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Enhanced Cytotoxic Effect of TAT–PLGA-Embedded DOXO Carried by Biomimetic Magnetic Nanoparticles upon Combination with Magnetic Hyperthermia and Photothermia

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Aim

The rationale behind this work lies in an optimization of the nanoformulation DOXO-BMNPs, already demonstrated to be more efficient against tumor cells, both *in vitro* and *in vivo*, than systemic traditional therapies. By embedding DOXO-BMNPs into PLGA, which is further functionalized with the cell-penetrating TAT peptide, the resulting nanoassembly is able to mediate drug transport (using DOXO as a drug model) and behaves as a hyperthermic agent (induced by an alternating magnetic field (AMF) or by laser irradiation with a laser power density of 2 W/cm2).

Summary Results

Our results obtained using the HepG2 cell line show that there is a synergy between chemotherapy and thermal therapy that results in a stronger cytotoxic effect when compared to that caused by the soluble DOXO. This is probably due to the enhanced DOXO release occurring upon the application of the thermal therapy.

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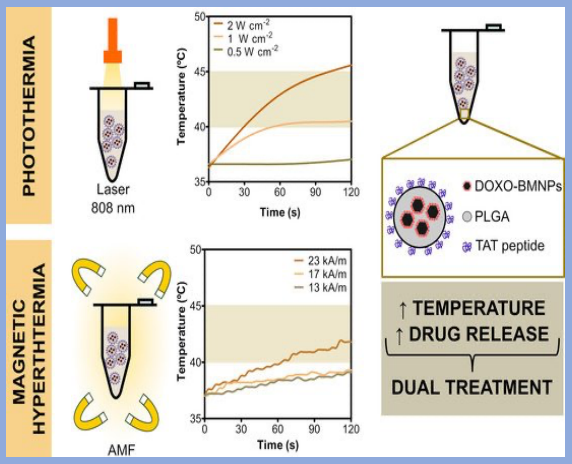
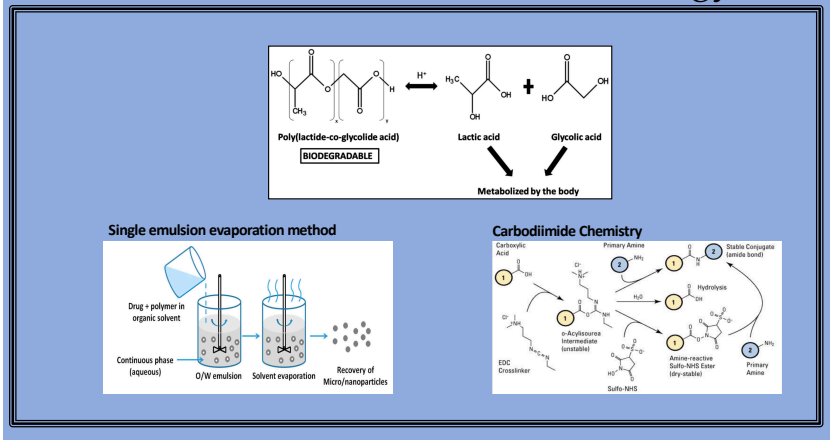


Aim

PLGA Nanotechnology



Conclusion

TAT-PLGA(DOXO-BMNPs) nanoassembly was able to exert both directed chemotherapy and hyperthermia treatment (either magnetic hyperthermia or photothermia) using the same nanoplatform: its cytotoxic effect is similar (or stronger) when directed chemotherapy is combined with magnetic hyperthermia or with photothermia. This synergy is caused by the enhanced DOXO release following treatment combination and the locally induced temperature increase. Therefore, the results of this work represent a step forward in the use of combined therapies to increase the antitumor efficiency of treatments, as well as a transition from systemic to local treatments with the goal of reducing drug doses and undesirable secondary effects.

Acknowledgment

A special thanks to all the Spanish group, especially to Prof. C. Jimenez-Lopez who hosted me at her laboratory in the Microbiology Department of Universidad de Granada; I sincerely thank Ylenia with whom I worked closely for the preparation of the nanoassembly and I also thank her for taking care of the graphics. Last but not least, a special thanks goes to my supervisor Prof. Massimiliano Perduca who is accompanying me in this PhD experience.

Results

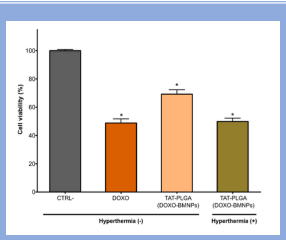


Figure 6. Cytotoxicity in HepG2 cell line following treatment with culture medium (control), DOXO (30 μg/mL DOXO), and TAT-PLGA(DOXO-BMNPs) (containing 300 μg/mL BMNPs and 30 μg/mL DOXO) in the absence or in combination with magnetic hyperthermia. Data represent the means ± SEM of three independent experiments performed in triplicate; $p < 0.05$ (*).

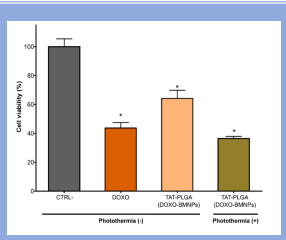


Figure 7. Cytotoxicity in HepG2 cell line following treatment with culture medium (control), DOXO (30 μg/mL DOXO), and TAT-PLGA(DOXO-BMNPs) (containing 300 μg/mL BMNPs and 30 μg/mL DOXO) in the absence or in combination with Photothermia. Data represent the means ± SEM of three independent experiments performed in triplicate; $p < 0.05$ (*).

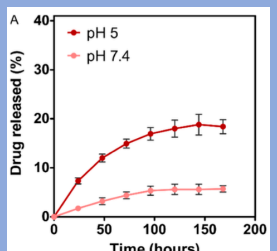


Figure 4. TAT-PLGA(DOXO-BMNPs) as drug nanocarriers. DOXO release at physiological and acidic pH values in (A) absence of magnetic hyperthermia and/or photothermia. (B) DOXO release at physiological and acidic pH values in combination with photothermia (2 W/cm2) or magnetic hyperthermia (frequency 120 kHz, H~ 23 kA/m) treatment.

References

I. García Rubia, G.; Peigneux, A.; Jabalera, Y.; Puerma, J.; Oltolina, F.; Elert, K.; Colangelo, D.; Gómez Morales, J.; Prat, M.; Jimenez-Lopez, C. pH-Dependent adsorption release of doxorubicin on MamC-Biomimetic Magnetite Nanoparticles. Langmuir 2018, 34, 13713–13724.

II. Jabalera, Y.; Oltolina, F.; Peigneux, A.; Sola-Leyva, A.; Carrasco-Jiménez, M.P.; Prat, M.; Jimenez-Lopez, C.; Iglesias, G.R. Nanoformulation design including MamC-mediated biomimetic nanoparticles allows the simultaneous application of targeted drug delivery and magnetic hyperthermia. Polymers 2020, 12, 1832.

III. Jabalera, Y.; Sola-Leyva, A.; Carrasco-Jiménez, M.P.; Iglesias, G.R.; Jimenez-Lopez, C. Synergistic Photothermal-Chemotherapy Based on the Use of Biomimetic Magnetic Nanoparticles. Pharmaceutics 2021, 13, 625.

IV. Gaglio, S.C.; De Rosa, C.; Piccinelli, F.; Romeo, A.; Perduca, M. Complexes of rare earth ions embedded in poly(lactic-co-glycolicacid)(PLGA)nanoparticles: Characterization and spectroscopic study. Opt. Mater. 2019, 94, 249–256.