

Evaluation of gastric motility of *Phyllanthus emblica* and *Asparagus racemosus* in cold stress induced gastric damage

Shirish Joshi¹, Snehalata Vijayanand Gajbhiye^{1*}, Urmila Thatte²

¹Department of Pharmacology, and Therapeutics, ²Department of Clinical Pharmacology, Seth GS Medical College and KEM Hospital, Mumbai, India

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***Correspondence to:**

Dr. Snehalata Vijayanand Gajbhiye,

Email: dr.ssborkar@gmail.com

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ABSTRACT

Background: Gastric emptying is known to be delayed in gastritis and gastric ulcer. *Phyllanthus emblica* and *Asparagus racemosus* are known to be gastroprotective. The objective of the study is to evaluate the effects of *Phyllanthus emblica* and *Asparagus racemosus* on gastric motility per se and by using the cold stress model of gastric damage.

Methods: 84 wistar rats were used and divided into 7 groups. Different extracts of *Phyllanthus emblica* was administered to rats. Other groups received distilled water (control), *Asparagus racemosus* and ranitidine. All rats were given a test meal of methyl cellulose (1.5%) mixed with phenol red (50 mg/100 ml) orally and gastric emptying was measured 20 minutes later.

Results: Gastric emptying was found to be 58.00 ± 8.36 in normal rats (group I). None of the study drugs had any per se effect on gastric motility. Cold stress significantly reduced the gastric emptying 35.33 ± 5.46 ($p < 0.05$). *Phyllanthus emblica* and *Asparagus racemosus* showed increase in gastric motility 82.66 ± 6.43 (*Phyllanthus emblica* hot water extract) and 68.50 ± 4.54 respectively which was statistically significant ($p < 0.01$). Ranitidine also showed statistically significant increase in gastric motility 70.00 ± 5.40 ($p < 0.01$).

Conclusions: *Phyllanthus emblica* and *Asparagus racemosus* have gastric motility enhancing effect and this could be one of the mechanisms of decrease in gastric erosions.

Keywords: Ayurveda, Gastric motility, Phenol red

INTRODUCTION

Phyllanthus emblica (syn. *Emblica officinalis*), commonly known as Indian gooseberry or amla, family euphorbiaceae, is an important herbal drug used in ayurvedic systems of medicine. The clinical uses of *Phyllanthus emblica* have been listed for various disorders in ayurvedic systems of medicine. Various plant parts show antidiabetic, hypolipidemic, antibacterial, antioxidant, antiulcerogenic, hepatoprotective, gastroprotective, and chemopreventive properties.¹

P. emblica has been shown to possess anti-inflammatory effects.^{2,3} As the current anti-inflammatory agents are known to possess GI related adverse effects, agents which have gastro protective effects are required. In a

study published by Bandyopadhyay SK and Shirish SS et al *Phyllanthus emblica* has shown to have protective effect on gastric ulcer.^{4,5}

Another such agent, *Asparagus racemosus* (*A. racemosus*) belongs to family liliaceae and commonly known as Shatawari. It has been used for a variety of disorders including nervous disorders, dyspepsia, diarrhoea, dysentery, tumors, inflammations, hyperdipsia, neuropathy, hepatopathy, cough, bronchitis, hyperacidity and certain infectious diseases.⁶ Also *Asparagus racemosus* has been found to be an effective antiulcerogenic agent, whose activity can well be compared with that of ranitidine hydrochloride.⁷ It heals duodenal ulcers and may have cytoprotective action similar action to that of prostaglandin.⁸

An important property that contributes to gastritis is the rate of gastric emptying. It is known that the gastric emptying is delayed in gastritis, which can be significantly correlated with increased severity of histologic gastritis.⁹ Cold stress markedly reduces gastric emptying which may be the reason for the gastric erosions produced by this model.¹⁰ Thus, it was of interest to examine whether the gastro-protection offered by the test drugs is related to its effect on gastric motility. Hence, we planned to conduct this study with the objective of studying the effects of *Phyllanthus emblica* and *Asparagus racemosus* on gastric motility per se and by using the cold stress model of gastric damage.

METHODS

Animals and husbandry conditions

A total of 84 wistar rats of either sex weighing between 200-250 gms were used for the study. The rats were kept fasting for a period of 24 hours, prior to the day of experimentation with free access to drinking water up to the beginning of the experiment. Standard ethical guidelines were followed during the study.

Study drugs

Four different formulations of *Phyllanthus emblica*, namely dry powder (PEDP), hot water extract (PEHWE), cold water extract (PECWE) and incinerated powder (PEIP) were administered orally in the dose of 270 mg/kg.

