CADMIUM-INDUCED HYPERTENSION AND THE PROTECTIVE EFFECT OF STANDARDIZED EXTRACTS FROM ANDROGRAPHIS PANICULATA (BURM.F.) NEES

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Cadmium-Induced Hypertension and the Protective Effect of Standardized Extracts from Andrographis paniculata (Burm.f.) Nees

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Abstract

This research aims to investigate the effects of cadmium on blood pressure and the protective effects of standardized extracts from Andrographis paniculata (Burm.f.) Nees. Cadmium is known to increase blood pressure in both humans and experimental animals. Moreover, it has been reported that the extracts of Andrographis paniculata and its major compound, 14-deoxy-11,12-didehydroandrographolide (AP3), have a blood-pressure-lowering effect. However, no studies have been conducted to determine the effects of Andrographis paniculata and its major compound on blood pressure in cadmium-induced hypertension and the mechanisms of action of cadmium and Andrographis paniculata.

In this study, we exposed groups of white mice to cadmium (0.5, 0.75, 1 mg/kg; orally; 14 days) and treated them with Andrographis paniculata extracts or verapamil (50 mg/kg; orally) by oral gavage. The results showed that both groups of mice that received Andrographis paniculata extracts had significantly higher mean systolic blood pressure and cadmium levels in the kidneys, heart, blood vessels, and blood compared to the control group. There was no significant change in the response of the heart to NE and ACh in all groups. The results also showed that the extracts of Andrographis paniculata and verapamil have the potential to reduce blood pressure, indicating the efficacy of standardized extracts of Andrographis paniculata in the treatment of hypertension induced by cadmium.
ABSTRACT

Cadmium (Cd) has been reported to induce hypertension in humans and animals, while *Andrographis paniculata* (AP) and its active diterpenoid, 14-deoxy-11,12-didehydroandrographolide (AP3), have been reported to exhibit hypotensive and vasorelaxation effects. However, there is no study on the effects of AP and its active constituents on Cd-induced hypertension. Furthermore, the mechanisms of action of Cd and AP are not well understood. Therefore, to investigate the effects of Cd on the cardiovascular system, one group of rats was treated with Cd (0.5, 0.75, 1 mg/kg; i.p.; 14 days) and another group was exposed to Cd (5, 10, 50 ppm; 1 and 3 months) via drinking water. Significant increases in systolic blood pressure as well as in Cd content in kidney, heart, aorta and blood were detected in both groups. Norepinephrine (NE)-induced cardiac responses were not altered in the isolated right atria of both groups. Cd decreased the sensitivity of M2 receptors to acetylcholine (ACh) but did not alter the expression of M2 receptors. In addition, 14 days and 3 months of Cd exposure decreased NE-evoked vascular contraction whereas 1 month of exposure increased NE-induced vascular contraction in the isolated aorta. These results indicated that duration of exposure was crucial. Cd also decreased ACh-induced relaxation but did not alter M3 receptor expression in both groups. The reduction of ACh-induced relaxation may be mediated through the alteration of NO/cGMP pathways and through the decreased expression of endothelial nitric oxide synthase (eNOS) which was dependent on Cd content in the aorta.

To determine the effects of *A. paniculata* extracts containing different contents of AP3 on the cardiovascular system, rats were orally treated with Extracts A and B (6 and 60 mg/kg), Extract C (19 mg/kg) or verapamil (50 mg/kg) for 8 days. Extract B (high level of AP3) had greater hypotensive effect than Extract A (low level of AP3). Verapamil (a positive control) had less hypotensive effect than Extract C (high level of AP3). The responses of the Extract A-treated aorta to NE, and the vascular responses to ACh of both extracts A and B were decreased. However, neither extract altered cardiac response to NE or ACh. The extract containing high content of AP3 had the most potent hypotensive effect. In addition, Extract C decreased blood pressure in Cd-induced hypertensive rats. These results demonstrate, for the first time, the contribution of muscarinic cholinergic function and NO/cGMP dependent pathways in blood vessels of Cd-induced hypertensive rats. Furthermore, this study demonstrates the potential role of standardized AP extract in attenuating hypertension in human. Further study should be conducted to evaluate this hypothesis.

KEY WORDS: CADMIUM / HYPERTENSION / ANDROGRAPHIS PANICULATA / MUSCARINIC / eNOS

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