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Cardiovascular effects of total soyasaponin in central nervous system and its relationship with monoamine transmitters

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KEY WORDS soyabeans; saponins; blood pressure; heart rate; brain; biogenic monoamines

AIM: To study the cardiovascular effect of total soyabeans saponins (TS) in brain and its relationship with monoamines. **METHODS**: After injection of TS (75 μg) into ventriculus lateralis cerebri (VLC) the changes of blood pressure (BP) and heart rate (HR) were observed and the contents of monoamines both in peripheral blood and brain (telencephalon, diencephalon, brainstem) were measured respectively by HPLC-ECD and fluorophotometry. **RESULTS**: After injection of TS into VLC, BP rised from 11.59 ± 0.84 to 14.59 ± 0.69 kPa; HR increased from 411 ± 21 to 465 ± 14 bpm; the contents of NE and E in peripheral blood increased from 6 ± 3 to 64 ± 44, from 6 ± 2 to 38 ± 34 nmol/L plasma, respectively, NE in brainstem increased from 14 ± 0 to 18 ± 3 nmol/g wet tissue respectively, but the contents of 5-HT in the 3 areas measured in the experiment decreased: in telecephalon from 9 ± 1 to 5 ± 1, in diencephalon from 14 ± 2 to 7 ± 2, in brainstem from 14 ± 3 to 6 ± 1 nmol/g wet tissue. **CONCLUSIONS**: The cardiovascular effects of TS in CNS were involved in the monoamine transmitters.

Total soyasaponin (TS) had cardiovascular effects and was used clinically as a drug[1]. However, it was very little known whether TS in CNS affected the cardiovascular actions and what relationship was between TS and monamines. The purpose of this study was to investigate the cardiovascular effects of TS in CNS and its relationship with monoamines.

MATERIALS AND METHODS

Wistar rats (n = 41) weighing 250 ± s 20 g were divided randomly into TS and control groups. Rats were anesthetized with urethane 1.0 mg·kg^{-1} ip. The tracheas of all animals were cannulated with a polyethylene tube, and the femoral arteries were cannulated for recording arterial blood pressure (BP) and heart rate (HR) with 2 channels physiologic recorder (LMS-2B). A stainless steel cannula was inserted into VLC according to atlas Konig and Klippel[2], and the soyasaponins was injected into VLC (5 μL·min^{-1}, 75 μg). TS was from Department of Organic Chemistry of Norman Bethune University of Medical Sciences. TS consisted of all kinds of saponins extracted from soyabeans. TS was a white color powder. It was stable under regulary temperature and easily soluble in water, and it is hydrolyzed when it is heated in the acid solution. The purity of TS in this study was over 90 %. The control group rats were injected the same volume saline as TS into VLC.

In the second TS group, 30 min after injection of TS into VLC, the peripheral blood was collected and then the rats were decapitated. The brain was sectioned into telencephalon, diencephalon, and brainstem. The contents of NE, E, DA in peripheral blood were measured by Mefford method[3]. The contents of NE, DA, 5-HT, and 5-HIAA (5-hydroxyl-indol-acetate) in brain were measured by the flourophotometry of Curzon and Green[4]. The control group rats were injected the same volume saline as TS into VLC.

RESULTS

In the first TS group, 10 min after injection of TS into VLC, the blood pressure (BP) rose from 11.6 ± 0.8 to 14.6 ± 0.7 kPa (P < 0.05), and the heart rate (HR) increased from 411 ± 21 to 465 ± 14 beat·min^{-1} (P > 0.05). They recovered to the normal levels at 60th min. There were no significant differences in the BP and HR of the control group rats after injection of saline into VLC (P > 0.05).

In the second TS group, 30 min after injection of TS into VLC, the contents of NE and E in peripheral blood in TS group rats were elevated obviously (P < 0.05) *vs* those of the control group rats, but there were no significant difference between the content of DA in peripheral blood in TS

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group rats and that in the control group rats ($P > 0.05$) (Tab 1). Thirty minutes after injection of TS into VLC, both of the 5-HT and 5-HIAA in telencephalon, diencephalon, and brainstem were declined ($P < 0.05$), but the DA in telencephalon and brainstem was elevated ($P < 0.05$), and the NE in brainstem was also increased ($P < 0.05$) (Tab 2).

Tab 1. Effects of injection TS (75 μg) into VLC on NE, E, DA in peripheral blood.
$n = 10$, $\bar{x} \pm s$. $^aP > 0.05$, $^bP < 0.05$.

nmol/L plasma	Control	TS
NE	6 ± 3	64 ± 44[b]
E	6 ± 2	38 ± 34[b]
DA	2 ± 2	2 ± 2[a]

Tab 2. Effects of injection TS (75 μg) into VLC on monoamines in brain. $\bar{x} \pm s$. $^aP > 0.05$, $^bP < 0.05$, monoamines: nmol/g wet tissue.

