# Graphene-based materials as platforms for skin disease treatment

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## Abstract

Skin diseases are one of the leading causes of global disease burden, affecting millions of people worldwide. In the United States of America (USA), nearly 85 million people are seen by a physician for at least 1 skin disease every year. Guidelines for treatment of Psoriasis, Atopic Dermatitis (AD), and Vitiligo include as first or second line options phototherapy with ultraviolet radiation combined or not with drugs while for Basal Cell Carcinoma (BCC), photodynamic therapy (PDT) with photosensitizers activated by near-infrared (NIR) radiation are listed in the first line of treatments. [1-3] However, these treatments still present limitations due to the low stability, toxicity, and skin penetration of commonly used drugs. Graphene-based materials (GBM) properties allow targeted drug delivery, sustained release, improved biostability and, low toxicity. In addition, they posse a high coefficient extinction in near-infrared (NIR) region making them good candidates to act as photothermal agents. [4]

In this study, we propose the use of nanographene oxide (GOn) and reduced nanographene oxide (rGOn) as platforms for skin diseases treatment. GO was produced from graphite (Gt) powder through the modified Hummer's method, [4] and further sonicated and centrifuged to obtain GOn. This material was later photo-reduced to obtain rGOn. Gt water dispersions stabilized with Pluronic P-123 (Gt-P-123) were also prepared. Particle size and morphology were evaluated by transmission electron microscopy (TEM), optic microscopy, and using a zetasizer; zeta potential was also measured. Absorbance spectra (200-850 nm) were obtained using a UV-Vis spectrophotometer. GOn and rGOn were irradiated with a LED source of 812 nm (150 mW $cm^{-2}$) and temperature increase recorded using a thermocouple. GOn and rGOn biocompatibility with primary human fibroblasts (HFF-1) was evaluated using the Alamar Blue assay. The permeability of GOn, rGOn and Gt-P-123 water suspensions through human skin was determined using a Franz cell system.

Single layer GOn and rGO 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. rGOn temperature reached 59.4 ºC after 30 min irradiation, around 1.3-fold higher than GOn heating. GOn and rGOn (100-500 µg $mL^{-1}$) did not affect HFF-1 cell viability after 24 h 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. Gt-P-123 presented sizes between a few to hundreds (agglomerates) of microns. Due its large size, no skin permeation was observed for Gt-P-123.

These results demonstrate for the first time the potential of GBM for use in skin disease treatment, as biocompatible photothermal agents able to penetrate deep into skin.

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