ANTI-ULCER ACTIVITY OF SAARANAIVER CHOORANAM (TRIANTHEMA DECANDRA LINN.,) FOR THE TREATMENT OF PEPTIC ULCER DISEASE (PUD)

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Abstract:

Peptic ulcers are a comprehensive term that includes ulcers of digestive tract in the stomach or duodenum. The formation of peptic ulcers depends on the presence of acid and peptic activity in gastric juices and breakdown in mucosal layers. A number of synthetic drugs are available to treat ulcers. But these drugs are expensive and are likely to produce more side effects when compared with the herbal medicines. The literature revealed that many medicinal plants and poly herbal formulations are used for the treatment of ulcers in gastro intestinal tract .One of the Poly herbal preparation was *Saaranaiver chooranam* mentioned in the Siddha literature the solitary ingredient, root of Trianthema decandra Linn., (*Vellai saaranai-Punarnavi*) which possess an anti-ulcerogenic activity. The present study was performed in pylorus ligation induced ulcer model in Wister rats, in which ability to provide gastric protection was studied at two different doses 200 and 400 mg/kg calculated based on the acute toxicity study. Gastric protection was evaluated by assessing various parameters like gastric volume, pH, total acidity, free acidity, ulcer index and percentage inhibition of ulceration. Ranitidine at 50 mg/kg was used as the standard drug. The test drug, *Saaraanaiver chooranam* (especially at 200mg/kg dose) was found to be equally efficacious with the reference drug, ranitidine (50mg/kg showed significant ($P<0.001$) decrease in the gastric volume, total acidity and free acidity. However, pH of the gastric juice significantly ($P<0.001$) increased at the dose, 400 mg/kg. It also showed a significant ($P<0.001$) decrease in number of ulcers and ulcer score index. In conclusion the anti-ulcer activity is evident from its significant reduction in degree of ulceration. Hence the study represents *Saaraanaiver chooranam* (Trianthema decandra Linn) has good anti-ulcer activity.

Keywords: Peptic Ulcer, Medicinal Plants, *Saaranaiver Chooranam***,** Pylorus Ligation, Anti-Ulcer Activity

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1. INTRODUCTION

A peptic ulcer is defined as disruption of the mucosal integrity of the stomach and/or duodenum leading to a local defect or excavation due to active inflammation. Although burning epigastric pain exacerbated by fasting and improved with meals is a symptom complex associated with peptic ulcer disease (PUD), it is now clear that >90% patients with this symptom complex (dyspepsia) do not have ulcers and that the majority of patients with peptic ulcers may be asymptomatic. Ulcers occur within the stomach and/or duodenum and are often chronic in nature.[1]PUD significantly affects quality of life by impairing overall patient well- being and contributing substantially to work absenteeism. Moreover, an estimated 15,000 deaths per year occur as a consequence of complicated PUD. The financial impact of these common disorders has been substantial, with an estimated burden on direct and indirect health care costs of ~$6 billion per year in the United States, with $3 billion spent on hospitalizations, $2 billion on physician office visits, and $1 billion in decreased productivity and days lost from work.[1]In symptomatic patients, the most common presenting symptoms are epigastric pain, which may be associated with dyspepsia, bloating, abdominal fullness, nausea, and averse to ingest the enough quantity of food because of bloating. These symptoms could be correlated with the disease "*Gunmam*" mentioned in Siddha texts.[2]Plant extracts and their crude are the most significant sources of new drugs, and have been shown to cause promising results in the treatment of gastric ulcer as well.[3,4]