		Control ($n = 11$)	TS ($n = 10$)
Telencephalon	NE	11 ± 2	11 ± 2[a]
	DA	13 ± 4	20 ± 2[b]
	5-HT	9 ± 1	5 ± 1[b]
	5-HIAA	7 ± 1	4 ± 1[b]
Diencephalon	NE	19 ± 3	19 ± 3[a]
	DA	41 ± 13	43 ± 10[a]
	5-HT	14 ± 2	7 ± 2[b]
	5-HIAA	11 ± 1	8 ± 1[b]
Brainstem	NE	14 ± 0	18 ± 3[b]
	DA	33 ± 7	45 ± 8[b]
	5-HT	14 ± 3	6 ± 1[b]
	5-HIAA	8 ± 2	6 ± 1[b]

DISCUSSION

The data from this experiment showed clearly that TS injected into VLC induced a pressor effect and maintained the level till near 1 h. The reasons may be as follows. First, injection of TS into VLC decreased the 5-HT, 5-HT in brain could decrease blood pressure and inhibit the pressor effect induced by some factors[5-8]. Second, injection of TS into VLC elevated the NE in peripheral blood and brainstem and the E in peripheral blood. NE and E both have pressor and speeding heart rate. Third, injection of TS into VLC made the DA in telecephalon and diencephalon rise. Injection of DA into cerebral ventricles induced a dose-dependent effect of pressor and tachycardiac[9].

In brief, the action that TS in CNS induced the pressor effect may be mediated by the NE, E elevation in peripheral blood strem from the excitation of sympathetic nerve by 5-HT, DA, and NE in brain.

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大豆总皂甙在中枢引起的心血管效应及其与单胺类递质的关系

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关键词 大豆类; 皂苷类; 血压; 心率; 脑; 生物单胺类

目的: 研究注入脑内大豆总皂甙(TS)的心血管效应及其与单胺类递质的关系. 方法: 记录大鼠侧脑室注入 TS (75 μg)引起的血压和心律的变化,

并用高压液相电化学检测法和荧光法测定端脑、间脑、脑干的单胺类递质含量 结果：TS 注入侧脑室后，血压由 11.59 ± 0 84 升至 14 59 ±0.69 kPa，心率由 411 ± 21 增至 465 ± 14 次/分；外周血中 NE，E 的含量分别由 6 ± 3 和 6 ± 2 升至 64 ± 44 和 38 ± 34 nmol/L 血浆；脑干内的 NE 由 33 ± 7 升至 45 ± 8 nmol/g 湿组织；端脑、间脑及脑干内的 5-HT 分别由 9 ± 1，14 ± 2 及 14 ± 3 降至 5 ± 1，7 ± 2 和 6 ± 1 nmol/g 湿组织。结论：中枢内的 TS 的心血管效应与单胺类递质有关。

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Electrophysiological effects of felodipine on guinea pig papillary muscles

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KEY WORDS felodipine; papillary muscles; action potentials; patch-clamp techniques; nifedipine; verapamil

AIM: To determine whether felodipine (Fel) has Ca^{2+} channel blocking effect in mammalian myocardium in comparison with those of nifedipine (Nif) and verapamil (Ver). **METHODS**: The action potentials (AP), the slow AP and the inward slow Ca^{2+} currents of guinea pig papillary muscles were studied using intracellular microelectrodes and voltage-clamp techniques. **RESULTS**: Fel 1, 3, and 10 μmol·L^{-1} concentration-dependently shortened APD_{30}, APD_{50}, and APD_{90} of the AP, while V_{max} and APA were not affected. The effect of Fel was not reversible on washout. At 0.1, 1, 3, and 10 μmol·L^{-1}, Fel depressed V_{max}, APA, APD_{30}, APD_{50}, and APD_{90} of the slow AP in a dose-dependent manner. The inward slow Ca^{2+} currents were reduced by Fel 3 μmol·L^{-1}. APD_{30}, APD_{50}, and APD_{90} of the first AP after rest were still shortened by Fel. When the stimulation frequency was elevated, the effect of Fel on the AP and slow AP decreased. The effect of Fel 3 μmol·L^{-1} on the slow AP was abolished in preparation pretreated with trifluoperazine. The threshold concentrations of Nif and Ver for the inhibition of APD_{50} of the slow AP ($P < 0.05$) were 0.1 and 1 μmol·L^{-1}, respectively. The effect of Ver 3 μmol·L^{-1} on the fast AP was not reversible on washout, but that of Nif 3 μmol·L^{-1} was. When the stimulation frequency was elevated from 0.5 to 2 Hz, the effect of Nif 3 μmol·L^{-1} on the fast AP was reduced, but that of Ver 3 μmol·L^{-1} was increased. **CONCLUSION**: Fel inhibited mainly the resting state of the cardiac Ca^{2+} channel. The potency of Fel was about the same as that of Nif and about 10 times more potent than that of Ver.

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Felodipine (Fel) is a calcium antagonist in vascular muscles[1,2]. Unlike verapamil (Ver) and nifedipine (Nif), Fel was an intracellular Ca^{2+} blocker rather than Ca^{2+} channel blocker[3]. In vascular muscle Fel was a Ca^{2+} channel blocker[4]. A WHO Committee proposed that demonstration with electrophysiological techniques of its ability to block Ca^{2+} entry into myocardial cells was considered mandatory for a Ca^{2+} channel blocker[5]. However, we have not seen the reports about the electrophysiological effect of Fel on cardiac tissues. This paper was to determine whether Fel had Ca^{2+} blocking effect in mammalian myocardium in comparison with those of Nif and Ver.

MATERIALS AND METHODS

Guinea pigs (weighing 250 ± *s* 31 g) of both sexes were stunned, and the papillary muscle from right ventricle was perfused with Tyrode solution 8 mL·min^{-1} at 35 ℃ gassed with 95 % O_2 + 5 % CO_2. The muscle was stimulated at 1 Hz by square pulse (duration: 1 ms; intensity: 2 ·