Egypt. J. Zool., 48: 387- 401 (June 2007)

ANTI-INFLAMMATORY EFFECTS OF SOMATOSTATIN, *FERULA NARTHEX* AND *CYMBOPOGON SCHOENANTHUS* EXTRACTS ON INTESTINAL PERISTALTIC REFLEX IN SCHISTOSOMIASIS- INFECTED MICE

FAIZA ABDU
Department of Bioscience, King Abdulaziz University, Jeddah, Saudi Arabia

ABSTRACT

Somatostatin (SOM) is an important neuromodulator in regulation of gastrointestinal motility. It acts as anti-inflammatory mediator during parasitic infection. Recently, many people prefer to use medicinal plants rather than chemical drugs. Herbal medicines such as *Ferula narthex* (*Fn*) and *Cymbopogon schoenanthus* (*Cs*) have been used to cure intestinal disorders in several countries including Saudi Arabia. However, the pharmacological and physiological characteristics for their effectiveness in intestinal inflammation associated with parasitic infection have not been fully determined. Therefore, the aim of this study was to investigate the pharmacological and physiological characteristics of SOM, *Fn* gum and *Cs* in reducing schistosomiasis-induced hyperactivity of gastrointestinal smooth muscle associated with severe pain during infection. Experiments were performed on Swiss male mice 4 and 8-wk following infection with *S. mansoni* compared to uninfected control mice. Jejunal contraction was assessed using a modified Trendelenburg type preparation to study aboral directed motor complexes (MCs). SOM (300nM) inhibited jejunum contractions in control and 4-wk-infected jejunum. However, in 8-wk post infection with *S. mansoni*, the inhibitory effect of SOM was less pronounced. *Fn* (3 mg/ml) and *Cs* (10 mg/ml) extracts inhibited the contractions in the jejunum from control and 4-wk-infected mice, while after 8-wk of infection, the inhibitory effect of *Fn* and *Cs* were more effective as compared to controls. In conclusion, the response to SOM is disturbed during schistosomiasis possibly due to the disturbance of neuroregulatory circuits of enteric neurotransmission in the small intestine. The inhibitory action of *Fn* and *Cs* extracts on gastrointestinal motility may represent an interesting therapeutic agents that lead to relieve schistosomiasis-related gastrointestinal dysmotility.

Key words: Chronic inflammation; enteric neurotransmission; schistosomiasis; SOM; *Ferula narthex; Cymbopogon schoenanthus*.

INTRODUCTION

Enteric nervous system (ENS) neurons and immune system both produce somatostatin (SOM) and express SOM receptors that respond to endogenous and exogenous SOM. In the gastrointestinal tract, SOM regulates intestinal fluid secretion that modulates intestinal peristalsis and enteric neurotransmission (De

Man *et al.*, 2002; Grider, 2003). SOM is known as an anti-inflammatory mediator which down-regulates lymphocyte proliferation, reduces immunoglobulin production and inhibits the release of proinflammatory cytokines (Ten Bokum *et al.*, 2000). SOM exerts its effects through interaction with five SOM receptors (sst_1-sst_5), which belong to the family of G-protein-coupled receptors with seven transmembrane spanning domains (Benali *et al.*, 2000). Within the ENS, SOM is present in descending interneurons that synapse mainly with other neurons in the myenteric plexus, but does not project into either the longitudinal or circular muscle layers of the intestine (Furness, 2000). The integrated circuit of modulatory interneurons during peristaltic reflex consists of SOM neurons coupled to opioid neurons that are coupled to inhibitory vasoactive intestinal polypeptide (VIP), pituitary adenylate cyclase activating peptide(PACAP) and nitric oxide NOs motor neurons innervating circular muscle (Grider, 1994). The intestinal distension (descending phase of peristalsis) stimulates SOM neurons to release SOM leading to a decrease in the activity of opioid neurons, thus eliminating the opioid neurons action on inhibitory motor neurons and resulting in an increase in release of the inhibitory motor neurotransmitters VIP/ PACAP/ NO (Grider, 1994) leading to descending relaxation of circular muscle.

During schistosomiasis, SOM has been known to have an anti-inflammatory effect. *Schistosoma mansoni* granulomas release significant amounts of SOM (Weinstock *et al.*, 1990; Elliott *et al.*, 1998) which upregulates the expression of its own receptors (Bruno *et al.*, 1994; Hukovic *et al.*, 1996; Tannenbaum *et al.*, 2001). Previous studies (Chatterjee *et al.*, 2001; Chatterjee *et al.*, 2005) indicated that exogenous administration of SOM has a beneficial antifibrotic effect in the infected liver and reduces portal pressure, the weight of the spleen and the liver, liver egg load and granulomas size. Thus, SOM may be an effective therapeutic agent for intestinal Schistosomiasis-induced hyper contractile activity (Mansy *et al.*, 1998; Chatterjee *et al.*, 2001).

