# Effects of nobiletin on blood pressure, vascular function and oxidative stress in L-NAME-induced hypertensive rats

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## Abstract

Nobiletin is a polymethoxylated flavone found in citrus peels. The beneficial effects of nobiletin have been reported such as anticancer and anti-oxidation. This study investigated whether nobiletin could alleviate hypertension, vascular dysfunction and oxidative stress in by L-NAME induced hypertensive rats. Male Sprague-Dawley rats weighing 220-250 g were given L-NAME (40 mg/kg/day) in drinking water for five weeks to induce hypertension. Hypertensive rats were intragastrically administered with nobiletin (20 or 40 mg/kg/day) or captopril (5 mg/kg/day) for the last two weeks (n = 6/each group). Systolic blood pressure (SP) and heart rate (HR) were measured once a week. Contractile responses to electrical field stimulation (EFS, 5-40 Hz, 1ms, 90V, 30s) and exogenous norepinephrine (NE) were tested in isolated mesenteric vascular beds (MVBs). Vasorelaxation responses to acetylcholine (ACh) and sodium nitroprusside (SNP) were performed in MVBs. In addition, vascular superoxide production, plasma malondialdehyde (MDA) and plasma nitric oxide metabolites (NOx) were evaluated. Rats treated with L-NAME had high SP and HR and these were alleviated by nobiletin and captopril treatment ($p<0.05$). Nobiletin or captopril suppressed the enhancement of contractile response to EFS in L-NAME hypertension ($p<0.05$). Both agents also improve vasorelaxation responses to ACh in MVBs in L-NAME rats, while the response to NE and SNP did not differ among groups. Moreover, high levels of vascular superoxide production and plasma MDA, and low level of plasma NOx were observed in L-NAME rats. These were restored by either nobiletin or captopril treatment ($p<0.05$). In conclusion, antihypertensive effect of nobiletin was associated with suppressing contractile response to sympathetic nerve stimulation, improving endothelium-dependent vasorelaxation, reducing oxidative stress and increasing NO bioavailability in L-NAME-induced hypertensive rats.

***Keywords:*** *Hypertension; L-NAME; Nobiletin; Vascular function; Oxidative stress.*