucosal protection. Many herbal drugs are being used for the management of peptic ulcer.³

Ulcer: Local defect on surface of organ produced by inflammation. Common sites are stomach, duodenum and intestinal ulcer in typhoid fever. Peptic ulcer is an ulcer of GIT at an area exposed to acid pepsin mixture. That is the mucosa of GIT in this area is digested by pepsin.⁴

With emphasis so many antiulcer drugs are available in the market like H_2 blockers e.g. Ranitidine, Cimetidine; Anticholinergics, PPIs;⁵⁻⁷ but herbal preparations or drugs

don't have any side effects hence which are beneficial for health than other therapy. With the same respect jivan mixture currently useful for stomachic, carminative and having ingredients like Haritaki which having antisecretory property as per US Patent 6,187,313.⁸⁻¹⁰

MATERIALS AND METHODS

Materials

Standard drug Ranitidine was procured from GSK Nasik, Test drug Jivan mixture procured from local market Nasik, Tophers reagent procured from Research lab Mumbai and other all the chemicals are laboratory grades which was procured from Mahendra chemicals Mumbai.

Apparatus

Centrifuge machine (Remi), pH meter (Max), Dissection box (Camel).

Animals

Albino rats (Wistar strain) of either sex having body weight 225-275gm were used as experimental animals.^{11,12}

Experimental groups

All rats are divided into three groups containing six animals in each group.

Table 1: experimental groups

Group	Treatment	Dose and Routes of administration
1- Control group	Only Ethanol	1 ml/kg, orally
2-Test Group	Jivan Mixture	1 ml/kg, orally
3- Standard Group	Ranitidine	27 mg/kg, orally



The rats were keeping fasting for 24 hrs before the experiment proceeds, also kept in restraining cages to avoid corpophagy.¹³

1) Pyloric ligation induced ulcer

Rats were anaesthetized with the help of anesthetic ether; the abdomen was open by a small incision. Pyloric portion of the stomach was slightly lifted out and ligated according to method of Shey *et al.*, avoiding traction to the pylorus or damage to its blood supply. The Stomach was carefully replaced and abdominal wall was closed by interrupted sutures. Rats were sacrificed by an over dose of anesthetic ether after four hours of pyloric ligation. The abdomen was opened, cardiac end of the stomach was dissected out and contents were drained into glass tube. The inner surface of free stomach was examined for gastric lesion. Centrifuge the contents to get a clear liquid which is titrated with 0.01N NaOH by using Topher's Reagent as an indicator, by using statistical analysis to calculate free acidity and total acidity, also to check its pH.¹³

2) Ethanol induced ulcer

Animals were orally administered with 1 ml absolute Ethanol each and then keep it for 1 hours in a cage, sacrifices it by an over dose of anesthetic ether and their intact stomach were removed and observe the stomachs scores as:^{14, 15}

0 – Normal stomach

1 – Spot ulceration

1.5 – Hemorrhagic streaks

2 – Ulcer ≥ 3 but ≤ 5

Statistical analysis¹⁵

Data of independent observations are represented as the mean+SEM. Statistical analysis was performed using one-way analysis of variance (ANOVA).

Comparisons test (Dunnett test) was used for analysis. $P < 0.05$ was considered as statistically significant.

Calculations

The calculations of free acidity and total acidity were done as follows:

$$\text{Free acidity and Total acidity} = \frac{\text{Normality of NaOH} \times \text{Volume of NaOH} \times 100}{0.1} \text{ meq/L/100gm.}$$

pH was measured by using pH meter.

RESULTS

The pretreatment of rats with Jivan mixture (1ml/kg) produced significant ($P < 0.05$) decreases in ulcer index, free acidity, total acidity and gastric volume. Where as, pH was significantly ($P < 0.05$) increased when compared with control group. (Tables 2-4; figures 1-3).

