Gold nanoparticles conjugated with anti-CD133 monoclonal antibody and 5-fluorouracil chemotherapeutic agent as nanocarriers for cancer cell targeting

ABSTRACT

The enhanced permeability and retention effect allows for passive targeting of solid tumours by nanoparticles carrying anticancer drugs. However, active targeting by incorporation of various ligands onto nanoparticles can provide for a more selective and enhanced chemotherapeutic effect and complement the deficiencies of the passive targeting approach. Here we report on the design of the carboxyl-terminated PEGylated gold nanoparticles (AuNPs), their functionalization with anti-CD133 monoclonal antibody (mAb) via a crosslinking reaction, and subsequent 5-fluorouracil (5-FU) drug loading. The synthesized products in the form of stable colloids were characterised using a range of physicochemical techniques, including X-ray diffraction (XRD), UV-Vis spectroscopy, transmission electron microscopy (TEM), and dynamic light scattering (DLS). Conjugation of anti-CD133 mAb onto PEGylated AuNPs was confirmed with the use of UV-Vis, BCA protein assay and fluorescence microscopy. HCT116 colorectal cancer cells abundantly expressed CD133: 92.4 ± 1.3%, as measured by flow cytometry. Whereas PEGylated AuNPs not conjugated with anti-CD133 mAb accumulated mainly at the cellular membrane, nanoparticles conjugated with anti-CD133 mAb were contained within the nuclear region of the cells. Anti-CD133 mAb conjugation facilitated the specific intracellular uptake due to specific antigen–antibody binding interaction. In vitro cytotoxicity studies on HCT116 cells showed that PEGylated AuNPs and PEGylated AuNPs-CD133 did not elicit any toxicity at any of the tested concentrations. Meanwhile, 5-FU-PEGylated AuNPs-CD133 significantly reduced the cell viability relative to the treatment with 5-FU-PEGylated AuNPs without anti-CD133 mAb conjugates ($p < 0.0001$). This study shows that the conjugation of nanocarriers with the anti-CD133 antibody improves the specific targeting of 5-FU against colorectal cancer cells. These results demonstrate that simultaneous functionalisation of PEGylated AuNPs with antibodies and chemotherapeutic drugs is a viable strategy to combat cancer through targeted drug delivery.