

三七皂甙 Rb<sub>1</sub> 和 Rg<sub>1</sub> 对心肌动作电位及慢内向电流的影响

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Effects of *Panax notoginseng* saponin Rb<sub>1</sub> and Rg<sub>1</sub> on myocardial action potential and slow inward current

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**ABSTRACT** The effects of Rb<sub>1</sub>, Rg<sub>1</sub> (purified saponin of *Panax notoginseng*) on contraction force, action potential and slow inward current of guinea pig papillary muscles were studied by intracellular micro-electrodes and voltage clamp techniques. The contraction force was decreased and the APD<sub>20</sub> was shortened in the presence of Rb<sub>1</sub> 1 mg/ml, while the RP, APA and V<sub>max</sub> remained unchanged. The amplitude of I<sub>si</sub> was decreased from a peak value of 9.8 ± 1.6 to 7.3 ± 3.4 μA after 20 min perfusion with Rb<sub>1</sub> solution. This effect was reversed by increasing calcium concentration. Rg<sub>1</sub> 1 mg/ml decreased the contraction force significantly without affecting the configuration of action potential and the amplitude of slow inward current. The results indicate that Rb<sub>1</sub> has a blocking effect on calcium channels, but Rg<sub>1</sub> has not.

**KEY WORDS** *Panax notoginseng*; saponins; papillary muscles; action potentials; calcium channel blockers

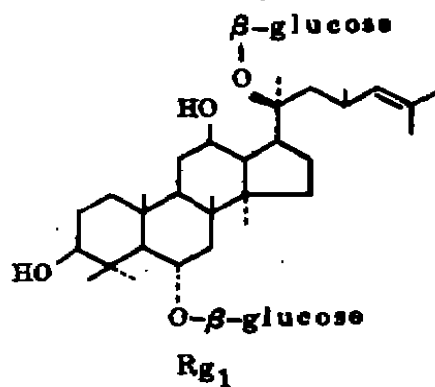
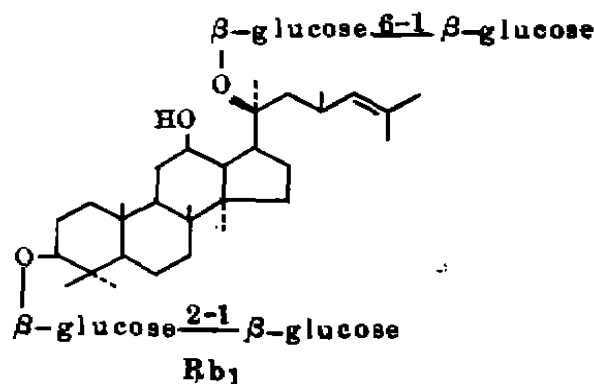
**摘要** 采用微电极方法及电压钳制技术, 观察三七皂甙 Rb<sub>1</sub>, Rg<sub>1</sub> 对豚鼠右心室乳头状肌动作电位 (AP)、收缩张力 (F<sub>c</sub>) 及慢钙电流 (I<sub>si</sub>) 的影响。Rb<sub>1</sub> 1.0 mg/ml 显著抑制 F<sub>c</sub>, 缩短动作电位的 2 相平台期并降低 I<sub>si</sub> 的幅度, 对 RP, APA 及 V<sub>max</sub> 无明显影响。Rg<sub>1</sub> 1.0 mg/ml 抑制 F<sub>c</sub>, 但对动作电位间期及 I<sub>si</sub> 的幅度均无影响。

Received 1988 Sep 22 Accepted 1989 Mar 22

表明 Rb<sub>1</sub> 可阻滞钙通道, Rg<sub>1</sub> 则无此作用。

**关键词** 三七, 皂甙类, 乳头状肌, 动作电位, 钙通道阻滞剂

三七皂甙 Rb<sub>1</sub>, Rg<sub>1</sub> 是从三七总皂甙 (total saponins of *Panax notoginseng*, PNS) 分离纯化得到的皂甙单体, 结构式如下:



它们虽是同一个来源,药理作用却不相同。 $Rb_1$ 能改善异丙肾上腺素诱发的心肌损伤并对结扎冠脉引起的心肌缺血损害有一定的保护作用, $Rg_1$ 则无(未发表资料)。对于去甲肾上腺素诱发的离体血管条收缩, $Rb_1$ 显著抑制胞外钙内流相, $Rg_1$ 则对胞内钙释放相有明显的抑制作用<sup>(1)</sup>。本文研究 $Rb_1$ 、 $Rg_1$ 对心肌动作电位、收缩张力及慢钙电流的影响,进一步探讨其作用机理。

## MATERIALS AND METHODS

三七皂甙 $Rb_1$ 、 $Rg_1$ 均由广州市医药工业研究所植化室提供,薄层层析显示单一斑点,扫描测定纯度大于95%。

采用豚鼠右心室乳头状肌进行实验,常规微电极方法记录动作电位。标本腱索端连接拉力换能器,同步记录收缩力。

膜电流记录采用单蔗糖间隙电压钳制方法,具体步骤见文献<sup>(2)</sup>。

## RESULTS

**$Rb_1$ 、 $Rg_1$ 对豚鼠右心室乳头状肌 $F_c$ 及AP的影响**  $Rb_1$  0.5, 1.0 mg/ml 灌流 20 min,  $F_c$  分别降低 10 和 23%,  $APD_{20}$  从给药前的  $92 \pm 16$  ms 分别缩短至  $87 \pm 16$  和  $86 \pm 17$  ms,  $APD_{50}$  及 ERP 略缩短但与给药前比较无显著性意义, RP, APA 及  $V_{max}$  均无明显变化 (Tab 1, Fig 1)。

$Rg_1$  0.5, 1.0 mg/ml 灌流 20 min,  $F_c$  分别

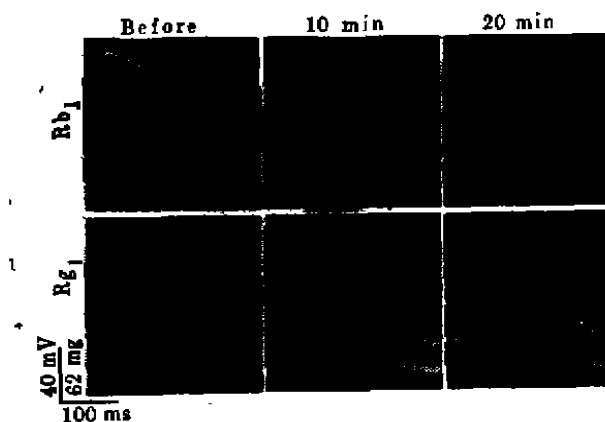


Fig 1. Effects of purified saponin of *Panax notoginseng*  $Rb_1$ ,  $Rg_1$  1.0 mg/ml on action potential and contraction force of guinea pig papillary muscles.

降低 14 和 19%,  $APD_{20}$  略缩短但与给药前比较无显著性意义,余参数均无明显改变 (Tab 1, Fig 1)。

**$Rb_1$ 、 $Rg_1$ 对心肌 $I_{Ca}$ 的影响** 将维持电位置于  $-40$  mV, 指令电位置于  $-20$  mV, 可记录到缓慢的内向电流, 即慢钙电流  $I_{Ca}$ 。  $Rb_1$  1.0 mg/ml 灌流 10 min,  $I_{Ca}$  峰值减小 15%, 20 min 减小 26%, 将灌流液中  $Ca^{2+}$  浓度由正常的 1.8 增加至 5.4 mmol/L,  $I_{Ca}$  逐渐恢复, 10 min 后达到给药前的 119%。  $Rg_1$  1.0 mg/ml 灌流 10 min,  $I_{Ca}$  峰值增加 4%, 20 min 减少 5%, 但与给药前比较均无显著性意义 (Tab 2, Fig 2)。

Tab 1. Effects of purified saponins of *Panax notoginseng*  $Rb_1$  and  $Rg_1$  0.5-1.0 mg/ml on action potentials and contraction force of guinea pig papillary muscles,  $n=9$ ,  $\bar{x} \pm SD$ . \* $P < 0.05$ , \*\* $P < 0.05$ , \*\*\* $P < 0.01$ .