In case of ethanol induced ulcer pretreatment of rats with Jivan mixture (1mg/kg) produced significant ($P < 0.05$) reduces ulcer index when compared with control group.

Table 2: Effect of Jivan mixture on gastric ulcer Induced by pylorus ligation in rats

Design of treatment	Standard Dose	Volume of gastric secretion (ml)	pH
Control (Ethanol)	1ml/kg	7.8±0.2309	1.87±0.3756
Jivan mixture	1ml/kg	4.9±0.1155*	2.8±0.2309*
Ranitidine	27mg/kg	3.9±0.2818**	3.1±0.1732**

n=6, significantly different from control at $P < 0.05$ (Dunnett's test)

Table 3: Effect of Jivan mixture on gastric ulcer Induced by pylorus ligation in rats

Design of treatment	Standard Dose	Free acidity (mEq/1)	Total acidity (mEq/1)	Ulcer Index
Control (Ethanol)	1ml/kg	19.6±0.05774	54±5.85	5.85±0.2309
Jivan mixture	1ml/kg	10.2±0.04552*	26.4±3.2*	2.4±0.145*
Ranitidine	27mg/kg	8.7±0.05774**	18.3±2.4**	3.2±0.1155**

n=6, significantly different from control at $P < 0.05$ (Dunnett's test)

Table 4: Effect of Jivan mixture on rats by ethanol Induced method

Design of treatment	Ulcer scores
Control (Ethanol)	1.5 (Hemorrhagic streaks)
Ranitidine	0.5 (Red coloration)
Jivan mixture	1 (Spot ulceration)

DISCUSSION

The cause of ulceration in patients is mainly due to hyper secretion of gastric juice and many also due to hyper secretion of pepsin. The result indicates that, in case of pyloric ligation method, the ulcer index, free acidity, total acidity, and volume of gastric juice was significantly ($P < 0.05$) reduced in rats pretreated with Jivan mixture where as pH was found to be significantly ($P < 0.05$) increased in rats which were compared with control group.



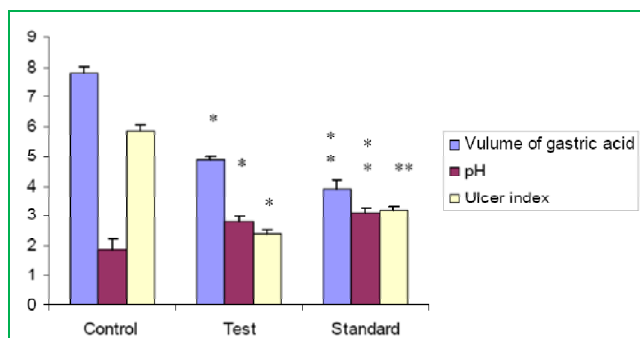


Figure 1: Comparison between 3 groups for Volume of gastric acid, pH and Ulcer index.

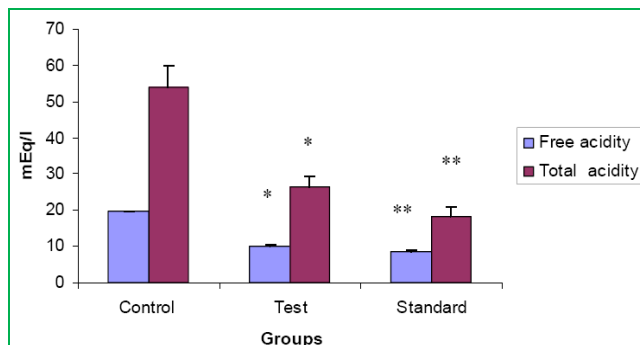


Figure 2: Graph showing comparison between 3 groups for Free and Total acidity.