Methods of preparation of formulations of Phyllanthus emblica

These were prepared as mentioned below.

Dry powder

Dried fruits were ground to get a fine powder which was then passed through # 100 mesh.

Hot water extract

25 gms of dried powder fruit were taken in a clean glass flask to which 250 ml of distilled water was added. The solution was boiled for 2 minutes, cooled and filtered to get a clear solution. The filtrate was then autoclaved at 1200° C for 15 minutes, cooled and dispensed in sterile 10 ml vials under aseptic conditions.

Cold water extract

10 gms of dried powdered fruit were taken in a clean glass powdered flask to which 100 ml of distilled water was added. The solution was sonicated for 1 hour and kept overnight. On the next day, the solution was filtered to get a clear solution and dispensed in sterile 10 ml vials under aseptic conditions.

Incinerated powder commercially available fruits were taken in a clean earthenware pot. The pot was closed with lid and sealed with mud. Sealed pot was kept in a muffled furnace at 200±5°C. After exactly 2 hours, pot was removed and cooled to room temperature. Seal was then opened and charred mass was ground to uniformly fine powder.

Methods of preparation of formulations of Asparagus racemosus

The dried root was obtained and identified using pharmacognostic methods. It was powdered and suspended in water. A decoction was prepared by boiling and the unfiltered decoction was administered orally to rats in the dose of 270 mg/kg.

Procedure

Effects of Indian medicinal plants on gastric emptying without stress.

One group of 42 rats was used. These were further subdivided into 7 groups of 6 rats each. Test drugs were administered for a period of 7 days prior to motility study. No cold stress was given after drug treatment and % gastric emptying was determined by carrying out gastric motility studies.¹¹

Preparation of the meal

Methyl cellulose was dispersed in water at 80°C at a final concentration of 1.5% under continuous stirring. The solution was allowed to cool at 37 °C and phenol red as a non- absorbable marker was added.

Rats were kept fasting for period of 24 hours prior to motility study. 1.5 ml of freshly prepared meal of methylcellulose containing phenol red as a marker (50 mg/100 ml) was administered orally to the rats. One animal from each group was sacrificed immediately following the test meal. This animal served as standard control for each group. Twenty minutes later all other rats were sacrificed by cervical dislocation. Their stomach were dissected out and rinsed in 0.9% saline. The stomachs were then placed in 100 ml of 0.5% NaOH, cut into small pieces and homogenised. The suspension was allowed to settle for 60 minutes at room temperature and 5 ml of supernatant was added to 0.5 ml of trichloroacetic acid (20%). After centrifugation of 2800 rpm for twenty minutes the supernatant was added to 4 ml 0.5 N NaOH and absorbance of the sample was read at wavelength of 560 nm with spectrophotometer.

% gastric emptying (GE) was then calculated as follows

$$\text{Mean} = \frac{\text{Amount of phenol red recovered from the test stomach}}{\text{Average amount of phenol red recovered from standard Stomachs}} \times 100$$

Stomachs

Effects of Indian medicinal plants on gastric emptying in rats subjected to cold stress.

The second group of 42 rats were kept fasting for 24 hours. These were further subdivided into 7 groups and administered the test drugs as mentioned in Table 1. Cold stress of 4°C for 4 hours was given 24 hours after administration of test drugs and % GE was estimated as described above.

Table 1: Drug treatment and distribution of groups.

Groups	Drugs	Dose (mg/kg)	Phase	No. of rats	Duration of treatment (days)
1	D/W	270	A	6	7
			B	6	1
2	PEDP	270	A	6	7
			B	6	1
3	PEHWE	270	A	6	7
			B	6	1
4	PECWE	270	A	6	7
			B	6	1
5	PEIP	270	A	6	7
			B	6	1
6	RAN	27	A	6	7
			B	6	1
7	AR	270	A	6	7
			B	6	1

Key- D/W-Distilled Water, PEDP- Phyllanthus Emblica Dry Powder, PEHWE- Phyllanthus Emblica Hot Water Extract, PECWE- Phyllanthus Emblica Cold Water Extract, PEIP- Phyllanthus Emblica Incinerated Powder, RAN- Ranitidine and AR-Asparagus Racemosus.

Statistical analysis

The data is represented as mean±SD. Unpaired t test and ANOVA with post hoc tukey test is used to analyse the data generated. p<0.05 will be considered significant.

