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The Efficacy of a Transferrin Targeted Dual Loaded Anticancer Drug Delivery System Using Functionalized Gold Nanoparticles as Delivery Vehicles

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Extended Abstract

The formulation of a safe and efficient drug delivery system, which can overcome the limitations faced by conventional methods of treatment, is seen as the next step towards successfully treating diseases such as cancer. Nanoparticles have gained much attention due to their desirable characteristics, facile synthesis and their adaptability in applications across various fields. Of these, gold nanoparticles (AuNP's) have emerged as potential vehicles for the delivery of chemotherapeutic drugs due to favourable attributes such as their apparent low toxicity, high surface area, biocompatibility, high loading capacity and ease of surface modification. It was hypothesized that gold nanoparticles used as delivery vehicles would improve anticancer activity of the drug towards cancerous cell lines, due to the ability of the nanoparticles in penetrating the leaky vasculature structure of cancerous tissue, this coupled with the mildly acidic pH of cancerous cells would result in the release of the anti-cancer drugs. Due to this there would be a decrease in cytotoxic effects towards noncancerous cell lines. This study involved the chemical synthesis of AuNP's via a modified Turkevich method. Subsequently, AuNP's were functionalized with the cationic polymer chitosan which encapsulated two anticancer drugs ie. 5-Fluorouracil (5-FU) and Doxorubicin (Dox) respectively, followed by functionalization with human transferrin. Nanoparticles and nanocomposites were fully characterized using ICP, FTIR, HR-TEM, UV-vis spectroscopy and Nanoparticle Tracking Analysis (NTA). To investigate the ability of the nanocomplexes in enhancing the activity of the selected drugs towards HeLa (Cervical adenocarcinoma), a cancerous cell line and lowering the cytotoxic effects of the drugs towards HEK293 (embryonic kidney), a noncancerous cell line, two *in vitro* cytotoxicity assays were performed.

NTA analysis and TEM imaging correlated well with each other, indicating that the nanocomplexes were of uniform shape, with high zeta potentials indicating they were stable and relatively small in size. In addition methods involving UV-vis spectroscopy, FTIR and NTA confirmed the successful conjugation of drug and successive components to AuNP's.

This study revealed that the dual loaded nanoparticles had a superior cytotoxic effect towards the cancerous cell lines when compared nanoparticles consisting of a single drug. While drug release studies over a 72-hour period showed that there was a steady and controlled release of the drug from the dual loaded nanocomposite at a pH of 4 which is desirable for effective cancer treatment. *In vitro* cytotoxicity assays were carried out on the two human cell lines viz. HeLa and HEK293, which showed the effectiveness of the nanocomposites towards the tumour cell lines with little or no significant toxicity towards the non-cancer cell line. The dual loaded nanoparticle exhibited greater anticancer activity on the Hep-G2 cell line when compared to the single loaded nanoparticle. Apoptosis assays were carried out to determine the mechanism of cell death, with the data correlating well with results from the MTT and SRB cytotoxicity assays. This highlights the immense potential of the dual loaded nanoparticles in providing safe and efficient drug delivery with limited side effects, due to selective targeting of cancerous tissue.

Keywords: Drug delivery, Doxorubicin, Gold nanoparticles Nanomedicine, Nanoparticles, 5-fluorouracil.