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论著

蛇床子素通过激活过氧化物酶体增殖物激活受体α调节肝细胞内脂肪酸代谢

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摘要 目的 探讨蛇床子素是否通过激活过氧化物酶体增殖物激活受体(PPAR)α调节肝细胞内的脂肪酸代谢。方法 大鼠肝细胞在用蛇床子素12.5~100 μmol·L^{-1}作用24 h后,用比色法测定细胞内甘油三酯(TG)和游离脂肪酸(FFA)含量,用逆转录聚合酶链反应法测定PPARα mRNA表达的变化。PPARα抑制剂MK886 1 μmol·L^{-1}预处理肝细胞2 h后,观察蛇床子素100 μmol·L^{-1}作用24 h后对细胞内TG和FFA含量以及PPARα调控的靶基因包括固醇调节元件结合蛋白(SREBP)-1/2、脂肪酸合酶(FAS)、二脂酰甘油酰基转移酶(DGAT)、肉碱软脂酰转移酶(CPT)-1a、脂肪酸转运蛋白(FATP)4和肝脂肪酸结合蛋白(L-FABP)mRNA表达的影响。结果 蛇床子素12.5~100 μmol·L^{-1}可明显降低肝细胞内 TG和FFA的含量(P<0.01),同时也能明显增加肝细胞内PPARα mRNA的表达(P<0.01)。在用PPARα抑制剂MK886预处理后,蛇床子素降低肝细胞内TG和FFA的作用则明显被减弱(P<0.01),同时抑制SREBP-1/2, FAS和DGAT mRNA表达的作用明显减弱或完全消失(P<0.01),增加CPT-1a, FATP4和L-FABP mRNA表达的作用也明显减弱或完全消失(P<0.01)。结论 蛇床子素通过激活肝细胞中PPARα后可降低细胞中的TG和FFA含量,其机制与激活PPARα后随后抑制SREBP-1/2, FAS和DGAT的基因表达以及增加CPT-1a, FATP4和L-FABP的基因表达有关。

关键词 蛇床子素 脂肪酸 过氧化物酶体增殖物激活受体α 肝细胞

分类号 R285.5 R963

Osthole regulates fatty acid metabolism in hepatocytes by activation of PPARα

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Abstract

OBJECTIVE To determine whether osthole regulates fatty acid metabolism in hepatocytes of rats by activating peroxisome proliferator-activated receptor (PPAR) α. **METHODS** Rat hepatocytes were cultured and treated with osthole 12.5-100 μmol·L^{-1} for 24 h, before triglycerides (TG) and free fatty acid (FFA) contents in hepatocytes were determined by colorimetric method. PPARα mRNA expression was determined by reverse transcription polymerase chain reaction. In order to determine whether the lipid-regulating effect of osthole was associated with activation of PPARα, hepatocytes were pretreated with PPARα inhibitor MK886 1 μmol·L^{-1} for 2 h before incubation with osthole 100 μmol·L^{-1} for 24 h. TG and FFA contents, PPARα-regulated target genes including sterol regulatory element-binding protein (SREBP)-1/2, fatty acid synthase (FAS), diacylglycerol acyltransferase (DGAT), carnitine palmitoyltransferase (CPT)-1a, fatty acid transporter protein (FATP)4, and liver fatty acid binding protein (L-FABP) mRNA expressions in hepatocytes were examined. **RESULTS** Osthole 12.5-100 μmol·L^{-1} could significantly reduce TG and FFA contents and enhance the PPARα mRNA expression in hepatocytes of rats(P<0.01), but reduction of TG and FFA contents were significantly alleviated after pretreatment with PPARα inhibitor MK886(P<0.01). Similarly, the reduction of SREBP-1/2, FAS and DGAT mRNA expressions as well as the increment of CPT-1a, FATP4 and L-FABP mRNA expressions in hepatocytes of rats by osthole were also alleviated or abrogated after pretreatment with PPARα inhibitor MK886(P<0.01). **CONCLUSION** Osthole can decrease TG and FFA contents in hepatocytes. The mechanisms might be associated with activation of PPARα, subsequent reduction of SREBP-1/2, FAS and DGAT gene expressions and increment of CPT-1a, FATP4 and L-FABP gene expressions.

Key words osthole fatty acids peroxisome proliferator-activated receptor α hepatocytes

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