It is known that numerous pharmaceutical agents such as proton pump inhibitors, anticholinergics, antacids, antimicrobial agents, H2-receptor antagonists, sucralfate, and bismuth are not fully effective, and produce numerous adverse effects such as impotence, arrhythmia, hematopoietic alterations, hypersensitivity, and gynecomastia.[3,4]Due to that, investigations of the new pharmacologically active agents through the screening of different plant extracts led to the discovery of effective and safe drugs with gastro-protective activity. Especially, plants with antioxidant capability as the main mechanism are used as the herbal reservoir for the treatment of ulcer disease.[5]Medicinal plants have achieved their therapeutic properties from their capability to produce renewable and various secondary metabolites, which are known as phytochemical constituents. Hence, numerous plants have used these phytochemicals as a protection mechanism against pathogens.[6]One of the vital potent herbal preparation was *Saaranai ver chooranam* mentioned in the Siddha literature the solitary ingredient, root of Trianthema decandra Linn., (*Vellai saaranai-Punarnavi*) which possess an anti-ulcerogenic activity and also easily accessible, reliable and feasible and cost effective than the conventional modern medications and also a potent alternative for their adverse effects.[7]

Henceforth, I preferred the herbal medicine "*Saaranai ver chooranam*" for Anti-ulcer, Anti-secretory and Antacid activities as per authentic siddha literature named ***"Agasthiyar Mani 4000 ennum vaithiya sinthamani venba Muthal pagam"***, Page No-180 indicated for Gunmam.[8]

2. MATERIALS AND METHODS

Preparation of the drug

According to this dissertation, the herbal formulation of **"*SAARANAI VER CHOORANAM*"** was taken as a trail drug for Anti-ulcer, Anti-secretory and Antacid activities has been taken from the Siddha aboriginal literature ***"Agasthiyar Mani 4000 ennum vaithiya sinthamani venba Muthal pagam"***, Page No-180[8]

Ingredients of the drug: *Saaranai ver (*Punarnavi) - *Trianthema decandra Linn.,*

Procurement of raw drug

The raw drug *Saaranai ver* (Trianthema decandra Linn,) was procured from outskirts of Dharmapuri, Tamilnadu, and South India.

Identification authentication

The solitary ingredient T.decandra roots are recognized and certified by the Professionals from Botanist at Government Siddha Medical College, Arumbakkam, and Chennai. The Voucher specimen Trianthema decandra Linn was labelled as 1014/PGG/321912104/GSMC-CH/2019-2022 and deposited to the laboratory of P.G *Gunapadam* department for prospective considerations.

Preparation and purification

The selection, preparation and purification was done as per the verses denoted in *Siddha* classical literature *"Agasthiyar Mani 4000 ennum vaithiya sinthamani venba- Muthal pagam"*, Page No-180.[8]

Purification of saaranai ver[8]

Materials required

1. Cow's milk (Bos taurus)
2. Goat's milk (Capra aegagrus hircus)

The well matured *saaranai* roots were selected cut into pieces and then boiled with cow's milk and goat's milk separately for purification. Repeat this process for about 7 times.

Preparation of the *Saaranai Ver Chooranam (SVC):*

SAARANAI VER - Trianthema decandra

Procedure:

Purified T.decandra roots were taken in anhydrous form pound well and grounded in stone mortar. The powder was sieved through a mesh (80- 100) particle size and kept it in a clean air tight container. It was labelled as "*Saaranai ver chooranam" (SVC).* The contents were examined frequently to evade wetness and microbes

Purification of the chooranam:

***Pittaviyal murai* (Steaming process):**

The *Saaranai ver chooranam (SVC)* was purified by *Pittaviyal* method (steam cooking in milk) as per *Siddha* classical literature. A mud pot was taken and it was half filled by mixture of milk with equal quantity of water. The mouth of the pot was sealed with a cloth. This *chooranam* was placed over the cloth and tied firmly around the mouth of mud pot by another pot. The gap between mud pots was tied with a wet cloth to avoid evaporation. The mud pot was kept on fire and boiled until the cow's milk $^{3}/_{4}$ part reduced in the lower pot. The same drug was later dried and powdered then sieved again. It was used for the further study.

Storage of the drug:

The prepared test drug was stored in a clean, dried, air tight container. The contents were explore frequently to avoid moisture and microbes.

