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ANTI ULCER ACTIVITY OF ETHANOLIC EXTRACT OF *TANACETUM PARTHENIUM* IN ASPIRIN PLUS PYLORUS LIGATION INDUCED GASTRIC ULCERS IN ALBINO RATS

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ABSTRACT

The aim of the study was to determine anti ulcer activity of Ethanolic extract of *Tanacetum parthenium* (EETP) on pylorus ligation and Aspirin-induced gastric ulcers in Wistar albino rats. The plant extract (200mg/kg and 400 mg/kg) in different doses was subjected for anti ulcer activity, omeprazole (20mg/kg) used as standard for the evaluation of activity. A significant dose dependant reduction in the acid parameters like gastric volume, pH, total acidity, total acid output and ulcer index were observed after treatment with 200 mg, 400 mg/kg *Tanacetum parthenium* extracts in Pylorus ligation plus aspirin induced ulcers. The EETP with 400 mg/kg dose was shown significant anti ulcer activity. The antiulcer activity is determined by the reduction in acid-secretary parameters (total acid and free acid), gastric volume and ulcer index suggesting that acid inhibition accelerates ulcer healing, thereby strengthening of mucosal barrier. EETP with 400 mg/kg shown significant antiulcer activity when compared with control group.

INTRODUCTION:

Ulcers are characterized by sloughing of inflamed dead tissue or superficial loss of tissue. [1] Ulceration caused by the abnormal equilibrium caused by either enhanced aggression or reduced mucosal resistance. There are different types of ulcers, such as mouth ulcer, esophagus ulcer, peptic ulcer, and genital ulcer, among these, peptic ulcer is most common. Bile acids, pepsin, Helicobacter pylori, alcohol, various food constituents and some pharmaceutical drug products are probable cause for ulcers. These agents may play a key role in the pathogenesis of gastric ulcer. These agents usually cause harm by enhancing gastric acid secretion or inhibition of prostaglandin synthesis or by increasing pepsin.[2-4] Various plants used in traditional medicine showed stomach antiulcer activity due to the presence of different phytochemical constituents.[5-7] Feverfew (*Tanacetum parthenium* L.) belonging to the family Asteraceae, is a daisy-like perennial plant found commonly in gardens and along roadsides. The name stems from the Latin word *febrifugia*, "fever reducer." [8-10] Feverfew (*Tanacetum parthenium* L.) has traditionally been used as an HMP for fever, women's ailments, inflammatory conditions, psoriasis, toothache, insect bites, rheumatism, asthma and stomach-ache. During the last decades, it has been increasingly employed as a

remedy for migraine prophylaxis. The plant contains a large number of natural products, including one or more of the sesquiterpene lactones are known to be present as active constituent, including parthenolide. [11] Other constituents include flavonoid glycosides and pinenes. Feverfew has multiple pharmacologic properties, such as anticancer, anti-inflammatory, cardio tonic, antispasmodic, and as an enema for worms.[12] In this study, Omeprazole was used as the reference anti-ulcer drug. It is a proton pump inhibitor which has been widely used as acid inhibitor agent for the treatment of disorders related to gastric acid secretion for about 15 years (Li et al., 2004). The present study was undertaken to evaluate anti-ulcerogenic properties of Ethanolic extract of *Tanacetum parthenium* in rats.

MATERIALS AND METHODS:

Collection of Plant material and extraction: The whole plant of *Tanacetum parthenium was* collected from the village of Manala, Rajanna Siricilla District, situated in the state of Telangana (India) and shade dried and powdered mechanically. The plant specimen was authenticated by botanist of Osmania University and authenticated voucher specimen Number 453 of the plant has been preserved in department for future reference. The dried plant were then milled to coarse powder mechanically and successively extracted with petroleum ether, chloroform, ethyl acetate and Ethanol in Soxhlet's apparatus and method of maceration was allowed for water at a duration of 72 hours. The crude extracts were evaporated to dryness under vacuum and dried in vacuum desiccators. Later Stored in refrigerator. Preliminary phytochemical investigation was performed. Based on the presence of Phyto constituents, Ethanolic extract of *Tanacetum parthenium* was selected for screening the anti-ulcerogenic potential in experimental animals.

