

# Marjoram Increases Basal Gastric Acid and Pepsin Secretions in Rat

Fatemeh Nabavizadeh Rafsanjani<sup>1\*</sup>, Mehrdad Shahrani<sup>2</sup>, Zakieh Vahedian Ardakani<sup>3</sup> and Mohammad Vahedian Ardakani<sup>3</sup>

<sup>1</sup>Department of Physiology, Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup>Shahr Kord University of Medical Sciences, Shahr kord, Iran

<sup>3</sup>Tehran University of Medical Sciences, Tehran, Iran

Considering the high consumption rate of marjoram in the Iranian population, this study was designed to investigate the effects of marjoram extract on gastric acid and pepsin secretion. In this study, Wistar rats ( $n = 12$ ) were divided into two equal case and control groups. Under general anaesthesia with 50 mg/kg i.p. sodium thiopental, laparotomy was done and a cannula inserted in the duodenum. In the case animals marjoram (12.5 mg/kg) was injected into the stomach through the mentioned cannula. The gastric contents were collected by the wash-out technique. Acid and pepsin secretions were then measured by titration and the Anson method, respectively. In the marjoram group, basal acid and pepsin secretions were significantly increased compared with the control group (acid:  $20 \pm 3.36$  vs  $4.1 \pm 0.36$   $\mu\text{mol}/15$  min; pepsin:  $9.04 \pm 0.01$  vs  $5.62 \pm 0.12$   $\mu\text{g}/15$  min;  $p < 0.001$ ). In the control group, pentagastrin stimulation increased acid secretion in comparison with the basal level ( $10.14 \pm 1.34$  vs  $4.1 \pm 0.36$   $\mu\text{mol}/15$  min,  $p < 0.001$ ), while in the marjoram group, there was a significant decline ( $16.46 \pm 3.23$  vs  $20 \pm 3.36$   $\mu\text{mol}/15$  min,  $p < 0.001$ ). In the marjoram group pentagastrin increased pepsin secretion in comparison with the basal state ( $12 \pm 0.11$  vs  $9.04 \pm 0.1$   $\mu\text{g}/15$  min,  $p < 0.001$ ). It seems that marjoram contains some components that activate chief and parietal cells and increase basal acid and pepsin secretion. Copyright © 2007 John Wiley & Sons, Ltd.

**Keywords:** marjoram; acid secretion; pepsin secretion; pentagastrin; rat.

## INTRODUCTION

There is an increasing interest in the use of herbal drugs for therapeutic purposes. Marjoram is a plant that has been used in traditional medicine and is widely used as a condiment in different pickles and foods (Zargari, 1996).

Its fruit powder which is called Furanocoumarin is useful in sunburn (Zargari, 1996). Although palpitation has previously been reported as a side effect when used in high doses, it is still a therapeutic substance used for flatulence and dyspepsia (Zargari, 1996). The plant leaves also contain many substances, i.e. B-penin, P-cimene, terpinolone, anethole, stragole, 2, 5 dimethyl esterin, B-spirophenol and *trans*-anethole which is mostly found (82.8%) in the leaf (Zargari, 1996).

Although the strengthening and antibloating effects of marjoram have been mentioned in traditional medicine texts (Zargari, 1996), no academic study regarding its effect on gastric secretion was found.

Accordingly, this study was designed to elucidate the acute effects of marjoram on basal and pentagastrin-stimulated gastric acid and pepsin secretions in rat.

## MATERIALS AND METHODS

In this study, two groups ( $n = 12$ ) of Wistar rats weighing 200–250 g were used. The rats were maintained in a temperature-controlled environment on a 12:12-h light-dark cycle with free access to food and water (Blandazzi *et al.*, 1990; Dehghani, 1999; Yang and Tache, 1997). Twenty four hours before the experiment, the animals were deprived of food but free to drink water (Nabavizadeh *et al.*, 2004; Yang and Tache, 1997). In order to omit the effect of circadian rhythms, the experiments were started at 8 every morning. The animals were anaesthetized by an intraperitoneal injection of 50 mg/kg sodium thiopental (Nabavizadeh *et al.*, 2004), tracheostomy was then performed (McTigue and Rogers, 1995; Nabavizadeh *et al.*, 2004). Cervical oesophagus was tied in order to prevent gastric reflux into the oral cavity.

