

# Magnetic Graphene Quantum Dots Nanovectors for Targeted Drug Delivery System

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Magnetic iron oxide-graphene oxide (Fe<sub>3</sub>O<sub>4</sub>-GO) were synthesized by green hydrothermal means that concurrently reduced and shattered graphene nanosheets to form the dots. To characterize the structure, morphology, and properties of Fe<sub>3</sub>O<sub>4</sub>-GO the TEM, XRD, XPS, BET and XANES/EXAFS were examined. The BET surface area of Fe<sub>3</sub>O<sub>4</sub>-GO (88.98 m<sup>2</sup>/g) was much higher than that of iron oxide nanoparticles (IONPs) (11.18 m<sup>2</sup>/g), revealing that Fe<sub>3</sub>O<sub>4</sub>-GO have high surface area which enables the Fe<sub>3</sub>O<sub>4</sub>-GO nanovector to encapsulate more drug. Furthermore, the XANES spectra of Fe atoms in Fe<sub>3</sub>O<sub>4</sub>-GO demonstrated an absorbance feature (Fe = 7112 eV) of a 1s to 3d transition. The EXAFS results suggest that Fe<sub>3</sub>O<sub>4</sub>-GO have Fe atoms at the center that are primarily coordinated by Fe–O. The Fe–O bond distance in MGQDs was 1.95 Å, with a co-ordination number of 3.95. The MTT cell viability results of MGQDs revealed that these nanovectors were nontoxic to 3T3 and BE–2–M17 cells.

**Keywords:** *Magnetic graphene quantum dots, Nanovectors, 3T3, BE-2-M17, XANES/EXAFS*

## Introduction

Graphene, and its chemically oxidized derivative graphene oxide (GO), have been investigated for drug delivery system (DDS), cancer photothermal therapy as they have a large surface area, ample functional groups on the surface, and low cytotoxicity [1]. Iron oxide nanoparticles (Fe<sub>3</sub>O<sub>4</sub> NPs) have also been studied for biomedical purposes. Their superparamagnetic behavior allows for them to be used for targeted therapeutic delivery [3]. They can be imaged in vivo by magnetic resonance imaging (M.R.I.), enabling the visualization of tumors and the circulatory system, as well as finding use in magnetic hyperthermia [2]. Fe<sub>3</sub>O<sub>4</sub> are nontoxic and their biocompatibility is very high, hence, the Food and Drug Administration (FDA) accepted ferumoxytol, which is one of the Fe<sub>3</sub>O<sub>4</sub> nanoparticles, as an iron supplement [3]. Fe<sub>3</sub>O<sub>4</sub> can be deposited onto GO to form magnetic iron oxide-graphene oxide (Fe<sub>3</sub>O<sub>4</sub>-GO) nanovectors hybrids which can combine the interesting aspects of both individual nanoparticles [4]. The combination of the properties of Fe<sub>3</sub>O<sub>4</sub>-GO offers the remote-triggered drug release while reducing the toxic effects of the drug. Recently, magnetic Fe<sub>3</sub>O<sub>4</sub>-GO demonstrated that the nanocomposite could also be utilized as the T<sub>2</sub>-weighted magnetic resonance (MRI) contrast agent for in vitro cell labeling [5]. Even though the use of Fe<sub>3</sub>O<sub>4</sub>-GO for drug delivery and MRI has already been proposed, to the best of our knowledge, the magnetic properties of Fe<sub>3</sub>O<sub>4</sub>-GO have not yet been fully utilized to guide drug delivery, and in vivo MRI using graphene-based nanocomposite.

In the present study, the XANES and EXAFS techniques were used to provide insights into the speciation of Cu in contaminated-oyster tissues.

## Experimental

### XAS Data analyses

XANES/EXAFS spectra was be collected on the Wiggler beam line 17C1 at the National Synchrotron

Radiation and Research Center (NSRRC) of Taiwan. The electron storage ring was operated at an energy of 1.5 GeV and a ring current of 100-200 mA. Data was collected in transmission mode by a Lytle detector in the regions of Fe K-edge at room temperature. The data will be subsequently normalized using Athena (vi) software, with linear pre-edge and polynomial post-edge backgrounds subtracted from the raw  $\ln(I_t/I_0)$  data ( $I_t$  is the light intensity after it passes through the sample and  $I_0$  is the initial light intensity), and then analyzed using Artemis (vi) software utilizing FFEF code-8. The spectra will be first energy-calibrated by simultaneously recording transmission spectra of Fe<sub>3</sub>O<sub>4</sub>-GO in Athena (vi), where the energy of the first inflection point for the reference sample absorption edge will be defined as 5989 eV, respectively. After calibration, the samples will be background-corrected (using a linear pre-edge region and a polynomial for the post-edge region) and normalized. EXAFS energy spectra will be then converted to the wave vector K-space form. These data directly reflected the average local environment around the absorbing atoms. Spectra will be analyzed using the IFEFFIT software package. Theoretical paths of Fe-Fe and Fe-O in Fe species will be used to fit the first coordination shell of experimental data that will be generated using the FEFF-8 program based on the crystallographic data of individual species. The coordination number, interatomic distance, Debye-Waller factor, and inner potential correction will be used as variables for the fitting procedures.

