Graphene-based materials for cancer-targeted chemo-photothermal dual therapy

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Cancer, the second leading cause of death worldwide, requires more effective treatment strategies. Photothermal therapy (PTT) is a non-invasive alternative based on the use of near-infrared (NIR) light energy. It results in hyperthermia (39-47 °C), leading to increased membrane permeability, which, in turn, induces higher nanoparticle/drug uptake and consequent tumor cell apoptosis. In this study, we explored graphene-based materials (GBM), owing to their large surface area and strong radiation absorption [1], as platforms for chemo-photothermal therapy.
For this purpose, nano-graphene oxide (GOn) was firstly produced using a modified Hummer's method [2] and subsequently thermally reduced and functionalized with poly(ethylene) glycol (PEG) to obtain stable aqueous dispersions (rGOn-PEG) [3]. GOn and rGOn-PEG (0.25 mg/mL) were mixed with 5-fluorouracil (5-FU), an anti-cancer drug, at a drug concentration varying between 0.25 and 5 mg/mL. GBM aqueous dispersions were irradiated with a LED source of 812.8±29.9nm (150 mW/cm2) and temperature change was recorded. The effect of GBM and NIR irradiation was evaluated by resazurin cell viability assay using human foreskin fibroblasts (HFF-1) and a human skin carcinoma cell line (A431 cells).
GOn was obtained with mean lateral dimensions of 248 nm, as determined by TEM. 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), respectively. Loading capacity of 5-FU on GBM reached 5.8±0.8 mg 5-FU/mg GOn and 3.6±1.2 mg 5-FU/mg rGOn-PEG by simple molecular physisorption, preventing drug inactivation. NIR irradiation increased rGOn-PEG temperature to 47 °C after 30 min, which is within temperature ranges of hyperthermia. GBM alone did not affect cell viability of healthy fibroblasts (HFF-1) and carcinoma-derived A431 cells up to the highest concentrations tested (250 μg/mL). rGOn-PEG concentrations above 100 μg/mL in combination with NIR significantly reduced A431 cells viability, pointing out the great potential of GBM-based platforms for dual PTT/chemotherapy in cancer treatment, namely using selective mild-hyperthermia, which constitutes an advantage comparing with current common approaches.

References

[1] Zhang B, *et al.*, Curr Med Chem, 24 (2017) 268
[2] Pinto AM, *et al.*, Carbon, 99 (2015) 318
[3] Chen J, *et al.*, Biomaterials, 35 (2014) 4986

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