Laparotomy was done and a polyethylene cannula with a 3 mm diameter was placed in the stomach via a duodenal incision. Residual gastric secretions were removed by performing lavage several times with 1–2 mL of normal saline at 37 °C, and allowed 30 min to reach steady state (Nabavizadeh and Vahedian, 2004). After 30 min recovery time, gastric acid and pepsin secretions were measured in both groups.

In the control group, 1 mL normal saline and in marjoram group 1 mL marjoram extract (12.5 mg/kg) were introduced into the stomach. The marjoram extract effective dose was obtained dose dependently.

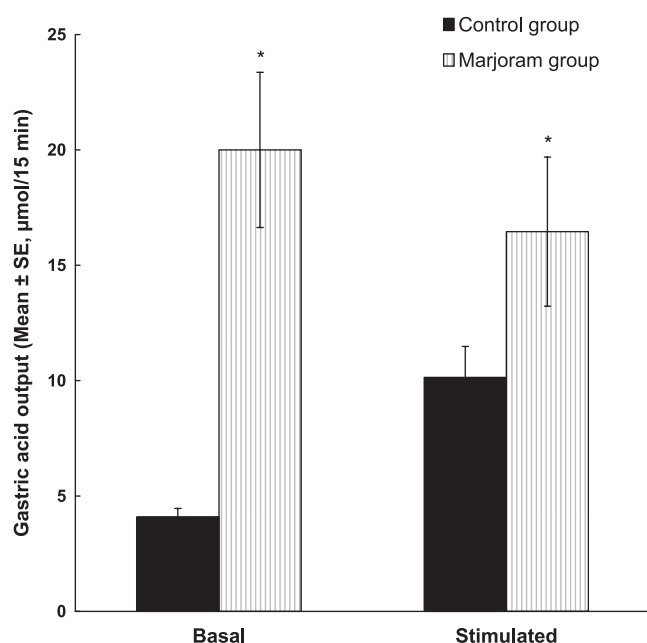
\* Correspondence to: Fatemeh Nabavizadeh Rafsanjani, Tehran University of Medical Sciences, Tehran, Iran.  
E-mail: Nabavizadeh2000@yahoo.com  
Contract/grant sponsor: Research Affairs of Kerman University of Medical Sciences.

After 15 min, 1 mL normal saline was injected and immediately all the gastric contents were collected by the wash out technique (Salim, 1988) for measuring basal secretion. From the collected secretion, 1 mL was used for acid titration and the remainder used for pepsin measurement by the Anson method (Berstad, 1970). In order to measure pentagastrin-stimulated acid and pepsin secretions, pentagastrin 25  $\mu\text{g}/\text{kg}$ , i.p. (Kato *et al.*, 1997) was used. Data are shown as mean  $\pm$  SE. Differences between groups were assessed by paired and unpaired *t*-test.  $p < 0.05$  was considered to be statistically significant.

