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YASTIMADHU GHRITA-AN EXPERIMENTAL STUDY

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ABSTRACT

Antiulcer activity of Yastimadhu ghrita was evaluated in rats employing pylorus ligated ulcer model to experimental gastric ulcers. Treatment with yastimadhu ghrita provided significant antiulcer activity in pylorus ligated ulcer model. These results suggested that the Yastimadhu ghrita significantly inhibits the gastric acid secretion. It was also observed that it exhibits significantly increased Gastric pH, providing a direct, protective effect on the gastric mucosa.

KEYWORDS: *Anti ulcer activity, Yastimadhu ghrita, Antisecretory activity.*

INTRODUCTION

Acid Peptic disorders are the victim of impaired *Agni.* These disorders are not uncommon because of changed lifestyle of mankind. Acid peptic disorders include Gastritis, Gastric ulcer, duodenal ulcer etc. Acid peptic disorders can be correlated with *pittapradhana vyadhis* like *Amlapitta, Annadravashula, Parinamashoola* where there is dominancy of *Pitta dosha* in *Ayurveda.*

Helicobacter pylori is important etiological factor in peptic ulcer disease accounting for 70% of gastric ulcer 90% duodenal ulcer If these peptic disorders are not treated in time & properly may lead to hematemesis, maleana, perforation of duodenal ulcer.

Sneha kalpanas proves more beneficial as it is having medicinal as well as nutritional values. important one is that it absorbs the maximum fat soluble active principles from the drugs which increases the potency of *sneha kalpanas* specially *ghrita kalpanas.*

The importance of *ghrita* which is having a cardinal quality of enhancing the active principles from the drug into the *ghrita* without leaving its own qualities. This increases the potency of individual *ghrita kalpanas*. *Ghrita* is also having the qualities viz. Antioxidant Lipophilic action etc.

Yastimadhu ghrita which is an *anubhuta yoga* and herbal preparation is taken for experimental study. Yastimadhu is well known drug for treating *pitta pradhana vyadhis* which are correlated with Acid peptic disorders *Pittashamaka* property of *Yastimadhu* is explained in many *nighantus* like *Bhavaprakasha nighantu, Dhanwantari nighantu* etc.

MATERIALS AND METHODS

Yastimadhu Ghrita is planned to neutralise the acid secretion and to cure the ulcers related to Acid peptic disorders where there is a hypersecretion of HCl, may leads to ulcer. In order to evaluate this, studies were conducted on experimental animals to access Antiulcer & Antisecretory effect of *Yastimadhu Ghrita*.

Evaluation of Antisecretory and Antiulcer activity using **Pylorus Ligated Ulcer**

Model[1]

Albino rats of either sex weighing between 150gms – 200gms were taken from D.G.M. Ayurvedic Medical College, Gadag, Karnataka and the whole study was carried out in the experimental laboratory attached with the institute.

Requirements

Animal : Albino Rats (150-200gms, overnight fasted)

Drugs : Anesthetic ether, Ranitidine, NaOH (0.01N), Topfer's reagent
Trial drug -- Yastimadhu Ghrita

Equipments : Dissecting table, Microscope, pH meter, Burette stand, Burette, Beakers, and Surgical equipments.

Selection of Rats

24 healthy Albino rats of either sex weighing 150-200 gms were selected and grouped into four (Group A, Group B, & Group C), Such that each group consisted of 6 rats. They were marked for their individual indentification in different parts of the body namely head, middle of the body, four limbs, and hind limbs, junction between body & tail, and tail were named as per the group respectively.

Group A: Received 1ml of tween 80 by oral route and served as normal Control group.
Group B: Received 27mg/kg body weight of Ranitidine with tween 80 orally and served as Standard group.
Group C: Received 4.32ml/kg body weight of Trial drug *Yastimadhu ghrita* with tween 80 and in warm water orally served as Trial group.

Fixation of Rat Dose: To calculate the Rat dose from Human dose, the formula is
Rate dose = Human dose x surface area factor 0.018 x 5 gives per kg body weight dose.

The human dose is multiplied with the constant 0.018 and multiplied by 5 to get per kg body weight dosage of Rat.

Ranitidine – 27mg/kg body wt
Yastimadhu Ghrita – 4.32 ml / kg body wt.

