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Toxicity of curcumin nanoparticles towards alveolar macrophage: Effects of surface charges

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Abstract

Curcumin has been used for chronic lung diseases management due to its diversified molecular actions. However, the potential cytotoxicity which occurs in cells following the exposure to high concentrations of curcumin has been overlooked. This study evaluated the toxic events of curcumin nanoparticles (Cur-NPs) with alterable surface polarity in alveolar macrophages (NR8383). We aimed to establish the correlation between the toxicity of Cur-NPs with different surface charges and the internalization mechanisms of the NPs. Toxicity data showed that positively charged Cur-NPs (IC_{50}: 9.77±0.5μg/mL) was the most potent against NR8383, followed by negatively charged Cur-NPs (IC_{50}:13.33±0.9μg/mL) and neutral Cur-NPs (IC_{50}:18.68±1.2μg/mL). Results from mitochondrial membrane potential, ATP content and intracellular ROS in NR8383 showed similar ranking to the toxicity assay. The predominant uptake pathway for positively and negatively charged Cur-NPs was via clathrin-mediated endocytosis, while neutral Cur-NPs was internalized via phagocytosis, micropinocytosis and clathrin-mediated endocytosis. Positively charged Cur-NPs mediates the cytotoxicity of NR8383 via lysosomal and mitochondrial-associated destabilization upon entry. In conclusion, the cytotoxicity of Cur-NPs on NR8383 is surface-charge dependent, which in turn is associated to the uptake pathway and localization of Cur-NPs in cells.

Graphical abstract