

论著

# 纳米铜经口染毒大鼠血清的代谢组学研究

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**摘要** 背景与目的: 运用代谢组学技术检测纳米铜染毒大鼠的血清代谢成分变化, 结合常规血液生化及组织病理学检查, 探讨纳米铜短期暴露的损害特征, 寻找损害早期的代谢标记物, 揭示血液代谢表型变化与纳米铜靶器官损害间的关系。材料与方法: 雄性Wistar大鼠30只, 分为溶剂对照组(1%HPMC), 微米铜(200 mg/kg)组和3个不同纳米铜剂量(50、100 和200 mg/kg)组, 共5组, 每组6只, 10 ml/kg经口染毒, 每日1次, 连续5 d, 次日麻醉采血制备血清, 进行核磁共振和血液生化分析, 同时摘取肝肾作组织病理学检查。结果: 纳米铜200 mg/kg组大鼠血清丙氨酸氨基转移酶、天冬氨酸氨基转移酶、甘油三酯、总胆红素、总胆汁酸、尿素氮和肌酐均明显升高, 伴随碱性磷酸酶和总胆固醇明显降低; 肝细胞出现点状坏死, 肾小管上皮细胞广泛坏死, 管腔内可见蛋白管型和棕黄色结晶物沉积, 肾小球亦受累及; 50、100 mg/kg剂量组甘油三酯和总胆固醇升高, 组织病理检查显示肝脏无明显损害, 肾小管上皮细胞出现肿胀; 微米铜染毒大鼠仅出现肾小管上皮细胞肿胀。血清代谢组学分析表明50~200 mg/kg纳米铜短期暴露可引起能量代谢紊乱和剂量依赖性的血清甘油三脂、不饱和脂肪酸和磷脂水平升高。结论: 相同质量浓度的纳米级铜粉毒性明显大于微米级铜粉, 肝脏和肾脏是大鼠纳米铜暴露的潜在靶器官, 其损害可能与细胞的能量代谢紊乱有关。

关键词 [1H NMR](#); [纳米铜](#); [代谢组学](#); [模式识别](#)

## Metabonomic Analysis of Serum from Rats Orally Dosed the Nano-copper Particles

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**Abstract** BACKGROUND AND AIM: [1H nuclear magnetic resonance \(1H NMR\)](#) spectroscopic methods were used to analyze serum obtained from rats treated with a range of doses of nano-copper particles in order to reveal the characteristics of the damage caused by nano-copper and identify the latent NMR biomarkers associated with the earlier damage. MATERIALS AND METHODS: 30 male Wistar rats were randomly assigned into five groups (6 rats per group), rats were given daily orogastric vehicle(1% Hydroxypropylmethylcellulose), nano-copper (50, 100, 200 mg/kg) or micron-copper(200 mg/kg) for 5 days, and sacrificed on Day 6. The serum samples from all rats were collected and their [1H NMR](#) spectra were acquired. PC analysis, blood biochemical analysis and histopathology examination for liver and kidney were performed simultaneously. RESULTS: For the rats dosed with 200 mg/kg nano-copper, increased levels in serum ALT, AST, TP, TG, TBA, TBILI, BUN and CREA, together with decreased ALP and TCHOL were marked compared with controls. Histopathology examination found hepatocellular dot necrosis, and widespread necrosis in the renal proximal tubules with protein cast in the tubule lumen, in which orange crystal deposition could also be found. For rats fed 50 and 100 mg/kg nano-copper, abnormalities included increased serum level of TCHOL and TG, as well as renal proximal tubular epithelial cellular swelling. The rats dosed with 200 mg/kg micron-copper particles showed slight damage. The metabonomic analysis of the serum samples revealed nano-copper disturbing cellular energy metabolism and serum lipid metabolism. These results were in agreement with the changes of serum biochemical and histopathology examinations. CONCLUSION: Liver and kidney were the potential target organs

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of nano-copper exposure. The damages of the target organs were associated with the disturbance of the cellular energy metabolism.

**Keywords** [1H NMR](#) [metabonomic](#) [pattern recognition](#) [nano-copper](#)

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