Drug delivery to tumours using a novel 5-FU derivative encapsulated into lipid nanocapsules

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Mots-clés	5-Fluorouracil [14], Cancer treatment [15], Lipid nanoparticles [16], nanomedicine [17]
Résumé en anglais	In this work, a novel lipophilic 5-fluorouracil (5-FU) derivative was synthesised and encapsulated into lipid nanocapsules (LNC). 5-FU was modified with lauric acid to give a lipophilic mono-lauroyl-derivative (5-FU-C12, MW of about 342 g/mol, yield of reaction 70%). 5-FU-C12 obtained was efficiently encapsulated into LNC (encapsulation efficiency above 90%) without altering the physico-chemical characteristics of LNC. The encapsulation of 5-FU-C12 led to an increased stability of the drug when in contact with plasma being the drug detectable until 3 h following incubation. Cytotoxicity assay carried out using MTS on 2D cell culture showed that 5-FU-C12-loaded LNC had an enhanced cytotoxic effect on glioma (9L) and human colorectal (HTC-116) cancer cell line in comparison with 5-FU or 5-FU-C12. Then, HCT-116 tumour spheroids were cultivated and the reduction of spheroid volume was measured following treatment with drug-loaded LNC and drugs alone. Similar reduction on spheroids volume was observed following the treatment with drug-loaded LNC, 5-FU-C12 and 5-FU alone, while blank LNC displayed a reduction in cell viability only at high concentration. Globally, our data suggest that the encapsulation increased the activity of the 5-FU-C12. However, in-depth evaluations of LNC permeability into spheroids are needed to disclose the potential of these nanosystems for cancer treatment.
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