Fluorouracil-Loaded Gold Nanoparticles for the Treatment of Skin Cancer: Development, in Vitro Characterization, and in Vivo Evaluation in a Mouse Skin Cancer Xenograft Model

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Abstract:

Fluorouracil (5-FU) is an antimetabolite drug used in the treatment of various malignancies, such as colon and skin cancers. However, its systemic administration results in severe side effects. Topical 5-FU delivery for the treatment of skin cancer could circumvent these shortcomings, but it is limited by the drug poor permeability through the skin. To enhance 5-FU efficacy against skin cancer and reduce its systemic side effects, it was loaded into a gold nanoparticle (GNP)-based topical delivery system. 5-FU was loaded onto GNPs capped with CTAB through ionic interactions between 5-FU and CTAB. GNPs were prepared at different 5-FU/CTAB molar ratios and evaluated using different techniques. GNP stability and drug release were studied as a function of salt concentration and solution pH. Optimum 5-FU/CTAB-GNPs were incorporated into gel and cream bases, and their ex vivo permeability was evaluated in mice dorsal skin. The in vivo anticancer efficacy of the same preparations was evaluated in A431 tumor-bearing mice. The GNPs had spherical shape and a size of ~16-150 nm. Maximum 5-FU entrapment was achieved at 5-FU/CTAB molar ratio of 1:1 and pH 11.5. Drug release from GNPs was sustained and pHdependent. 5-FU GNP gel and cream had around 2-fold higher permeability through mice skin compared with free 5-FU gel and cream formulations. Further, in vivo studies in a mouse model having A431 skin cancer cells implanted in the subcutaneous space showed that the GNP gel and cream achieved 6.8- and 18.4-fold lower tumor volume compared with the untreated control, respectively. These results confirm the potential of topical 5-FU/CTAB-GNPs to enhance drug efficacy against skin cancer.

Keywords:

Gold nanoparticles, 5-fluorouracil, cetyltrimethylammonium bromide, skin cancer

Published In:

Molecular Pharmaceutics, DOI: 10.1021/acs.molpharmaceut.8b00047, Vol. 15, No. 6, pp. 2194-2205