

Antihypertensive effect of hesperidin and losartan in renovascular hypertensive rats

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Introduction: Activation of renin-angiotensin system (RAS) and oxidative stress has been characterized in two-kidney, one-clip, 2K-1C hypertension model¹. Hesperidin, a flavonoid derived from citrus fruits, has several biological effects including anti-oxidation and anti-inflammation². The aim of this study is to investigate the effect of hesperidin on blood pressure, RAS and oxidative stress in renovascular hypertensive rats.

Method: Male Sprague-Dawley rats were anaesthetized with pentobarbital-sodium (60 mg/kg, i.p.) and a silver clip (0.2 mm width) was placed on the left renal artery to induce 2K-1C hypertension. Hypertensive rats were treated with hesperidin (40 mg/kg/day) or losartan (10 mg/kg/day) for four weeks while sham-operated control group and 2K-1C untreated group received vehicle, propylene glycol (n=7/each group). Systolic blood pressure (SP) was measured using a tail cuff method. Serum Angiotensin II (Angiotensin II Enzyme immunoassay kit), angiotensin converting enzyme (ACE) activity (fluorescent assay) and vascular superoxide production (lucigenin-enhanced chemiluminescence method) were evaluated. In addition, AT₁ receptor expression in the thoracic aorta was measured using the Western blot method. Data are expressed as mean ± S.E.M which compared using one-way ANOVA followed by Fisher's Least Significant Difference test.

Results: After seven weeks of experiment, the 2K-1C rats had high SP comparing to the sham-operated control rats (204.58±11.86 vs. 129.23±2.36 mmHg, p<0.05). Treatment with hesperidin or losartan significantly decreased SP comparing to untreated 2K-1C rats (143.96±3.65 or 141.11±3.12 mmHg, p<0.05). Significant increases in ACE activity (215.80±3.85 vs. 170.11±3.75 mU/ml), serum Angiotensin II level (47.92±2.38 vs. 25.16±1.66 pg/ml) and AT₁ receptor protein expression (168.20±23.86 vs. 100.00±0.00 % of control) were found in hypertensive rats comparing to sham-operated control rats (p<0.05). These were alleviated in hypertensive rats treated with hesperidin or losartan (ACE activity, 167.13±5.63 or 171.15±9.68 mU/ml; Angiotensin II level, 25.81±2.21 or 31.61±1.87 pg/ml; AT₁ receptor protein expression, 84.15±10.52 or 95.20±22.06 % of control, p<0.05). There was an increase in vascular superoxide production (107.72±10.65 vs. 58.98±5.62 count/mg dry wt/min) in hypertensive rats comparing to a sham-operated control group (p<0.05), this was reduced by hesperidin (52.44±3.80 count/mg dry wt/min) or losartan (51.58±10.32 count/mg dry wt/min) treatment, p<0.05.

Conclusion: Hesperidin has antihypertensive effect in renovascular hypertensive rats. The possible mechanism is likely to involve the inhibition of RAS activation and antioxidant property.

References:

1. Maneesai P, et al. (2017). *Naunyn-Schmiedeberg's Archives of Pharmacology* 1-11.
2. Jain M, et al. (2011). *Inflammation Research* **60(5)**: 483-491.