## Results

As shown in Fig. 1 (a), XANES spectra of Fe atom in Fe standards, IONPs and Fe<sub>3</sub>O<sub>4</sub>-GO samples exhibited an absorbance feature (Fe=7114 eV) of 1s to 3d transition. In comparison with the standard spectra, XANES spectra of products were similar to those of the Fe standard. The

transition intensity was very sensitive to the coordination symmetry. For iron oxides,  $1s \rightarrow 3d$  peak intensity of Fe  $K$ -edge XANES was governed by the average coordination number and the symmetry of oxygen anions coordinated to the central iron cation. Fe  $K$ -edge EXAFS spectroscopy may provide information about the atomic arrangement of Fe species in terms of bond distance, coordination number, and types of neighbors. Fig. 1 (b) shows the fine structure parameters of Fe standards, IONPs and  $\text{Fe}_3\text{O}_4$ -GO. EXAFS fitting results for the oxygen shell listed in **Table 2** suggest that Fe standards, IONPs and  $\text{Fe}_3\text{O}_4$ -GO have Fe atoms at the center that are primarily coordinated by Fe–O. The standard Fe–O bond distance in FeO,  $\text{Fe}_2\text{O}_3$ ,  $\text{Fe}_3\text{O}_4$ , IONPs and  $\text{Fe}_3\text{O}_4$ -GO is 1.96, 1.80, 1.96, 1.96, 1.97 Å with coordination numbers of 4.27, 4.20, 3.71, 3.66, and 3.75, respectively. In all samples, Debye–Waller factor ( $\Delta\sigma^2$ ) was less than 0.014 (Å<sup>2</sup>). The co-ordination number of the nearest O shell oscillated between samples, suggestive of the protective role of the coated GO material.

**Table 1**

EXAFS fine structural parameters of IONPs samples compared with that of Fe standards.

Samples	First shell	CN ( $\pm 0.05$ ) <sup>a</sup>	R ( $\pm 0.02$ Å) <sup>b</sup>	$\Delta\sigma^2$ (Å <sup>2</sup> ) <sup>c</sup>
FeO	4.27	4.27	1.96	0.0029
$\text{Fe}_2\text{O}_3$	4.20	4.20	1.80	0.0050
$\text{Fe}_3\text{O}_4$	3.71	3.71	1.96	0.0019
<i>Samples</i>				
IONPs	3.66	3.66	1.96	0.0046
$\text{Fe}_3\text{O}_4$ -GO	3.75	3.75	1.97	0.0047

Notes:

<sup>a</sup> Coordination number;

<sup>b</sup> Bond distance;

<sup>c</sup> Debye–Waller factor.

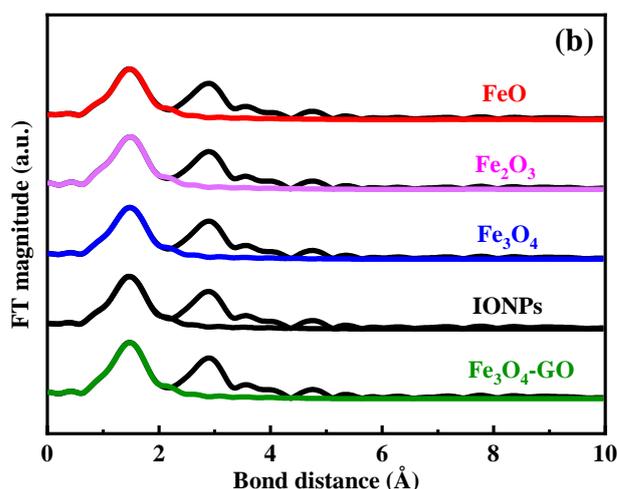
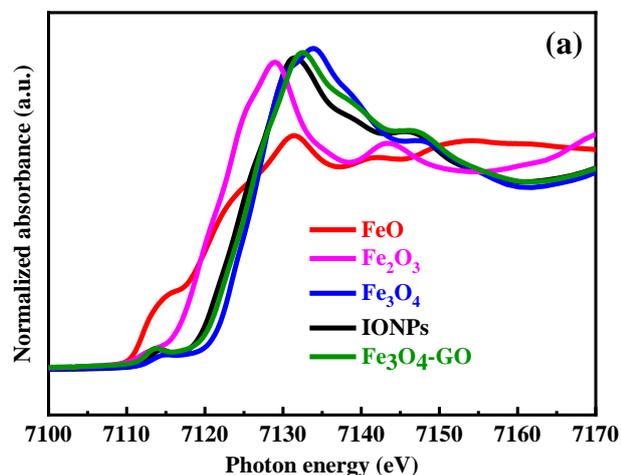


Fig. 1 (a)–(b) Fe  $K$ -edge derivative XANES spectra of FeO,  $\text{Fe}_2\text{O}_3$ ,  $\text{Fe}_3\text{O}_4$ , IONPs and  $\text{Fe}_3\text{O}_4$ -GO. (b) Fe  $K$ -edge EXAFS Fourier transformed spectra of FeO,  $\text{Fe}_2\text{O}_3$ ,  $\text{Fe}_3\text{O}_4$ , IONPs and  $\text{Fe}_3\text{O}_4$ -GO.

## Discussion

The more pronounced coordination number was attributed to the higher oxygen density, which could be associated with the magnetization and poor crystallization, which is in line with the previous studies

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