Injectable thermo-responsive hydrogel incorporating graphene-based nanomaterials and a dual drug combination for breast cancer chemo-photothermal therapy

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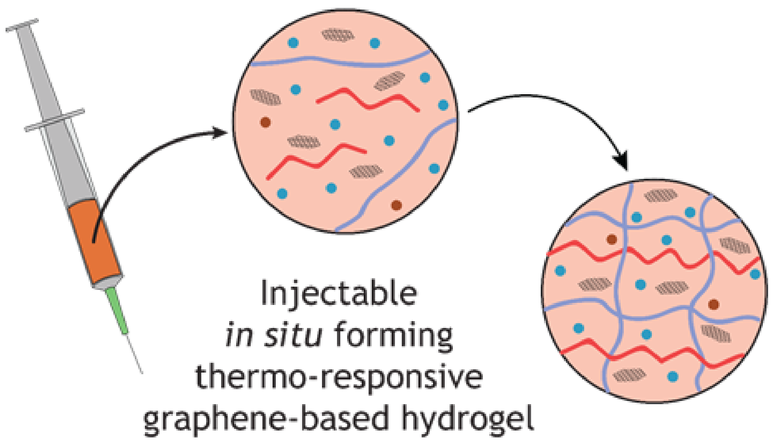
Introduction

- Graphene oxide (GO) and reduced graphene oxide (rGO) nanomaterials hold great potential for cancer combinatorial therapy due to their photothermal and loading capabilities. However, these materials lack colloidal stability, being unable to reach the tumor [1]. To overcome this limitation, injectable *in situ* forming hydrogels are now starting to be explored for the local delivery of nanomaterials into the tumor site.
- In this work, injectable *in situ* forming thermo-responsive hydrogels integrating GO (thermogel-GO) and rGO (thermogel-rGO) were assembled. Then, an optimized Doxorubicin:Ibuprofen combination (1:5 molar ratio) was incorporated into the thermogel-rGO (thermogel-rGODI) in order to explore it in the combinatorial chemo-photothermal therapy of breast cancer cells [2].

Materials and Methods

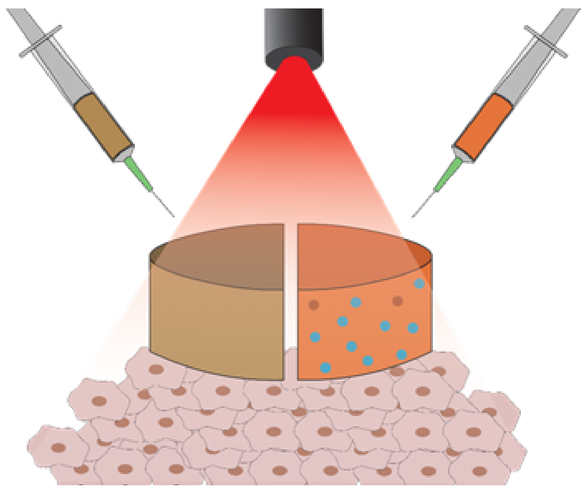


Physicochemical characteriazation

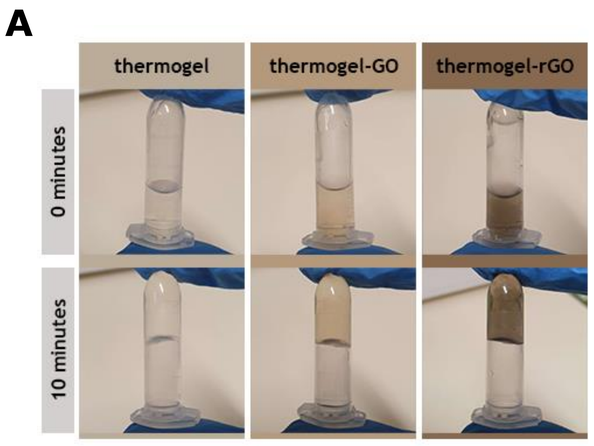
Thermo-responsive gelation
Swelling ratio
Degradation
Photothermal capacity