Administration of the drug

Form of the medicine: *Chooranam*
Route of Administration: Enteral route
Dose: 1 to 2 grams twice a day
Vehicle: Ghee or Palm jiggery
Indications: *Gunmam* (Peptic Ulcer Disease)

Evaluation of anti-ulcer activity

Methodology of pylorus-ligated-induced peptic ulcers

Female Wistar Rat (Weight 150-170 gm. and starved for 48 hour having access drinking water) Housed in wide single wire cage, to avoid cannibalism & coprophagy - 10 animals are used as control under anesthesia a midline abdominal incision made Pylorus is ligated care being exercised that neither damage to blood supply nor traction on the pylorus occurs.

Grasping the stomach with instrument is meticulously avoided else ulceration will invariable develop at the same place
The abdominal wall is closed by sutures and the test compound given either orally or injected subcutaneously

Animal is placed in plastic cylinder (44 mm. diameter) which is closed on both side by wire mesh. Animal are sacrificed with CO_2 anesthesia. The abdomen is opened and a ligature is placed around the esophagus close to the diaphragm. The stomach is removed and the contains are drained in centrifuge tube. The stomach is opened and pinned in cork plate. Mucosa is examined with stereo-microscope

Calculation of ulcer index UI = UN + US + UP X 10-1 UI = Ulcer index
UN = Average of number of ulcer per animal
US = Average of severity score
UP = Percentage of animal with ulcer

Pylorus ligated rats
The Antiulcer activity was conducted on shay rat model. Twenty albino rats of either sex (200-400gm) were taken. They were divided into four groups of five rats each group. The animals were fasted for 24 hours before the experiment but had free access to water. After the fasting period, the rats were anaesthetized with light ether. The abdomen was opened and the pyloric end was ligated with a thread. All the samples were given 60 minutes prior to pyloric ligation. The animals were treated as follows.

Group I	Treated with distilled water (1ml/kg, P.0) and was kept as control
Group II	Treated with Ranitidine (50mg/kg, P.O) and was kept as standard.
Group III	Treated with SVC (200mg/kg, P.O)
Group IV	Treated with SVC (400mg/kg, P.O)

Biochemical parameters
After 24 hours of pylorus ligation all the animals were sacrificed. The stomach was excised carefully keeping the esophagus closed. Open along the greater curvature and the luminal contents were removed. The gastric contents were collected in a beaker and centrifuged at 1000 rpm for 10 minutes. The samples were analyzed for gastric volume, pH, free and total acidity. The mucus was flushed with saline and stomach was pinned on a frog board and scored.

Collection of gastric juice
Gastric juice was collected from the pylorus ligated rats. The gastric juice thus collected was centrifuged and the volume of gastric juice (ml) as well as pH of gastric juice was noted. Then the gastric juice was subjected to biochemical estimation.

Determination of pH
A liquor of 1ml of gastric juice was diluted with 1ml of distilled water and PH of the solution was measured using pH meter.

Ulcer score
The gastric mucosa was examined for ulcers by magnifying lens and the ulcer scored according to its comparison with that of standard. Ulcer score was recorded as follows: -

ULCER SCORE

SEVERITY	APPEARANCE
0	Normal colored stomach

0.5	Red coloration
1	Spot ulcers
1.5	Hemorrhagic streaks
2	Ulcers > 3mm but < 5mm
3	Ulcer > 5mm

Mean ulcer score for each animal is expressed as ulcer index. Percentage protection

The percentage protection can be calculated by the using the formula,

Percent protection=100 – Ut / Uc X 100

(or)

Percentage protection = UI = UN +U

(or)

Percentage protection = UI = (C – T) / C

Where, C -Severity score in control rat / T-Severity score in test rat.

Determination of free and total acidity in gastric juice:

One ml of gastric juice was pipetted into a 100 ml conical flask, and add 2 to 3 drops of Topfers reagent and titrated with 0.01N NaoH (which was previously standardized with 0.01 N Oxalic acid) until all traces of the color disappears and the color of the solution was yellowish orange. The volume of alkali added was noted. This volume corresponds to free acidity. Then 2 – 3 drops of phenolphthalein solution were added and titration was continued until a definite red tinge reappears. Again, the total volume of alkali added was noted. This volume corresponds to total acidity.

