

Temperature controlled theranostics for pancreatic cancer

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INTRODUCTION

Pancreatic cancer is the 4th most aggressive cancer in the western world with less than 34% of patients surviving past 5 years [1]. Lack of specific symptoms results in a delay in diagnosis. Theranostics are new platforms, which offer simultaneous diagnosis and therapy resulting in a decrease in treatment time [2]. Here treatments are conjugated onto diagnostics by stimuli responsive binding allowing for controlled drug release resulting in a rapid and localised clinical effect. Hybrid nanoparticles are composed of an iron oxide core surrounded by a rigid gold shell [3]. These particles undergo manipulation due to inherent magnetism of the core whilst laser irradiation of their gold shell results in localised heating due to surface plasmon resonance. Hence, they can be utilised as diagnostics using MRI and laser irradiation can be used as a trigger for drug release.

MATERIALS AND METHODS

Proof of concept studies have been carried out using a novel bisnaphthalamido (BNIP) based drug series. BNIPs are a series of novel compounds, which have exhibited exciting potential as chemotherapy agents [4,5]. HNPs were fabricated and characterised using photon correlation spectroscopy (PCS), transmission electron microscopy (TEM), magnetic resonance imaging (MRI), super quantum interference device (SQUID) and zeta potential measurement. Drug conjugation and release was quantified using reverse phase high performance liquid chromatography (HPLC). Cellular response and cytotoxicity assays were carried out using trypan blue exclusion, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and atomic force microscopy.

RESULTS AND DISCUSSION

In our studies, we designed hybrid nanoparticles (50 nm) capable of drug loading onto their surface (3:1:0.25, Drug:Fe: Au). By exploiting the gold surface-to-drug interaction of a range of novel Bisnaphthalamido based agents (Fig. 1) a system with heat triggered drug release was produced. *In vitro* studies of these formulations showed the novel formulations possess a 10-fold lower IC₅₀ value when compared with the free drug after only 24 h. These cytotoxicity studies combined with cellular uptake studies showed the formulations to be significantly more effective compared with gemcitabine (a nucleoside analogue marketed as Gemzar). *In vivo* trials have commenced to further elucidate their viability for use as theranostics.

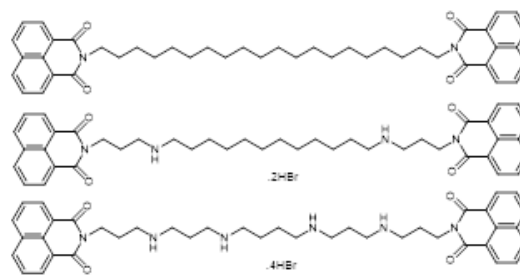


Fig. 1. Drug compounds attached to HNPs

CONCLUSIONS

These data highlight the potential of HNPs as dual imaging agents and contrast agents for pancreatic cancer therapy.

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