Experimental Animals: Wistar albino rats weighing 150-250 gm of either sex were maintained in a 12 hour light/dark cycle at a constant temperature 25ºC with free access to feed and water. All animals were fasted prior to all assays and were allocated to different experimental groups each of 6 rats. Moreover the animals were kept in specially constructed cages to prevent coprophagia during the experiment. All animal experiments were carried out according to CPCSEA guidelines, after getting the approval of the Institutional Animal Ethics Committee Reg .No: CPCSEA/IAEC/JLS/011/11/19/13). Food was provided in the form of dry pellets and water *ad-libitum.*

Experimental methodology: Pylorus ligation model: The rats will be randomly assigned into 4 different groups (n=6). Animals were divided into three groups (n=6). All the animals received 200 mg/kg of aspirin once daily for three days.

Group I : Normal control receiving Distilled water
Group II : Omeprazole (20mg/kg) p.o.
Group III : Ethanolic extract of Tanacetum *parthenium*(EETP) (200mg/kg) p.o
Group IV : Ethanolic extract of Tanacetum *parthenium* (EETP) (400mg/kg) p.o

On the 3rd day, all group rats were fasted 24 h prior to induction of gastric ulcer. Pyloric ligation was done by ligating the pyloric end of the stomach of rats after 1 h of drug administration.[13] Animals were allowed to recover and stabilized in individual cage and were deprived of water during post-operative period. After 4 h of surgery, rats were sacrificed by cervical dislocation and ulcer index were examined on the dissected stomachs as described below. The stomachs were excised and were examined for hemorrhagic lesions in glandular mucosa. After the animals were sacrificed, their stomachs dissected out, and then cut along the greater curvature and the mucosa was rinsed with cold normal saline to remove blood contaminant, if any. The sum of the length (mm) of all lesions for each stomach was used as the ulcer index (UI), and the percentage of inhibition (%I) was calculated

as described by using the following Formula [14]

$$\%I = \frac{(USc - USt)}{USc} \times 100$$

Where USc = ulcer surface area in control and USt = ulcer surface area in treated animals. The gastric juice was titrated against 0.01N sodium hydroxide using Topfer's reagent as indicator to find out the free acidity and total acidity. (Ganguly et al., 1973)

Measurement of mucus production: Gastric mucus production was measured in rats subjected to pylorus ligation. The mucus covering of each stomach was gently scraped using a glass slide and weighed immediately using a digital precision electronic balance.

Estimation of pepsin activity: The centrifuged (5000 g for 10 minutes) gastric juice (0.1 mL) was added to 1 mL bovine albumin (0.5% w/v in 0.01 N HCl; pH 2) and incubated for 20 minutes at 37°C. A duplicate background control tube (gastric juice blank), in which 1 mL albumin was replaced with 1 mL of 0.01 N HCl, was simultaneously run. Hydrolysis was stopped by adding 2 mL of 10% TCA. All of the tubes were heated in boiling water for 5 minutes, then cooled. After denaturation of the proteins by heating in a boiling water bath for 5 minutes, the precipitate was removed by centrifugation (9000 g for 10 minutes). A total of 1 mL of the supernatant was mixed with 0.4 mL of 2.5 N NaOH and ml of the Folin-Ciocalteu reagent and then the volume was adjusted to 10 mL using distilled water. Absorbance was measured at 700 nm. The peptic activity was calculated in terms of micrograms of tyrosine liberated per milliliter of gastric juice. [15]

Statistical analysis: Comparisons between treatment means were performed using the Student's *t*-test. Values in tables are expressed as arithmetic mean±S.E.M.