Several studies have been focused on the novel therapeutic components from medicinal plants. *Ferula narthex* (*Fn*) and *Cymbopogon schoenanthus* (*Cs*) are medicinal plants grown in eastern countries, including Iran, Egypt and Saudi Arabia. Both plants have been used traditionally during inflammation for their anti-inflammatory effects as well as their drug relaxant effect on smooth muscle contraction. Using other species of *Cymbopogon, (Cymbopogon goeringii)* was reported to have anti-arrhythmic action in isolated guinea pig smooth muscle (Liu and Feng, 1989), while *Cymbopogon citrates* extract has an inhibitory action on both secretory and contractile mechanisms in diarrheal conditions (Tangpu and Yadav, 2004).

Several species of *Ferula* were submitted to pharmacological studies that revealed the relaxant effect of *Ferula* gum extract on contraction of gastrointestinal tract in mammals. The extract of *Ferula ovina* and *Ferula*

sinaica roots inhibited the spontaneous movements of rabbit jejunum and guinea pig ileum (Al-Khalil *et al.*, 1990).

Ferula gummosa essential oil (FGEO) as well as hydro-alcoholic, etheric, petrolic and methanolic extracts all inhibited the response to KCl in a concentration-dependent manner and attenuated the response of the acetylcholine-induced contraction (Sadraei *et al.*, 2001). *Ferula asafoetida* gum extract caused relaxation in the smooth muscle of isolated guinea pig ileum. Similar inhibitory effect of the extract was observed on the precontracted ileum by histamine and KCl. The relaxant component of plant extract might be interfering with muscarinic, adrenergic and histaminic receptor activities (Fatehi *et al.*, 2004). However, the effect of *Fn* gum and *Cs* extract on smooth muscle contraction during inflammation is not fully determined.

Therefore, the aim of this study was to investigate the effect of SOM as a neuromodulator and anti-inflammatory drug during intestinal inflammation and to examine the potential role of *Fn* gum and *Cs* extract as medicinal plants on motor activity induced by intraluminal distention in both normal and inflammatory conditions.

MATERIAL AND METHODS

Animal preparation

Male Swiss mice (8 weeks old) were used in this study. Experiments were set up using three groups of animals, one control and two treatments, representing two different phases 4 and 8-wks post infection. Each group of animals consisted of 6-7 mice. All experiments were approved by the Ethics Committee of King Fahad medical research centre (KFMRC).

Schistosoma mansoni infection

The maintenance of the *S. mansoni* life cycle and the transcutaneous infection of mice with *S. mansoni* were carried out according to the methods of Bogers *et al.* (2000) and Moreels *et al.* (2001). Mice were transcutaneously infected with about 100 S. mansoni cercariae of a Biomphalaria alexandrina strain. The cercariae were allowed to penetrate during 30 min after which the water was removed and checked for remaining cercariae.

Tissue preparation

Control and infected animals were stunned by a blow on the head and then sacrificed by cervical dislocation. A mid-line laparotomy was performed and a segment of proximal jejunum was rapidly excised and placed in gassed (95% O2 and 5%CO2) Krebs bicarbonate buffer solution (composition in mM: NaCl 117, KCl 4.7, NaHCO3 25, CaCl2 2.5, MgCl2 1.2, $NaH_2PO4.2H_2O$ 1.2 and D-glucose 11) cleared of any mesenteric connective tissue and the lumen flushed with Krebs solution.

Experimental protocol

Jejunal segments approximately 5 cm in length were prepared from each animal, and two in total were mounted horizontally in separate 20 ml perfusion chambers. Tissues were maintained at 37°C, perfused with Krebs solution at a rate of 5 ml/min, and allowed to equilibrate for at least 30 min before experiments started. Motor complex (MCs) of jejunum in infected and uninfected mice were monitored and analyzed by using Neurolog\NL 900D (Digitimer Ltd, Hertfordshire, England) to record contractile activity as changes in intraluminal pressure under isovolumetric conditions to compare their responsiveness to SOM, *Fn* and *Cs* extracts.

Isolated jejunal segment was distended to 2-3.5 cmH_2O to evoke MCs. Only preparations in which regular MCs were maintained were used for subsequent experiments. SOM, *Fn* and *Cs* extracts were added to the chambers 15 min after stopping perfusion and recording was continued for a further 20 min before washing out (SOM, *Fn* and *Cs*) and re-instating perfusion.

Plant extract

Plants were identified at the Botany Department at King Abdulaziz University. *Cs* dried powder and *Fn* gum were purchased from local markets, western area of Saudi Arabia. The extract was prepared according to the method of Fatehi *et al.* (2004). *Fn* (600mg) and *Cs* (1g) were soaked over night in 100 ml distilled water at room temperature (22°C) to prepare stock solutions. Bath volume was considered when preparing the stock solution in order to reach the required concentrations of *Fn* (3 mg/ml) and *Cs* (10 mg/ml). Freshly diluted aliquots were maintained on ice during the course of the experiments and added to the bath in micro litre volumes.

Drugs

SOM was purchased from Sigma Chemical (USA), and dissolved in 1% bovine serum albumin in distilled water. SOM was stored at –20°C. Freshly diluted aliquots were maintained on ice during the course of the experiments and added to the bath in microlitre volumes.

