Design And Characterisation Of Novel Sorafenib-Loaded Carbon Nanotubes With Distinct Tumour-Suppressive Activity In Hepatocellular Carcinoma

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Purpose: Over the past 30 years, no consistent survival benefits have been recorded for anticancer agents of advanced hepatocellular carcinoma (HCC), except for the multikinase inhibitor sorafenib (Nexavar®), which clinically achieves only ~3 months overall survival benefit. This modest benefit is attributed to limited aqueous solubility, slow dissolution rate and, consequently, limited absorption from the gastrointestinal tract. Thus, novel formulation modalities are in demand to improve the bioavailability of the drug to attack HCC in a more efficient manner. In the current study, we aimed to design a novel sorafenib-loaded carbon nanotubes (CNTs) formula that is able to improve the therapeutic efficacy of carried cargo against HCC and subsequently investigate the antitumour activity of this formula.

Materials and methods: Sorafenib was loaded on functionalized CNTs through physical adsorption, and an alginate-based method was subsequently applied to microcapsulate the drug-loaded CNTs (CNTs-SFN). The therapeutic efficacy of the new formula was estimated and compared to that of conventional sorafenib, both in vitro (against HepG2 cells) and in vivo (in a DENA-induced HCC rat model).

Results: The in vitro MTT anti-proliferative assay revealed that the drug-loaded CNTs formula was at least two-fold more cytotoxic towards HepG2 cells than was sorafenib itself. Moreover, the in vivo animal experiments proved that our innovative formula was superior to conventional sorafenib at all assessed end points. Circulating AFP-L3% was significantly decreased in the CNTs-SFN-MCs-treated group (14.0%) in comparison to that of the DENA (40.3%) and sorafenib (38.8%) groups. This superiority was further confirmed by Western blot analysis and immunofluorescence assessment of some HCC-relevant biomarkers.

Conclusion: Our results firmly suggest the distinctive cancer-suppressive nature of CNTs-SFN-MCs, both against HepG2 cells in vitro and in a DENA-induced HCC rat model in vivo, with a preferential superiority over conventional sorafenib.

Keywords: carbon nanotubes, sorafenib, DENA, hepatocellular carcinoma, microcapsules