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Hypotensive Effect of Bunitrolol at Low Plasma Concentrations in Conscious, Unrestrained Spontaneously Hypertensive Rats

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Effects of bunitrolol on mean arterial pressure (MAP) and heart rate (HR) were studied in conscious, unrestrained spontaneously hypertensive (SHR) rats at rest and during handling stress. Propranolol was employed as a reference drug. Plasma drug concentrations were determined to related with the cardiovascular effects of the drugs. Bunitrolol produced a tachycardia for the first 2 hr and a significant reduction in resting MAP at 3 and 4 hr after the oral dose (5 mg/kg) when plasma bunitrolol concentration was less than 10 ng/ml, indicating the difference between cardiac and vascular beta adrenoceptors in sensitivity to intrinsic sympathomimetic action or direct vasodilator action. Propranolol (5 mg/kg) produced no discernible effects on resting MAP and HR. Stress-induced tachycardia was significantly inhibited by both drugs throughout the experiment, while significant inhibition of hypertensive response was observed only at 4 hr after the treatment. Both bunitrolol and propranolol were rapidly absorbed from the gastrointestinal tract. Plasma half-life of these drugs were almost the same values of around 2 hr. These results indicate that dose size, plasma concentrations, and procedures and the timing of blood pressure measurement are the important factors to be considered when the antihypertensive effect of *beta*-blockers is studied in SHR rats.

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