Graphene Magnetic Nanoparticles as multifunctional smart drug delivery nanosystems for cancer theranostics

Victor Gonçalves
Vânia Costa, Teresa Lage, Raquel Rodrigues, Nuria Genicio, Graça Minas, Juan Gallo and Manuel Bañobre-Lopez
International Iberian Nanotechnology Laboratory, Av. Mestre José Veiga 4715-330 Braga, Portugal
victor.goncalves@inl.int

The purpose of this study was to validate the theranostic performance of graphene-based magnetic nanoparticles (GbMNPs) against tumoral hepatic cell lines. In the GbMNPs, the core nanoparticle made of magnetic material is located in the hollow cavity enclosed by an outer carbonaceous shell. The unique properties of GbMNPs combine physicochemical properties from both graphene and iron oxide (Fe3O4) counterparts, such as biocompatibility and non-toxicity, superparamagnetic behaviour with high saturation magnetization, and high drug encapsulation efficiency and loading capacity provided by the hydrophobic interactions between the certain drug molecules and the particular bidimensional structure of graphene. The in vitro tests revealed the ability of GbMNPs in combining magnetic resonance imaging (MRI) with therapy, exhibiting (i) a r_2 relaxivity value of ~364 $mM^{-1}s^{-1}$, (ii) a high heating efficiency under an alternating (AC) magnetic field – magnetic hyperthermia – (independent loss power of 1.83 nHm^2 kg-1) and (iii) a drug (doxorubicin, DOX) loading efficiency of 96% with a pH- and temperature-dependent release. Cytotoxicity studies with HepG2 cell line showed that the cell viability was reduced to 36% when tested with DOX-loaded GbMNPs (GbMNP@DOX) under an AC magnetic field. In order to study the nanoparticles cellular internalisation, cells were incubated with increasing concentrations of GbMNPs for 24h and imaged by MRI. A concentration-dependent T2-MRI contrast enhancement was observed, as denoted by the remarkable decrease in the T2 relaxation time as Fe concentration increases. Additionally, a 3D liver cancer organoid was bioengineered as a more representative human model of disease to in vitro validate the therapeutic performance of GbMNP@DOX. Cell viability studies performed in the liver tumoroid over time indicated that it remained viable beyond the 2 weeks mark, showing an enhanced functional activity when compared to 2D cultured cells, as denoted by an increase in the transferrin and albumin production levels of 46% and 86%, respectively. In order to assess the therapeutic performance of GbMNP@DOX in a relevant model of disease, a functional validation was performed against the developed 3D liver cancer organoid. Results showed showing a large decrease in cell viability, with 65% of viable cells, which was further reduced to only 2% of viable cells with application of magnetic hyperthermia.

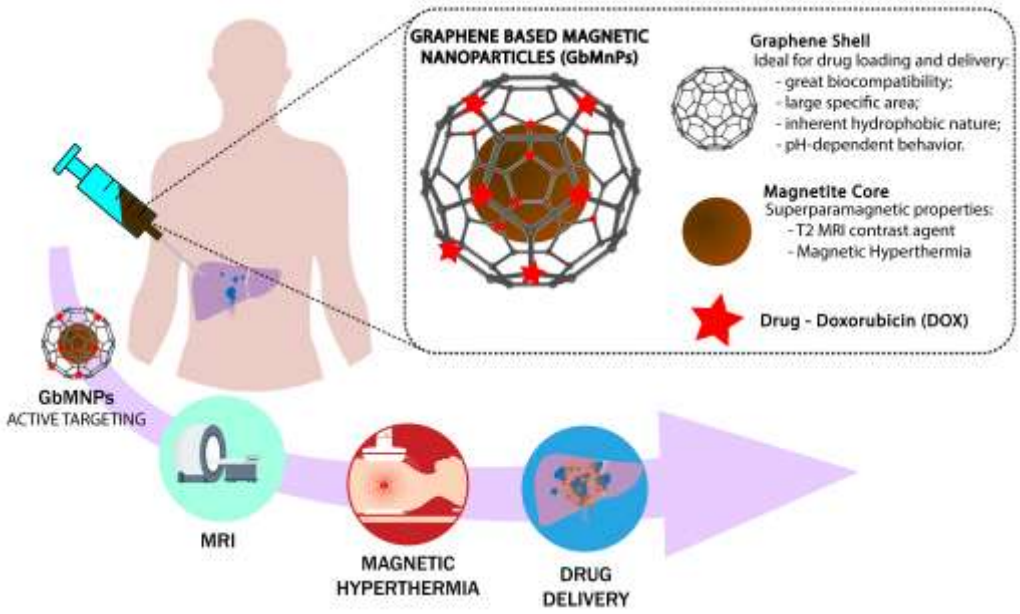

Figure 1: Schematic representation of the graphene based magnetic nanoparticles as multifunctional smart drug delivery nanosystems for cancer theranostics