RESULTS:

In the present study, Ethanolic extracts of *Tanacetum parthenium* have been shown to possess anti ulcer activity against experimentally induced ulcer model (Aspirin + Pylorus ligation Method). Ethanolic extract of *Tanacetum parthenium*, significantly reduced the acid secretary parameters i.e. Total and free acidity as well as the gastric volume and ulcer index suggests that acid inhibition accelerates ulcer healing. The decrease in gastric volume and simultaneous decrease in acidity may be one of the causes of ulcer healing. The significant antiulcer activity (ulcer index, % ulcer inhibition, volume of gastric juice, free acidity, total acidity) of Ethanolic extract of *Tanacetum parthenium* (EETP) at different doses(200mg/kg and 400mg/kg) on aspirin plus pylorus ligation induced gastric ulcers in rats is evaluated using Omeprazole as standard and the results were shown in table1. The results were shown graphically. Ulcer index, % ulcer inhibition, free acidity and total acidity were calculated.

DISCUSSION:

Aspirin causes mucosal damage by interfering with prostaglandin synthesis. Disturbances in gastric juice secretion, damage to gastric mucosa, alteration in permeability, gastric mucus depletion, increase in the pepsin are reported to be the pathogenic effects of aspirin plus pylorus-ligated ulcer. Ulcer index was significantly reduced in plant extracts and Omeprazole treated groups compared to the control treatments. It is evident from results that these plant extracts (200mg/kg and 400mg/kg) causes a reduction in the intensity of gastric ulcerations as observed from the reduced ulcer index in the drug treated groups. The Ulcer index was measured(mean ± SEM) at both doses 200mg/kg and 400mg/kg(Table 1, figure 1), but the dose 400 mg/kg shows closer response to standard drug(Omeprazole) Percentage of ulcer protection of 400 mg/kg is more when compared to 200 mg/kg, but not as standard .

Table 1. Effect of EETP on various parameters in pylorus ligation induced gastric ulcers in rats.

Sl. No	Treatment	Ulcer index (mean ± SEM)	% Ulcer protection	pH of gastric juice	Gastric juice (ml)	Free acidity meq/ltr	Total acidity meq/ltr
1	Control	14.8±0.15	……..	3.1±0.25	8.8	91.61	110.34
2.	Omeprazole(20mg/kg)	2.6±0.06***	82%	5.85±0.05	2.6	35.53	62.61
3.	EETP (200 mg/kg)	3.5±0.04*	76%	3.51±0.13	4.2	45.21	67.45
4.	EETP (400mg/kg)	2.9±0.05**	80%	4.52±0.15	4.1	40.6	64.13

Values are expressed as mean± SEM. Test and standard groups were compared with control group. Statistical comparison was performed using analysis of variance (ANOVA) followed by t-test. $*P < .05$; $**P < .01$; $***P < .001$, when compared with control groups.

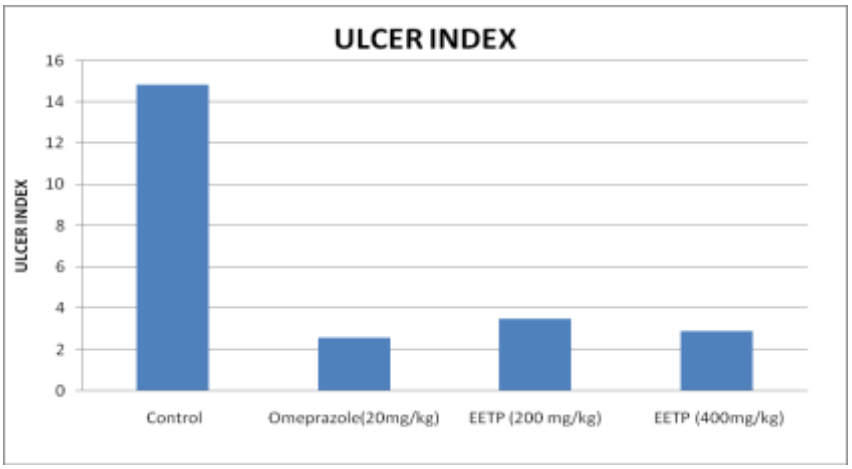

Fig 1. Effect of EETP (200mg/kg and 400mg/kg) on ulcer index in pylorus ligation induced gastric ulcers in rats