Procedure: All the animals were fasted for 24 hours before pyloric ligation, but water ad libitum was supplied. However, no water was supplied during the experiment. The test drug Yastimadhu Ghrita, Tween 80 and the standard drug Ranitidine were administered orally. After half an hour under ether anesthesia, the pylorus of the stomach was ligated i.e. the abdomen was opened by a small midline incision below the xiphoid process. Pyloric end was slightly lifted out and ligated avoiding traction to the pylorus or damage to its blood supply closed the abdomen wall by putting the sutures. Cleaned the skin from any blood spots and bleeding. Collodion was applied over the wound. Rats were kept in a separate cage and allowed them to recover. After 4 hours of pyloric ligation sacrified the animals by the over dose of anesthetic ether. Abdomen was opened and oesophageal end (cardiac end) of the stomach was tied. The entire stomach was removed from the body of the animal by cutting it.

A small cut is given to the pyloric region just above the ligation and contents of the stomach were collected in a graduated centrifuge tube.

The stomach was opened along the greater curvature and washed it slowly under the running tap water. The stomach was kept on the slide glass and observed under
10 x magnification for ulcers. All the samples of Stomach were done in the same manner and scoring of ulcers was done as below:
0 = Normal coloured stomach
0.5 = Red colouration

1 = Spot ulcers.

1.5 = Haemorrhagic streaks

2 = Ulcers ≥ 3 but ≤ 5

3 = Ulcers > 5

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

The percentage protection was calculated using the formula

Percentage protection = Ut/Uc x 100

Where Ut = Ulcer index of treated group

Uc = Ulcer index of control group.

In order to calculate the difference between the control and the treatment animals, the results were subjected to ANOVA test.

Methods for Estimation of Volume of Gastric Juice, Free Acidity, Total Acidity and pH

Procedure: After collecting the contents of the stomach in a graduated centrifuge tube as said above, Centrifuge of gastric content was done at 1,000 rpm for 10min, the volume of gastric juice was noted.

One ml of supernatant of gastric juice liquid was pipetted out and diluted with 10ml of distilled water, the pH of this solution was noted with the help of pH meter. Titration of the solution against 0.01N Sodium hydroxide using Topfer's reagent as indicator was carried out to the end point when the solution turns to orange colour. The volume of NaOH was noted which corresponds to the free acidity. Further titration till the solution regains pink colour was carried out the volume of NaOH was noted which corresponds to the total acidity. Acidity (meq/1/100g) can be expressed as.

$$\text{Acidity} = \frac{\text{Volume of NaOH x 0.01 x 100 meq/L/100g}}{0.1}$$

The statistical significance was determined by using ANOVA and 't' test, as Alkaline phosphates not concern with the Anti ulcer activity so it was not estimated.

i) Antiulcer Activity

Table 01: Data of Antiulcer activity.

Group	Body weight (gm)	Treatment	Ulcer Index						Total score	Mean Ulcer Index ± Sem	% Protection
			Normal colour stomach	Red colour stomach	Spot ulcers	Heamorrhagic streaks	Ulcer ≥3 but≤5	Ulcer >5			
A [Control]	160	Tween 80 (1ml)	-	0.5	1	1.5	2.0	-	5	6.30 ± 0.85	0 %
	180		-	0.5	1	1.5	-	3.0	6		
	170		-	0.5	1	1.5	2.0	3.0	8		
	180		-	0.5	1	1.5	2.0	3.0	8		
	150		-	0.5	1	1.5	-	-	3		
	160		-	0.5	1	1.5	2.0	3.0	8		
B [Standard]	170	Ranitidine 27 mg/kg body wt with Tween 80	-	0.5	-	-	-	-	2.0	0.90 ± 0.27	86 %
	150		-	0.5	-	-	-	-	0.5		
	180		-	0.5	-	-	-	-	0.5		
	170		-	0.5	-	-	-	-	0.5		
	170		-	0.5	-	-	-	-	0.5		
	175		-	0.5	1	-	-	-	1.5		
	180		-	0.5	-	-	-	-	0.5		
C [Trial]	175	Yastimadhu ghrita 4.32ml/kg body wt with Tween 80	-	0.5	1	-	-	-	1.5	1.50 □± 0.22	76.19 %
	170		-	0.5	-	-	-	-	0.5		
	180		-	0.5	-	1.5	-	-	2.0		
	160		-	0.5	1	-	-	-	1.5		
	160		-	0.5	-	1.5	-	-	2.0		
	180		-	0.5	1	-	-	-	1.5		

Table 02: Summary of Data of Anti ulcer activity.

Group	No of animals	Mean	SD	SEM	't' value	P value
A (Control)	6	6.3	2.06	0.85	7.41	P < 0.001
B (Standard)	6	0.9	0.66	0.27	3.33	P<0.05
C (Yastimadhu Ghrita)	6	1.5	0.54	0.22	6.80	P < 0.01

Table 03: Anova Test of Anti ulcer Activity.