Data Analysis

MCs were measured in terms of their peak amplitude above baseline (cmH_2O), duration(s) and interval(s) between them. Baseline values were taken during the 15 min before drug application and the response effect in the 15 min following application. Responses are expressed as absolute values ± standard error of mean S.E.M with N = number of animals.

RESULTS

Effect of SOM on jejunual smooth muscle contractility

Exposure of the jejunal segments to SOM (300nM) inhibited MCs in the uninfected control and *S. mansoni*-infected mice 4 and 8-wk of infection (Fig.1). This inhibition appeared as a period of contractile quiescence followed by a return of activity at nearly the rate observed before the addition of drug. In control animals intervals increased from 44.14± 1 to 279.29 ± 50s, $P < 0.05$,*n* =

7 while in 4-wk- infected animals intervals were changed from 43.05± 0.9 to 144.69 ± 41s, $P < 0.04$, $n = 6$ (Fig. 2A). The amplitude did not record any significant change in both control and 4-wk-infected jejunum (5.53 ± 0.9 *vs* 4.56 ± 1 cmH_2O, $P < 0.1$, $n= 7$ and 5.41 ± 1.6 *vs* 4.82 ± 2 cmH_2O, $P < 0.5$, $n= 6$ respectively, Fig. 2B). After 8-wk of infection with *S. mansoni*, the effect of SOM on interval was attenuated .The intervals increased from 31.23 ± 1 to 81.58 ± 20s, $P < 0.05$, $n = 6$ and the amplitude decreased from 21.57± 4 to 16.58 ± 3.9 cmH_2O, $P< 0.1$, $n= 6$, respectively. However, the magnitude of the inhibition was higher in control animals as compared to 4 and 8-wk-infected mice (Fig. 2C).

Effect of *Ferula narthex* gum extract on jejunual smooth muscle contractility

The gum extract of *Fn* (3 mg/ml) produced an inhibition of MCs frequency and amplitude in control, 4 and 8-wk-infected mice jejunum (Fig. 3). In uninfected control jejunum the MCs between intervals increased from 39.77 ± 4 to 202.09 ± 18s, $P < 0.002$, $n = 6$, (Fig. 4A) and the amplitude decreased from 4.56 ± 0.7 to 1.84 ± 0.9 cmH_2O, $P < 0.004$, $n= 6$ (Fig. 4B). Similar effect was observed in 4-wk-infected animals. The intervals increased from 40.94 ± 11 to 162.82 ± 47s, $P < 0.05$, $n = 6$ and the amplitude decreased from 4.40 ± 1.1 to 1.86 ± 1.2 cmH_2O, $P < 0.001$, $n= 6$. *Fn* extract was more effective and abolished MCs in 8-wk-infected animals compared to the control ($n= 6$, Fig. 4B). The inhibitory effect of *Fn* gum extract remained for 20 min and was irreversible after washing the segment.

Effect of *Cymbopogon schoenanthus* extract on jejunual smooth muscle contractility

The inhibitory effect of *Cs* extract continued for 20 min and was reversible after washing in control and 4-wk but not 8-wk-infected animals (Fig.5). *Cs* (10 mg/ml) produced a significant increase in the intervals (Fig.6A) and decrease in the amplitude in control and 4-wk-infected mice (Fig.6B). In control jejunum the interval was 44.99± 1.9 *vs* 80.95 ± 2.9s, $P < 0.001$, $n = 6$. The amplitude was decreased from 4.74 ± 0.8 to 2.84 ± 1 cmH_2O, $P < 0.05$, $n= 6$, (Fig. 6B). In 4-wk -infected mice, the effect of *Cs* on MCs intervals was attenuated. The interval was (40.50 ± 1 *vs* 65.08 ± 6s, $P < 0.04$, $n = 6$), while the amplitude was (4.79 ± 1.57 *vs* 2.97 ± 2 cmH_2O, $P < 0.01$, $n= 6$). 8-wk post infection MCs were completely abolished after the addition of *Cs* aqueous extract ($n = 6$, Fig. 6B).

DISCUSSION

It has been reported that SOM inhibits intestinal motility in normal and pathological conditions (De Man *et al.*, 2002; Grider, 2003). In the present study, the potential role of SOM to reduce the intestinal hyper contractile activity that is produced by *S. mansoni* infection has been investigated. The data of the present study showed that SOM reduced contractile activity in the small intestine of control and 4-wk-infected mice. This effect was similar to the previous studies of De Man *et al.* (2002) and De Jonge *et al.* (2003), where SOM inhibited neuronal cholinergic activity in the small intestine. The present study also showed that in 8-wk post infection a different response to exogenous SOM was observed, the inhibitory effect of SOM was less pronounced as compared to control mice. These results are consistent with those of De Man *et al.* (2002) and De Jonge *et al.* (2003), since the response to SOM was attenuated in 8-wk and remained unchanged through the time course of the experiments. The inhibitory effect of SOM during schistosomiasis could be due to oxidative damage to enteric nerve cells (Van Nassauw *et al.*, 2001) as SOM is released from granulomas (De Man *et al.*, 2002) during the chronic stage of schistosomiasis (Weinstock *et al.*, 1990). The release of SOM from the intestinal granulomas in and around the intestinal mucosa and muscle layers might lead to endogenous SOM receptor desensitization which in turn leads to inactivation of SOM receptors and down-regulation instead of upregulation of SOM receptors thus attenuated the effect of exogenous SOM. Our results were also supported by those of De Jonge *et al.*(2003) who found that the infection with *S. mansoni* results in disturbed SOM levels of enteric cholinergic neurons, and SOM levels in inflamed mouse ileum were elevated during the chronic stage (from 8- 15-wk post- infection). Similarly, Feniuk *et al.* (1995), noticed that in the guinea pig ileum, SOM receptors desensitization occurs rapidly after addition of SOM analogues. Thus, desensitization of the SOM receptors on the cholinergic neurons may result in a diminished effect of exogenously administered SOM during 8-wk post infection.

