Nanographene oxide and PEGylated reduced nanographene oxide as platforms for anti-cancer drug delivery

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Cancer is the second leading cause of death globally. Currently used pharmacological treatments (chemotherapy) present several drawbacks, including the need for high doses of cytotoxic drugs, systemic administration and consequent long-term and late developing severe side effects. Hence, there is a pressing need for more effective drug delivery strategies. Over the past decades, several therapeutic nanocarriers have been explored to deliver anti-cancer drugs to cancerous tissues. Graphene-based materials (GBM) possess large surface area, holding potential for synergistic biologic and drug release effects [1]. In this study, we explored nanographene oxide and PEGylated reduced nanographene oxide as platforms for drug delivery using 5-fluorouracil (5-FU), a widely used drug with anti-cancer activity [2]. Nano-sized graphene oxide (GOn) was produced through the modified Hummer's method [3] followed by ultrasonication using a custom-built industrial grade system. Through this method, we assure the achievement of reproducible large-scale batches of nano-sized GBM. Afterwards, following a single-step procedure, GOn was thermally reduced and non-covalently functionalized with poly(ethylene) glycol bis(amine) (PEG-NH_2) to obtain stable aqueous dispersions (rGOn-PEG) [4]. Oxidation degree, reduction and PEGlyation of GOn were characterized by XPS, FTIR and UV-vis spectroscopy, as well as thermal analysis by TGA. Particle size was determined by transmission electron microscopy (TEM). Surface charge was measured using a zetasizer. GOn and rGOn-PEG (0.125 mg/mL) were sonicated for 30 min and mixed with 5-FU dispersions at a drug concentration varying between 0.25-5 mg/mL, in water. Aliquots were collected from 0 min to 72h, centrifuged (13000 rpm), and the difference in free 5-FU quantified by measuring its absorbance (265 nm). GBMs and drug absorbance spectra (200-850 nm) were obtained using a UV-Vis spectrophotometer. GOn and rGOn-PEG were obtained with mean lateral dimensions of 287 nm and 521 nm, respectively, as determined by TEM. XPS analysis revealed that the O at.% was of 31.95% and 15.87% for GOn or rGOn-PEG, respectively. GOn reduction was further confirmed by a redshift in the characteristic absorbance peak and increased rGOn-PEG absorbance in the near-infrared range of UV-vis spectra, in comparison to unmodified GOn. GOn and rGOn-PEG dispersions showed colloidal stability with zeta potential values around -25.6±0.8 mV and -10.2±0.3 mV (pH=7.4), respectively. 5-FU was successfully loaded by simple molecular physisorption on GOn and rGOn-PEG. Maximum drug loading efficiency was achieved almost immediately after mixing GBMs with 5-FU, regardless of concentrations tested. Drug loading capacities of 5.8±0.8 mg 5-FU/mg GOn and 3.6±1.2 mg 5-FU/mg rGOn-PEG were achieved. This can be explained by favorable interaction between GOn oxygen-containing groups and hydrophilic 5-FU, and possibly by PEG hinderance of drug adsorption. This study shows the successful production and single-step functionalization of nano-sized GBM and the potential using GOn and rGOn-PEG as platforms for anti-cancer drug delivery.

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ACKNOWLEDGMENTS

This work was financed by FEDER funds through the COMPETE 2020 - Operacional Programme for Competitiveness and Internationalisation (POCI), Portugal 2020, and by national funds (PIDDAC) through FCT/MCTES in the framework of the project POCI-01-0145-FEDER-031143, and Base Funding - UIDB/00511/2020 of the Laboratory for Process Engineering, Environment, Biotechnology and Energy – LEPABE.