Near-infrared light emitting diode based photothermal therapy with graphene: skin permeation studies

Filipa A. L. S. Silva
Filipa A. L. S. Silva[1,2], Raquel Costa-Almeida[1,2], Licínia Timochenco[3], Soraia Pinto[1,2], José Ramiro Fernandes[4], Fernão D. Magalhães[3], Bruno Sarmento[1,2,5], Artur M. Pinto[1,2,3]
[1]i3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Porto, Portugal; [2]INEB - Instituto de Engenharia Biomédica, Porto, Portugal. [3]LEPABE, Faculdade de Engenharia, Universidade do Porto, Porto, Portugal; [4]CQVR – Centro de Química Vila Real, Universidade de Trás-os-Montes e Alto Douro, Portugal,[5]CESPU, IINFACTS – Institute for Research and Advanced Training in Health Sciences and Technologies, Rua Central de Gandra 1317, 4585-116 Gandra, Portugal
flsilva@i3s.up.pt; arturp@i3s.up.pt

Abstract

Basal cell carcinoma (BCC) is the most common form of human cancer, and treatment usually involves surgery. However, several non-invasive strategies such as photothermal therapy (PTT) have been explored. Graphene-based materials (GBM) are good candidates to act as photothermal agents since they can absorb near-infrared (NIR) light energy that can induce hyperthermia (39-47°C), leading to tumour cells apoptosis. We have demonstrated that low power (150 mW cm^{-2}) NIR irradiation using light emitting diodes (LED) resulted in reduced nanographene oxide modified with polyethylene glycol (rGOn-PEG) heating up to 47 °C, which is within the mild PTT temperature range. PEGylation strongly enhanced the dispersibility of rGOn in physiological media (phosphate buffered saline, fetal bovine serum, and cell culture medium) and also improved the biocompatibility of rGOn-PEG, in comparison to GOn (25–250 µg mL^{-1}). After a single NIR LED irradiation treatment of 30 min, a decrease of ≈38% in A-431 cells viability was observed for rGOn-PEG (250 µg mL^{-1}). [1,2]

In this study, we propose the use of nano graphene oxide (GOn) and rGOn, non-PEGylated, as platforms for PTT treatment of BCC. To perform this, GO was produced through the modified Hummer's method, [1,2] and further sonicated and centrifuged to obtain GOn. GOn was photo-reduced to obtain rGOn. Materials obtained were characterized in terms of physical-chemical and optical properties. Particle size and morphology were determined by transmission electron microscopy (TEM) and by using a zetasizer equipment, zeta potential was also measured. GBM absorbance spectra (200-850 nm) were obtained using a UV-Vis spectrophotometer. GOn and rGOn were irradiated with a LED source of 810 nm (150 mW cm^{-2}) and temperature increase recorded using a thermocouple. Biocompatibility of the materials with primary human fibroblasts (HFF-1) was tested using the Alamar Blue method. The permeability of GOn and rGOn water suspensions through human skin was determined using a Franz cell system. Skin samples were analysed by TEM and stained with haematoxylin and eosin for histological analysis.

Single layer GBM were obtained with average lateral dimensions below 200 nm. GOn and rGOn dispersions showed colloidal stability with zeta potential values of -39.4 ± 1.8 and -37.8 ± 1.2 mV (neutral pH), respectively. The increment of rGOn temperature triggered by NIR irradiation revealed to be time-dependent. rGOn temperature reached 59.4 ºC after 30 min irradiation, around 1.3 fold higher than GOn heating. GOn and rGOn (100-250 µg mL^{-1}) didn't affect HFF-1 cell viability after 24h of incubation. Both materials were able to cross epidermis and dermis in a time-dependent manner. Skin permeability of rGOn revealed to be lower and slower than GOn permeability, during the 1st hour of contact with the skin. After 6 h, the amount of rGOn that permeated to the receptor compartment was 1.2-fold lower than for GOn.

Together, our results demonstrate the potential of irradiating GBM using lower energy, cheaper, smaller, and safer LED, as alternative to high power lasers, for NIR mild hyperthermia therapy of cancer, namely BCC. The potential use of GBM for BBC treatment as biocompatible photothermal agents able to penetrate deep into skin is also demonstrated, a step towards translation to clinics.

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