Gastrodin Improved Baroreflex Sensitivity and Increased Gamma-Amino Butyric Acid Content in Brains without Decreasing Blood Pressure in Spontaneously Hypertensive Rats

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Gastrodin, a bioactive component in *Gastrodia elata* Bl., has been approved as a drug for the treatment for dizziness and headache in China [1]. Combined with antihypertensive drugs, gastrodin was employed to deal with refractory hypertension in the elderly, but the effect of gastrodin alone on hypertension remains unknown.

Arterial baroreflex plays a crucial role in the regulation of cardiovascular activities, and baroreflex function impairment should be regarded as an independent risk factor in hypertension. A new strategy, improving the impaired arterial baroreflex function, has been promoted to treat cardiovascular disease [2]. Glutamate (GLU) and gamma-amino butyric acid (GABA), the most common neurotransmitters in the central nerve system (CNS), were both involved in baroreflex regulation [3]. Our present experiment was designed to investigate the effect of gastrodin on hypertension, baroreflex sensitivity (BRS) and content of GLU and GABA in the CNS in spontaneously hypertensive rat (SHR).

Spontaneously hypertensive rat (20–22 weeks of age) received gastrodin (Xi'nan Co., Chongqing, China) *via* the left femoral vein in doses of 8, 80 and 800 mg/kg ($n = 7$ per group). Blood pressure, heart period (HP) and BRS were recorded 0.5 h before and 2 h after drug administration in conscious freely moving SHR [4]. It was found that BRS was significantly enhanced after administration in 80 and 800 mg/kg (Figure 1D), while no significant difference was found (Figure 1A–C) in systolic blood pressure, diastolic blood pressure and HP.

In another experiment, 2 h after bolus injection of gastrodin (80 or 800mg/kg, *ip*) or vehicle ($n = 7$ –9 per group), content of GLU and GABA in whole brain of SHR was determined [4] using HPLC/MS. Gastrodin increased GABA content significantly in 800 mg/kg group (Figure 2A). No similar results were found about GLU content (Figure 2B).

The present study has directly demonstrated for the limited times that, independent of blood pressure reduction, gastrodin can significantly improve baroreflex function. The blood pressure was not the unique but the most common factor that influence arterial baroreflex. When a drug lowers blood pressure, BRS often increased. Gastrodin, similar to low dose of ketanserin [5], was one of the few drugs that can enhance BRS, not attributable to the normalization of BP levels. As baroreflex was an independent factor that causes end-organs damage in hypertension [2], the study of baroreflex mechanism became more and more important. The effect of gastrodin improving baroreflex without reducing blood pressure may help investigating baroreflex mechanism from more directions than blood pressure reduction.

Common mechanism of blood pressure and baroreflex in the CNS, especially in the nucleus of the solitary tract (NTS), was well reported [6, 7]. GABA regulated both blood pressure and baroreflex in the NTS, and injection of GABA agonists within the NTS produced an inhibition of NTS neurons, which resulted in reduction in the baroreflex bradycardia and an increase in arterial pres-

Figure 1 The effects of gastrodin(GAS) on (A) systolic blood pressure (SBP), (B) diastolic blood pressure (DBP), (C) heart period (HP) and (D) baroreflex sensitivity (BRS) in conscious SHR in doses of 8, 80, 800 mg/kg. The values are expressed as mean $\pm$ SD. Paired Student *t*-test, * $P < 0.05$ for after drug versus before drug. $n = 7$ in each group.

sure [6]. Meanwhile, GLU receptor antagonists block arterial baroreflex as well as regulate blood pressure in the NTS or in the caudal ventrolateral medulla [8]. Gastrodin decreased

immunoreactivities of GABA shunt enzymes in the hippocampus [9] and ameliorated the cerebral injury in the rats of cerebral ischaemia reperfusion by improving the level of GABA in striatum [10]. Our present study indicated gastrodin increased GABA content in the CNS. All these evidence suggested that GABA increased as a secondary effect in the CNS owing to the gastrodin administration.

In summary, gastrodin improved BRS without decreasing blood pressure in SHR.

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Conflict of Interest

The authors declare no conflict of interest.

Figure 2 Effect of gastrodin on content of the gamma-aminobutyric acid (GABA) and glutamate (GLU) in the central nerve system in doses of 80, 800 mg/kg or vehicle. (A) GABA, (B) GLU. Values are expressed as mean $\pm$ SD. Dunnett *t*-test, * $P < 0.05$ for treatment group versus control group. $n = 7-9$ in each group.

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