The Effects of Surface Coatings on the Drug Delivery Capacity of Oxidized Graphene Nanoribbons

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Introduction

What are oxidized graphene nanoribbons (O-GNRs)?

- GONRs are thin, elongated strips of graphene with straight edges.
- Derived from multi-walled carbon nanotubes (MWCNTs), a more widely known carbon nanoparticle.

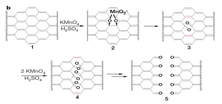

Figure 1: GONRs synthesized from MWCNT by converting ketones into carboxylic acids at the ends of the nanotubes in a longitudinal manner[1].

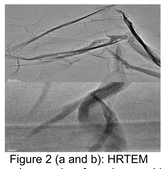

Figure 2 (a and b): HRTEM micrographs of graphene oxide nanoribbons.

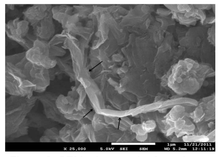

Figure 3: SEM micrograph of graphene oxide nanoribbons. Scale bar correspond to 1 µm.

What are the benefits of studying O-GNR?

- Photoluminescence in the visible and infrared region, allowing for live cell imaging.
- Can be multi-functionalized, allowing for optimizing solubility and half-life, which is an important factor for efficient drug delivery.
- Biocompatibility issue of having aggregates of nanoparticles in aqueous solutions can be solved through functionalization of GONR[2].

How can this be used in future for breast cancer diagnosis and treatment?

- Multi-functionalized → molecular imaging probes to consist of O-GNR functionalized with a targeting agent that recognizes a biomarker specific to tumor.
- Currently, most chemotherapy drugs target all cells, consequently destroying not only cancer cells, but also other rapidly dividing cells such as stomach lining, blood cells, and hair follicles. As a result, side effects like nausea, low blood cell counts, and hair loss result.
- However, because targeted drug delivery would deliver drugs directly to the cancer cells, these painful side effects caused by chemotherapy would be avoided. By coating nanoparticles with proteins that recognize receptors on cell membranes, a wide range of drugs and imaging agents can enter cells through endocytosis[].
- The method of functionalizing a targeting agent to specific cells would use O-GNR in a way that also enhances the contrast between malignant and benign tissue in a MRI scan, making it easier to detect the tumor[
- Consequently this method allows for the quick diagnosis and an improved accuracy, localization, and efficiency of drug delivery agents.

The purpose of this experiment was to determine the efficacy of various surface coatings for solubilization and for drug delivery into cells.

Methods

Synthesizing and Coating O-GNR.

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Loading O-GNR with Doxorubicin.

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Cell Line Collection and Maintenance.

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Colorimetric (Fluorimetric and Absorbance-based) Assay.

Coating O-GNR

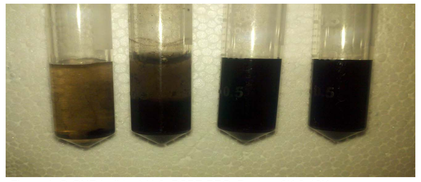

Figure 4: O-GNR in (l to r) H_20, DSPE-PEG, Dextran 6K & 10K.

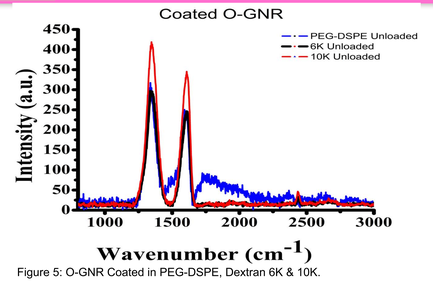

Figure 5: O-GNR Coated in PEG-DSPE, Dextran 6K & 10K.

How can O-GNR become soluble in water?

- O-GNR must be functionalized to make them water-soluble so that they are stable in biological media and blood before potential applications are realized.
- O-GNR can be functionalized with many different surface coatings, including:
  - 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[amino(polyethylene glycol)-2000] (PEG-DSPE)
  - Dextran with a molecular weight of six kilodaltons
  - Dextran with a molecular weight of ten kilodaltons.

Loading O-GNR with Doxorubinicin

- The coated nanoparticles were loaded with the anti-cancer drug doxorubicin via simple π-stacking.
- Raman spectra and UV-Vis of the O-GNRs were taken and analyzed to ensure that the structures and bonds of the nanoparticles were not disrupted during the coating and loading process, and that Doxorubinicin (DOX) was successfully loaded onto the O-GNR.

