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Actions of Ya-hom, a herbal drug combination, on isolated rat aortic ring and atrial contractions

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Abstract

The effect of the Thai popular medicine Ya-hom on cardiovascular function was studied in isolated rat aortic ring and atrium by comparison with norepinephrine (NE). Water extraction of Ya-hom at concentrations of 0.83, 1.67, 8.33 and 16.67 mg/ml stimulated aortic ring contraction dose-dependently. The maximum contraction, at 16.67 mg/ml, was about 14% that of NE. This stimulatory effect of Ya-hom was inhibited partially by phentolamine, which indicated that the effect of Ya-hom was partially dependent on the α receptor, similar to NE. Administration of Ya-hom with NR decreased the force of aortic ring contraction as compared to the effect of NE alone, indicating that Ya-hom may have a partial α-agonist activity.

Ya-hom at concentrations of 1.67, 8.33 and 16.67 mg/ml showed a dose-dependent, positive inotropic and negative chronotropic effects. Ya-hom increased the force of isolated atrial contraction with a slow onset and prolonged action. In contrast to norephinephrine, which acted on β_1 receptor, causing positive inotropic and chronotropic effects, propranolol did not alter the effect of Ya-hom on the atrial contraction. This shows that the action of Ya-hom on atrial contraction does not involve β receptor.

This study demonstrated that the selected Ya-hom preparation increased vascular smooth muscle contraction, and increased the force but decreased the rate of atrial contraction.

Keywords: Ya-hom; Aortic ring; Rat atrium; Cardiovascular effects

Introduction

Ya-hom, one of the most popular Thai folk medicines, has been used for treatment of fainting, nausea and vomiting. Ya-hom preparations are marketed under different trade names with different compositions as well as different proportion of medicinal plants. The cardiovascular effects of some principal ingredients in Ya-hom have been reported. *Aquilaria agallocha* Roxb (Benbassat et al., 1959), Kote-sor (Khadzhai and Sokolova, 1960) and Chinese cinnamon (Kong et al., 1976) have been reported to cause vasodilation and decrease blood pressure, whereas aqueous and alcoholic extracts of Kote-kra-dook caused an increase in blood pressure (Bose et al., 1961). The methanol extract of Kote-kra-dook, however, inhibited KCl-induced aortic contraction (Shoji et al., 1986) and was also shown to

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have a hypotensive action (Gupta and Ghatak, 1967). Reports showed that licorice decreased (El-Mahdy et al., 1973; Shihata and Elghamry, 1963) and increased blood pressure (Hano et al., 1950; Fournier and Lagrue, 1971; Girerd et al., 1958), stimulated and depressed myocardium function and caused vasoconstriction and vasodilation according to concentration (El-Mahdy et al., 1973). Most of the Ya-hom recipes are composed of both cardiovascular stimulatory and inhibitory herbal medicines. Therefore, the exact action of each formula must be investigated.

There have been few reports about the effect of Ya-hom on both animal and human cardiovascular function. Ya-hom slowed the pulse rate and widened the pulse pressure in humans (Matangkasombat, 1973). In the rat, the water-soluble fraction of a chloroform extract and a water extract of Ya-hom extracts raised blood pressure, whereas the alcohol extract and water-insoluble fraction of the chloroform extract lowered blood pressure (Matangkasombat, 1974). In addition, Ya-hom extracts have a direct stimulating effect on the rat heart, whereas they show no effect on the rabbit heart (Matangkasombat, 1974). Another report using water extraction indicated that four brands of Ya-hom decreased blood pressure but had no effect on the heart rate, pulse pressure or electrocardiogram of rats (Wangmad et al., 1986). Two of these four brands (nos. 1 and 4) had a positive inotropic effect, two of them (nos. 1 and 3) had negative chronotropic effect, whereas the remaining one (no. 2) had no effect on the isolated atrium (Na Pattaloong and Sawasdimongkol, 1995). According to some controversial results, determination of the effect of Ya-hom on the cardiovascular function remains inconclusive. This may be due to use of the different brands, extraction methods and experimental models. Because most Ya-hom formulae contain similar major ingredients, the most famous brand of Ya-hom has been selected for the study of its cardiac and vascular effects, *in vitro* in this present study and using an *in vivo* model for the next study. The pharmacological actions of this brand have never been reported. A massive single preparation of a lyophilized water extract of Ya-hom was prepared for the entire experiment in order to reduce variation among extractions.

Materials and methods

Ya-hom preparation

The selected brand of Ya-hom was purchased from the Ya-hom producing company, Bangkok, Thailand. A 100-g sample of Ya-hom contains: 7.1 g *Agastache rugosa* (Fisch. et Mey.) O. Kuntze; 3.5 g *Acorus gramineus* Soland (Wan-num-lek); 3.3 g *Lysimachia foenum graecum* Hance; 7.1 g *Citrus nobilis* Lour.; 11.8 g *Magnolia officinalis* Rehd. et Wils; 7.1 g *Cinnamonum cassia* Presl (Chinese cinnamon); 3.5 g *Mentha arvensis* L.; 2.3 g *Asarum sieboldii* Mig. (Soie-cheng); 9.3 g *Ligusticum wallichii* Franch; 4.8 g *Glycyrrhiza glabra* L. (licorice); 7.1 g *Eugenia caryophyllata* Thunb. (clove); 7.1 g *Saussurea lappa* Clarke (Kote-kra-dook); 7.1 g *Aquilaria agallocha* Roxb.; 9.3 g *Atraetlis ovata* Thunb.; (Kote-kae-ma); 4.7 g menthol; 1.4 g Borneo camphor; and 3.5 g *Angelica anomala* Lallem (Kote-sor).

Ya-hom powder was boiled in water in a ratio of 1 g: 20 ml for 15 min, filtered through cotton and muslin cloth, and the filtrate lyophilized and kept at −20 °C until use. One gram of Ya-hom powder yielded 0.136 g of lyophilized product. Ya-hom solution was freshly prepared on the day of experiment by redissolving the lyophilized powder in Kreb–Henseleit solution for aorta (KH aorta) and Kreb–Henseleit solution for heart (KH heart) to investigate the effect of Ya-hom on isolated aortic ring and isolated atrium, respectively. The concentrations of Ya-hom are expressed as concentrations of Ya-hom powder in the organ bath (mg/ml).

HPLC analysis of Ya-hom

Lyophilized Ya-hom water extract was dissolved in methanol, sonicated for 20 min and then adjusted to a concentration of 0.01 g/ml with methanol. The sample was filtered through a Sep-pack® C18 cartridge before applying to HPLC using LiChrosphere® 100RP-18, Merck (5 μm) column and eluted with deionized water for 5 min, followed by a linear gradient of 10–100% acetonitrile for 15 min. The HPLC analysis of lyophilized Ya-hom water extract is shown in Fig. 1.

Animals

Male Wistar rats weighing between 180–220 g each were obtained from the National Laboratory Animal Center at Salaya, Mahidol University, Nakornpratom, Thailand. The rats were housed in hanging cages in the animal room at the Faculty of Pharmacy, Mahidol University, and fed with commercial rat diet (FE Zeullic) and tap water ad libitum.

Chemicals

Norepinephrine (NE) bitartrate, phentolamine and propranolol were purchased from Sigma Chemical Co., St. Louis, USA. Other chemicals were of analytical grade.