“Development of functionalized-graphene as a promising nano-carrier for drug delivery applications”

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Graphene has attracted massive interest in numerous biomedical applications such as anti-cancer therapy, drug delivery, bio-imaging and gene delivery. Therefore, it is important to ensure that graphene is nontoxic, and that its cellular biological behavior is safe and biocompatible. Herein, a new route was used to enhance the biocompatibility of graphene, using several natural deep eutectic solvents (DESs) as functionalizing agents, owing to their capability to introduce various functional groups and surface modifications. To meet this end, different combinations of binary and ternary natural DESs were synthesized using choline chloride salt with several hydrogen bond donors (i.e., urea, glucose, fructose, sucrose, glycerol and malonic acid). Characterizations of the physicochemical changes in DES-functionalized graphene were conducted by FESEM, FTIR, XRD, and Raman spectroscopy. There were considerable improvements in the cytotoxicity profile of DES-functionalized graphene on human breast adenocarcinoma (MCF-7), human gastric adenocarcinoma (AGS) and macrophage cell line (RAW264.7), compared to pristine graphene and oxidized graphene, as demonstrated by cell viability, cell cycle progression, and reactive oxygen species evaluation assays. The association between cellular toxicity of DES-functionalized graphene and their physicochemical properties were also revealed. To the best of our knowledge, this is the first study on the cytotoxicity profile improvement of graphene using DESs as functionalizing agents, and its cellular biological behavior. Next, it was selected tamoxifen, as a representative of common anti-cancer drugs, to load on the best DES-functionalized graphene samples. The application of DESs as functionalizing agents, especially for DES choline chloride (ChCl):malonic acid (1:1), significantly reduced the cytotoxicity level of graphenes. DES ChCl:malonic acid (1:1) also demonstrated higher tamoxifen entrapment efficiency and loading capacity in comparison to the functionalization with DES ChCl:glucose (2:1), ChCl:fructose (2:1) and ChCl:urea (2:1). Therefore, DES ChCl:malonic acid (1:1) is considered the most promising nanocarrier for drug delivery applications, owing to its lower cytotoxicity and higher drug loading capacity.

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