

Synthesis of chitosan oligomer conjugated methotrexate nanomicells for purpose of co-delivery of anticancer drugs

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Background and Aims: Cancer as a proliferative disease constantly to be one of the major problems in all over the world. For cancer treatment so many considerations such as surgery, radiotherapy, and chemotherapy have been proposed. Creating new chemotherapeutic agents with high efficacy and low side effect would give a new promising view in cancer treatment. Methotrexate (MTX) as an antifolate agent with high toxicity is one of the best candidate for fabricating new conjugated nanomicells effective targeted drug delivery system. As our main hypothesis to make nanomicells, the hydrophobic moiety of MTX was reacted with the effective hydrophilic part of chitosan.

Methods: MTX –chitosan oligomer with different molar ratios of MTX (25, 12.5, 6.25) were synthesized for the first time. The synthetic procedure was involved activation of carboxylic functional group of MTX using dicyclohexylcarbodiimide and NHS and then the activated moiety was reacted with chitosan. After filtration and separation of dicyclohexylurea the product purification was carried out using dialysis membrane with cut off 3000 against DMSO. Validity of products was investigated by HNMR and FTIR spectroscopy which indicate the successful conjugation. The MTX –chitosan micelles were produced by ultrasonication using probe type sonicator.

Results: Micelles from feeding ratio of 12.5 were shown smaller size and polydispersity with average of 217.9 ± 49.32 and 0.375 ± 0.063 , respectively.

Keywords: Methotrexate; Nanomicells; Methotrexate-chitosan oligomer