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Development and cytotoxicity evaluation of respirable nanomicelle carriers for delivery of tretinoin by jet nebulizer

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Background & Objectives: Lung cancers are serious and lethal problems in cigarette smoking patients. Direct deposition of cytotoxic drugs to the site of neoplasm (lungs) and avoiding the systemic side effects and drug interactions are some benefits following inhalation of anticancer agents which can be an effective and safe alternative to systemic administration. The aim of present study is to prepare and characterize chitosan-stearic acid conjugate nanomicelles for encapsulation of all-trans retinoic acid (ATRA).

Methods: Water soluble chitosan was grafted to stearic acid (SA) chains via 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide mediated coupling reaction. The chemical structure of depolymerized chitosan (DC)-SA copolymers and degree of amino substitution was determined by 1H NMR. ATRA loaded micelles were prepared by film hydration, solvent evaporation and dialysis method. The physicochemical properties and formation of polymeric micelles were studied by dynamic light scattering and fluorescence spectroscopy methods. Nanomicelle size and zeta potential and ATRA entrapment efficiency were determined and the cytotoxicity of the formulations was also evaluated on A549 cell line by MTT assay. ATRA-loaded micelles were also characterized for their nebulization efficiency and retention of ATRA in the micelles after nebulization.

Results: ATRA was loaded in nanomicelles with entrapment efficiencies more than 70%. Nanomicelles possessed positive charges with mean particle sizes of less than 300 nm. The IC50 of ATRA nanomicelles showed increased cytotoxic potential of drug. Transmission electron microscopy (TEM) revealed the spherical shape of prepared nanomicelles. The nebulization efficiency was up to 89% and the fine particle fraction (FPF) varied from 38% to 47%. The micelles had enough stability to remain encapsulation of the drug during nebulization process.

Conclusions: The results exhibited the potential of DC-SA micelles as a suitable carrier for delivery of ATRA by different routes of administration, specially the pulmonary route via jet nebulization.

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