Some studies have investigated the bioactive action of the genus *Ferula* that are traditionally used for treatment of intestinal hyperactivity (Sadraei *et al.*, 2001; Fatehi *et al.*, 2004). In the current study, the potential role of *Fn* aqueous extract to reduce the intestinal hyper contractile activity associated with intestinal inflammation has been investigated. *Fn* extract produced a significant inhibition on the contractile activity in control mice. These results are similar to those of Fatehi *et al.* (2004), who found that application of *Ferula* extracts can suppress gut motility, and reduce blood pressure. These activities may emphasize the benefits of using *Ferula* in the treatment of increased contractile activity during diarrheal diseases. Similar inhibitory effects of other *Ferula* species were previously described in rabbit jejunum, guinea-pig ileum (Al-Khalil *et al.*, 1990; Aqel *et al.*, 1991; Fatehi *et al.*, 2004) and in isolated rat ileum (Sadraei *et al.*, 2001). In the present study, *Fn* inhibited the

hypercontractility of 4 and 8-wk inflamed jejunum. However, the mechanism of action of *Fn* or other *Ferula* species extracts on contractile activity during intestinal inflammation associated with parasitic infection was not investigated so far. Al-Khalil *et al.* (1990) suggested that *Ferula ovina* has non-specific anti-cholinergic and anti-histaminic effects, while the study of Fatehi *et al.* (2004) revealed that the relaxant components in *Ferula asafoetida* gum extract might interact with a variety of muscarinic, adrenergic and histaminic receptors activity or with the mobilization of calcium ions required for smooth muscle contraction. The authors also observed that the cyclo-oxygenase inhibitor indomethacin inhibited the relaxatory effect of *Ferula asafoetida* which suggested that PGE_2 may be involved in this inhibition. Thus, it is possible to refer the effect of *Fn* on MCs during intestinal inflammation to the interaction between the active components of the plant *Fn* extract and the cholinergic or adrenergic receptors.

In the present study, the effect of *Cs* extract was examined on contractile activity in isolated segments of jejunum from control, 4 and 8-wk-infected mice. *Cs* extract inhibited jejunal contraction of control and 4-wk-infected mice. Surprisingly, at 8-wk post infection, *Cs* abolished the jejunal contractile activity. However, the mechanisms of action of Cs extract on contractile activity during inflammatory conditions have not been fully investigated. The inhibitory effect of *Cymbopogon* observed previously using other species in isolated guinea pig papillary muscles and atrium suggested that volatile oil of *Cymbopogon goeringii* may possess anti-arrhythmic action (Liu and Feng, 1989). Tangpu and Yadav (2004) suggested that the *Cymbopogon citrates* extract has the ability to inhibit both secretory and motility activity of diarrhoea implying to the presence of an intestinal anti-motility components.

Thus, *Fn* and *Cs* extracts may act *via* two pathways. First, by activating the release of some inhibitory neurotransmitters from inhibitory interneurons and cholinergic motor neurons that are stimulated by distension and supply each muscle layer (Furness *et al.*, 2004). Second, by blocking the cholinergic, nicotinic and muscarinic receptors pathways.

Taken together, SOM plays an important role as an anti-inflammatory drug during infection with *S. mansoni*. *Fn* and *Cs* may have therapeutic benefits to cure inflammatory conditions but the mechanism of action of both extracts on intestinal peristalsis in abnormal condition still needs to be elucidated.

REFERENCES

AL-Khalil, S., Aqel, M., Afifi, F. and AL-Eisawi, D. (1990). Effects of an aqueous extract of *Ferula ovina* on rabbit and guinea pig smooth muscle. J. Ethnopharmacol., **30**: 35-42.

Aqel, M. B., AL-Khalil, S. and Afifi, F. (1991). Effects of a *Ferula sinaica* root extract on the uterine smooth muscle of rat and guinea pig. J. Ethnopharmacol., **31**: 291-297.

Benali, N., Ferjoux, G., Puente, E., Buscail, L. and Susini, C. (2000). Somatostatin receptors. Digestion., **62**: 27-32.

Bogers, J., Moreels, T., DE Man, J., Vrolix, G., Jacobs, W., Pelckmans, P. and Van Marck, E. (2000). *Schistosoma mansoni* infection causing diffuse enteric inflammation and damage of the enteric nervous system in the mouse small intestine. Neurogastroenterol. Motil., **12**: 431-440.