Group	Treatment	Ulcer Index	% Protection
A	Control with tween 80	6.30± 0.85	0 %
B	Ranitidine with tween 80	0.90± 0.20*	86 %
C	*Yastimadhu Ghrita* with tween 80	1.50± 0.22*	76 %

* = P< 0.001

It is evident from Table No. 03 that the ulcer index and percentage protection in control group A is 6.30 ±0.85 and 0%, Ranitidine (Standard) group B is 0.90 ±0.20 and 86% & *Yastimadhu Ghrita* (Trial) group C is 1.50 ±0.22 and 76%. The results are statistically significant by ANOVA test. When compared with control group, the treatment groups Ranitidine & *Yastimadhu Ghrita* showed more significant by unpaired 't' test.

It follows that, standard group is more significant than *Yastimadhu Ghrita* & *Yastimadhu Ghrita* showed effect on Pylorus ligated ulcer model.

ii. Antisecretory Activity

Table 04: Data of Antisecretory activity.

Group	Body weight (gm)	Treatment	Volume of Gastric juice (in ml)	Volume of Gastric juice (ml/100gm)	Free acidity meq /L/100gm	Total acidity (meq/L/100gm)	pH
A [Control]	160	Tween 80 (1ml)	10.1	5.56	89	177	2.66
	180		10.8	6.0	86	186	3.00
	170		10.2	6.11	91	196	2.81
	180		11.0	6.10	97	195	2.75
	150		11.2	6.09	96	196	3.01
	160		10.2	6.08	97	192	2.8
			10.58 ± 0.197	5.99 ± 1.122	92.66 ± 1.916	190.33 ± 3.09	2.83 ± 0.056
B [Standard]	170	Ranitidine 27 mg/kg body wt with tween 80	4.1	2.41	39	98	5.31
	150		3.6	2.10	42	97	5.1
	180		3.8	2.11	42	86	4.63
	170		4.0	2.05	40	100	5.2
	170		4.4	2.42	42	89	5.6
	175		3.6	2.23	43	101	5.5
			3.916 ± 0.13	2.2 ± 0.06	41.33 ± 0.61	95.16 ± 2.53	5.20 ± 0.141
C [Trial]	175	*Yastimadhu Ghrita* 4.32ml/kg body wt. with tween 80	4.8	2.82	82	100	4.8
	170		5.2	3.15	79	100	5.4
	180		5.3	3.12	80	100	4.6
	160		5.0	3.76	71	102	5.6
	160		5.6	4.00	65	94	5.3
	180		5.1	3.87	68	96	5.3
			5.16 ±0.113	3.453 ±0.196	74.16 ±2.90	102.00 ±3.809	5.16 ±0.157

Table 05: Anova Test of Anti Secretory Activity.

Group	Treatment	Volume of Gastric juice (in ml)	Volume of Gastric juice (ml/100gm)	Free acidity meq/L/100gm	Total acidity meq/L/100gm	pH
A	Control with tween 80	10.58 ± 0.197	5.99 ± 1.122	92.66 ± 1.916	190.33 ± 3.09	2.838± 0.056
B	Ranitidine with tween 80	3.916 ± 0.13	2.20 ± 0.06	41.33 ± 0.61	95.16 ± 2.53	5.20 ±0.141
C	*Yastimadhu Ghrita* with tween 80	5.16 ± 0.113	3.453 ± 0.196	74.16 ± 2.90	102.00 ± 3.809	5.16 ± 0.157

Table 06: Comparison of Percentage decrease in Groups.

Group	Treatment	Decrease in Volume of Gastric juice (inml)	Decrease in Volume of Gastric juice (ml/100gm)	Decrease in Free acidity meq/L/100gm	Decrease in Total acidity meq/L/100gm
A	Control with tween 80	O %	O %	O %	O %
B	Ranitidine with tween 80	62.98 %	63.27%	55.4 %	50 %
C	*Yastimadhu Ghrita* with tween 80	51.22%	42.35%	20%	46.4%

It is evident from Table No.06 that the Volume of Gastric juice (in ml) secreted in Control group A is 10.5±0.197, Ranitidine (Standard) group B is 3.916±0.13, & *Yastimadhu Ghrita* (Trial) Group C is 5.16 ±0.113. The results are statistically significant by ANOVA test. When compared with Control group, the treatment groups Ranitidine, *Pittantaka Yoga* & *Yastimadhu Ghrita* showed more significant by unpaired 't' test

It follows that Standard group is more significant than *Yastimadhu Ghrita* and *Yastimadhu Ghrita* showed equipotent effect in Volume of Gastric juice (in ml).

