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别嘌呤醇对大鼠CYP450酶活性的影响

Effects of Allopurinol on Cytochrome P450 Isoforms in Rats

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中文关键词： Cocktail 别嘌呤醇 CYP450 探针药物

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作者	单位	E-mail
朱海燕	温州医学院附属第一医院药剂科，浙江 温州 325000	zhyan929@163.com
陈翔	温州医学院附属第一医院药剂科，浙江 温州 325000	
张秀华*	温州医学院附属第一医院药剂科，浙江 温州 325000	wzzhangxiuhua@yahoo.cn

中文摘要:

目的 用Cocktail探针药物法研究别嘌呤醇对大鼠细胞色素P450(CYP450)同工酶的影响。方法
将SD大鼠随机分为2组，别嘌呤醇组为实验组，生理盐水组为对照组，采用高效液相色谱-质谱联用技
测定连续给药14 d后大鼠血浆中相应探针药物的浓度及其药动学参数。结果 别嘌呤醇体内给药14 d
后，大鼠体内非那西丁的$AUC_{(0-\infty)}$(P<0.01)、C_{max}(P<0.05)和$t_{1/2}$(P<0.05)显著大于对照组，CL显
低于对照组(P<0.01)；而甲苯磺丁脲、奥美拉唑和右美沙芬探针药物的药动学参数均无显著变化。结
别嘌呤醇抑制大鼠CYP1A2酶，对CYP2C9、CYP2C19和CYP2D6酶的影响不显著。

英文摘要:

OBJECTIVE To study the change of the hepatic CYP450 activity following administration of allopurinol by Cocktail probe drugs in rats. METHODS The rats were randomly divided into two groups: rats were given allopurinol once daily orally for days as the test group, another group received orally normal saline once daily as the blank control group. The plasma concentrations of Cocktail probe drugs were determined by HPLC-MS and their corresponding pharmacokinetic parameters were calculated. RESULTS $AUC_{(0-\infty)}$, C_{max} and $t_{1/2}$ of phenacetin notably increased and the CL decreased significantly after administered allopurinol for 14 consecutive days. But the pharmacokinetic parameters of tolbutamide, omeprazole and dextromethorphan had no statistical significance. CONCLUSION Allopurinol can inhibit CYP1A2 enzyme, but has little influence on metabolism of CYP2C9, CYP2C19 and CYP2D6 enzyme in rats.