Bruno, J. F., Xu, Y. and Berelowitz, M. (1994). Somatostatin regulates somatostatin receptor subtype mRNA expression in GH3 cells. Biochem. Biophys. Res. Commun., **202**: 1738-1743.

Chatterjee, S., De Man, J. and Van Marck, E. (2001). Somatostatin and intestinal schistosomiasis: therapeutic and neuropathological implications in host-parasite interactions. Trop. Med. Int. Health., **6**: 1008-1015.

Chatterjee, S., Vrolix, G., Depoortere, I., Peeters, T. and Van Marck, E. (2005). The therapeutic effect of the neuropeptide hormone somatostatin on *Schistosoma mansoni*-caused liver fibrosis. BMC Infect. Dis., **5**: 45.

De Jonge, F., Van Nassauw, L., De Man, J. G., De Winter, B. Y., Van Meir, F., Depoortere, I., Peeters, T. L., Pelckmans, P. A., Van Marck, E. and Timmermans, J. P. (2003). Effects of *Schistosoma mansoni* infection on somatostatin and somatostatin receptor 2A expression in mouse ileum. Neurogastroenterol. Motil., **15**: 149-159.

De Man, J. G., Chatterjee, S., De Winter, B. Y., Vrolix, G., Van Marck, E. A., Herman, A. G. and Pelckmans, P. A. (2002). Effect of somatostatin on gastrointestinal contractility in *Schistosoma mansoni* infected mice. Int. J. Parasitol., **32**: 1309-1320.

Elliott, D. E., Blum, A. M., Li, J., Metwali, A. and Weinstock, J. V. (1998). Preprosomatostatin messenger RNA is expressed by inflammatory cells and induced by inflammatory mediators and cytokines. J. Immunol., **160**: 3997-4003.

Fatehi, M., Farifteh, F. and Fatehi-Hassanabad, Z. (2004). Antispasmodic and hypotensive effects of *Ferula asafoetida* gum extract. J. Ethnopharmacol., **91**: 321-324.

Feniuk, W., Dimech, J., Jarvie, E. M. and Humphrey, P. P. (1995). Further evidence from functional studies for somatostatin receptor heterogeneity in guinea-pig isolated ileum, vas deferens and right atrium. Br. J. Pharmacol., **115**: 975-980.

Furness, J. B. (2000). Types of neurons in the enteric nervous system. J. Auton. Nerv. Syst., **81**: 87-96.

Furness, J. B., Jones, C., Nurgali, K. and Clerc, N. (2004). Intrinsic primary afferent neurons and nerve circuits within the intestine. Prog. Neurobiol., **72**: 143-164.

Grider, J. R. (1994). Interplay of somatostatin, opioid, and GABA neurons in the regulation of the peristaltic reflex. Am. J. Physiol., **267**: G696-G701.

Grider, J. R. (2003). Reciprocal activity of longitudinal and circular muscle during intestinal peristaltic reflex. Am. J. Physiol., **284**: G768-G775.

Hukovic, N., Panetta, R., Kumar, U. and Patel, Y. C. (1996). Agonist-dependent regulation of cloned human somatostatin receptor types 1-5 (hSSTR1-5): subtype selective internalization or upregulation. Endocrinology., **137**: 4046-4049.

Liu, M. and Feng, G. H. (1989). [Effects of *Cymbopogon goeringii* (Steud.) A. Camus volatile oil on physiologic properties of the isolated guinea pig myocardium]. Zhongguo Zhong Yao Za Zhi., **14**: 620-623.

Mansy, S. S., Yehua, H. A., Hassan, M. M., Hassan, E. A., Youssef, M. M., Hadi, A. A. and Mackenzie, C. D. (1998). Effect of octreotide on the pathology of hepatic schistosomiasis. Arzneimittelforschung., **48**: 855-861.

Moreels, T. G., De Man, J. G., Bogers, J. J., De Winter, B. Y., Vrolix, G., Herman, A. G., Van Marck, E. A. and Pelckmans, P. A. (2001). Effect of *Schistosoma mansoni*-induced granulomatous inflammation on murine gastrointestinal motility. Am. J. Physiol., **280**: G1030-G1042.

Sadraei, H., Asghari, G. R., Hajhashemi, V., Kolagar, A. and Ebrahimi, M. (2001). Spasmolytic activity of essential oil and various extracts of *Ferula gummosa* Boiss. on ileum contractions. Phytomedicine., **8**: 370-376.

Tangpu, V. and Yadav, A. K. (2004). Antidiarrheal activity of *Rhus javanica* ripen fruit extract in albino mice. Fitoterapia., **75**: 39-44.

Tannenbaum, G. S., Turner, J., GUO, F., Videau, C., Epelbaum, J. and Beaudet, A. (2001). Homologous upregulation of sst2 somatostatin receptor expression in the rat arcuate nucleus in vivo. Neuroendocrinology., **74**: 33-42.

Tenbokum, A. M., Hofland, L. J. and Van Hagen, P. M. (2000). Somatostatin and somatostatin receptors in the immune system: a review. Eur. Cytokine. Netw., **11**: 161-176.

