Title (6)	:	**Evaluation of curcumin nanoparticles of various sizes for targeting multidrug-resistant lung cancer cells via inhalation**
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Abstract	:	Introduction: Inhalation drug delivery can deliver high doses of chemotherapeutic drugs to the lung tumor. This study evaluates the efficacy and the mechanistic pathways of nebulized Cur NPs at various sizes to treat multidrug resistant lung cancer. Methods and results: Cur-NPs (30 nm and 200 nm) were nebulized separately onto the multidrug-resistant lung cancer cells (H69AR). Smaller NPs induced significantly higher cell death owing to a higher rate of particle internalization via dynamin-dependent clathrin-mediated endocytosis. Owing to the higher lysosome trafficking of Cur-NP30 nm compared to Cur-NP200 nm, oxidation of lysosome was higher (0.47 ± 0.08 vs 0.38 ± 0.08), contributing to significantly higher mitochondrial membrane potential loss (1.57 ± 0.17 vs 1.30 ± 0.11). MRP1 level in H69AR cells was reduced from 352 ± 12.3 ng/μg of protein (untreated cells) to 287 ± 12 ng/μg of protein (Cur-NP30 nm) and 303 ± 13.4 ng/μg of protein (Cur-NP200 nm). NF-κB, and various cytokine expressions were reduced after treatment with nebulized Cur-NPs. Conclusions: Nebulized Cur-NPs formulations could be internalized into the H69AR cells. The Cur-NPs toxicity toward the H69AR was size and time-dependent. Cur-NP30 nm was more effective than Cur-NP200 nm to retain within the cells to exert higher oxidative stresss-induced cell death. Keywords: Curcumin nanoparticles; H69AR; drug-resistant; endocytosis; inhalation; lysosome.