

## Effect of Rice-Based Solution on Intestinal Water Movement and Motility: Studies in a Model of Prostaglandins-Induced Secretory Diarrhea and the Myoenteric Plexus Preparation

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**Abstract:** Rice-based solution was studied for its antidiarrheal potencies. Two experiments were conducted to test its antisecretory and antimotility properties on intestine. In experiment 1, studies in a model of prostaglandins-induced secretory diarrhea in rat jejunum and colon have been performed to verify the antisecretory effect of a rice-based solution. When administered intraluminally, rice water reduced dose dependently the prostaglandin E1-induced net fluid secretion in both intestinal segments. In experiment 2, rice water was tested for its potency as inhibitor of electrically-evoked contractions of the myenteric plexus-longitudinal muscle preparation of guinea-pig small intestine. Aqueous rice extract exerts a myorelaxant effect, it decreases twitch heights of the intestinal strip by acting either on the mucosal or the serosal side. This effect seems to be mediated by an intramural modulatory influence on smooth muscle excitability.

**Key words:** Rice, diarrhea, water movement, myorelaxation

### INTRODUCTION

Many major diarrheal states usually result from chemical actions that cause the intestinal mucosa to secrete fluid and electrolytes into the lumen of the bowel until secretory volume exceeds absorptive capacity. The net accumulation of fluid in the lumen produces unformed or watery feces and rapid loss of body weight. The antidiarrheal properties of rice water were widely admitted. Rice water had been proposed in the management of acute diarrhea in infants<sup>[1]</sup> and in adult patients with severe cholera<sup>[2]</sup> It had been shown that clinical outcomes improve when rice water is incorporated into oral rehydration therapy for patients with secretory diarrhea.

In animals, the protective effects of diet based on cooked white rice against post weaning diarrhea in piglets was confirmed<sup>[3,4]</sup>. Mathews *et al.*<sup>[5]</sup> proposed that a factor purified from boiled rice blocks the secretory response of intestinal crypt cells to cyclic-AMP. The target of this rice inhibitor factor is the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) chloride channel.

However, the effect of an antidiarrheal on gastrointestinal propulsion is partly due to a decrease in intestinal hypersecretion and partly due to a decrease in intestinal hyperperistalsis<sup>[6]</sup>.

As part of an ongoing effort to evaluate the antidiarrheal potentials of rice water, we studied the

antisecretory and the antimotility properties of an aqueous extract from boiled rice in rodents. The antisecretory effect of the rice solution was tested in a prostaglandins-induced secretory diarrhea model<sup>[7]</sup>. Both small intestine and colon were used to investigate water movement since they have been shown to be target organs of the antisecretory effect of drugs with antidiarrheal property<sup>[8]</sup>. The antimotility activity of rice water was tested for its inhibitory effect on electrically-evoked contractions of longitudinal muscle of Guinea Pig Ileum (GPI)<sup>[9]</sup>.

### MATERIALS AND METHODS

**Preparation of rice-based solution:** Rice from commercial source (40g) was boiled in 400 mL phosphate buffer saline 0.45 M, pH 7.4, NaCl 0.1M. Rice water was obtained by draining rice after cooking for 30min. Solution was centrifuged 20000 g for 5 min and supernatant was aliquoted and stored at -20°C. Dry matter was estimated after incubation at 90°C for 48 h. Along the text we express rice water quantization as mg dry matter.

**Preparation of animals:** Experiments were performed on female wistar rats weighing 180-220 g. Animals were deprived of food for 24 h before experiments, but had free

access to water. Following anaesthesia, with urethane (50 mg 100 g<sup>-1</sup> of body weight i.p), the abdomen was opened. A catheter was placed in the jejunum about 8-12 cm distal to the pylorus and fixed by ligation. The second ligation was made about 8 -12 cm distal to the first.

A second catheter was placed in the ascending colon before ligation within 0.5 cm distal to the caecum. The cannulated segments were flushed three times with warm tyrode solution and returned to the abdominal cavity. Thirty minutes after the preparation, tyrode solution was instilled into the jejunal loop (1.5 to 2 mL) and the colonic lumen (0.5 to 1 mL).