Van Nassauw, L., Bogers, J., Van Marck, E. and Timmermans, J. P. (2001). Role of reactive nitrogen species in neuronal cell damage during intestinal schistosomiasis. Cell Tissue Res., **303**: 329-336.

Weinstock, J. V., Blum, A. M. and Malloy, T. (1990). Macrophages within the granulomas of murine *Schistosoma mansoni* are a source of a somatostatin 1-14-like molecule. Cell. Immunol., **131**: 381-390.

EXPLANATION OF FIGURES

Fig. 1: Effect of SOM on MCs in the Mice Jejunum:
Representative traces showing the transient increase in the interval between MCs produced by SOM (300nM) in control, 4 and 8-wk post infection.

Fig. 2: Effect of SOM on MCs Intervals and Amplitude in Control and Infected Mice Jejunum:
Histograms showing the increase in interval **(A)** and the decrease in amplitude **(B)** between MCs before and after addition of SOM (300nM). Note that the effect of SOM on MCs intervals was deteriorated in 8-wk

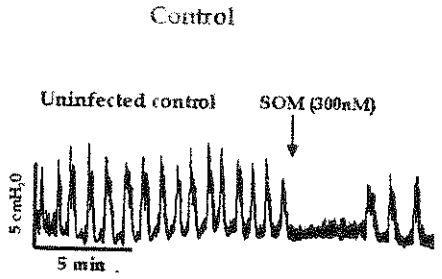
post infection. *=$P < 0.05$ compared to pre-drug control. **(C)** Histograms showing the magnitude of increase in intervals in control, 4 and 8-wk infected mice. *=$P < 0.05$

Fig. 3: Effect of *Ferula narthex* Extract on MCs in the Mice Jejunum:
Representative traces showing the increase in the interval and the decrease in amplitude produced by *Fn* (3 mg/ml) in control, 4 and 8-wk post infection. Note that MCs was abolished after 8-wk of infection.

Fig. 4: Effect of *Ferula narthex* Extract on MCs Interval and Amplitude in Control and Infected Mice Jejunum:
Histograms showing the interval **(A)** and amplitude **(B)** between MCs in control and 4-wk post infection before and after addition of *Fn* extract (3 mg/ml). *=$P < 0.05$ and ***=$P < 0.004$ compared to pre-drug control.

Fig. 5: Effect of *Cymbopogon schoenanthus* Extract on MCs in the Mice Jejunum:
Representative traces depicting the increase in the interval and the decrease in amplitude produced by *Cs* (10 mg/ml) in control, 4 and 8-wk infected jejunum. Surprisingly, *Cs* extract abolished MCs after 8-wk of infection.

Fig. 6: Effect of *Cymbopogon schoenanthus* Extract on MCs Intervals and Amplitude in Control and Infected Mice Jejunum:
Histograms showing the increase in interval **(A)** and the decrease in amplitude **(B)** before and after addition of *Cs* extract (10 mg/ml) in control and 4-wk infected animals. Note that MCs was abolished in 8-wk infected animals *= $P < 0.05$, **= $P < 0.01$ and ***= $P < 0.001$ compared to pre-drug control.



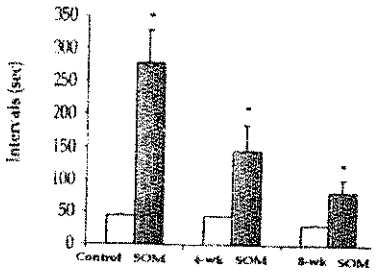
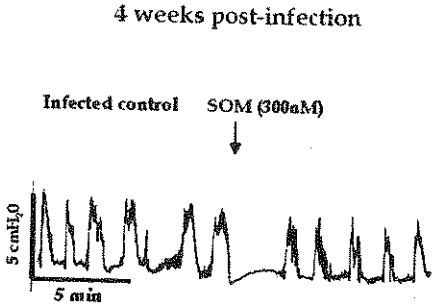


