药学学报 2006, 41(6) 498-505 DOI: ISSN: CN:

论文

三七皂苷的口服吸收机制

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摘要：

目的研究三七总皂苷(PNS)的口服吸收机制。方法采用Caco-2细胞和动物等模型研究PNS中人参皂苷Rb_1(Rb_1)和人参皂苷Rg_1(Rg_1)的胃肠道内稳定性、肠道黏膜吸收机制及吸收过程中胃、肠及肝对药物的影响。结果Rb_1和Rg_1在胃液酸性环境下易被破坏，而在近中性环境内基本保持稳定。Rb_1和Rg_1在大肠内容物中易降解，尤以Rb_1降解较为明显；二者在小肠内容物中则相对稳定。Rb_1和Rg_1在Caco-2细胞层的摄取受温度的影响，而pH的变化及环孢菌素A的加入对二者摄取均无显著性影响。在实验考察的浓度范围内，细胞内Rb_1(或Rg_1)的摄取量随Rb_1(或Rg_1)的浓度的增加而呈线性增加，Rb_1(或Rg_1)单体与总皂苷中的Rb_1(或Rg_1)在Caco-2细胞模型中的吸收特性无明显差异。而Rg_1的细胞摄取量［(1.07±0.16) μg·mg^{-1}(protein)］(C_0=1 mg·mL^{-1})相对Rb_1［(0.77±0.03) μg·mg^{-1}(protein)］(C_0=1 mg·mL^{-1})较高。Caco-2细胞转运实验表明，Rb_1和Rg_1单体的转运透过系数(P_{app})分别为50.56%。结论三七皂苷(包括Rb_1和Rg_1)的吸收机制为单纯被动扩散，吸收过程不受细胞膜内P-gp和MRP外排载体的调控，PNS中其他成分对Rb_1或Rg_1的吸收特性无明显影响。胃液的酸性环境、大肠菌丛产生的酶及肝脏的首过作用均对其口服吸收产生影响，而肠道黏膜的透过性低是其口服吸收差的主要影响因素。

关键词： 三七总皂苷 Caco-2细胞 生物利用度 人参皂苷Rb_1 人参皂苷Rg_1

Mechanism of oral absorption of panaxnotoginseng saponins

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Abstract:

AimTo study the mechanism of absorption after oral administration of panaxnotoginseng saponins (PNS). MethodsCaco-2 cells and rat models were applied to evaluate the degradation of both ginsenoside Rb_1(Rb_1) and ginsenoside Rg_1(Rg_1) in PNS in gastrointestinal lumen, and the transport mechanism of PNS across the intestinal mucosa, and the barrier function of stomach, intestine and liver involved in absorption process. ResultsRb_1 and Rg_1 proved to be readily eliminated in stomach, but stable in relatively neutral circumstance. Both Rb_1 and Rg_1 in PNS, especially for Rb_1, degraded significantly in the contents of large intestine. However, both of them kept mainly intact in the contents of small intestine. Uptake of both Rb_1 and Rg_1 by Caco-2 cell monolayer was inhibited at low temperature, but not by cyclosporine A, and the change in the apical pH showed no pronounced effect. Uptake and transport were non-saturable and increased linearly with increasing of concentrations of Rb_1 and Rg_1 over the range of concentration tested, which indicated a passive transport. There was no significant difference of absorption characteristic between monomer (Rb_1 and Rg_1) and mixture (PNS). Uptake amount of Rg_1［(1.07±0.16) μg·mg^{-1}(protein)］ (C_0=1 mg·mL^{-1}) in Caco-2 cells was a little higher than that of Rb_1［(0.77±0.03) μg·mg^{-1}(protein)］ (C_0=1 mg·mL^{-1}). Meanwhile, apparent permeability coefficient of Rg_1 were not influenced by cyclosporine A. The P_{app} from Rb_1 ((2.59±0.17)×10^{-7} cm·s^{-1} (C_0=1 mg·mL^{-1}) for Rg_1 from apical compartment to basolateral compartment predicted an incompletely absorption. Transports of both Rb_1 and Rg_1 were not influenced by cyclosporine A. The P_{app} from Rb_1 ((2.59±0.17)×10^{-7} cm·s^{-1} (C_0=1 mg·mL^{-1}) for Rg_1 from apical compartment to basolateral compartment predicted an incompletely absorption. Transports of both Rb_1 and Rg_1 after different routes of administration to rats showed that the absolute bioavailability after peroral (po), intraduodenal (id), and portal venous (pv) administration is 0.71%, 2.75% and 65.77% respectively for Rb_1, and 3.29%, 6.60% and 50.56% respectively for Rg_1. ConclusionTransport across Caco-2 cell monolayer for PNS (include Rb_1 and Rg_1) is a simple passive diffusion process. No efflux transporters in Caco-2 cells and other components in PNS showed effects on it. The elimination in stomach, large intestine and liver contributed to the low bioavailability of PNS, but the low membrane permeability might be a more important factor dominating the extent of absorption.

Keywords: Caco-2 cells bioavailability ginsenoside Rb_1 ginsenoside Rg_1 panaxnotoginseng saponins

收稿日期 2005-09-29 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 方晓玲

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