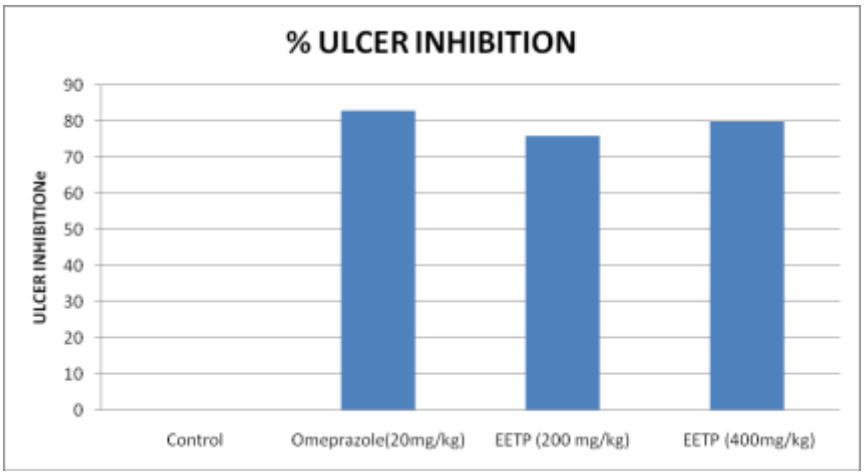

Fig 2. Effect of EETP(200mg/kg and 400mg/kg) on % ulcer inhibition in pylorus ligation induced gastric ulcers in rats

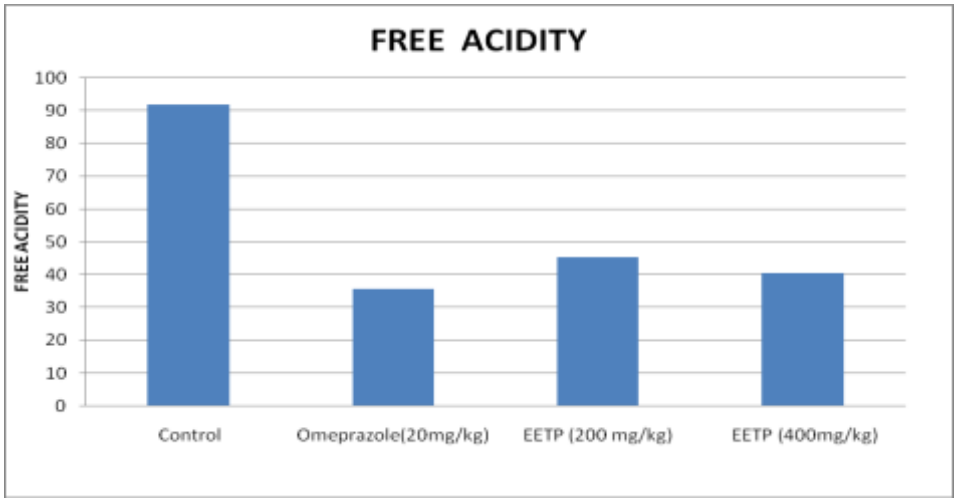

Fig 3. Effect of EETP (200mg/kg and 400mg/kg) on free acidity in pylorus ligation induced gastric ulcers in rats