**Administration of substances:** Misoprostol (15-Desoxy-(16RS)-16-hydroxy-16-methylprostaglandin-E<sub>1</sub> methyl ester), a synthetic analogue of prostaglandin-E<sub>1</sub> (32 ng min), or 0.9% NaCl was infused intra-arterially into a branch of the mesenteric artery (0.9 mL h) using a peristaltic pump (minipuls 2-Gilson-France). Preliminary experiments showed that infusion of PGE-1 analogue affected fluid transfer both in the jejunum and the colon but the infusion of 0.9% NaCl solution did not cause any changes in water movements. Rice-based solution was given intraluminally by adding various volumes to the tyrode solution with which the jejunal or colonic loops were filled. Concentrations of the rice extract were given in mg dry matter per mL of tyrode solution.

**Determination of net fluid transfer:** Net fluid transfer rates were determined gravimetrically 30 min after the introduction of tyrode solution, according to the procedure described by Bubbler and Badhri<sup>[7]</sup>. At the end of the experiments, the intestinal segments were stripped from the mesentery and their weight determined. In order to compare transport rates in segments that varied somewhat in length, the volumes transported were expressed as  $\Delta V$  in mL 30 min<sup>-1</sup> g<sup>-1</sup> wet weight of the jejunum or the colon. Positive values indicate net absorption and negative values indicate net secretion.

**Intestinal motility:** The tissue was mounted in a 10 mL organ bath. All measurements were done at 37°C in Krebs solution aerated with 95%O<sub>2</sub>-5%CO<sub>2</sub>. The composition of the Krebs solution was 118 mM NaCl; 4.75 mM KCl; 2.54 mM CaCl<sub>2</sub>·2H<sub>2</sub>O; 1.19 mM MgSO<sub>4</sub>·7H<sub>2</sub>O; 25 mM NaHCO<sub>3</sub>; 0.93 mM KH<sub>2</sub>PO<sub>4</sub>; 11 mM D+ Glucose; 0.027 mM EDTA. In the GPI assay, a length of about 5 cm was used after discarding the 5 cm nearest the ileo-caecal junction and removing any food residue. Since addition of tested substances in the organ bath solicits the serosal side of the intestinal tissue, strip of GPI was mounted in a configuration which allowed the introduction of tested

samples into the luminal side by mean of a tube attached to its upper end. The contractions of the longitudinal muscle were induced by coaxial electric stimulation. The tissue was stimulated by single shocks with a pulse width of 0.1 to 1 m sec delivered at a frequency of 0.1 Hz. The voltage was adjusted initially to give a maximal response (40 to 100 volts)<sup>[10,11]</sup>. Rice water was tested for an inhibitory effect on the electrically induced contractions of organ preparation.

## RESULTS

Fluid was absorbed in all control rats receiving intra arterially infusion of NaCl 0.9%. The infusion of PGE1-synthetic analogue (32ng min) significantly reversed fluid absorption into net fluid secretion in both jejunal and colonic segments. Rice water administered intraluminally, doesn't affect net absorption in jejunum and colon of controls. Nevertheless, the secretory effect induced by PGE1-synthetic analogue was dose dependently and significantly reduced by rice water in both intestinal segments (Fig.1 and 2).

Furthermore, rice water produced decreases in the amplitude of evoked contractions of the myenteric plexus preparation of the guinea pig ileum. Figure 3 shows the time course for inhibition of the evoked twitch response of the GPI bioassay caused by rice-based solution (560 mg dry matter) both on serosal and mucosal sides of intestinal tissue. The rate of onset of inhibition was more pronounced when rice water is introduced into the organ bath and acts on the serosal side of the mounted intestinal strip. The degree of inhibition reaches a plateau more quickly. At the same concentration, the onset of action of rice water introduced intraluminally was slower and reaches a plateau within a few minutes.

## DISCUSSION

Although diarrhea was attributed primarily to a disordered motility, it is generally recognized that abnormalities, in the intestinal transport of electrolytes and water, play an important role in the pathology of diarrhea<sup>[12]</sup>. In this regard, experiments were achieved to study the effects of rice-based solution on fluid transport across the intestinal mucosa *in vivo* and its antipropulsive activity *in vitro*. The antisecretory effects of rice water were tested on intestinal fluid secretion induced by prostaglandins in the jejunum and the colon of rats. Rice water administered intraluminally and dose dependently, reduced misoprostol-induced net fluid secretion in the jejunum and the ascending colon. This prostaglandin E1-