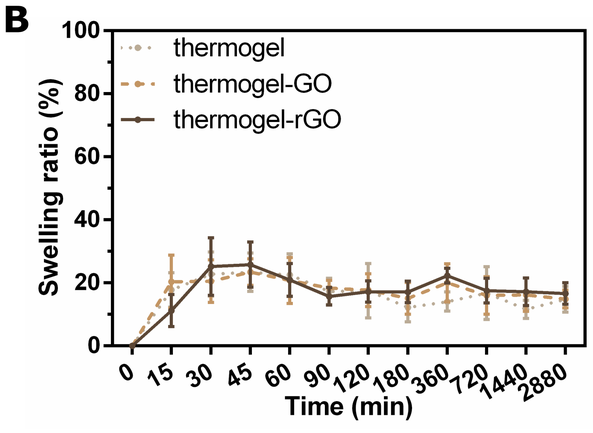
Biological characteriazation

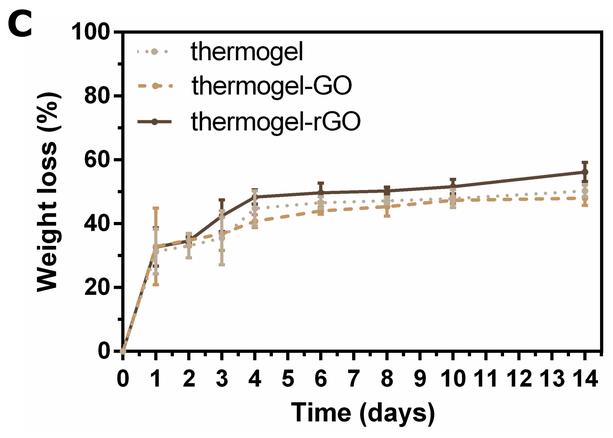
Cytocompatibility
Photothermal therapy
Chemo-Photothermal therapy

