

Right Place, Right Time: GQDs for Controlled Chemotherapy Release

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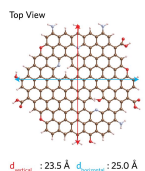
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Abstract

With cancer rates increasing at an alarming rate, many traditional methods for cancer treatment begin to feel outdated. This is where engineering nanomaterials, such as Graphene Quantum Dots (GQDs), offer a promising approach to making chemotherapy a more targeted treatment and therefore minimizing the side effects. This study focuses on optimizing drug delivery mechanisms using GQDs, specifically Reduced Graphene Quantum Dots (RGQDs) synthesized via a top-down approach from reduced graphene oxide, and Hyaluronic Acid Graphene Quantum Dots (HAGQDs) synthesized bottom-up from hyaluronic acid. The process is done by loading chemotherapeutics Gemcitabine, Paclitaxel, and Doxorubicin (DOX) HCl onto GQDs through sonication, this is followed by a centrifugal purification which isolates properly drug-loaded GQDs. To evaluate their controlled release, photothermal properties of GQDs are utilized. Samples are excited with an 808 nm laser at 1, 5, and 10 minutes, and they are later compared to a control group. This analysis provides insights into how laser stimulation affects drug release efficiency, paving the way for advancements in GQD based cancer treatments.

Intro

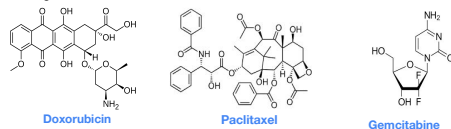
GQDs and Their Importance in Cancer Therapeutics



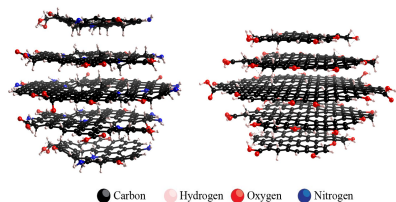
- Enhanced cellular uptake and tissue penetration:** Their nanoscale size allows for efficient cell entry and deeper penetration into tumor tissues.
- Functionalization capabilities for targeted delivery:** GQDs can be modified to attach targeting molecules, enabling precise drug delivery to specific cancer cells.
- Low inherent toxicity:** GQDs exhibit low cytotoxicity compared to other nanomaterials, improving their biocompatibility and safety.
- Triggered drug release via external stimuli:** GQDs can be designed to release drugs upon light exposure, allowing for controlled drug delivery.

Utilizing Different Chemotherapeutics

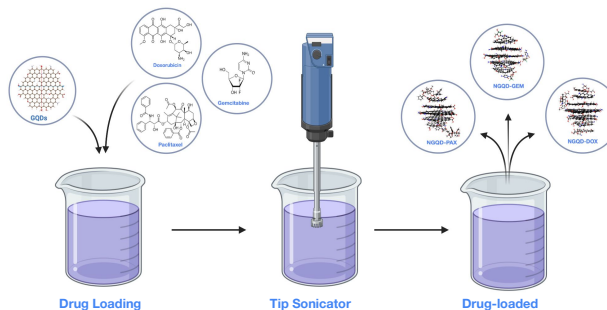
- Doxorubicin (DOX):** A drug that damages the DNA of cancer cells, preventing their growth.
- Paclitaxel (PAX):** A drug that interferes with the cell division process, stopping cancer cells from multiplying.
- Gemcitabine (GEM):** A drug that blocks the production of DNA in cancer cells, leading to their death.



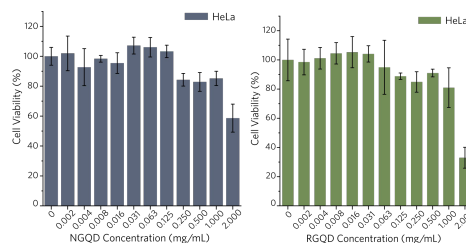
Molecular Structures of GQDs



Drug Loading

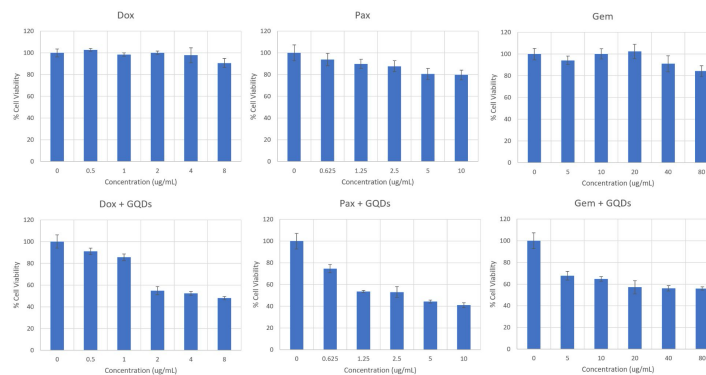


Cell Viability of GQDs

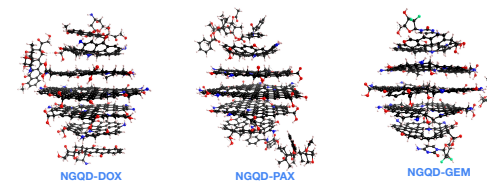


- More than **80% cell viability at 1 mg/mL** means that it is a **safe dosage** to use

Cell Viability of Chemotherapeutics



A Closer Look at Drug Loaded GQDs



Conclusion

- Controlled Drug Release Engineering:** 808 nm laser stimulation successfully triggered controlled drug release from RGQDs and HAGQDs, confirmed by spectroscopy, demonstrating the ability to engineer on-demand delivery.
- Biocompatibility for Delivery:** The safety profile of GQDs was confirmed by a MTT assays on HeLa cells, which showed >80% cell viability at 1 mg/mL, supporting its use as a biocompatible concentration.
- Release Kinetics Optimization:** By comparing the drug release profiles at 1, 5, and 10 minutes laser exposure, we were able to optimize laser-triggered release kinetics, gaining insights into the release process.
- Cytotoxicity with GQDs:** Dox, Pax, and Gem all showed concentration dependant cytotoxicity, and with the combination of GQDs this led to a significant reduction in cell viability at all concentrations tested. This suggests GQDs enhance the drugs efficacy.

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Graphene Quantum Dots (GQDs) show great promise as a controlled drug delivery for cancer therapy. By optimizing the engineered release mechanism of the GQDs it offers an edge to the current on market chemotherapeutics. While the release mechanism is still a big challenge, this precise control is crucial for maximizing its efficacy and minimizing the effects on healthy cells. Our research has shown that 808 nm laser stimulation can effectively trigger drug release and that GQDs exhibit good biocompatibility in HeLa cells at specific concentrations. However, the long-term stability, biodistribution, and cellular uptake mechanisms of these drug-loaded GQDs are still largely unexplored. Future studies will need to focus on optimizing GQD design for sustained release, minimizing potential immunogenicity, and developing strategies for targeted delivery to specific tumor microenvironments. Ultimately this research aims to advance the development of nanomedicines which can revolutionize cancer treatment by providing a tailored, on-demand drug delivery.

References

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- Topkiran, U. C., Valmukhametova, A. R., Vashani, D., Paul, H., Dorsky, A., Sottile, O., Johnson, D. A., Burnett, W., Coffey, J. L., Akkaraku, G. R., & Naumov, A. V. (2023). Holistic Investigation of Graphene Quantum Dot Endocytosis. *Small*, 21(8), 2406095. <https://doi.org/10.1002/smll.202406095>