DEVELOPMENT OF SMART POLYMERIC NANOCONTAINERS AS TARGETED DRUG DELIVERY SYSTEMS FOR THE TREATMENT OF PEDIACTRIC BRAIN MALIGNANCIES

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Introduction: Pediatric pilocytic astrocytomas (PA) and medulloblastomas (MB) account for >20% of all primary brain tumours and 20% of all malignant cases, respectively. Although, several molecular and genetic factors that drive their development and progression have been uncovered, little progress has been made in the field of curative therapeutics. Current chemotherapeutic agents lack in specificity and selectivity, resulting in unpleasant side effects for the child. One approach to improve drug efficacy and subsequently the therapeutic outcome is to encapsulate drugs within nanocontainers (NCs). Biocompatible and biodegradable polymeric NCs can cross the blood-brain-barrier without causing any damage, due to their nano-size and suitable modified surface. The aim was to synthesize polymeric NCs capable of delivering first-line chemotherapy drugs at the tumour site to increase their efficacy and reduce their side effects.

Methods: Hollow NCs were synthesised following three steps: 1) PMAA core synthesis, 2) Coating it with MAA and EGDMA copolymers (crosslinked by MBA) and 3) Removal of the PMAA core to obtain hollow polymeric NCs P(MAA-*co*-MBA-*co*-EGDMA). Throughout the synthesis stages, polymeric NCs were characterized structurally by Fourier Transform Infrared Spectroscopy and Dynamic Light Scattering, and morphologically by Scanning Electron Microscopy. Daunorubicin was used to test the loading capacity of the nanocontainers as gold standard drug. The NCs were used for the following biological evaluations: haemolysis assay, wound healing assay, MTT assay, and fluorescence microscopy.

Results: The NCs' compatibility and loading capacity were investigated. The haemolysis assay showed <2% haemolysed RBCs for the three concentrations of nanocontainers tested. Daunorubicin was loaded in NCs by 53.8%. Free NCs were shown to be non-cytotoxic in MTT assay and loaded NCs showed good cellular uptake in fluorescence microscopy.

Conclusion: Re-synthesis of the polymeric NCs will take place to optimise their size, stability, and loading capacity, for a sustained drug release and prolonged drug biodistribution whilst further experiments will be performed to evaluate their efficacy further in PA and MB cell cultures and mouse models using different drugs.

References:

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