Orachorn Boonla. 2015. **Anti-Hypertensive and Anti-Oxidative Effects of Rice Bran Peptides and Curcumin in Experimental Models of Hypertension in Rats.** Doctor of Philosophy Thesis in Medical Physiology, Graduate School, Khon Kaen University.

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ABSTRACT

Increased free radical production, reduced nitric oxide bioavailability, and reduced activity of antioxidants in the vascular system are involved in the development of hypertension and cardiovascular disease. Consumption of dietary antioxidants has demonstrated their beneficial role in the prevention and treatment of hypertension. Rice bran protein hydrolysates or rice bran peptides (RBP) which was prepared extracted from rice bran protein via enzymatic hydrolysis possess important pharmacological activities, such as antidyslipidemic, antidiabetic and antihypertensive effects. Curcumin (CUR), a phenolic compound present in the rhizomes of turmeric, possesses cardiovascular protective, anti-inflammatory and antioxidant properties. Nonetheless, the mechanisms of RBP and CUR involved with the vascular protective effects, especially against hypertension have not yet been clarified.

The present study aimed to investigate the beneficial effects of RBP and CUR on hypertension, hemodynamic disturbance, oxidative stress, endothelial dysfunction and arterial structural changes during the development of hypertension in animal models of 2kidney-1clip (2K-1C) renovascular hypertension and N^{ω}–nitro-L-arginine metyl ester (L-NAME)-induced hypertension in male Sprague-Dawley rats.

The 2K-1C hypertension was induced in rats by placing a silver clip onto the left renal artery while sham-operated rats were served as sham controls. Sham-operated or 2K-1C rats were intra-gastrically administered with RBP or CUR at a dose of 50 or 100 mg/kg/day, or vehicle for 6 weeks. The L-NAME hypertension was induced in rats by administering L-NAME, a nitric oxide synthase (NOS) inhibitor at

a dose of 50 mg/kg/day in drinking water for 3 weeks whereas rats receiving tap water were served as normotensive controls. The rats were administered simultaneously with RBP or CUR at a dose of 50 or 100 mg/kg/day, or vehicle for 3 weeks.

At the end of experimental periods, it was found that RBP or CUR significantly improved hemodynamic performance in 2K-1C and L-NAME hypertensive rats by reducing high blood pressure, increasing hindlimb blood flow and decreasing hindlimb vascular resistance, when compared to normotensive rats ($P<0.05$). The improvement of hemodynamics in rats was associated with reduced plasma angiotensin converting enzyme and increased plasma nitrate/nitrite. Endothelium-dependent vasorelaxation, in response to acetylcholine, of aortic rings and mesenteric artery beds isolated from 2K-1C and L-NAME hypertensive rats-treated with RBP or CUR was significantly increased ($P<0.05$). In addition, RBP and CUR also attenuated hypertension-induced oxidative stress and vascular structural modifications in both thoracic aortas and mesenteric arteries. The ameliorative effects of RBP and CUR were associated with up-regulation of eNOS expression, down-regulation of $p47^{phox}$ NADPH oxidase and decreased superoxide production in vascular tissues of 2K-1C and L-NAME hypertensive rats.

The study suggest the mechanisms responsible for the antihypertensive effect of RBP and CUR in 2K-1C and L-NAME hypertensions-induced endothelial dysfunction and vascular remodeling involve the improvement of NO bioavailability and reduction in oxidative stress.