Fig. 2 A



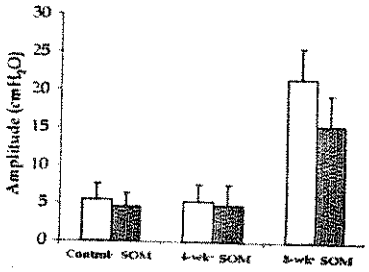


Fig. 2 B

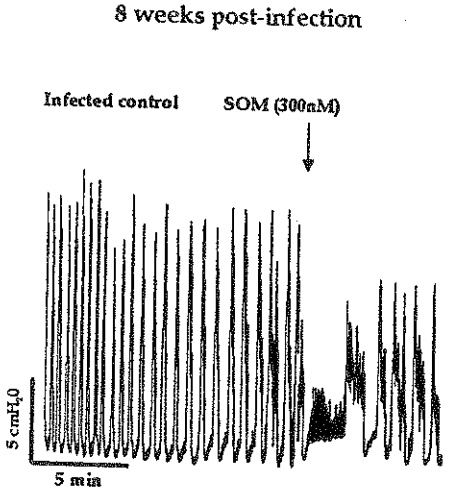


Fig. 1

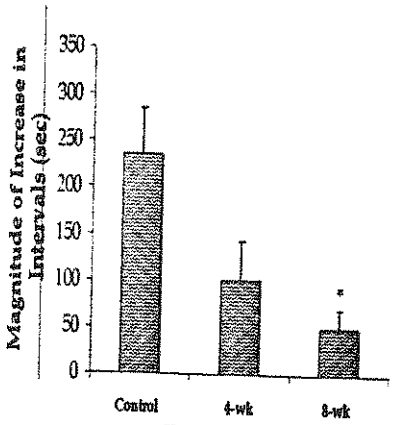


Fig. 2C

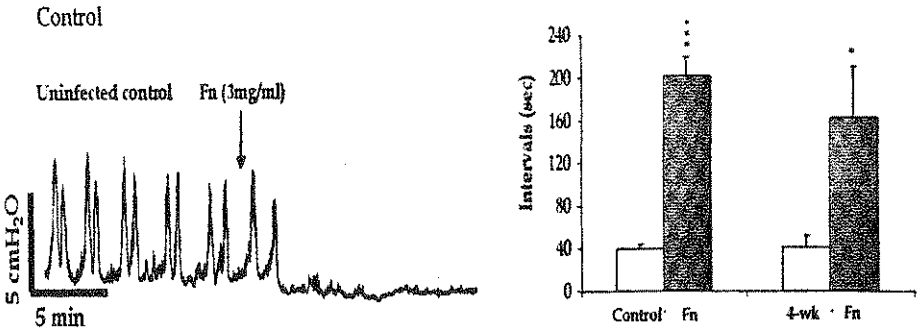


Fig. 4 A

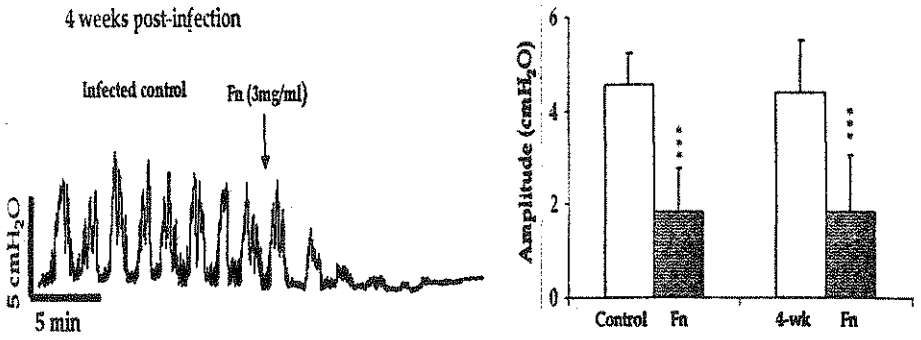


Fig. 4 B

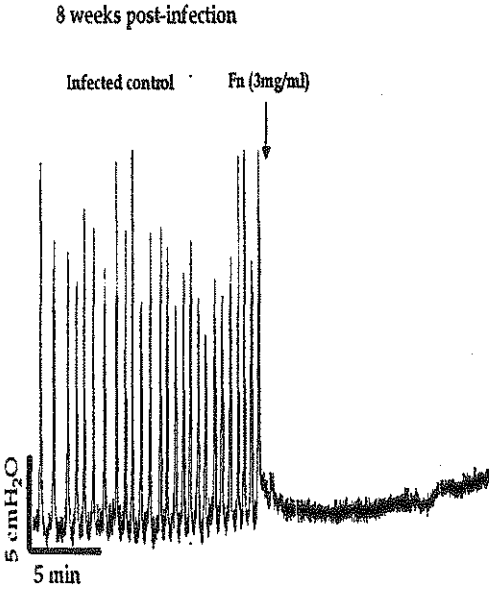


Fig. 3

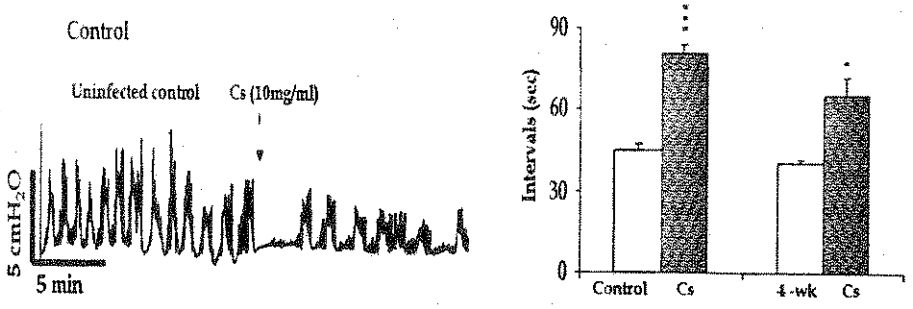


Fig. 6 A

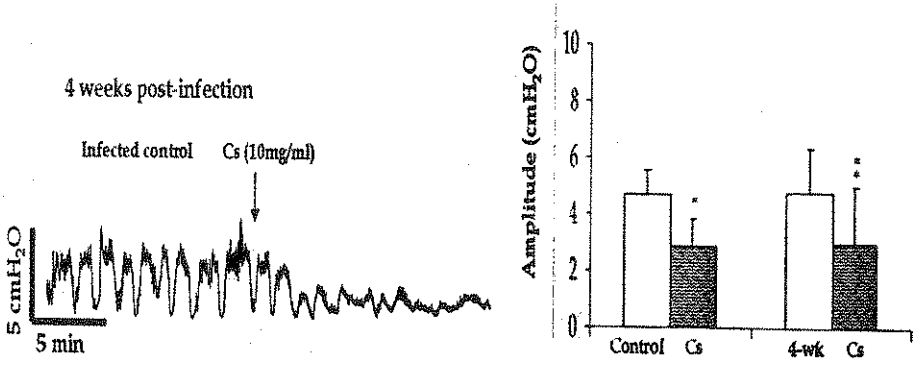


Fig. 6 B

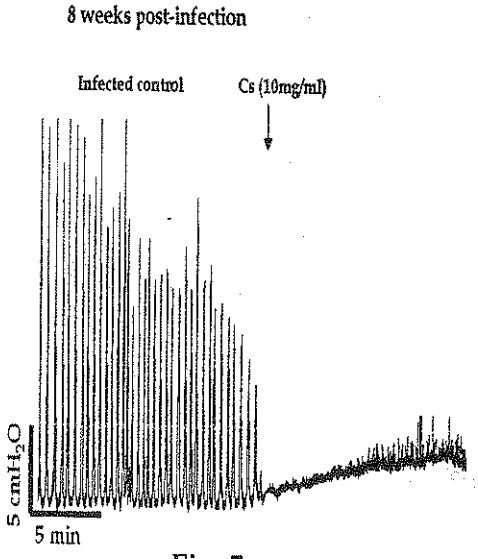


Fig. 5

المجلة المصرية لعلم الحيوان
المجلد ٤٨ (يونيو ٢٠٠٧)

التأثيرات المضادة للالتهاب لكل من السوماتوستاتين ومستخلصات الحلتيت والإذخر على التقلص المعوي اللاإرادي في الفئران المصابة *بالبلهارسيا*

فايزة عبده
قسم علوم الأحياء- كلية العلوم- جامعة الملك عبد العزيز

يعتبر السوماتوستاتين Somatostatin أحد الناقلات العصبية الهامة في تنظيم الحركة الانقباضية للمعدة وللأمعاء، كما يعمل مضاداً للالتهابات في أثناء الإصابة الطفيلية.

وحديثاً، يفضل كثيرٌ من الناس استخدام النباتات الطبية بدلاً من العقاقيرّ الكيميائية ومن هذه النباتات الطبية الحلتيت والإذخر (*Ferula narthex* and *Cymbopogon schoenanthus*) اللذان يستخدمان لمعالجة بعض أمراض الأمعاء في بعض الدول ومنها المملكة العربية السعودية. إلاّ أن الخصائص الفارماكولوجية و الفسيولوجية لتأثيرهما في أثناء إصابة الأمعاء الدقيقة