

论著

基于MDCK II细胞的中药成分体外肾毒性评价

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摘要 目的 用狗肾近端小管上皮(MDCK II)细胞系研究中药成分的肾毒性, 探讨其作为评价中药成分肾毒性体内动物实验替代方法的可能性。方法 以氯化汞(HgCl₂)为阳性对照, 研究已知有肾毒性的马兜铃酸 I (AA I) 和马兜铃酸 II (AA II), 以及未见肾毒性报道的苦参碱、氧化苦参碱和肉豆蔻醚对MDCK II细胞的毒性作用。用MTT法检测细胞存活; 倒置显微镜观察细胞形态改变; 乳酸脱氢酶(LDH)释放实验检测细胞膜损伤; 流式细胞术分析细胞周期及细胞凋亡, 用Hoechst 33258染色法观察凋亡细胞形态变化。结果 AA I 和AA II 分别与MDCK II细胞作用24, 48和72 h细胞存活均被明显抑制, AA I 的IC₅₀值分别为(63.4±6.6), (44.8±6.0)和(37.3±4.6) μmol·L⁻¹, AA II 的IC₅₀值分别为(125.7±6.2), (106.7±20.4)和(94.2±9.7) μmol·L⁻¹; 在5~300 μmol·L⁻¹时AA I 和AA II 分别与MDCK II细胞作用24 h, LDH的释放率明显增高; AA I (75 μmol·L⁻¹) 和AA II (150 μmol·L⁻¹) 分别与MDCK II细胞作用24 h, 倒置显微镜下可见细胞收缩变圆, 部分细胞破裂脱落; 用流式细胞仪和Hoechst 33258染色法观察亦发现, AA I 和AA II 均可使细胞周期S期阻滞, 诱导MDCK II细胞发生凋亡。苦参碱、氧化苦参碱和肉豆蔻醚在2~10 mmol·L⁻¹浓度范围内分别与MDCK II细胞作用24 h, 对上述指标均无明显影响。结论 MDCK II细胞系对有肾毒性的AA I 和AA II 和未见肾毒性报道的苦参碱、氧化苦参碱和肉豆蔻醚的反应不同, 可用于中药成分体外肾毒性评价。

关键词 [肾毒性](#) [MDCK II细胞](#) [中草药](#)

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Evaluation of nephrotoxicity induced by Chinese herbal ingredients with MDCK II cells *in vitro*

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Abstract

AIM To evaluate the nephrotoxicity induced by Chinese herbal ingredients with Madin Darby canine kidney type II (MDCK II) cells and explore the possibility of using MDCK II cells to early assess the nephrotoxicity of Chinese herbal ingredients *in vitro*. **METHODS** The cytotoxicities of aristolochic acid I (AA I), aristolochic acid II (AA II), matrine, oxymatrine and myristicin were investigated. The cell survival inhibition rate of MDCK II cells after treatment of these drugs were studied by MTT assay, and the morphological changes of MDCK II cells were examined with contrast microscopy. Cell membrane injury was observed by detecting lactate dehydrogenase (LDH) release rate. Cell cycle and apoptosis rate were determined by using flow cytometry. The morphological changes of apoptosis cells were examined with Hoechst 33258 staining. **RESULTS** MDCK II cell survival was inhibited after exposed to AA I and AA II, respectively. The IC₅₀ values of AA I for 24, 48 and 72 h were (63.4±6.6), (44.8±6.0) and (37.3±4.6) μmol·L⁻¹, respectively. The IC₅₀ values of AA II for 24, 48 and 72 h were (125.7±6.2), (106.7±20.4) and (94.2±9.7) μmol·L⁻¹, respectively. The LDH release rate of MDCK II cells significantly increased after treated with AA I or AA II for 24 h. MDCK II cells were contracted and rounded after treated with AA I (75 μmol·L⁻¹) or AA II (150 μmol·L⁻¹) for 24 h. The further research also indicated that AA I and AA II affected cell cycle and induced cell apoptosis. After treated with matrine, oxymatrine and myristicin (2-10 mmol·L⁻¹) for 24 h, all above the parameters of MDCK II cells had no obvious changes. **CONCLUSION** MDCK II cells have different responses to AA I and AA II with nephrotoxicity, and matrine, oxymatrine and myristicin without reports of nephrotoxicity. MDCK II cells may be useful for assessment of nephrotoxicity of Chinese herbal ingredients *in vitro*.

Key words [kidney toxicity](#) [MDCK II cells](#) [drugs](#) [Chinese herbal](#)

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