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论文

# *N*-甲基(3,4-亚甲二氧基苯甲酰)甲基-乙酰胺(SY-640)对化学致癌剂苯并芘与小鼠肝细胞核DNA共价结合的抑制作用

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摘要:

用小鼠肝细胞核制备和肝微粒体制备,研究了化合物SY-640对致癌剂苯并芘(BP)损伤肝细胞核的保护作用及与P-450的关系。结果表明,SY-640可显著抑制$^{3}$H-BP与小鼠肝细胞核的DNA共价结合。SY-640连续po 3 d,可显著诱导小鼠肝微粒体细胞色素P-450含量及氨基比林脱甲基酶活性;给药1次2h内却只抑制氨基比林脱甲基酶活性。体外温孵实验表明,SY-640对小鼠肝微粒体氨基比林脱甲基酶活性也具有明显的抑制作用。差示光谱分析表明,SY-640可与细胞色素P-450形成络合物。提示该化合物对肝微粒体细胞色素P-450酶系的影响与其对化学致癌剂BP所致肝细胞毒性的保护作用有关。

关键词: N-甲基(3.4-亚甲二氧基苯甲酰)甲基-乙酰胺 苯并芘 脱氧核糖核酸 氨基比林-N-脱甲基酶 细胞色素P-450

# INHIBITORY EFFECT OF 2-(*N*-ACETYL-METHYL AMINO)-3′,4′-METHYLENEDIOXYACETYL-AMINOPHENE(SY-640) ON COVALENT BINDING OF CARCINOGENIC BENZO(a)PYRENE WITH MOUSE HEPATOCYTE NUCLEAR DNA

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Abstract:

Many carcinogens must be first transformed into electrophilic ultimate carcinogens via metabolic activation in liver microsomes before covalent binding to nucleophilic center of DNA. SY-640 is a synthetic compound with hepatoprotective activity. Results of the present study indicate that the covalent binding of $^{3}$H-benzo(a)pyrine to mouse hepatocyte nuclear DNA *in vitro* and *in vivo* was markedly inhibited by SY-640. Further studies found that the liver microsomal cytochrome P-450 content and aminopyrine demethylase activity were significantly increased in mice treated with SY-640(150 mg·kg$^{-1}$ po) once daily for three days, while the hepatic microsomal aminopyrine demethylase activity was obviously inhibited two hours after oral administration of SY-640 150 mg·kg$^{-1}$ in mice. The aminopyrine demethylase activity of liver microsomes from normal, PB- and 3-MC-treated mice was also significantly inhibited by the addition of SY-640 *in vitro*. When SY-640 was incubated with NADPH reduced mouse liver microsomes, a metabolic-intermediate(MI) complex at 457 nm was formed. The effects of SY-640 on cytochrome P-450 and its formation of MI complex with cytochrome P-450 may partially explain why SY-640 could inhibit covalent binding of BP to mouse hepatocyte DNA *in vitro*.

Keywords: Benzo(a)pyrine DNA Covalant binding Aminopyrine-*N*-demethylase Cytochrome P-450 2-(*N*-acetyl-methyl amino)-3′,4′-methylenedioxyacetyl-aminophene

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