Acidity was calculated by using following formula:

$$\text{Acidity} = \frac{\text{Volume of NaOH x normality of NaOH x 100}}{0.1} = \text{(mEq /lit)}$$

Histopathological examination

The stomach tissue samples after ulcer scoring were fixed in 10 % buffered formalin and processed with paraffin wax. For histopathological examination, 5 micrometer sections were stained with hematoxylin and eosin. The extend and depth of ulceration and hemorrhage were evaluated**.**

3. RESULT AND DISCUSSION

Anti-ulcer activity [9,10]

Table no: 30 Effect of Saaranaiver Chooranam on Pylorus Ligation induced gastric ulceration

(Gastric volume and acidity).

Groups	**Treatment**	**Dose (mg/kg /p. o)**	**Gastric volume (ml)**	**Free acidity mEq/l**	**Total acidity**	**pH**
Group I	Control	-	4.2±0.012	4.6±0.42	22.3±0.22	2.2±0.12**
Group II	Ranitidine	50	2.4±0.12**	2.9±0.32**	6.8±0.12**	3.9±0.22**

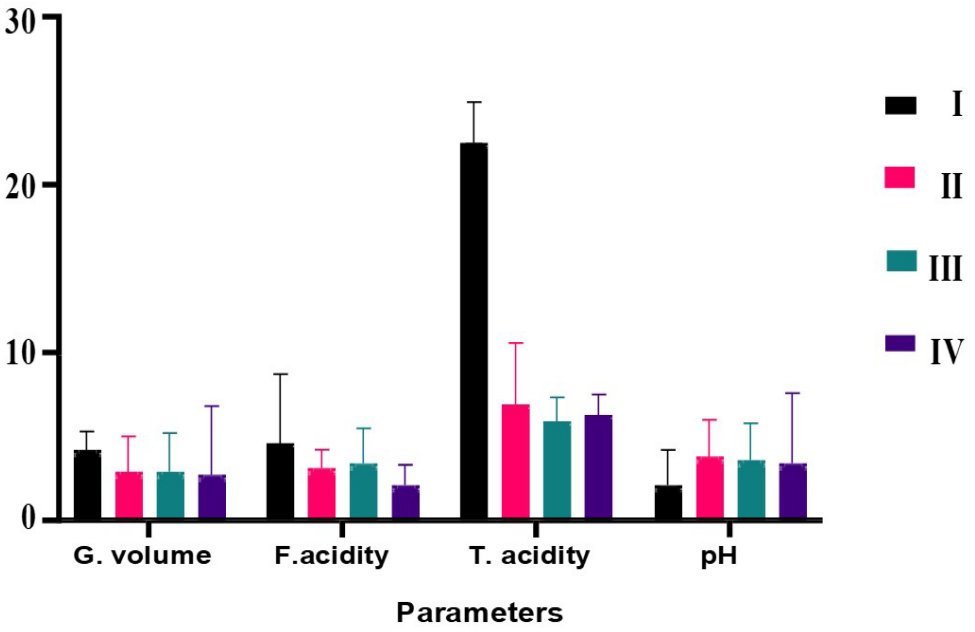
Group III	SVC	200	3.2±0.22**	3.6±0.52**	6.2±0.32**	4.2±0.32**
Group IV	SVC	400	2.5±0.21**	2.6±0.22**	5.8±0.02**	3.4±0.42**