RESULTS

Part A

The % gastric emptying (%GE) of rats from group 1 who were administered distilled water for period of 7 consecutive days was found to be 58.00±8.36. The % GE for drug treated groups was 64.16±17.29, 58.33±5.95, 50.00±7.56 and 64.50±16.15 in rats treated with PEDP, PEHWE, PECWE and PEIP respectively. The % gastric emptying of rats administered Ranitidine was 58.00±19.51. % GE shown by AR was 76.66±5.88, which was significantly greater than the control group. None of the *Phyllanthus emblica* groups showed significant gastric motility changes as compared to control group and ranitidine (p>0.05).

Part B

Cold stress significantly reduced gastric emptying in the rats administered distilled water to 35.33±5.46%. Treatment of all formulations of *Phyllanthus emblica* and *Asparagus racemosus* reversed the stress induced decrease in gastric emptying. Rats receiving PEHWE showed highest improvement in % gastric emptying. All test groups showed improvement in % gastric emptying time which was found to be statistically significant as compared to control group. Group administered ranitidine also showed improvement in % gastric emptying. Details of the study are as shown in Table 2.

Table 2: Effect of study drugs on percentage gastric emptying (mean±SD).

Groups	Drugs	No stress	Cold stress
1	D/W	58.00±8.36.	35.33±5.46 [@]
2	PEDP	64.16± 17.29	66.00±3.22**
3	PEHWE	58.33± 5.95	82.66±6.43**
4	PECWE	50.00±7.56	77.03±3.74**
5	PEIP	64.50±16.15	60.00±9.31**
6	RAN	58.00±19.51	70.00±5.40**
7	AR	76.66±5.88*	78.50±4.54**

*-p<0.05 vs control group, **-p<0.01 vs control group, @ - p<0.05 vs no stress D/W group; Key- D/W-Distilled Water, PEDP- Phyllanthus Emblica Dry Powder, PEHWE- Phyllanthus Emblica Hot Water Extract, PECWE- Phyllanthus Emblica Cold Water Extract, PEIP- Phyllanthus Emblica Incinerated Powder, RAN- Ranitidine and AR-Asparagus Racemosus; Statistical tests - Unpaired t test and ANOVA with post hoc Tukey test.

DISCUSSION

The results of our study show that there was no effect per se of *Phyllanthus emblica* on gastric emptying when the rats were not exposed to stress. However, *Asparagus racemosus* showed an increase in gastric emptying in animals not exposed to stress. The reduction in gastric emptying induced by cold stress was significantly reversed by the study drugs *Phyllanthus emblica* and AR. The ability of *Phyllanthus emblica* and *Asparagus racemosus* to reverse the stress induced suppression of gastric motility may be one of the reasons for its cytoprotective effect on gastric erosions. As gastric emptying which is delayed in gastritis, is significantly correlated with increased severity of gastritis.

The other effects of *Phyllanthus emblica* which are responsible for its protection against gastric erosions can be explained by its effects on inducing PGE(2) synthesis and augmenting e-NOS/i-NOS ratio.¹² Also, *A. racemosus* has shown to heal duodenal ulcers without inhibiting acid secretion which indicates that it may have cytoprotective action similar to that of prostaglandin.⁸

The effect of increase in gastric motility by *Phyllanthus emblica* and *Asparagus racemosus* can also be explained by its effect on prostaglandin. Though the role of prostaglandin is complex, it is known that in the proximal stomach prostaglandins promote tonic contraction and

gastric emptying.¹³ Also *A. racemosus* is known to act as a galactagogue and is known to be to be anti-dopaminergic which explains its prokinetic effect in animals that were not exposed to stress.¹⁴ The study done by Dalvi SS et al also confirms the prokinetic effects of *A. racemosus*. In this study Oral administration of powdered dried root of *A. racemosus* has been found to promote gastric emptying in healthy volunteers. The delayed gastric emptying may play a role in etiology of gastric ulcer.¹⁵ On the other hand, very rapid gastric emptying with gastric acid hypersecretion may be important in the pathogenesis of duodenal ulcer.¹⁵

The cold stress model is a well-known model that causes gastric erosions and is known to reduce gastric motility. Hypothermia and possibly other factors induced by cold-restraint stress results in depressed gastric motility.¹⁶ Since the purpose of the study was to understand the effect of the drugs on stress induced decrease in gastric motility, cold stress model was chosen. Ranitidine was used in the study as it is a known antiulcer agent and its effect on gastric motility could be compared to the test drugs. Our finding of ranitidine's effect on increase in gastric motility is in confirmation with study conducted by Scarpignato C et al.¹⁷

CONCLUSION

Thus we conclude that *Phyllanthus emblica* and *Asparagus racemosus* have gastric motility enhancing effect and this could be one of the mechanisms of decrease in gastric erosions.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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