

**Title:** Gold Nanoparticles Capped with Benzalkonium Chloride and Poly (ethylene imine) for Enhanced Loading and Skin Permeability of 5-Fluorouracil

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**Objective:** *To enhance 5-fluorouracil (5-FU) permeability through the skin by loading onto gold nanoparticles (GNPs) capped with two cationic ligands, benzalkonium chloride (BC) or poly (ethylene imine) (PEI). Whereas 5-FU has excellent efficacy against many cancers, its poor permeability through biological membranes and several adverse effects limit its clinical benefits. BC and PEI were selected to stabilize GNPs and to load 5-FU through ionic interactions.*

**Methods:** *5-FU/BC-GNPs and 5-FU/PEI-GNPs were prepared at different 5-FU/ligand molar ratios and different pH values and were evaluated using different techniques. GNPs stability was tested as a function of salt*

concentration and storage time. 5-FU release from BC- and PEI-GNPs was evaluated as a function of solution pH. Ex vivo permeability studies of different 5-FU preparations were carried out using mice skin.

**Results:** 5-FU-loaded GNPs size and surface charge were dependent on the 5-FU/ligand molar ratios. 5-FU entrapment efficiency and loading capacity were dependent on the used ligand, 5-FU/ligand molar ratio and solution pH. Maximum drug entrapment efficiency of  $59.0 \pm 1.7\%$  and  $46.0 \pm 1.1\%$  were obtained for 5-FU/BC-GNPs and 5-FU/PEI-GNPs, respectively. 5-FU-loaded GNPs had good stability against salinity and after storage for 4 months at room temperature and at 4°C. In vitro 5-FU release was pH- and ligand-dependent where slower release was observed at higher pH and for 5-FU/BC-GNPs. 5-FU permeability through mice skin was significantly higher for drug-loaded GNPs compared with drug-ligand complex or drug aqueous solution.

**Conclusion:** Based on these results, BC- and PEI-GNPs might find applications as effective topical delivery systems of 5-FU.

**Keywords:**

Gold nanoparticles; 5-fluorouracil; poly (ethylene imine); benzalkonium chloride; skin permeability.