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论著

非诺贝特对凝胶包埋培养的原代大鼠肝细胞的毒性

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摘要 **目的** 研究非诺贝特对凝胶包埋培养的原代大鼠肝细胞内氧化压力和脂质含量的影响。**方法** 将收获得到的 新鲜原代大鼠肝细胞进行胶原凝胶包埋，构建肝细胞体外凝胶包埋培养模型，同时构建传统平板模型作为对照。在肝细胞培养过程中加入非诺贝特25和100 μmol·L^{-1}，分别于培养3和7 d后，检测细胞内活性氧类(ROS)、丙二醛(MDA)、甘油三酯(TG)含量，并用尼罗红和油红O对细胞内中性脂滴进行定量分析和染色观察。**结果** 平板模型非诺贝特各组之间没有显著性差异，而凝胶包埋模型非诺贝特各组之间差异明显。对于凝胶包埋模型， 非诺贝特25和100 μmol·L^{-1}均导致细胞内ROS增加，其中非诺贝特处理3 d组细胞内ROS分别为对照组的(131±19)%和(149±10)%，非诺贝特处理7 d组细胞内ROS分别为正常对照组的(121±8)%和(117±5)%(P<0.01)；非诺贝特还导致了胞内MDA含量、TG和中性脂含量的显著增加(P<0.05)。**结论** 凝胶包埋培养原代大鼠肝细胞作为体外培养模型相对于平板模型能更好地反映非诺贝特的肝毒性作用。

关键词 非诺贝特 共同培养技术 肝 毒性作用

分类号 R972.6,R965.2

Toxic effect of fenofibrate on gel entrapped primary rat hepatocytes

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Abstract

OBJECTIVE To explore effect of fenofibrate on oxidative stress and intracellular lipid content of collagen gel-entrapped primary rat hepatocytes. **METHODS** Primary rat hepatocytes were gel-entrapped in hollow fiber or on monolayer as contrast after harvest. During the culture, fenofibrate 25 μmol·L^{-1} and 100 μmol·L^{-1} were added. After 3 and 7 d treatment, intracellular reactive oxygen species (ROS), malondialdehyde (MDA) and triglycerides (TG) contents were determined. The intracellular neutral lipid drops stained with both oil red O and Nile red were quantified and observed by light microscope, respectively. **RESULT** There were no significant difference between these groups in monolayer model. However, in the gel- entrapped model, distinct differences among groups was discovered. After 3 and 7 d treatment, both fenofibrate 25 and 100 μmol·L^{-1} induced the accumulation of intracellular ROS. Compared with normal control group, fenofibrate 25 and 100 μmol·L^{-1} increased the intracellular ROS up to（131±19）% and （149±10）% on the third day, but on the seventh day, ROS level was （121±8）% and （117±5）%, respectively. Fenofibrate also induced the increasing in intracellular MDA content and the accumulation of intracellular TG and neutral lipid drops (P<0.05). **CONCLUSION** Gel entrapment culture of primary rat hepatocytes better reflects the toxic effect of fenofibrate demonstrated by the increasing in the intracellular oxidative stress and intracellular lipid accumulation.

Key words fenofibrate co-culture techniques liver toxic actions

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