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Protein–drug nanoconjugates: Finding the alternative proteins as drug carrier

Iqra Munir
University of Karachi, Pakistan

The present study was designed for the identification of protein bovine serum "fetuin-A" as a new drug carrier candidate, and justified through the most potential drug delivery systems i.e. as protein-drug nanoconjugates and green nanoparticle synthesis approach. For this purpose, a study was conducted to establish the interaction of bovine fetuin-A to validate its binding modalities with doxorubicin (Dox). Fetuin-A was purified to highest form of purity and monodispersity. Green synthesis of fetuin-A conjugated gold nanoparticles (F-GNPs) has been performed giving typical UV-maxima with subtle variation in fourier transform infrared spectroscopy (FTIR). Atomic force microscopy (AFM) revealed spherical shaped, polydisperse F-GNPs of varying sizes, complementing the radius of hydration (19.5–62.4 nm) by dynamic light scattering (DLS). Circular dichroism (CD) analysis of fetuin-A with respect to Dox interaction shows remarkable reduction in ellipticity with increasing concentrations of Dox (20–120 µM). Fetuin-A:Dox and F-GNPs:Dox at variable concentrations revealed significantly enhanced absorption spectra, while a continuous decrease in florescence (560 nm) was observed. This effect was more drastic when Dox interact with fetuin-A as compared to F-GNPs. Some known antimicrobial drugs were also investigated under similar conditions, giving strong quenching effects in a dose dependent manner suggesting the significant yet differential interactions. In cytotoxicity assay, fetuin-A:Dox conjugates revealed less toxicity as compared to F-GNPs:Dox and Dox alone. *In silico* studies of the fetuin-A:Dox complex suggest that the drug binds in the major grove between beta-sheet and long loop region of D1 domain and stabilized by several hydrogen bonds. Hence, fetuin-A was identified as a new carrier protein for the targeted and sustained drug release and/or delivery approach as demonstrated by comparative anticancer activities.

iqramunir2010@hotmail.com