Parameter	$Rb_1$			$Rg_1$		
	Before	0.5	1.0 mg/ml	Before	0.5	1.0 mg/ml
RP (mV)	$82 \pm 2$	$81 \pm 2^*$	$82 \pm 1^*$	$84 \pm 3$	$85 \pm 4^*$	$85 \pm 4^*$
APA (mV)	$112 \pm 3$	$111 \pm 4^*$	$110 \pm 4^*$	$116 \pm 6$	$117 \pm 7^*$	$117 \pm 7^*$
$V_{max}$ (V/s)	$225 \pm 17$	$217 \pm 28^*$	$220 \pm 30^*$	$234 \pm 44$	$231 \pm 45^*$	$236 \pm 45^*$
$APD_{20}$ (ms)	$92 \pm 16$	$87 \pm 16^{**}$	$86 \pm 17^{***}$	$86 \pm 17$	$84 \pm 18^*$	$82 \pm 19^*$
$APD_{50}$ (ms)	$183 \pm 28$	$179 \pm 25^*$	$180 \pm 27^*$	$185 \pm 20$	$184 \pm 23^*$	$183 \pm 25^*$
ERP (ms)	$188 \pm 26$	$186 \pm 26^*$	$185 \pm 29^*$	$190 \pm 28$	$191 \pm 34^*$	$190 \pm 36^*$
$F_c$ (mg)	$60 \pm 15$	$54 \pm 14^{***}$	$46 \pm 18^{***}$	$57 \pm 10$	$50 \pm 15^{**}$	$46 \pm 14^{***}$

Tab 2. Effects of Rb<sub>1</sub>, Rg<sub>1</sub> 1.0 mg/ml on amplitude of I<sub>si</sub> (μA) in guinea pig papillary muscles. Holding potential (E<sub>H</sub>) was -40 mV, command potential (E<sub>c</sub>) was -20 mV.  $\bar{x} \pm SD$ . \*P>0.05, \*\*P<0.05, \*\*\*P<0.01.

	I <sub>si</sub> (μA)	
	Rb <sub>1</sub> (n=8)	Rg <sub>1</sub> (n=9)
Before	9.8±1.6	9.6±1.8
10 min	8.3±2.7**	10.0±3.7*
20 min	7.3±3.4**	9.1±4.0*
CaCl <sub>2</sub> 5.4 mmol/L	11.7±2.8**	12.0±3.4***

## DISCUSSION

Rb<sub>1</sub> 抑制心肌收缩力, 缩短动作电位的 2 相平台期, 降低心肌慢钙电流的幅度且可以被外钙浓度的增加所逆转, 结合文献(1), 符合钙通道阻滞剂的基本特征<sup>(3)</sup>, 可以认为 Rb<sub>1</sub> 具钙通道阻滞作用。

Rg<sub>1</sub> 对心肌动作电位的 2 相平台期无影响, 对慢钙电流的幅度无抑制, 提示无钙通道阻滞作用。它对心肌收缩力的抑制可能是通过影响其它环节, 如抑制胞内钙释放等而发挥的。

致谢 广州市医药工业研究所植化室提供三七皂甙; 本室马郁琪老师协助薄层鉴定。

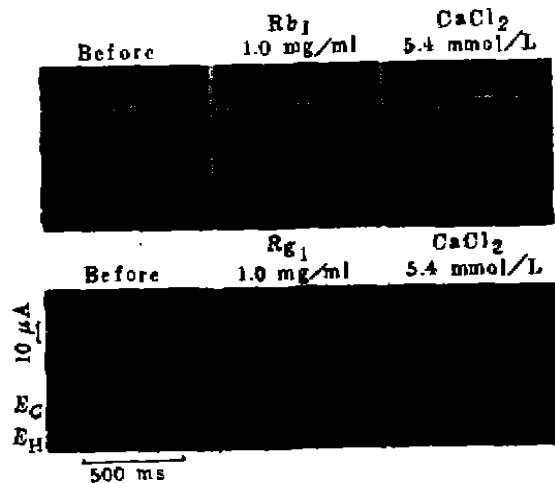


Fig 2. Effects of Rb<sub>1</sub> and Rg<sub>1</sub> 1.0 mg/ml on slow inward current of guinea pig papillary muscles. Upper trace, transmembrane current; lower trace, transmembrane potential. Holding potential (E<sub>H</sub>) was -40 mV, command potential (E<sub>c</sub>) was -20 mV.

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1990 Jul 17-22

Bonn, FRG

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