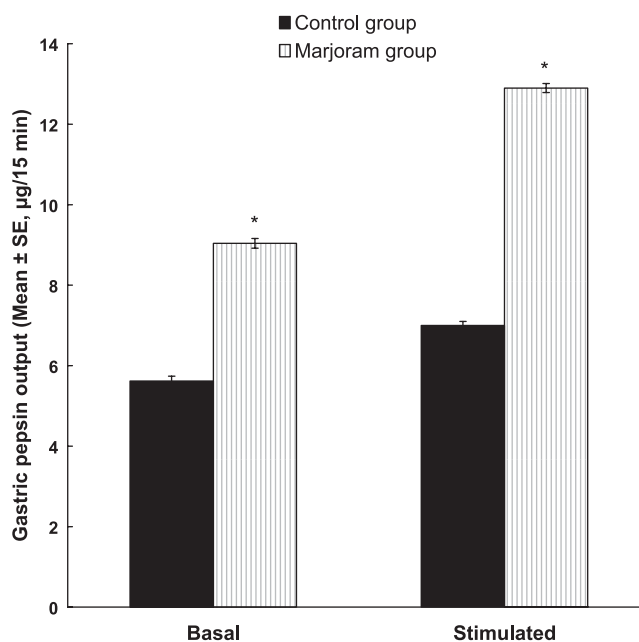
## RESULTS

Basal acid secretion in the marjoram group showed a significant increase in comparison with the control group ( $20 \pm 3.36$  vs  $4.1 \pm 0.36$   $\mu\text{mol}/15$  min,  $p < 0.001$ ) (Fig. 1). In the control group, pentagastrin-stimulated acid secretion was significantly increased in comparison with the basal state ( $10.14 \pm 1.34$  vs  $4.1 \pm 0.36$   $\mu\text{mol}/15$  min,  $p < 0.001$ ) (Fig. 1). Although pentagastrin is an increasing factor on acid secretion, it produced a significant decline in stimulated acid secretion in the marjoram group compared with the basal level ( $16.46 \pm 3.23$  vs  $20 \pm 3.36$   $\mu\text{mol}/15$  min,  $p < 0.001$ ) (Fig. 1).

Basal pepsin secretion in the marjoram group showed a significant increase in comparison with the control group ( $9.04 \pm 0.01$  vs  $5.62 \pm 0.12$   $\mu\text{g}/15$  min,  $p < 0.001$ ) (Fig. 2). In the marjoram and control groups, pentagastrin-stimulated pepsin secretion had a significant increase in comparison with the basal status ( $12.0 \pm 0.11$  vs  $9.04 \pm 0.1$   $\mu\text{g}/15$  min in marjoram group,  $p < 0.001$  and  $7.9 \pm 0.12$  vs  $5.62 \pm 0.12$   $\mu\text{g}/15$  min in control group,  $p < 0.001$ ) (Fig. 2).



**Figure 1.** Comparison of the acid secretion between the control and marjoram groups ( $n = 12$  in each group) \*  $p < 0.001$ .



**Figure 2.** Comparison of the pepsin secretion between the control and marjoram groups ( $n = 12$  in each group) \*  $p < 0.001$ .

## DISCUSSION

In this study marjoram increased basal acid secretion compared with the control state (Fig. 1). This effect may be mediated through an increase in the intracellular  $\text{Ca}^{2+}$  concentration (Dufner *et al.*, 2005; Puscas *et al.*, 2001).

Pentagastrin, a gastrin-like pentapeptide, can also bind to gastrin receptors (CCK-B) and activate parietal and enterochromaffin cells (Berne *et al.*, 2003; Bertaccini and Coruzzi, 1998; Hansen *et al.*, 1998; Hills *et al.*, 1996). Stimulation of acid secretion by gastrin has been shown to be mostly mediated by histamine release from enterochromaffin cells in rats (Kato *et al.*, 1997; Kato *et al.*, 1998). But surprisingly, pentagastrin-induced acid secretion was significantly less than that the basal state in marjoram administered animals ( $p < 0.001$ , Fig. 1). It should be kept in mind that the basal acid secretion in the marjoram group was significantly more than the control one. Therefore, it can be inferred that the marjoram extract should have an active ingredient that can stimulate gastrin or histamine receptors on parietal cells much more strongly than their original ligands (gastrin or histamine). Upon pentagastrin administration, these ingredients should competitively be removed by a less potent ligand and acid secretion declined.

Basal pepsin secretion was significantly more in the marjoram group than in the control group ( $p < 0.001$ , Fig. 1). Since  $\text{Ca}^{2+}$  ions have a pivotal role in pepsin exocytosis from chief cells (Johnson, 2001), this effect may be due to intracellular  $\text{Ca}^{2+}$  elevation induced by marjoram administration.

Pentagastrin increased pepsin secretion in comparison with the basal state both in the control and marjoram groups ( $p < 0.001$ , Fig. 2). This is due to the pentagastrin effect on gastrin receptors (CCK-B), in

chief cells (direct effect) and enterochromaffin cells and histamine release (indirect effect) (Hansen *et al.*, 1998).

Although stimulated gastric acid secretion was reduced following marjoram administration, basal secretion was increased, in contrast with the plant's alleviating effects on dyspepsia. Therefore, the antibloating and stomach strengthening effects of marjoram can not be explained fully by acid and pepsin changes after a single dose extract administration.

More studies should be conducted to evaluate the plant's chronic effects and also gastric motility.

### Acknowledgements

The authors are grateful to the deputy of Research Affairs of Kerman University of Medical Sciences for financial support. We are indebted to Mr Hamid Sohanaky for technical editing.

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