

EFFECT OF DCPIB ON THE CONTRACTILE ACTIVITY OF THE ISOLATED PERFUSED HEART

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ABSTRACT. The concentration-dependent effects of DCPIB were assessed in Langendorff-perfused hearts. Increasing doses of DCPIB caused a progressive decline in HR and $\pm dP/dt$, while significantly elevating LVEDP. LVSP showed a slight, non-significant increase, and LVDP remained unchanged.

KEYWORDS. DCPIB; VSOR; HR; LVSP; LVEDP; LVDP.

After osmotic pressure changes, VSOR (volume-sensitive outwardly rectifying) channels are activated, promoting the efflux of Cl^- and organic anions. This leads to water efflux and restoration of normal cell volume, known as the Regulatory Volume Decrease (RVD) process. DCPIB, a selective VSOR channel blocker, exerts beneficial effects in cardiac tissues by preventing excessive cell swelling and preserving myocardial contractility, particularly under ischemic conditions.

In the present study, the effect of DCPIB on contractile activity was assessed in the Langendorff apparatus at the following concentrations: 2.5, 5 and 10 μM . The measured parameters included heart rate (HR), left ventricular systolic pressure (LVSP), left ventricular end-diastolic pressure (LVEDP), left ventricular developed pressure (LVDP), the rates of pressure increase and decrease ($+dP/dt$ and $-dP/dt$). No significant differences were observed in LVDP between the control group and the DCPIB-administered group, whereas all other measured parameters exhibited concentration-dependent changes. HR and dP/dt parameters decreased dose-dependently with increasing DCPIB concentration. HR in control was 243 ± 10 bpm, while it decreased to 236 ± 11 bpm at 2.5 μM DCPIB, 224 ± 12 bpm at 5 μM , and 210 ± 14 bpm at 10 μM ($n=5$). LVSP showed a slight increasing trend, but the differences were not statistically significant. LVEDP significantly increased with increasing DCPIB concentration: in control it was 20.7 ± 3.0 mm Hg, while at 2.5 μM it was 27.4 ± 2.3 mmHg, 28.4 ± 2.1 mm Hg at 5 μM , and 31.5 ± 2.9 mm Hg at 10 μM . $+dP/dt$ and $-dP/dt$ indicated a decrease in cardiac contractile strength with increasing DCPIB dose. $+dP/dt$ in control was 1842 ± 207 mm Hg/s, decreasing down to 1756 ± 227 mm Hg/s at 2.5 μM , 1683 ± 208 mm Hg/s at 5 μM , and 1457 ± 159 mmHg/s at 10 μM . Similarly,

-dP/dt in control was -1162 ± 93.6 mm Hg/s, changing to -1066 ± 110 mmHg/s at $2.5\mu\text{M}$, -1032 ± 116 mm Hg/s at $5\mu\text{M}$, and -929 ± 97 mm Hg/s at $10\mu\text{M}$ ($n=5$).

DCPIB exerts a concentration-dependent depressive effect on contractile activity, as reflected by decreased HR and $\pm\text{dP/dt}$, along with a significant elevation in LVEDP. In contrast, LVSP and LVDP showed no notable changes. These findings suggest that DCPIB impairs both systolic performance and diastolic relaxation in a dose-dependent manner, likely through modulation of VSOR channel activity.

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