Photothermal cancer therapy with graphene-based materials and their drug conjugates

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Oncological malignancies are the second leading cause of death globally, raising the need for novel treatment strategies. Photothermal therapy (PTT) may be applied as an effective non-invasive alternative treatment. Near-infrared (NIR) light energy can induce hyperthermia (39-47°C), inducing higher nanoparticle/drug uptake due to increased membrane permeability and tumor cell apoptosis. Graphene-based materials (GBM) present strong radiation absorption and possess large surface area, holding potential for synergistic biologic and drug release hyperthermia triggered effects [1]. Herein, GBM and GBM loaded with 5-fluorouracil (5-FU), an anti-cancer drug, are proposed as platforms for cancer PTT. Nano-sized graphene oxide (GOn) was produced through the modified Hummer's method [2] followed by ultrasonication through a custom-built industrial grade system, to assure the achievement of reproducible large-scale batches of nano-sized GBM. Following a one-step procedure, GOn was thermally reduced and functionalized with poly(ethylene) glycol (PEG) moieties to obtain stable aqueous dispersions (rGOn-PEG) [3]. GOn and rGOn-PEG (0.25 mg/mL) were mixed with 5-FU at a drug concentration varying between 0.25-5 mg/mL. GBM aqueous dispersions were irradiated with a LED source of 812.8±29.9nm (150 mW/cm^2) and temperature recorded using a thermocouple. The effect of GBM and NIR irradiation was evaluated by resazurin cell viability assay using a human skin carcinoma cell line (A431 cells, ATCC). 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. 5-FU was successfully loaded by simple molecular physiosorption on GOn and rGOn-PEG, with loading capacity being of 5.8±0.8 mg 5-FU/mg GOn and 3.6±1.2 mg 5-FU/mg rGOn-PEG. NIR irradiation increased rGOn-PEG temperature to 47ºC after 30 min, which is within temperature ranges of hyperthermia. rGOn-PEG in combination with NIR reduced A431 cells viability, in opposition to irradiated GOn or rGOn-PEG alone. This study opens new avenues for the development of GBM-based platforms for drug delivery and PTT of cancer.

REFERENCES

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