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论文

新型促吸收剂研究进展——以细胞间紧密连接为靶点

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摘要：

亲水性小分子药物、多肽和蛋白质主要通过胞旁通路吸收。这类药物膜通透性较差，口服生物利用度较低。紧密连接是构成胞旁通路的结构基础，传统的胞旁通路促吸收剂一般对黏膜损伤较大，限制了这些药物的临床应用。近年来，随着对紧密连接结构、功能认识日益加深，许多特异性的促吸收剂被发现，如NO供体、CPE和Zot等，实验表明，通过瞬间可逆的打开紧密连接，这些促吸收剂可显著增加胞旁转运标志物和亲水性药物的吸收，而其毒副作用较传统的促吸收剂大为降低。总之，新型促吸收剂提供了一个增加亲水性药物生物利用度的有益思路。

关键词： 胞旁通路 紧密连接 促吸收

Advances in study of novel absorption enhancers based on tight junctions

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Abstract:

Hydrophilic low molecular drugs, peptides and proteins, which are always poor in bioavailability, are mainly absorbed through the paracellular way in which the tight junction is the elementary framework. The tight junctions are a multiple unit structure composed of multiprotein complex that affiliates with the underlying apical actomyosin ring. Tight junction proteins are identified including transmembrane proteins (occludin, claudin and JAM), cytoplasmic plaque proteins (ZO-1, ZO-2, ZO-3 and cingulin) and cytoskeleton. Traditional absorption enhancers can usually impair mucous membranes which constraint the utilization of these enhancers. Recently, with the increasing knowledge of the structure and function of tight junctions, many new absorption enhancers have been developed such as NO donor, CPE, Zot, and so on. *In vivo* and *in vitro* studies have shown that these enhancers could be effectively used to increase the absorption of paracellular markers and low bioavailable drug across intestinal epithelium with lower side effect. In short, the transient opening of the tight junctions by these enhancers provides new ideas that could help in novel drug delivery of therapeutic agents.

Keywords: tight junction absorption enhancer paracellular pathway

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