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论著

纳米锰锌铁氧体颗粒对L-02细胞的氧化损伤作用

殷婕[1], 吴启南[1], 邵莹[1], 陈蓉[1], 张东生[2]
1. 南京中医药大学药学院, 江苏 南京 210046;
2. 东南大学医学院, 江苏 南京210009

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摘要 目的 探讨磁性锰锌铁氧体纳米颗粒($Mn_{0.5}Zn_{0.5}Fe_2O_4$)对人肝细胞株L-02的毒性作用机制。方法 $Mn_{0.5}Zn_{0.5}Fe_2O_4$ 800 mg·L^{-1}作用L-02细胞48 h,透射电镜观察细胞形态及超微结构的变化。$Mn_{0.5}Zn_{0.5}Fe_2O_4$ 200, 400和800 mg·L^{-1}作用48 h后,检测L-02细胞内丙二醛(MDA)的含量、超氧化物歧化酶(SOD)和还原型谷胱甘肽(GSH)的活性;荧光染色观察凋亡细胞形态;流式细胞术检测细胞周期及凋亡;荧光定量PCR仪检测胱天蛋白酶3 mRNA表达。结果 $Mn_{0.5}Zn_{0.5}Fe_2O_4$ 800 mg·L^{-1}作用48 h后,纳米颗粒进入细胞内,细胞膜发生破损,细胞器消失,染色体异常聚集。与正常对照组比较,$Mn_{0.5}Zn_{0.5}Fe_2O_4$ 200~800 mg·L^{-1}使细胞内MDA含量逐渐升高,SOD与GSH活性逐渐降低(P<0.05)。$Mn_{0.5}Zn_{0.5}Fe_2O_4$可使细胞周期发生改变,G_0/G_1期细胞百分率有降低的趋势,S期和G_2/M期细胞百分率有升高的趋势。Hoechst33258显示明显的细胞凋亡形态。$Mn_{0.5}Zn_{0.5}Fe_2O_4$可引起L-02细胞发生剂量依赖性的细胞凋亡,$Mn_{0.5}Zn_{0.5}Fe_2O_4$ 800 mg·L^{-1}作用48 h后,细胞凋亡率达到30.3%,是对照组细胞凋亡率(2.4%)的12.6倍。胱天蛋白酶3 mRNA表达量先增加后降低,但都明显高于正常对照组(P<0.05)。结论 $Mn_{0.5}Zn_{0.5}Fe_2O_4$可破坏细胞膜完整性并进入细胞内,诱导细胞发生氧化应激,改变细胞周期,引发细胞凋亡,产生细胞毒性。

关键词 纳米颗粒 $Mn_{0.5}Zn_{0.5}Fe_2O_4$ L-02细胞 氧化应激 细胞周期 细胞凋亡
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Oxidative damage of $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles to L-02 cells

YIN Jie[1], WU Qi-nan[1], SHAO Ying[1], CHEN Rong[1], ZHANG Dong-sheng[2]

1. College of Pharmacy, Nanjing University of Traditional Chinese Medicine, Nanjing 210046, China;
2. College of Basic Medical Sciences, Southeast University, Nanjing 210009, China

Abstract

OBJECTIVE To explore the toxic mechanisms of $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles on L-02 cells. **METHODS** Morphological changes were observed by transmission electron microscopy after L-02 cells were treated with $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles 800 mg·L^{-1} for 48 h. Malondialdehyde (MDA) content, superoxide dismutase (SOD) and glutathione(GSH) activities were determined after cells were exposed to $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles 200, 400 and 800 mg·L^{-1} for 48 h. Cell cycle and apoptosis were detected by flow cytometry. Morphologic changes were observed by Hoe fluorescence microscopes. Expression of caspase 3 mRNA was analyzed by real time PCR. **RESULTS** After L-02 cells were treated with $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles 800 mg·L^{-1} for 48 h, the ultrastructure of cells changed, cell organelles disappeared and the nucleus shrank in size, which served as evidence of apoptosis when nanoparticles went into L-02 cells. Compared with normal control group, MDA content in $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles 200-800 mg·L^{-1} groups significantly increased while GSH and SOD activities significantly decreased(P<0.05). Compared with normal control group, the percentage in S phase and G_2/M phase increased but decreased in G_0/G_1 phase in $Mn_{0.5}Zn_{0.5}Fe_2O_4$ treated cells. $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles could induce apoptosis in L-02 cells. After cells were exposed to $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles 800 mg·L^{-1} for 48 h, the cell apoptosis rate was 30.3%, 12.6 times that in normal control group. Compared with normal control group, the expression of caspase 3 mRNA significantly increased in $Mn_{0.5}Zn_{0.5}Fe_2O_4$ 200-800 mg·L^{-1} groups(P<0.05). **CONCLUSION** $Mn_{0.5}Zn_{0.5}Fe_2O_4$ nanoparticles can change the ultrastructure of cells, which results in apoptosis in L-02 cells through cell cycles and oxidative stress.

Key words nanoparticles $Mn_{0.5}Zn_{0.5}Fe_2O_4$ L-02 cells oxidative stress cell cycle apoptosis

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通讯作者 吴启南,E-mail: qnlxw@yahoo.com.cn; Tel: (025)85811059 qnlxw@yahoo.com.cn