

### 论文 酮洛芬及其异丙酯对HaCaT细胞构建的组织工程皮肤的渗透作用

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#### 摘要:

目的体外构建适用于经皮给药研究的组织工程皮肤。方法以表皮角质形成细胞系HaCaT细胞及人真皮成纤维细胞为细胞来源,用I型牛胶原蛋白为真皮基质包埋成纤维细胞,其上接种HaCaT细胞,采用气-液界面方式培养,观察不同的培养介质对组织工程皮肤的影响,HE染色切片观察培养皮肤结构形态。以酮洛芬及其异丙酯为模型药物研究经皮渗透和代谢特性。结果HaCaT细胞经气-液界面培养可形成类表皮层,但不能形成完整的角质层。维生素C可明显促进细胞增殖,维生素D<sub>3</sub>可促进细胞分化,雌二醇对此组织工程皮肤没有明显的影响。同皮肤细胞匀浆代谢相似,酮洛芬异丙酯被代谢成原药酮洛芬。结论HaCaT细胞在气-液界面培养条件下可形成多层分化不完全的表皮层,保留了一定的酶活性,可用于药物的经皮渗透和代谢等研究。

关键词: 组织工程皮肤 HaCaT细胞 经皮渗透

### Percutaneous penetration of ketoprofen and ketoprofen isopropyl ester through a tissue engineering skin reconstructed with HaCaT cells

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#### Abstract:

AimTo reconstruct of a tissue engineering skin *in vitro* for the study of the use of drug percutaneous penetration and metabolism. MethodsDermal fibroblasts were embedded in collagen type I. HaCaT cells were seeded on the top of the gel. The skin was generated through air-liquid interface culture. Effects of various culture media on tissues morphology were investigated. Sections of the cultured skin were stained with hematoxylin and eosin and examined under microscope. Permeation and metabolism of ketoprofen and its isopropyl ester through the cultured skin were investigated. ResultsHaCaT cells initially developed a multilayer epithelium at the air-liquid interface, but it showed a parakeratotic stratum corneum. Vitamin C enhanced cell proliferation obviously. Vitamin D<sub>3</sub> promoted cell differentiation. And estradiol showed little effect on the tissue engineering skin. Ketoprofen isopropyl ester was hydrolyzed into ketoprofen when penetrated through the cultured skin, which resembled in the skin cell homogenates metabolism. ConclusionCultured at the air-liquid interface, HaCaT cells developed a parakeratotic mutilayer epithelium. Enzyme activity was reserved. This cultured skin could serve as an appropriate model for drug percutaneous metabolism and skin irritation.

Keywords: HaCaT cell percutaneous penetration tissue engineering skin

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