Cytotoxicity and genotoxicity of lipid nanocapsules

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Résumé en anglais	Lipid nanocapsules (LNCs) offer a promising method for the entrapment and nanovectorisation of lipophilic molecules. This new type of nanocarrier, formulated according to a solvent-free process and using only regulatory-approved components, exhibits many prerequisites for being well tolerated. Although toxicological reference values have already been obtained in mice, interaction of LNCs at the cell level needs to be elucidated. LNCs, measuring from 27.0±0.1nm (25nm LNCs) and 112.1±1.8nm (100nm LNCs) and with a zeta potential between -38.7±1.2mV and +9.18±0.4mV, were obtained by a phase inversion process followed by post-insertion of carboxy- or amino-DSPE-PEG. Trypan blue, MTS and neutral red uptake (NRU) assays were performed to evaluate the cytotoxicity of LNCs on mouse macrophage-like cells RAW264.7 after 24h of exposure. The determination of 50% lethal concentration (LC50) showed a size effect of LNCs on toxicity profiles: LC50 ranged from 1.036mg/L (MTS) and 0.477mg/mL (NRU) for 25nm LNCs, to 4.42mg/mL (MTS) and 2.18mg/mL (NRU) for 100nm LNCs. Surfactant Solutol® HS15 has been shown to be the only constituent to exhibit cytotoxicity; its LC50 reached 0.427mg/mL. Moreover, LNCs were not more toxic than their components in simple mixtures. At sublethal concentration, 100nm LNCs only were able to induce a significant production of nitric oxide (NO) by RAW264.7 cells, as assessed by the Griess reaction. Again, surfactant was the only component responsible for an increased NO release (1.8±0.2-fold). Genotoxicity assays revealed no DNA damage on human lymphocytes in both the in vitro Comet and micronucleus assays using 4-hour and 24-hour treatments, respectively.
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