# Sonochemical Assembly of Copper/Iron-modified Graphene Oxide for Anti-Inflammatory Drug Delivery

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## Introduction

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly prescribed medications worldwide to treat the inflammation and pain. When the drug is delivered to the human body through the gastro-intestinal system, the latter undergoes bleeding and develops gastritis after repeated doses of ketorolac over prolonged duration. Many approaches are being put towards administration of ketorolac at a lower dose and shortening period of the systemic exposure while maintaining its therapeutic efficacy.

Nanomedicine offers tools based on molecular carriers aiming at an increase of the drug surface area by reducing particle size and modification of the surface thereby causing more rapid dissolution and absorption by target tissue. Graphene oxide (GO) in its pristine or modified form can be used as a successful drug molecular carrier due to its high surface area, biocompatibility and a very rich surface chemistry.

Acoustic cavitation (sonochemistry) is an efficient tool for the assembly of pre-formed GO modified with copper in aqueous solution via the interaction with gaseous bubbles at the cavitation interface; sonochemical encapsulation of the drug *(e.g.* ketorolac) in these new nanocomposites or in microspheres.

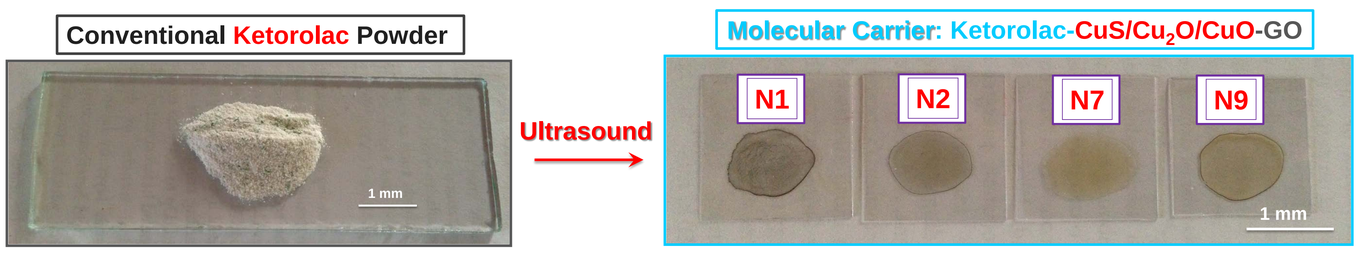



**Figure 1**. Optical phase contrast images of the conventional ketorolac (the anti-inflammatory drug) in powder (on the left) and ultrasonically prepared molecular carrier for this drug, which is introduced by the copper-modified graphene oxide (on the right): Ketorolac can be efficiently encapsulated into N1 (original GO), N2 (copper-modified GO), N7 (copper/iron-modified GO) and N9 (iron-modified GO) by our developed experimental methods.

