

**Effect of DC-015, a novel potent and selective
α₁-adrenoceptor antagonist on plasma lipid and
vascular reactivity in hyperlipidemic rats. Clin. Exp.
Pharmacol.**

許準榕

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Abstract

1. The effects of DC-015, a newly synthesized quinazoline derivative, on plasma lipids, lipoprotein levels and vascular reactivity were investigated in Wistar-Kyoto rats (WKY) and spontaneously hypertensive rats (SHR).
2. The hypotensive effect of DC-015 was compared with prazosin in SHR. Intravenous administration of DC-015 and prazosin (both at 0.01, 0.05 and 0.1 mg/kg) induced dose-dependent reductions in mean arterial pressure (MAP) which reached a maximal effect 5 min after injection and persisted over 2 h in SHR. DC-015 decreased MAP with equal efficiency compared with prazosin.
3. The plasma levels of total cholesterol (CE), low-density lipoprotein (LDL)-CE and total triglyceride (TG) were markedly increased and the levels of high-density lipoprotein (HDL)-CE were markedly decreased in both high fat-high cholesterol (HF-HC) diet fed WKY and SHR.
4. In HF-HC diet fed WKY and SHR, the total plasma CE, LDL-CE and total plasma TG were significantly reduced after oral administration of DC-015 (1 mg/kg, twice a day) for 4 weeks. Furthermore, DC-015 therapy was associated with increased HDL-CE levels and thus the ratio of total CE to HDL-CE was improved. The antihyperlipidaemic effect of prazosin was less than that of DC-015.
5. Significantly attenuated median effective concentration (EC₅₀) values and augmented maximal responses for phenyl-ephine-induced contraction of aortic rings were observed in HF-HC diet fed WKY and SHR. Endothelium-dependent relaxation to acetylcholine was impaired while endothelium-independent relaxation to nitroglycerin was well preserved.

6. Oral administration of DC-015 (1 mg/kg, twice a day) for 4 weeks significantly augmented EC50 values and attenuated maximal responses for phenylephrine-induced contraction of aortic rings in HF-HC diet fed WKY and SHR. Prazosin (1 mg/kg, twice a day) showed a lesser extent of efficiency than DC-015 at normalization of vasorelaxation in HF-HC diet fed WKY and SHR.

7. It is concluded that DC-015, a potent antihypertensive agent, may have additional advantage in also reducing hyperlipidaemia