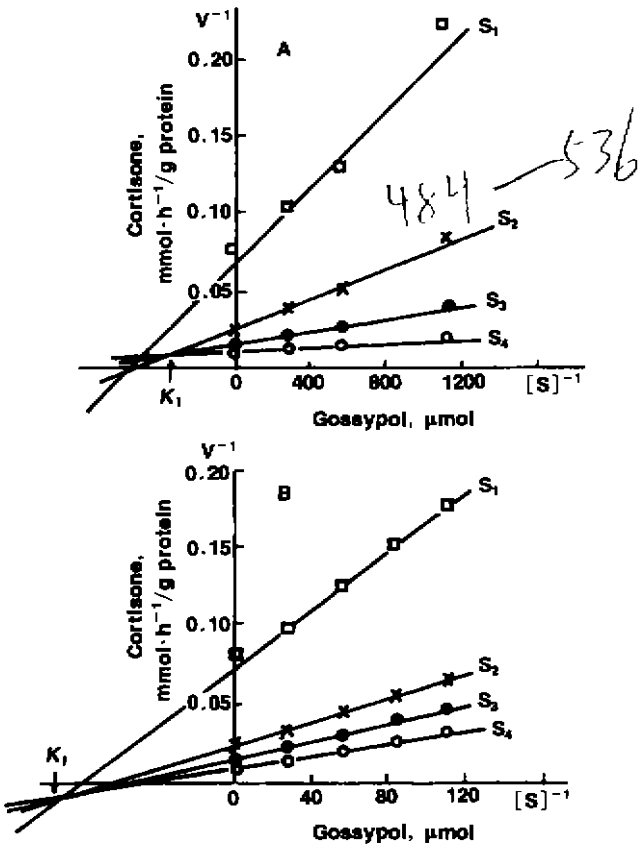

Fig 3. Effects of gossypol on kidney cortex microsome 11β-OHSD by Dixon plot. A: NADP-dependent enzyme; B: NAD-dependent enzyme. S_1: 1.58 μmol, S_2: 4.73 μmol, S_3: 7.88 μmol, S_4: 15.8 μmol of cortisol.

to the potent inhibitor-gossypol acetic acid were very different. The ratio of relative inhibitory potency of gossypol acetic acid is over twenty times in favor of NAD-dependent one. The dose of gossypol acetic acid used in clinical trial was usually 20 $mg \cdot d^{-1}$ per man. According to such low physiologic concentration of this compound, from a forementioned results, we can draw an inference that, the NAD-dependent 11β-OHSD isoform localized in the distal renal tubules may be a more critical physiologic mechanism in regulating renal glucocorticoid levels, then cause the hypokalemia when existence of a potential inhibitor. This hypothesis remains to be confirmed further *in vivo* in the prospective investigation.

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棉酚抑制豚鼠肾脏依赖 NAD 和 NADP 的 11β-羟基甾体脱氢酶同工酶

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关键词 羟基甾体脱氢酶类; 同工酶类; 棉酚; 低钾血症; 甾类

目的: 探讨棉酚诱发低钾血症机制. 方法: 从豚鼠肾脏皮质制备 11β-OHSD, 反相高效液相测定该酶活性. 结果: 依赖辅酶 I 的 11β-OHSD 的 V_{max} = 0.64 mmol·h^{-1}/g protein, K_m = 0.07 μmol; 依赖辅酶 II 的 11β-OHSD 的 V_{max} = 1.75 mmol·h^{-1}/g protein, K_m = 0.21 μmol. 棉酚对它们的抑制有显著差异, IC_{50}(95 %可信限) 前者为 50.2 (48.3 – 52.0) μmol, 后者为 1143 (1098 – 1188) μmol, 抑制常数 K_i 分别为 96 mmol·L^{-1}和 340 mmol·L^{-1}. 结论: 抑制依赖辅酶 I 的 11β-OHSD 是棉酚诱发低钾血症的更主要的生理因素.

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Effect of SR-140333, a neurokinin-1 receptor antagonist, on airway reactivity to methacholine in sedated rats[1]

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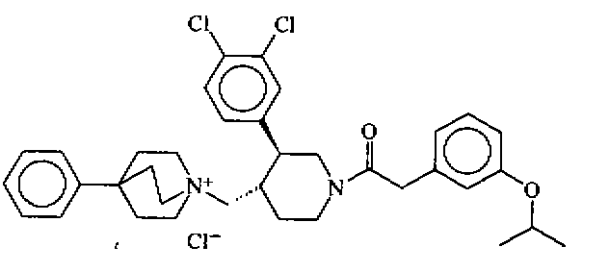
KEY WORDS SR-140333; methacholine chloride; atropine; neurokinin-1 receptors; albuterol; aminophylline; dexamethasone; trachea

AIM: To study the roles of neurokinins in the airway reactivity (AR) to methacholine chloride (MC). **METHODS**: The effects of (*S*)-1-(2-[3, 4-dichlorophenyl)-1-(3-isopropoxyphenylacetyl) piperidin-3-yl] ethyl)-4-phenyl-1-azoniabicyclo [2.2.2] octane·chloride (SR-140333), a neurokinin-1 receptor antagonist, on AR to inhaled MC in diazepam-sedated rats, and on MC-induced contraction of isolated tracheal spiral strips were observed. **RESULTS**: SR-140333 inhibited the increase in respiratory rate (RR) induced by MC aerosol (10 – 1000 μmol/m^3), and the ID_{50} for inhibiting the response to MC aerosol (1 mmol/m^3) was 4.9 μg·kg^{-1}(95 % confidence limits 1.4 – 17.2 μg·kg^{-1}). SR-140333 1 μmol·L^{-1} had no inhibitory effect on MC-induced tracheal contraction. Atropine blocked responses to MC both *in vivo* and *in vitro*. **CONCLUSION**: Endogenous neurokinins are involved in the AR to MC in rats, at least partly mediated via neurokinin-1 receptors.

Airway hyperreactivity to a wide variety of pharmacological and physical agents is one of the characteristics of asthma. Methacholine chloride (MC), is often used for measuring airway reactivity (AR) in humans[1] and animals[2]. Stimulation of sensory nerve C-fibers and the secondary release of tachykinins (TK), such as substance P (SP) and neurokinin A (NK-A), in the airways play an important role in AR to various stimuli[3], and antigen-induced airway inflammation[4,5] and bronchoconstriction[5,6]. MC or vagal nerve stimulation releases SP and NK-A from perfused guinea pig lungs[7,8]. Whether AR to MC relates to sensory nerve function and TK remains unclear. The present study was to clarify the contribution of endogenous TK to MC AR in rats using a neurokinin-1 receptor antagonist, SR-140333[9,10].



(*S*)-1-(2-[3,4-dichlorophenyl)-1-(3-isopropoxyphenylacetyl)piperidin-3-yl]ethyl)-4-phenyl-1-azoniabicyclo [2.2.2]octane·chloride

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