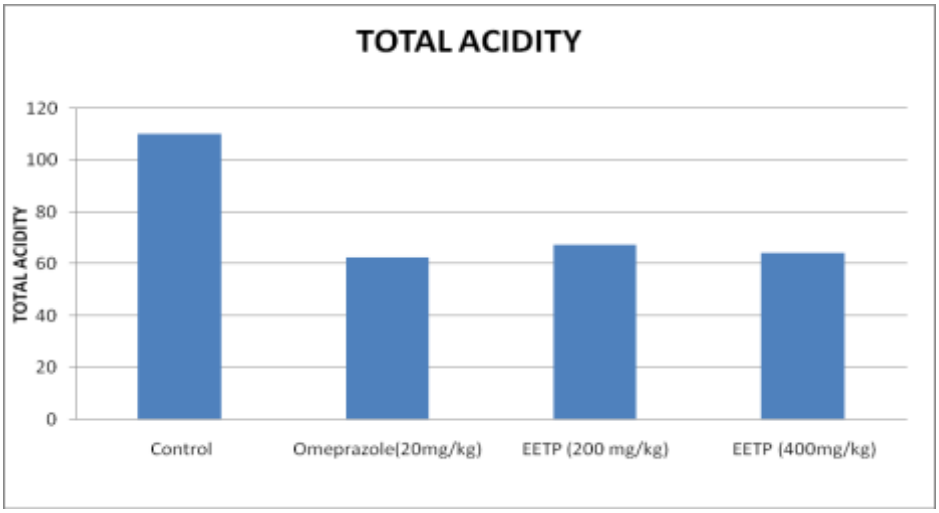

Fig 4 Effect of EETP (200mg/kg and 400mg/kg) on Total acidity in pylorus ligation induced gastric ulcers in rats

Table 2: Effect of EETP (200mg/kg and 400mg/kg) on mucus secretion and pepsin content

Sl. No	Treatment	mucus production(µg)	pepsin content (µ moles of tyrosine/ ml)
1	Control	34.8 0.56	21.63 ± 1.21
2	Omeprazole(20mg/kg)	64.45 0.66***	4.57 ± 1.13***
3	EETP (200 mg/kg)	45.3 0.34*	11.84 ± 1.22*
4	EETP (400mg/kg)	51.31 0.65**	10.72 ± 1.21**

Values are expressed as mean± SEM. Test and standard groups were compared with control group. Statistical comparison was performed using analysis of variance (ANOVA) followed by t-test. $*P < .05$; $**P < .01$; $***P < .001$, when compared with control groups.

Gastric juice was measured and the values were given in Table 1, figure 2. Free acidity, total acidity were also measured in meq/litre, it reveals, the 400mg/kg dose extract shows better activity compared to 200mg/kg dose extract. (Figure 3 and figure 4). Mucus is secreted by the mucus neck cells and coats the gastric mucosa, thereby preventing physical damage and back diffusion of hydrogen ions. The decreased mucus secretion in control rats indicates the decreased ability of the mucosal membrane to protect the mucosa from physical damage and back diffusion of hydrogen ions. Depletion of the gastric wall mucus has been significantly ($P < .001$) prevented by Tanacetum portulacastrum ethanolic fraction (dose dependent manner). depletion in pepsin content of the gastric fluid indicate the cytoprotective effect of Ethanolic extract of *Tanacetum parthenium*.(Table 2). Hence, it can be said that both extracts have anti ulcer activity, but EETP at 400 mg/kg is more potent.

CONCLUSION:

The antiulcer activity of Ethanolic extract of *Tanacetum parthenium* was done at two different doses (200 mg/kg and 400mg/kg) against aspirin plus pylorus ligation induced ulcer in Albino Wistar rats using Omeprazole as standard. Reduction in ulcer index, total acidity,free acidity, increased mucus secretion and depletion in pepsin content of the gastric fluid indicate the cytoprotective effect of Ethanolic extract of *Tanacetum parthenium* , 400mg/kg treated group shown significant anti ulcer activity compared to 200mg/kg treated group.

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