It is evident from Table No. 05 that the Volume of Gastric juice (in ml/100gms) secreted in Control group A is 5.99±1.22, Ranitidine (Standard) group B is 2.22 ± 0.06 & *Yastimadhu Ghrita* (Trial) Group C is 3.453 ±0.196. The results are statistically significant by ANOVA test. When compared with Control group, the treatment groups Ranitidine & *Yastimadhu Ghrita* showed more significant by unpaired 't' test.

It follows that Standard group is more significant than *Yastimadhu Ghrita* and *Yastimadhu Ghrita* showed effect in Volume of Gastric juice (ml/100gms).

It is evident from Table No. 05 that the Volume of Free acidity (in meq/L/100gms) secreted in Control group A is 92.66±1.916, Ranitidine (Standard) group B is 41.33±0.61 & *Yastimadhu Ghrita* (Trial) Group C is 74.16 ±2.90. The results are statistically significant by ANOVA test. When compared with control group, the treatment groups Ranitidine & *Yastimadhu Ghrita* showed more significant by unpaired 't' test.

It follows that Standard group is more significant than *Yastimadhu Ghrita & Yastimadhu Ghrita* is less significant in Free acidity (meq/L/100gms).

It is evident from Table No. 05 that the Volume of Total acidity (meq/L/100gms) secreted in Control group A is 190.33±3.09, Ranitidine (Standard) group B is 95.16±2.53 & *Yastimadhu Ghrita* (Trial) Group C is 102.00 ±3.809. The results are statistically significant by ANOVA test. When compared with Control group, the treatment groups Ranitidine & *Yastimadhu Ghrita* showed more significant by unpaired 't' test

It follows that all the two groups i.e Ranitidine, and *Yastimadhu Ghrita* showed almost equipotent effect in Total acidity (meq/L/100gms).

It is evident from Table No. 05 that the pH in control group A is 2.838±0.056, Ranitidine (Standard) group B is 5.20±0.141 & *Yastimadhu Ghrita* (Trial) Group C is 5.16 ±0.157. The results are statistically significant by ANOVA test. When compared with Control group, the treatment groups Ranitidine & *Yastimadhu Ghrita* showed more significant by unpaired 't' test.

It follows that all the two groups i.e Ranitidine and *Yastimadhu Ghrita*. showed almost equipotent effect in pH.

It is evident from Table no. 06 that Ranitidine (Standard) Group B showed decrease in Volume of Gastric juice (in ml) by 62.98%, Volume of Gastric juice (ml/100gm) by 63.27%, Free acidity (meq/L/100gms) by 55.4% and Total acidity (meq/L/100gms) by 50%.

Yastimadhu Ghrita (Trial) Group C as shown decrease in Volume of Gastric juice (in ml) by 51.22%, Volume of Gastric juice (ml/100gm) by 42.35%, Free acidity (meq/L/100gms) by 20.00% and Total acidity (meq/L/100gms) by 46.4%.

DISCUSSION

Probable Mode of Action of *Yastimadhu Ghrita*

As *Yastimadhu & Godugdha* are having best *pitta doshahara* property which is the prime cause for Acid peptic disorders & also mitigates *Tridosha*. It helps in reducing the symptoms of Acid peptic disorders.

Yastimadhu & Goghrita are best *vranaropana dravyas* which helps in healing of ulcer (Antiseptic).

Godugdha & Goghrita are acting as Antacid and helps in neutralizing the Acid and also helps in avoiding secretion of Acid & also having *Vatanulamana* property.

Yastimadhu is one of the best drug as Antibacterial which helps to eradicate Helicobacter polyri.

Thus these two formulations will help in treating and reducing the symptoms of Acid peptic disorders.

Modern aspect of Discussion

In 1950 Yastimadhu commonly used as European herbal medicine in Gastric ulcer. Further liqorice derived compound of *Yastimadhu* raise in concetration of prostaglandin in digestive system that promotes mucous secretion from stomach wall as well as it produces few cells in stomach which reduces the concentration of HCl and irritation in the stomach due to secretion of HCl. *Yastimadhu* also increases the life span of surface cells of stomach. By this it will increase the strength of stomach acting as immunomodulator. It also does tha Phagocytic action by secreting INTER LEUCIN-1. This avoids the infection of H. Pylori bacteria which is the main cause for Peptic ulcers. Thus *Yastimadhu* acts as Antiulcer & Antipepsin effect. It is also having Antispasmodic action where there is a pain in epigastric region which is a common symptom in Acid peptic disorders by increasing local blood flow & mucosal fluid transport.[2]