## Results

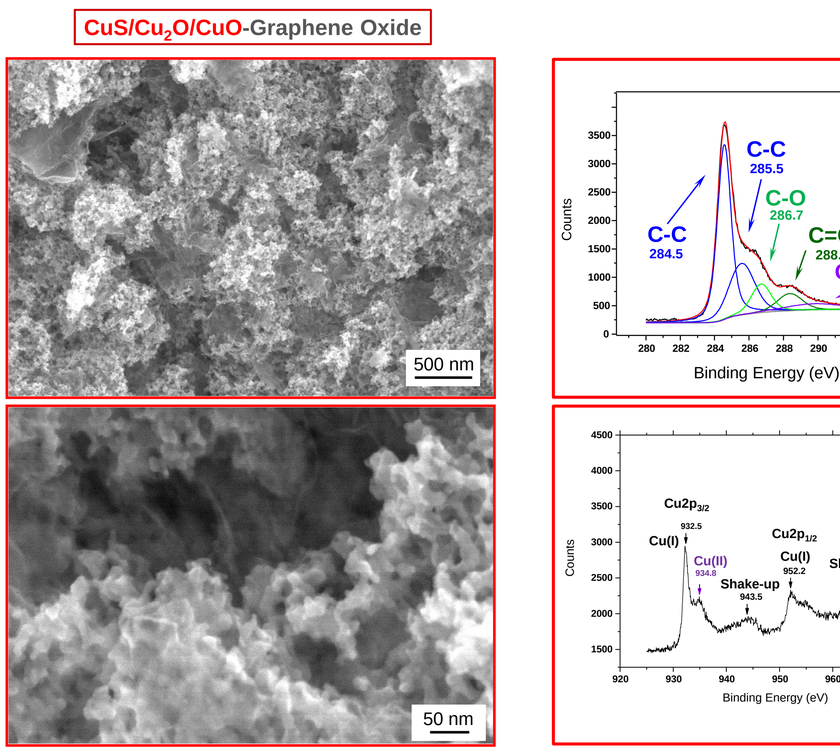



**Figure 2.** Representative FE-SEM images of ultrasonically prepared copper-modified GO (20 kHz, 8 and 18 W/cm$^2$).

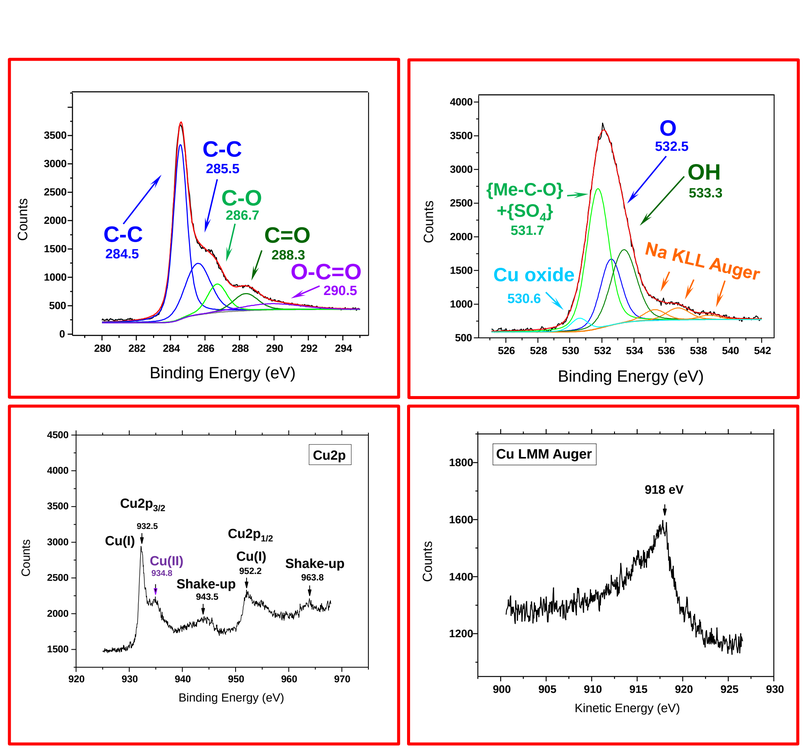



**Figure 2.** X-Ray photoelectron spectra of copper-modified GO: C1s and O1s (upper row), Cu2p and Cu LMM Auger lines (lower row) **.**

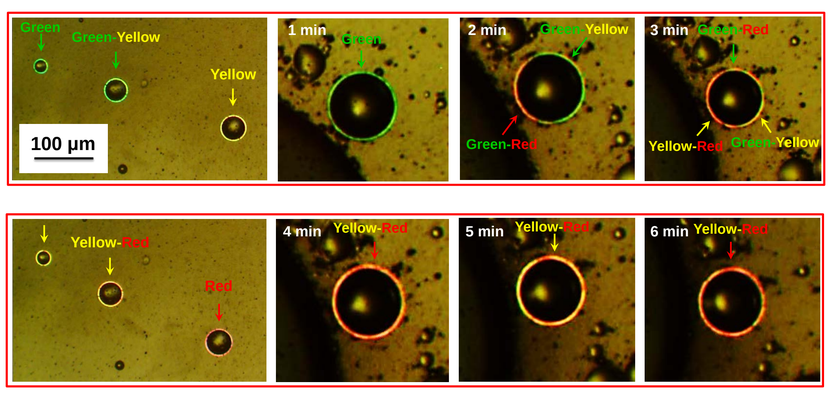



**Figure 3.** Representative optical phase contrast images of photoluminescent ultrasonically prepared oil-filled microspheres with the outer shell consisting of copper-modified GO in the matrix of polyvinyl alcohol (20 kHz, 18 W/cm$^2$).