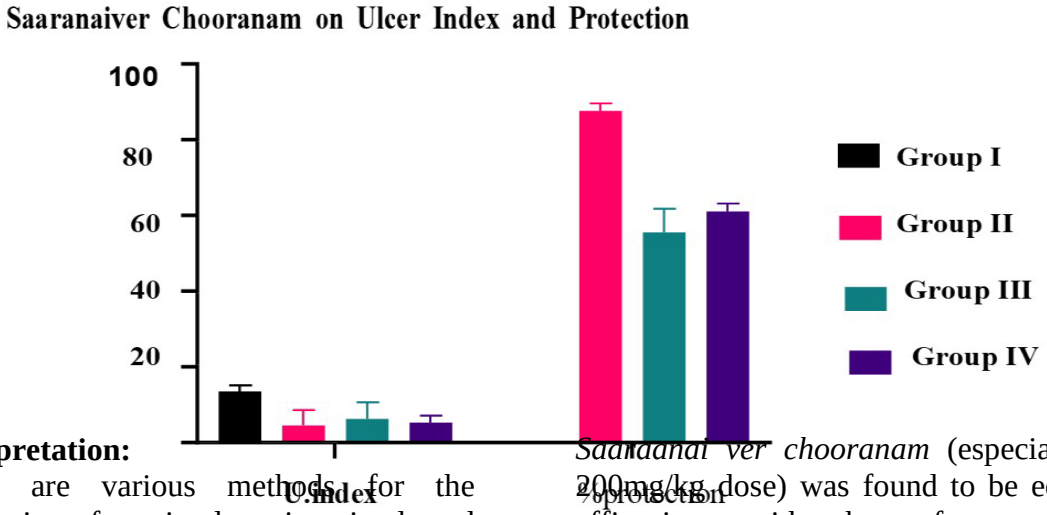
Effect of Saaranaiver Chooranam on Pylorus Ligation induced gastric ulceration

Groups	Treatment	Dose (mg/kg/p. o)	Ulcer index	% protection
Group I	Control	-	13.5 ± 0.16	-
Group II	Ranitidine	50	4.9 ± 1.12**	67.5%
Group III	SVC	200	6.5 ± 1.16***	57.54%
Group IV	SVC	400	4.8 ± 0.22**	65.66%

**P<0.01 ***P<0.001 Vs Control respectively, Values are represented as mean ± S.E.M (n=6). One-way ANOVA followed by Student-t test (P< 0.001)

Table no: 32 Effect of different doses of Saaranai ver Chooranam on Pylorus Ligation induced gastric ulceration ulcer index and protection





Interpretation:

There are various methods for the production of peptic ulcers in animals and pyloric ligation is one of the most commonly used methods.

Pyloric ligation causes accumulation of the gastric juice and hindrance of the gastric blood circulation, which lead to damage of the upper gastrointestinal tract and the formation of ulcers The pyloric ligation of the stomach causes accumulation of gastric acid which leads to development of ulceration in stomach. The fasting of rats for 24 hours followed by ligation of pyloric end of the stomach, the ulcer index is determined 4 hours after pylorus ligation.

The lesions produced by this method are located in the lumen region of the stomach. **In Group I**, Pylorus ligation induced ulcer control rats shown perforated ulcer, deep ulceration of granular epithelium and almost reducing the sub mucosa. **In Group II**, The standard drug Ranitidine 50mg/kg has shown reduced the ulcer volume [66.6%] and it heals the ulcer with few inflammatory cells. **In Group III,** The sample drug SVC 100mg/kg dose has shown mucosal erosion, the partial healing of ulcer with few inflammatory cells [55.56%]. **In Group IV**, the sample drug SVC 200 mg/kg has shown the healed ulcer, normal mucosa and no inflammatory cells [61.11%]. Ranitidine reduced the gastric acid secretion, it reduced the ulcer score and it increased the pH, thus showing an anti-ulcerogenic effect. The test drug, *Saaranai ver chooranam* (especially at 200mg/kg dose) was found to be equally efficacious with the reference drug, ranitidine (50mg/kg).

SVC reduced the ulcer index. The anti-ulcer activity is evident from its significant reduction in degree of ulceration. Hence the study represents SVC has good anti-ulcer activity.

4. CONCLUSION

The SVC was found to be an effective anti-ulcerogenic agent, whose activity can well be compared with that of ranitidine hydrochloride. The results of this study suggest that *Saaranai ver chooranam* causes an inhibitory effect on release of gastric hydrochloric acid and protects gastric mucosal damage.

5. REFERENCES

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