

论文

应用A549细胞单层模型研究蛋白多肽类药物肺部吸收的特性应用A549细胞单层模型研究蛋白多肽类药物肺部吸收的特性

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摘要:

关键词: 蛋白多肽类药物 A549 肺部吸收 表观渗透系数

Transport of proteins and peptides across human cultured alveolar A549 cell monolayers

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Abstract:

AimAn in vitro cultured monolayer system of alveolar epithelial cells was used as a model to investigate the transport pathway peptides or proteins, salmon calcitonin (sCT), insulin (INS), recombinant hirudin (rHAV2), and recombinant human growth hormone (rhGH), in pulmonary epithelium in vivo. MethodsHuman lung adenocarcinoma A549 cells formed continuous monolayers with growing polycarbonate filters of Transwell plate. Transport studies of macromolecules in the monolayer system were carried out after 6 days in culture. The transport of peptides or proteins with MW 3 400-22 000 was studied in cultured human lung adenocarcinoma A549 cell monolayers at different conditions. ResultsThe results showed that the apparent permeability coefficients (P_app) of these macromolecules across A549 cell monolayers ranged from 2x10^-6 to 5x10^-6 cm.s^-1 and exhibited good inverse correlation with molecule weight. No concentration, direction and temperature dependence were observed in the permeation of sCT, INS and rHAV2. While the P_app of rhGH in the BA direction (2.25x10^-6 cm.s^-1) was significantly less than that in the reverse direction. The P_app values of rhGH were concentration and temperature independent in the AB direction. ConclusionThese findings suggest that the hydrophilic peptides and proteins, salmon calcitonin, insulin, recombinant hirudin, and recombinant human growth hormone used in this study, appeared to penetrate the A549 cell monolayers via a paracellular pathway by passive diffusion mechanism.

Keywords: A549 pulmonary absorption apparent permeability coefficients proteins and peptides

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