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实验方法

非接触式共培养体外血脑屏障模型的跨膜电阻及通透性

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摘要 目的 建立大鼠脑毛细血管内皮细胞(BCEC)与星形胶质细胞共培养血脑屏障模型并评价其功能。方法 采用SD大鼠原代分离培养获得BCEC和星形胶质细胞。经细胞形态学观察、免疫组化检测相关抗原后建立非接触式共培养血脑屏障模型，测定共培养模型所形成的跨细胞电阻及荧光素钠的通透性。采用LC-MS检测6个化合物透过血脑屏障模型的通透性，并与文献报道的体内数据进行比较。结果 培养的BCEC多数为短梭形外观，免疫组化检测可见细胞高表达因子Ⅷ;星形胶质细胞呈现具有细胞突起的典型形态，免疫组化检测可见细胞高表达胶质纤维酸性蛋白。共培养的体外血脑屏障模型跨BCEC单层的电阻值为(373±41)Ω·cm^2，荧光素钠跨BCEC单层的通透性为(0.34±0.14)×10^{-3} cm·min^{-1}，符合体外血脑屏障模型要求。对所选6个化合物体内外透过BBB模型渗透系数的比较，表明具有一定的相关性(R^2=0.7679，P<0.05)。结论 建立的体外BBB模型在跨内皮电阻和通透性方面具备了在体BBB的基本特性，可以用于模拟体内环境，进行药物早期筛选方面的研究。

关键词 毛细血管内皮细胞，脑 星形胶质细胞 血脑屏障

分类号 R963

Transendothelial electric resistance and permeability of *in vitro* model of no-contact co-culture blood-brain barrier

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Abstract

OBJECTIVE To establish and evaluate a co-culture model of blood-brain barrier (BBB) using primary rat brain capillary endothelial cells (BCEC) and astrocytes. **METHODS** Primary cultures of BCEC and astrocytes were prepared from SD rats. Two kinds of cells were identified through cell morphology and immunohistochemistry. No-contact co-culture BBB model *in vitro* was developed and transendotheliar resistance and permeability of fluorescein sodium were measured. Additionally *in vitro* BBB permeabilities of six compounds were measured by LC-MS and compared their results with *in vivo* from literatures. **RESULTS** The cultured BCEC possessed the spindle-shaped morphology and expressed factor Ⅷ antigen. The cultured astrocytes possessed cell process morphology and expressed GFAP antigen. Transendothelial electric resistance (TEER) and permeability of fluorescein sodium were (373±41)Ω·cm^2 and (0.34±0.14)×10^{-3} cm·min^{-1}, respectively. These values were consistent with literatures. The correlation (R^2=0.7679, P<0.05) between *in vitro* permeability of selected six compounds and the *in vivo* published data was calculated. **CONCLUSION** TEER and permeability of