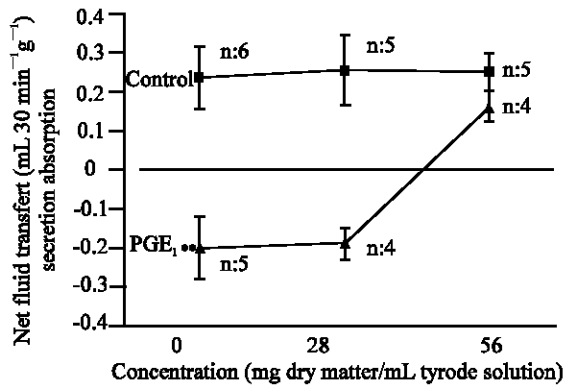


Fig 1: Effect of rice water on PGE<sub>1</sub>-induced net fluid secretion in the jejunum of rat and in controls. Each point represents the Mean  $\pm$  SEM. n refers to number of experiments. \*\* p<0.01 compared with control

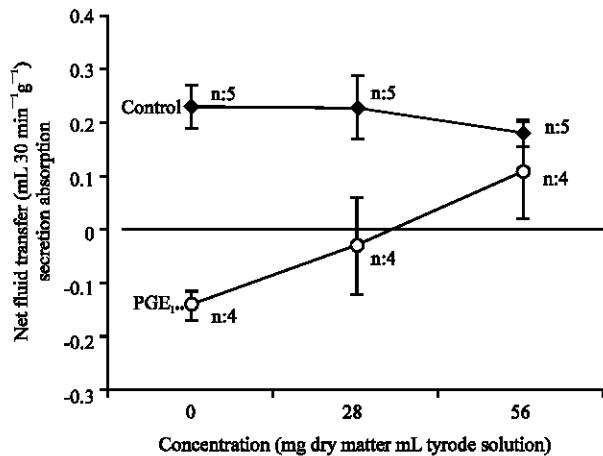


Fig 2: Effect of rice water on PGE<sub>1</sub>-induced net fluid secretion in the ascending colon of rat and in controls. n refers to number of experiments. Each point represents the Mean  $\pm$  SEM \*\* p<0.01 compared with control

synthetic analogue appears to cause less pronounced net fluid secretion in the colon and rice-based solution seems to be more potent in inhibiting the prostaglandin effect on this intestinal segment.

In order to investigate further the antipropulsive effect of rice water and its contribution to antidiarrheal activity, guinea pig ileum bioassay was used. The results obtained in the present study demonstrate that rice-based solution can produce a myorelaxant effect of the electrically-evoked twitch response of the longitudinal myenteric muscle. Since configuration of intestinal strip in the organ bath exhibited its serosal side, the observed effects induced by rice solution on this side suppose that active components act after delivery from the blood

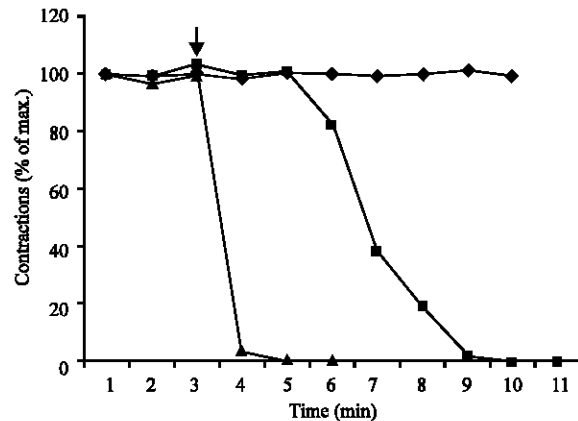


Fig 3: Time course of the inhibitory effect of rice water on electrically-evoked contractions of the myenteric plexus-longitudinal muscle preparation of guinea-pig ileum. Arrow indicates rice water administration. The symbols represent %inhibition of the twitch response caused by 560mg dry matter on (?) serosal and (l) mucosal side of the intestinal strip. (♦) = control

stream. Then, experimental model was modified so that it could be possible to introduce the tested solution into the luminal side and to check whether rice water could exert its myorelaxant effect via mucosa. Results showed an inhibitory effect of the electrically-evoked contractions of the ileal strip caused by the rice water on both serosal and mucosal sides. The observed difference in the rates of onset of inhibition could be probably explained by an intramural modulatory influence on smooth muscle excitability.

## CONCLUSION

Present data strengthen the physiological potencies associated with rice. Both antimotility potential of rice-based solution and its antisecretory effects may play an important role in its antidiarrheal action.

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