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| **Tackling the major challenges around lack of drug efficacy to improve pancreatic cancer patient prognosis. An evaluation into the properties of multifunctional silver ‑ iron oxide hybrid-nanoparticles.** |
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| **Background:** Lack of drug efficacy is one of the major challenges faced by pancreatic cancer patients, contributing to the dismal patient prognosis and survival rates seen globally. Conventional chemotherapeutics have harsh side-effects, penetrate poorly into the dense pancreatic tumour and are broken down by intratumoural bacteria before they can have therapeutic effect. We have designed and evaluated a clever nanoparticle system which aims to overcome these barriers and increase drug accumulation within the tumour and improve therapeutic efficacy. Silver iron-oxide nanoparticles (Ag HNPs) possess the capabilities for image guided drug delivery with triggered release and intrinsic antibacterial properties. |
| **Methods:** Microbiological studies which tested the susceptibility of *Escherichia coli* to Ag HNPs. Bacteria growth with and without Ag HNP treatment were evaluated using optical density measurements and agar disc diffusion method.The Ag HNPs ability to generate heat was evaluated *via* femtosecond laser irradiation of Ag HNPs suspended in agar. Electrostatic and covalent bond loading of anti-cancer drugs onto the particle surface was determined by high performance liquid chromatography and spectroscopic analysis. Cytotoxicity and cellular uptake analysis were evaluated using BxPC-3 cell line. Prior to the evaluation of particle properties, the particles were characterised using transmission electron microscopy, zeta potential and S.Q.U.I.D analysis. |
| **Results:** Ag HNPs prevent the growth of E. coli. Preliminary tests determined that the minimum inhibitory concentration is 0.1 ≥ 0.5 mgmL-1. Clear zones of inhibition were seen for Ag HNP concentrations > 1 mgmL-1 . Upon coating Ag HNPs in a thermoresponsive polymer the susceptibility to bacteria was decreased. Suggesting that bacteria killing could be controlled.  Efficient heating was observed, with Ag HNPs (Fe:Ag approx. 3:1) achieving a 36.7 °C increase over 50 second irradiation. The heat dissipation was evaluated ± 10 mm range from the point of impact. The temperature dropped dramatically as the distanced increased from the point of impact, implying that heating is localised and has potential for targeted therapy whereby collateral heat damage should be reduced.  Attachment of anti-cancer drugs to the Ag HNP surface, electrostatically and chemically, was achieved. The optimum ratio of particle to drug concentration is yet to be determined.  *In vitro* assessment provided promising findings that Ag HNPs have good cellular uptake and minimal cytotoxicity in pancreatic cancer cell lines.  On-going studies include investigating drug release profiles at various physiological conditions. Previous work within the group using gold-iron oxide nano-carriers achieved80 % drug release at 44°C, *via* a thermally labile linker. It is expected our silver system will behave in a similar way. |
| **Conclusions:** Findings thus far suggest that a synergistic effect of the Ag HNPs properties provide great potential for them to be used in a formulation for heat triggered drug release, overcoming barriers for drug efficacy. Further optimisation of the formulation is on-going and with favourable *in vitro* outcomes leading to *in vivo* evaluation. |