Milk contains rich amount of Ca^{++} ions which helps in neutralizing the Acid & soothens the mucous membrane of stomach.[3]

As *Godugdha & Goghrita* both are coming under the category of lipids. The major part of the lipids consists of natural fats with smaller amounts of phospholipids, steroids & glycolipids.[4]

Ghee is a fat can bond with lipid soluble nutrients & herbs to penetrate the lipid based cells walls of the body. Thus it increases the potency of certain herbs by carrying active components to the interior of cells, which helps to increase immunity and avoids formation of free radicals in the body due to oxidative injury and also improves the digestive power. It contains a butyric acid, a fatty acid which acts as Antibacterial.[5]

As per *Ayurveda Goghrita* is a *Yogavahi***,** an catalyst having the capacity to enhance the qualities from the drugs to which we have added without living its own qualities. Thus it increases the potency of individual *Ghrita kalpana*. In the same manner *Yastimadhu Ghrita* helps in quick action & effective for the Acid peptic disorders.

By the above explanation it can be inferred that the formulations *Pittantaka Yoga* & *Yastimadhu Ghrita* can effectively combat all the factors in the causation of the Acid peptic disorders.

DISCUSSION ON RESULTS

The Ulcer index in Control, Ranitidine & *Yastimadhu Ghrita* is 6.3 ± 0.85 and 1.5 ± 0.22. The Results are statistically significant by Student's 't' test. From the above results, when compared with Ranitidine, *Yastimadhu Ghrita* showed almost equipotent effect on Pylorus ligation induced ulcer model.

Ranitidine showed decrease in the Volume of Gastric juice by 3.916 ± 0.13, Free acidity 41.33 ± 0.61 and Total acidity 95.16 ± 2.53 when compared to Control which are statistically significant, while *Yastimadhu Ghrita* showed decrease in volume of Gastric Juice 5.16 ± 0.113, Free acidity 74.16 ± 2.90 and Total acidity 102.00 ± 3.809 which are statistically significant when compared to Control group. But in pH, there is a significant difference observed between Ranitidine, *Yastimadhu Ghrita* and Control animals.

In Pyloric ligation model, the significant reduction in basal Gastric secretion and complete inhibition of ulcers by *Yastimadhu Ghrita* after pylorus ligation suggest that the

Cytoprotective. Gastric acid is an important factor for the genesis of ulceration of Pylorus ligation ulcer in rats. Gastric acid secretion is regulated by many factors including anxietic effect in the CNS, Vagal activity, Cholinergic, Histaminergic and Gastrinergic neurotransmissions, the activities of various post-synaptic receptors and the proton pump. It is therefore difficult to elucidate the relationship between the mechanism of inhibitions of Gastric acid by *Yastimadhu Ghrita*. The current data clearly demonstrated that *Yastimadhu Ghrita* inhibited the aggressive factors, Gastric acid Secretion.

The Anti-ulcer *Yastimadhu Ghrita* was supported by the decrease in the aggressive factors like basal Gastric acid Secretion, Total acidity and increase in defensive factors like pH. However the Mechanism of its Ulcer healing activity needs to be explored experimentally. Further Clinical studies may help in extrapolating the result of present study to human beings.

CONCLUSION

1. *Yastimadhu ghrita* selected for the study was found to be effective as Gastric anti ulcerative & anti secretary. This has been proved here experimentally on selected Albino rats.
2. It can be concluded from the results of present study that *Yastimadhu ghrita* significantly inhibits the gastric acid secretion. It was also observed that it exhibits significantly increased Gastric pH in pylorus ligated model.
3. *Yastimadhu ghrita* has significantly reduces ulcer index in pylorus ligated model which is a positive sign for the Antiulcer activity.
4. Summarizing the above, it is concluded that Yastimadhu ghrita is having a significant effect as Gastric antiulcer & antisecretory activity.

REFRENCES

1. S.K. Kulkarni, Hand book of experimental Pharmacology, Chapter 3. Pharmacology of Gastrointestinal Tract, Experiment 3.13, 1st edition, New-Delhi, Vallabh prakashan, 1990.
2. Dr. M. Sabin's, Chemistry & Pharmacology of Ayurvedic Medicinal plants, First edition, Published by Choukamba Bharati, Varanasi, 2006.
3. www.ncbi.nlm.gov – R.K. Marton.
4. S.Ramakrishnan, Medical Biochemistry, Second edition, Published by Orient Longman Ltd, Madras, 1994; 11.
5. www.vedaliving.com.