

## **Mechanisms of O-1602 Induced Endothelium-Independent Vasorelaxation of Rat Small Mesenteric Artery**

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**Abstract :** A typical cannabinoid O-1602 induces vasorelaxation and activates the orphan G protein-coupled receptor GPR55 in human endothelial cells. The aim of this study is to characterize the mechanisms of endothelium-independent relaxation of O-1602 in the rat small mesenteric artery using wire myograph. In endothelium-denuded vessels, O-1602 partially produced concentration-dependent vasorelaxation. In vessels depleted of intracellular Ca<sup>2+</sup> (by EGTA and methoxamine), CaCl<sub>2</sub> produced concentration-dependent contraction. Preincubation with O-1602 (at 10 μM and 30 μM) abolished the contractile responses (P<0.01). The putative antagonist at novel "endothelial anandamide receptor" O-1918 (10 μM) significantly reversed the inhibitory effect of O-1602 on CaCl<sub>2</sub>-induced vasoconstriction. It is likely that the mechanism of endothelium-independent vasorelaxation to O-1602 is mediated by interfering with Ca<sup>2+</sup> entry via an O-1918-sensitive pathway.

**Keywords :** O-1602, endothelium, vasorelaxation, calcium

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