بالالتهاب الناجم عن الإصابة الطفيلية لم تتحدد بعد. لذلك كان الهدف من الدراسة هو تحديد هذه الخصائص لكلٍ من السوماتوستاتين و الحلتيت والإذخر في تثبيط التقلصات المعوية المتزايدة والمؤلمة في أثناء فترة الإصابة *بالبلهارسيا*.

وقد أجريت الدراسة على الفئران السويسرية السليمة والمصابة *بالبلهارسيا* لمدة ٤ و ٨ أسابيع، ثم قورنت نتائج الفئران المصابة بالفئران السليمة. وقد تم قياس التقلصات في جزء القناة الهضمية الصائم باستخدام طريقة Trendelenburg المعدلة وذلك لقياس الحركة التقلصية من الاتجاه الفمي إلى الاتجاه الشرجي. أدت المعالجة بالسوماتوستاتين (٣٠٠ نانو مول) إلى تثبيط التقلصات في الحيوانات السليمة وكذلك الحيوانات المصابة لمدة ٤ أسابيع، ولكن بعد ٨ أسابيع من إحداث الإصابة كان تأثير السوماتوستاتين أقل بكثير.

كذلك ثبط مستخلص كل من الحلتيت (٣ مج/مل) والإذخر (١٠ مج/مل) التقلص اللاإرادي في الحيوانات السليمة وكذلك المصابة لمدة ٤ أسابيع أما بعد ٨ أسابيع من الإصابة فإن استخدام الحلتيت والإذخر أدى إلى إزالة التقلص المعوي كلياً.

نستخلص من ذلك بأن الاستجابة للسوماتوستاتين تتعرقل أثناء الإصابة المزمنة *بالبلهارسيا* ويعزى ذلك إلى إخلال تنظيم النقل العصبي، وخاصة النقل العصبي الهضمي، للأمعاء الدقيقة. أما التأثير المثبط لكل من مستخلصي الحلتيت والإذخر لتقلصات القناة الهضمية فقد يمثل عقاراً هاماً لعلاج الإصابة *بالبلهارسيا* والتي تسبب خلل حركة القناة الهضمية.