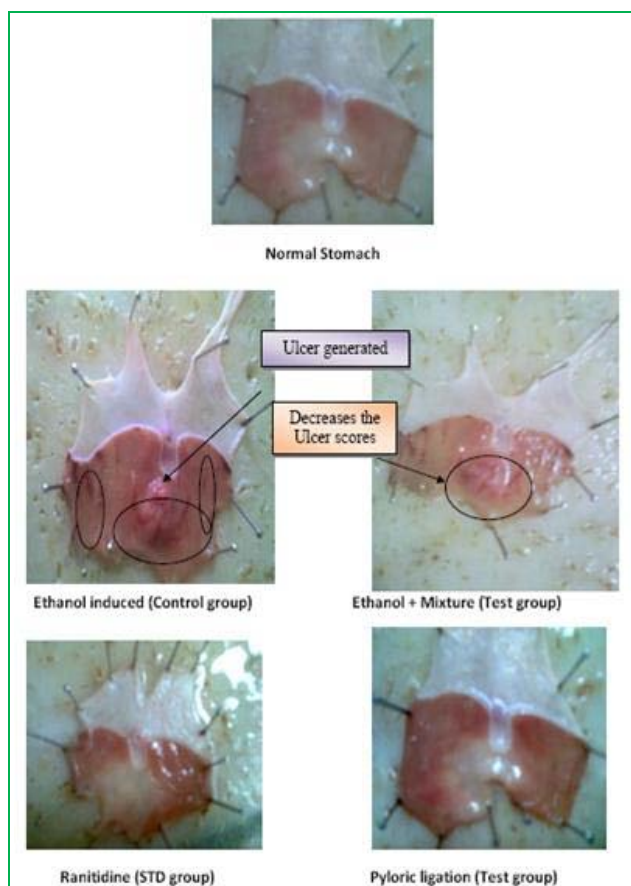


Figure 3: Physical observations of the study samples

which is responsible for anti-ulcer activity. The Jivan mixture significantly reduced the gastric acid secretion in the present study i.e. anti-ulcer effects.

The cyto-protective action which promotes the generation of prostaglandin and causes decreases in secretion of gastric acid, mixture significantly reduced the gastric ulceration in pyloric ligated rats without affecting the gastric secretion or pepsin.

In case of ethanol induced ulcer, the ulcer scores were significantly ($P < 0.05$) decreased in rats pretreated with Jivan mixture which were compared with control group.

The cyto-protective action has been decreases by ethanol, which is due to inhibition of synthesis of endogenous prostaglandin, which promote the formation of ulcer, the protective effect of mixture against ethanol induced ulcer in rats may show the anti-ulcer activity by decreasing the ulcer scores.

The result further point out that, the cyto-protection may be the major mechanism responsible for the anti-ulcer activity of the mixture.

On the other hand Ranitidine, a reference standard drug is H_2 blockers which blocked histamine induced gastric secretion, produced anti-ulcer effect by inhibiting the gastric secretion and decreased in pepsin activity.

The ethanolic extract of leaves of *T. chebula* possesses antioxidant property which could be the linked to its gastro-protective effect of the mixture.

The mixture show the anti-ulcer activity against both models, may be by generating the prostaglandin which causes inhibition of secretion of gastric fluid. Also it contains *Terminalia chebula* (tannins) which having property of protein precipitation and vasoconstrictor effect which could be advantages in preventing ulcer development and strongly suggest that it has potential to be used as a anti-ulcer drug without any side effects. From the above result it can be conclude that, the Jivan mixture was found to be effective against both the models of ulcer.

CONCLUSION

Study of anti-ulcer activity of Jivan mixture was performed by pyloric ligation and ethanol induced ulcer methods. This showed significantly ($P < 0.05$) decreased in ulcer index, volume of gastric content, free acidity and total acidity and pH of gastric content was significantly increased in pyloric ligation induced ulcer method where as significantly ($P < 0.05$) decreased in ulcer scores in ethanol induced ulcer.

However, more experimentation and details study is required for detection of exact mechanism of action.

Cyto-protective action by drugs has been considered to be due to the generation of prostaglandins or blockade of back diffusion of H^+ ions will be the major mechanism

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