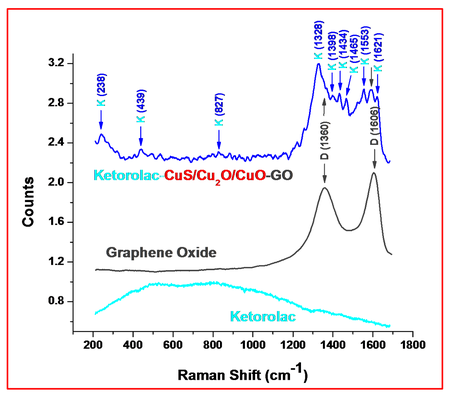
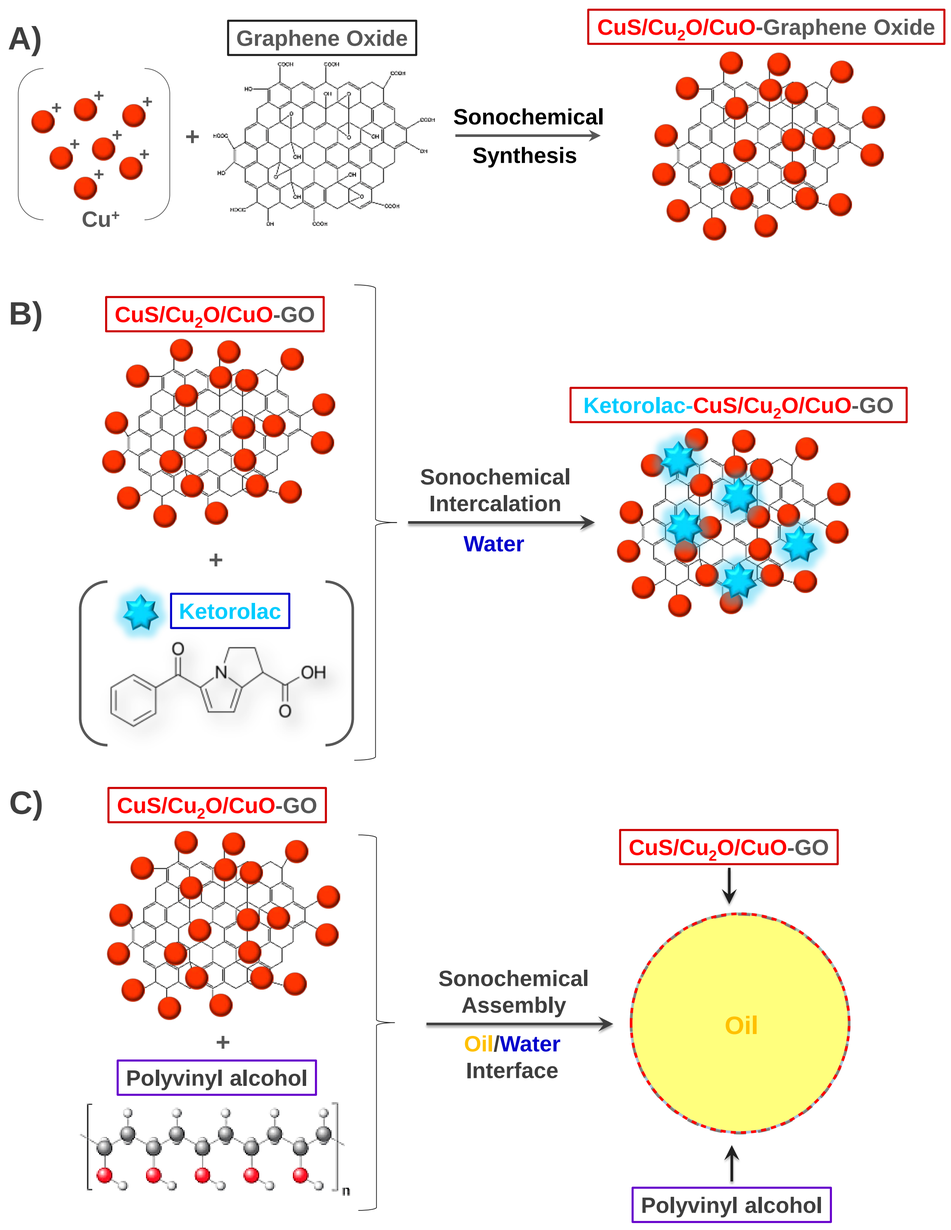



**Figure 4.** Raman spectra of ketorolac (lower row), original GO (middle row) and encapsulated ketorolac into the copper-modified GO (upper row).

## Experimental Methods




**Scheme 1**. Schematic illustration of our developed ultrasonic methods for the synthesis of copper-modified GO (A), sonochemical encapsulation of ketorolac into copper-modified GO (B) and sonochemical assembly of copper-modified GO with polyvinyl alcohol at the oil/water interface resulting in the formation of highly photoluminescent microspheres (C).

## Conclusions

- A **new sonochemical method** for the synthesis of novel p-type semiconductor **CuS/Cu$_2$O/CuO−GO** nanocomposites is developed. These new nanocomposites can be used as **drug molecular carriers** in aqueous solution.
- A **new ultrasonic encapsulation method** for intercalation of **the anti-inflammatory drug ketorolac** into these **CuS/Cu$_2$O/CuO−GO** nanocomposites acting as **molecular carriers** is developed. Submicron size of CuS/Cu$_2$O/CuO−GO and a larger surface area can significantly improve molecular interactions of the drug with other compounds thereby reducing the therapeutic dose and side effects in the gastrointenstinal tract.
- A **newly developed sonochemical approach** for the molecular assembly of **CuS/Cu$_2$O/CuO−GO** nanocomposites with **polyvinyl alcohol (PVA)** at the oil/water interface can yield **photoluminescent** microspheres in water. The remarkable photoluminescence of these microspheres is attributed to the H-bridging between PVA and CuS/Cu$_2$O/CuO−GO nanostructure due to the light absorption ability of Cu$_2$O and charge-transfer insulation by CuO.

## Reference

Darya Radziuk, Lubov Mikhnavets, Anastasia Tkach, Ludmila Tabulina, Vladimir Labunov. Sonochemically Assembled Photoluminescent Copper-Modified Graphene Oxide Microspheres. *Langmuir* **2018**, *34* (29), 8599-8610.

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