中国药理学与毒理学杂志 2010 24 (6): 481-487 ISSN: 1000-3002 CN: 11-1115/R

论著

纳米活性炭，纳米二氧化硅和纳米二氧化钛对人胃肿瘤BGC-823细胞的毒性作用

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收稿日期 2010-6-22 修回日期 网络版发布日期 2010-12-20 接受日期 2010-11-5

摘要 目的 探讨不同化学组成的纳米颗粒对人胃癌BGC-823细胞的毒性作用及其机制。方法 分别以纳米活性炭(ACNP)、纳米二氧化硅(SiO_2)和纳米二氧化钛(TiO_2)100，200，400，800和1600 mg·L^{-1}悬液作用BGC-823细胞24，48和72 h，MTT法检测细胞增殖，比色法检测乳酸脱氢酶(LDH)漏出量。ACNP 100 mg·L^{-1}，纳米SiO_2 200 mg·L^{-1}，纳米TiO_2 200 mg·L^{-1}作用BGC-823细胞24 h，透射电镜观察细胞形态及超微结构的影响。纳米SiO_2和纳米TiO_2 100，200，400 mg·L^{-1}作用细胞24 h后，Annexin Ⅴ-FITC/PI双染法检测细胞凋亡。ACNP、纳米SiO_2和纳米TiO_2 100，200 mg·L^{-1}作用细胞48 h后，用PI染色法检测细胞周期。结果 ACNP，纳米SiO_2和纳米TiO_2均能明显抑制BGC-823细胞的增殖，作用72 h后的IC_{50}分别为874.2，676.2和883.5 mg·L^{-1}。与正常对照组相比，纳米SiO_2 100~800 mg·L^{-1}组LDH漏出量均显著升高，并呈浓度依赖性（r=0.9751，P<0.01），而纳米TiO_2 100 mg·L^{-1}作用细胞24 h，LDH漏出量与对照组相比没有显著差异，但随着作用浓度增加和作用时间延长，各组LDH漏出量明显高于对照组(P<0.05)。ACNP 100 mg·L^{-1}作用24 h后，细胞出现细胞质浓缩、细胞核固缩和裂解。纳米SiO_2 200 mg·L^{-1}和纳米TiO2 200 mg·L^{-1}作用24 h后均出现细胞坏死。纳米颗粒ACNP，SiO_2和TiO_2作用组均可见纳米颗粒进入细胞及线粒体损伤。纳米SiO_2 100 mg·L^{-1}和纳米TiO_2 100 mg·L^{-1}作用24 h，细胞坏死率与正常对照组(4.59±1.20)%相比显著升高(P<0.01)，分别为(39.40±1.72)%和(14.12±0.90)%(P<0.05)；细胞凋亡率与对照组相比没有显著差异。ACNP，纳米SiO_2和纳米TiO_2 100和200 mg·L^{-1}作用细胞48 h后，S期细胞增多，G_0/G_1期细胞减少，细胞碎片增多；ACNP组亚二倍体细胞增多。结论 ACNP、纳米SiO_2和纳米TiO_2能够抑制BGC-823细胞的增殖。ACNP可诱导细胞凋亡。纳米SiO_2和纳米TiO_2能损伤细胞膜，造成以细胞坏死为主的毒性损伤。

关键词 纳米复合物 炭 二氧化硅 二氧化钛 胃肿瘤 细胞系,肿瘤 细胞毒性 细胞凋亡

分类号 R99，R735

Cytotoxic effects of activated carbon nanoparticles, silicon dioxide nanoparticles and titanium dioxide nanoparticles on human gastric carcinoma cell line BGC-823

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Abstract

OBJECTIVE To explore cytotoxic effects of activated carbon nanoparticles(ACNP), silicon dioxide nanoparticles (nano-SiO_2) and titanium dioxide nanoparticles (nano-TiO_2) on the human gastric carcinoma cell line BGC-823. **METHODS** BGC-823 cells were exposed to ACNP, nano-SiO_2 and nano-TiO_2 100, 200, 400, 800 and 1600 mg·L^{-1} for 24, 48 and 72 h. The inhibitory rate was observed by MTT assay. The lactate dehydrogenase (LDH) leakages in the culture medium were determined. The morphological changes were observed by transmission electron microscopy after cells were treated with ACNP 100 mg·L^{-1}, nano-SiO_2 200 mg·L^{-1} or nano-TiO_2 200 mg·L^{-1} for 24 h. The apoptotic rate was detected by Annexin Ⅴ-FITC/PI staining with flow cytometry after cells were treated with nano-SiO_2 or nano-TiO_2 100, 200, 400 mg·L^{-1} for 24 h. The cell cycle was detected by PI staining after cells treated with ACNP or nano-SiO_2 or nano-TiO_2 100 and 200 mg·L^{-1} for 48 h were collected. **RESULTS** ACNP, nano-SiO_2 and nano-TiO_2 significantly inhibited the proliferation of BGC-823 cells. The 50% inhibitory concentrations of ACNP, nano-SiO_2 and nano-TiO_2 after 72 h were 874.2, 676.2 and 883.5 mg·L^{-}

^{1}, respectively. The LDH leakages in nano-SiO_2 100-800 mg·L^{-1} groups significantly increased in a concentration-dependent manner (r=0.9751, P<0.01). The LDH leakage of nano-TiO2 100 mg·L^{-1} was not higher than that in normal control group. The LDH leakage in nano-TiO_2 groups increased with the concentration and time. Condensation of the cytoplasm, condensation and fragmentation of the nuclear chromatin were observed in ACNP 100 mg·L^{-1} for 24 h. The cells treated with nano-SiO_2 or nano-TiO_2 200 mg·L^{-1} for 24 h exhibited necrosis. Mitochondrial damage was observed in the cells treated with ACNP, nano-SiO_2 or nano-TiO_2. The necrotic rate of nano-SiO_2 and nano-TiO_2 100 mg·L^{-1} was (39.40±1.72)% and (14.12±0.90)%, respectively, which were significantly higher than that of the control group (4.59±1.20)% (P<0.05). The percentage of cells at S phase of ACNP, nano-SiO_2 and nano-TiO_2 100 and 200 mg·L^{-1} groups was higher than that in control group, while the percentage of G_0/G_1 phase cells decreased. The percentage of "sub-G_1" cells significantly increased in ACNP groups. **CONCLUSION** ACNP, nano-SiO_2 and nano-TiO_2 could inhibit proliferation of BGC-823 cells in vitro. ACNP could induce apoptosis of BGC-823 cells. Nano-SiO_2 and nano-TiO_2 could directly induce necrosis of BGC-823 cells by disintegrating plasma membrane.

Key words nanocomposites charcoal silicon dioxide titanium dioxide stomach neoplasma cell line tumor cytotoxicity apoptosis

DOI: 10.3867/j.issn.1000-3002.2010.06.007

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