



## Development and cytotoxicity evaluation of nanomicelle carriers for delivery of all-trans retinoic acid

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**Background and Aims:** 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. This is the first report on preparation and evaluation of all-trans retinoic acid (ATRA) in alkyl-grafted nanomicelles suitable for nebulization.

**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 <sup>1</sup>H NMR. ATRA was dissolved in methanol and was added dropwise to DC-SA solutions under magnetic stirring. The physicochemical properties and formation of polymeric micelles were studied by dynamic light scattering and fluorescence spectroscopy method. 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.

**Results:** ATRA was loaded in nanomicelles with entrapment efficiencies more than 90%. Nanomicelles possessed positive charges with mean particle sizes of less than 300 nm. The IC<sub>50</sub> of ATRA nanomicelles showed increased cytotoxic potential of drug.

**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.

**Keywords:** Retinoic acid; Nanomicelle; Chitosan