

三七皂甙 Rb₁ 和 Rg₁ 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 Rb₁ and Rg₁ on myocardial action potential and slow inward current

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ABSTRACT The effects of Rb₁, Rg₁ (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 APD₂₀ was shortened in the presence of Rb₁ 1 mg/ml, while the RP, APA and V_{max} remained unchanged. The amplitude of I_{si} was decreased from a peak value of 9.8 ± 1.6 to 7.3 ± 3.4 μA after 20 min perfusion with Rb₁ solution. This effect was reversed by increasing calcium concentration. Rg₁ 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 Rb₁ has a blocking effect on calcium channels, but Rg₁ has not.

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

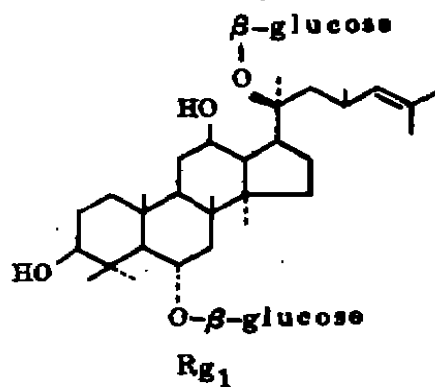
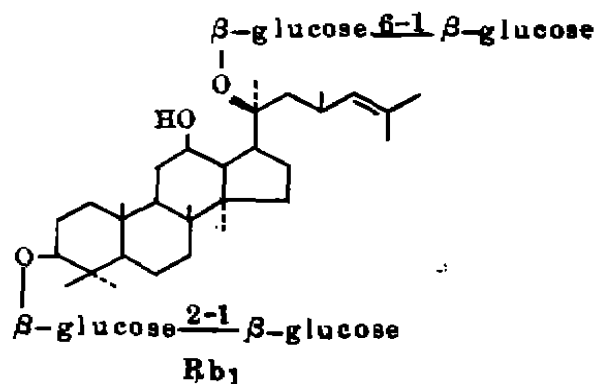
摘要 采用微电极方法及电压钳制技术, 观察三七皂甙 Rb₁, Rg₁ 对豚鼠右心室乳头状肌动作电位 (AP)、收缩张力 (F_c) 及慢钙电流 (I_{si}) 的影响。Rb₁ 1.0 mg/ml 显著抑制 F_c, 缩短动作电位的 2 相平台期并降低 I_{si} 的幅度, 对 RP, APA 及 V_{max} 无明显影响。Rg₁ 1.0 mg/ml 抑制 F_c, 但对动作电位间期及 I_{si} 的幅度均无影响。

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表明 Rb₁ 可阻滞钙通道, Rg₁ 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 Rb₁, Rg₁ 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⁽¹⁾。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⁽²⁾。

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 ± 16 ms 分别缩短至 87 ± 16 和 86 ± 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

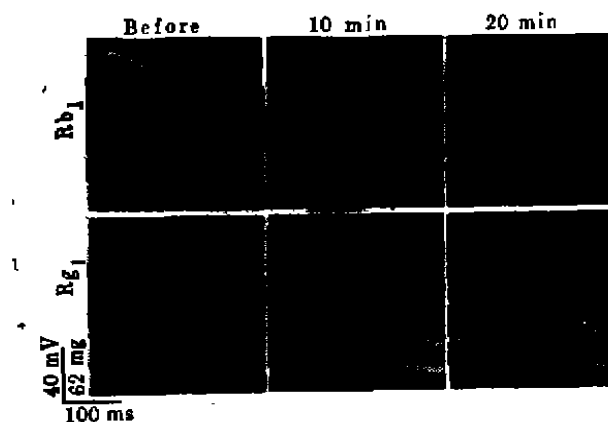


Fig 1. Effects of purified saponin of *Panax notoginseng* Rb_1 , Rg_1 1.0 mg/ml on action potential and contraction force of guinea pig papillary muscles.

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

Tab 2. Effects of Rb₁, Rg₁ 1.0 mg/ml on amplitude of I_{si} (μA) in guinea pig papillary muscles. Holding potential (E_H) was -40 mV, command potential (E_c) was -20 mV. $\bar{x} \pm SD$. *P>0.05, **P<0.05, ***P<0.01.

	I _{si} (μA)	
	Rb ₁ (n=8)	Rg ₁ (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 ₂ 5.4 mmol/L	11.7±2.8**	12.0±3.4***

DISCUSSION

Rb₁ 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⁽³⁾, 可以认为 Rb₁ 具钙通道阻滞作用。

Rg₁ 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。

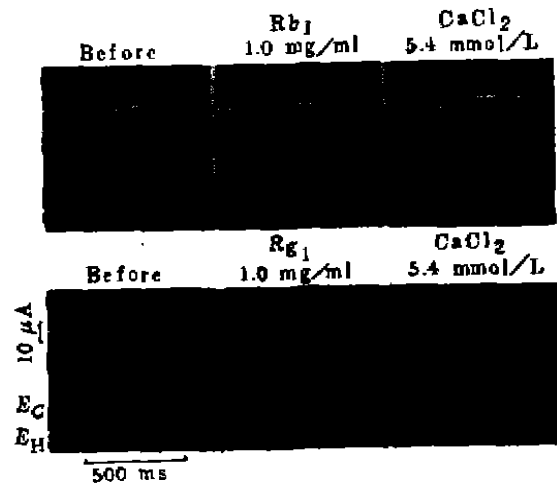


Fig 2. Effects of Rb₁ and Rg₁ 1.0 mg/ml on slow inward current of guinea pig papillary muscles. Upper trace, transmembrane current; lower trace, transmembrane potential. Holding potential (E_H) was -40 mV, command potential (E_c) was -20 mV.

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