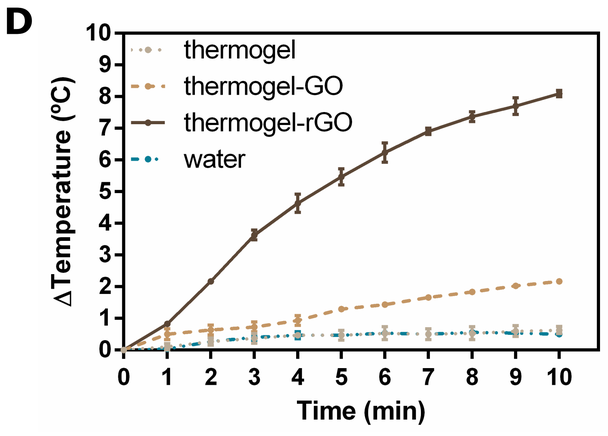


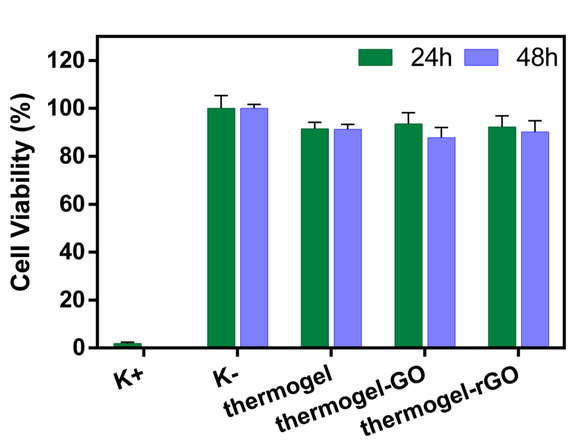
Results

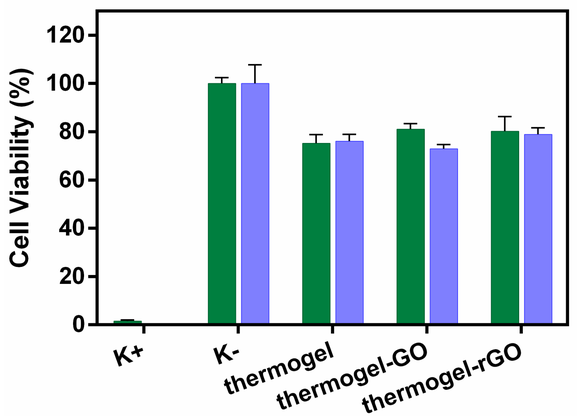


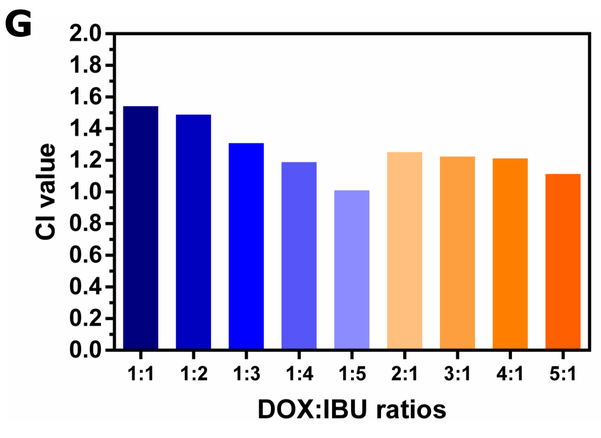












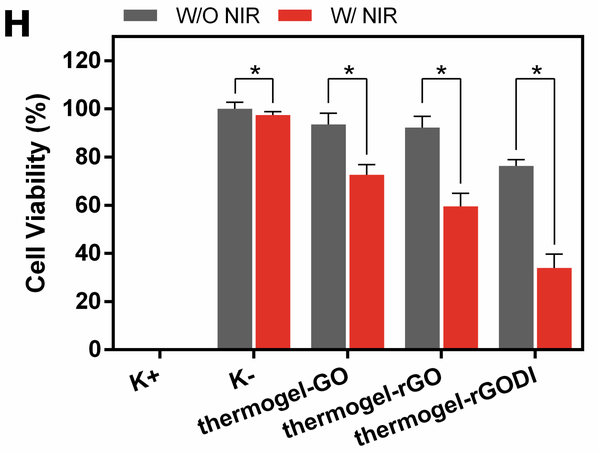


Figure caption: Macroscopic images of the thermogel, thermogel-GO, and thermogel-rGO gelation **(A)**. Evaluation of the hydrogels' swelling capacity over a period of 48 h **(B)**. Determination of hydrogels' weight loss over a period of 14 days **(C)**. Temperature variation curves of the different hydrogel formulations during 10 min of irradiation (808 nm, 1.7 W/cm^2). Data represent mean ± SD, n = 3 **(D)**. Cytocompatibility of thermogel, thermogel-GO and thermogel-rGO towards MCF-7 **(E)** and NHDF **(F)** cells after 24 and 48 h of incubation. Combination Index of the different DOX:IBU combinations against MCF-7 cells **(G)**. Effect of thermogel-GO, thermogel-rGO and thermogel-rGODI (at a concentration of 10 µg/mL of GO or rGO and 90.4 µM of the 1:5 DOX:IBU combination) towards MCF-7 cells without (W/O NIR) or with (W/ NIR) NIR laser irradiation (808 nm, 1.7 W/cm^2, 10 min) **(H)**.

Conclusion

- Thermogel-rGODI is a promising injectable *in situ* forming thermo-responsive hydrogel for the chemo-photothermal therapy of breast cancer cells.

References

[1] de Melo-Diogo, *et al.*, (2018), Functionalization of graphene family nanomaterials for application in cancer therapy, Colloids Surf., B., 171, 260-275.

[2] Lima-Sousa, *et al.*, (2020), Injectable *in situ* forming thermo-responsive graphene based hydrogels for cancer chemo-photothermal therapy and NIR light-enhanced antibacterial applications, Mater. Sci. Eng., C, 117, 111294.

Acknowledgments

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