

Investigation on the cardio-protective effect of Xin Su Ning on ischemia-reperfusion induced injury in isolated heart.

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Introduction: We previously reported that Xin Su Ning (XSN) prolongs action potential duration (APD) of isolated cardiac myocytes^{1,2}. In this study we aimed to identify the cardio-protective effect of XSN in Ischemia-reperfusion (I/R) induced injury in isolated heart.

Methods: CHL cell line stably transfected human NaV1.5 channel were used for electrophysiological assay using Axopatch 200B patch clamp system with external and internal solutions prepared as previously described³. For isolated hearts study, male Sprague-Dawley rats (280 ~ 320g) were divided into control, I/R, XSN 0.05 g/L and 0.1 g/L groups. The hearts were isolated and perfused in retrograde mode at constant pressure of 60 mmHg at 37°C as previously reported³. The extracts of XSN in the form of frozen dried powder were administrated by dissolving in the perfusing solution. The measurements used to evaluate XSN's effects were: Left ventricular developed pressure (LVDP), the rate of pressure development and rate of relaxation (max/min dP/dt), and heart rate (HR). Rate pressure product (RPP) was calculated by multiplying LVDP by HR. The differences between control and other groups were tested using Student's *t*-test.

Results: XSN blocks human NaV1.5 channel in a dose dependent manner with an $IC_{50} = 0.184 \pm 0.017$ g/L. XSN at 0.1 g/L produced the significant recovery of LVDP during 60 min reperfusion as shown in Figure 1. Max dP/dt, min dP/dt and HR after 60 min perfusion with vehicle and difference concentrations of XSN were shown in Table 1.

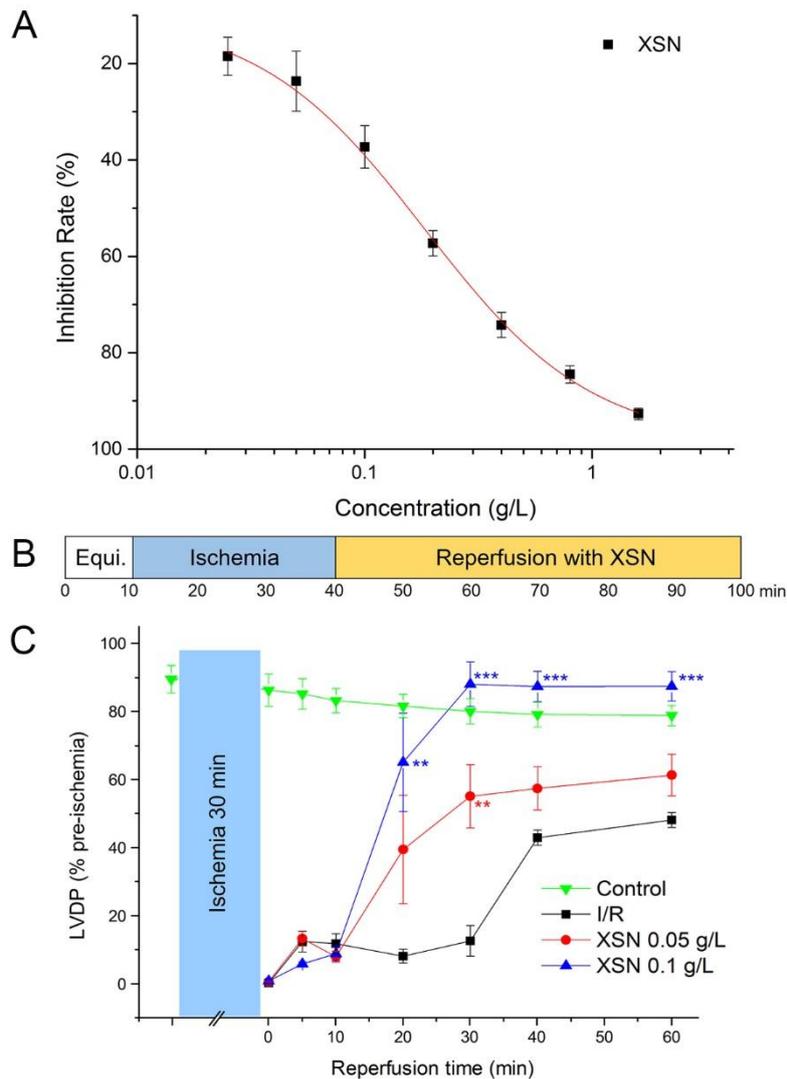


Fig. 1 (A) Dose response curve of XSN on human NaV1.5 channel (n=5); (B) Experimental protocol of contractile function of I/R perfused rat heart; (C) percent rate of LVDP of rat hearts with/without XSN treatment after reperfusion 0, 5, 10, 20, 30, 40, 60 min (n=5). The data were presented as mean±SEM. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. I/R group.

Table 1 Myocardial contractile function measured ex vivo in a rat I/R heart (mean±SEM, n=5).

%pre-ischemia	LVDP	max dP/dt	min dP/dt	HR	RPP
I/R	48.11±2.18	56.82±4.91	48.06±3.67	97.61±5.80	46.82±3.06
XSN 0.05 g/L	61.28±6.08	57.50±7.82	58.07±6.05*	79.15±4.34	48.85±6.43
XSN 0.1 g/L	87.36±4.34***	93.39±4.53**	90.27±4.25***	75.56±3.94*	70.57±5.38**

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. I/R group.

Conclusions: XSN blocked NaV1.5 channel dose dependently, and together with the APD prolongation which could be the cellular electrophysiological mechanisms of the anti-tachyarrhythmic effect of XSN. XSN improved cardiac systolic function on ischemia-reperfusion injured rat heart by increasing LVDP, RPP, max dP/dt and min dP/dt, the protective effect may contribute to the anti-arrhythmic effect of XSN on ischemic heart.

References:

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