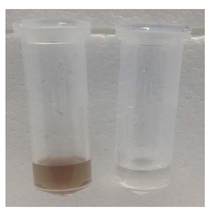

Figure 6: Supernatant from loaded O-GNR coated with 6K (l) and 10K (r) Dextran

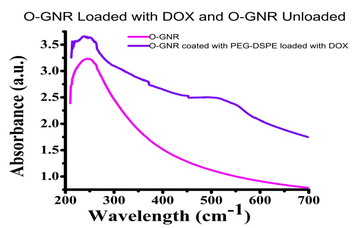

Figure 7: UV-Vis of O-GNR Loaded with DOX and O-GNR Unloaded

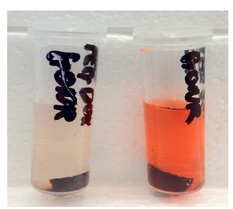

Figure 8: O-GNR coated with PEG-DSPE loaded at 200 ug/mL (l) and 500 ug/mL (r)

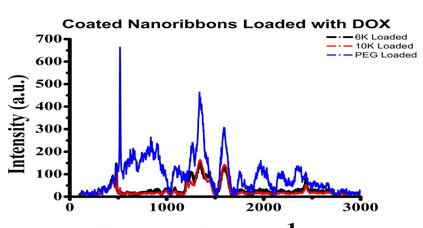

Figure 9: Raman Spectra of Coated O-GNR Loaded with DOX

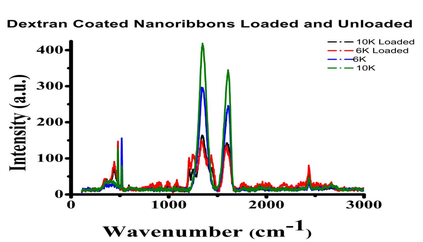

Figure 10: Raman Spectra of Dextran Coated O-GNR Loaded and Unloaded with DOX

Colorimetric Cytotoxicity Assays

Lactate Dehydrogenase (LDH) Assay

The lactate dehydrogenase assay (LDH) Kit (Sigma-Aldrich, New York) was performed. The percent viability averages were plotted, and they were normalized to the negative control (cells that were completely lysed) to take into account the absorbance values with 0% viability.

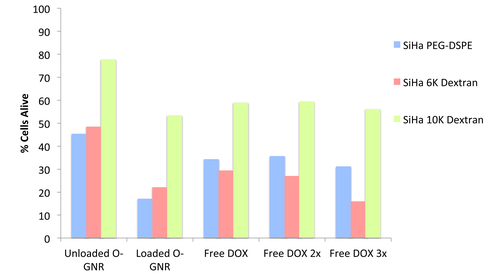

Figure 11. The percentage of SiHa cells alive after exposure to O-GNR Coated with PEG-DSPE, 6K Dextran, and 10K Dextran.

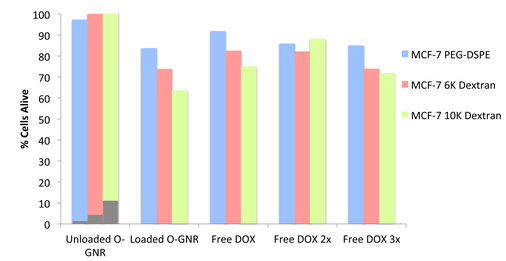

Figure 12. The percentage of MCF-7 cells alive after exposure to O-GNR Coated with PEG-DSPE, 6K Dextran, and 10K Dextran.

Conclusion & Future Work

- The coating that provided the most effective drug delivery in MCF-7 cells was dextran with a molecular mass of ten thousand kilodaltons (Dextran 10K); in SiHa cells, PEG-DSPE was the most effective.
- It was determined that in both cell lines, the nanoparticles delivered three times more doxorubicin than the cells would take up without the nanoparticles. This effect may have a large impact on the efficacy of drug therapy, and may significantly reduce the side effects of the cancer drug treatments.
- The future applications of O-GNRs seem promising, thus researching the environmental impact of O-GNR before it reaches the consumer is imperative.

Acknowledgments

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References

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