**Title:** Gold Nanoparticles Enhance 5-Fluorouracil Anticancer Efficacy Against Colorectal Cancer Cells

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5-Fluorouracil (5-FU), an antimetabolite drug, is extensively used in the treatment solid tumors. However, its severe side effects limit its clinical benefits. To enhance 5-FU anticancer efficacy and reduce its side effects it was loaded onto gold nanoparticles (GNPs) using two thiol containing ligands, thioglycolic acid (TGA) and glutathione (GSH). The GNPs were prepared at different 5-FU/ligand molar ratios and evaluated using different techniques. Anticancer efficacy of 5-FU/GSH-GNPs was studied using flow cytometry in cancerous tissue obtained from patients having colorectal cancer. The GNPs were spherical in shape and had a size of ~9–17 nm. Stability of the GNPs and drug release were studied as a function of salt concentration and solution pH. Maximum 5-FU loading was achieved at 5-FU/ligand molar ratio of 1:1 and 2:1 for TGA-GNPs and GSH-GNPs, respectively. GNPs coating with pluronic F127 improved their stability against salinity. 5-FU release from GNPs was slow and pH-
dependent. 5-FU/GSH-GNPs induced apoptosis and stopped the cell cycle progression in colorectal cancer cells. They also had a 2-fold higher anticancer effect compared with free 5-FU. These results confirm the potential of GNPs to enhance 5-FU anticancer efficacy.