Natural diatoms dopped with AuNPs as drug delivery systems and comparison with diatoms decorated with graphene

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Abstract

The use of natural diatoms is currently a topic of interest for therapeutic applications due to its facilities, low cost, and biocompatibility. Here a comparison between a previous work of diatoms dopped with AuNPs and the possibility of what oculd be adding graphene to the system, or as a replacement of the AuNPs. Here, are reported the chemical modification of diatoms *Aulacoseria genus* microalgae-derived biosilica from Guayllabamba - Ecuador decorated with gold nanoparticles by *In-situ* and *Ex-situ* methods to study the *in vitro* gentamicin loading and release properties in simulated body fluid (SBF) from the paper "Natural diatoms dopped with AuNPs as drug delivery systems" . Successful decoration of the diatoms and loaded with gentamicin was confirmed using Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), Raman spectroscopy and Fluorescence Microscopy. It follow the *In-vitro* drug release by using Ultraviolet-Visible Spectroscopy (UV–vis). The results revealed that diatoms decorated with gold nanoparticles using the *Ex-situ* method (Au/CTAB-Diatom) showed a faster release reaching a maximum of 93% in 10 days and a lower loading rate, while the samples decorated by the *In-situ* method presented longer and slower release behavior. Fluorescence properties were enhanced after the gentamicin loaded. The advantage of this work is the control of the structural and optical properties of diatoms deco- rated with gold nanoparticles for the gentamicin drug delivery. As for the graphene adhesion is a similar protocol as the decoration with AuNPs, acquiring new features that would be study in next works.

Results

Raw diatoms were characterized using the Brunauer-Emmett-Teller technique, obtaining a surface area and pore volume of 59.52 m2/g and 0.24 cm3/g respectively. After the dealumination treatment, the surface area increased and the pore volume decreased to 102.30 m2/g and 0.22 cm3/g, respectively. The increase in the surface area on the diatoms frustules is due to the removal of impurities during the dealumination treatment. In Fig. 1 visible absorption spectra spectrum of the diatoms decorated with gold nanoparticles using the *In-situ* method Fig. 1(a) shows an absorbance peak at 540 nm attributable to the surface plasmon resonance band (SPR) of the gold nanoparticles on the diatom surface. Fig. 1(b) shows the CTAB-modified gold nanoparticles spectrum, and we observe an absorption band at 239 nm attributed to the electronic transitions (d-orbitals) of the Au/Br− aqua-complex presented in CTAB aqueous solution and the absorption band of gold nanoparticles at 526 nm. FTIR spectra show the characteristic peaks of diatom frustule (Fig. 2(a)), which includes the Si-O-Si bending at 431 and 795 cm-1, and Si- O-Si stretching at 1041 cm−1. Diatoms coated with gold nanoparticles and loaded with gentamicin in Fig. 2(d) and (e) show a new vibration peak at 1617 cm−1 ascribed to the NH vibrational bending of primary aromatic amines and a strong OH stretching of surface-bound hydroxyl groups at 3320 cm−1, demonstrating the successful loaded of the diatoms with gentamicin. In Fig. 3(a) the XRD patterns show some peaks corresponding mainly to quartz and cristobalite. The amorphous part in the region of 20–30 degrees corresponds to the structure of the diatom as a random network of tetrahedrally bound silicon atoms. The XRD pattern of the diatoms decorated with gold nanoparticles in Fig. 3(b) shows the reflections at 38°, 44°, 64°, and 77° that correspond to the (111), (200), (220), and (311) planes of the face-centered cubic (fcc) gold, respectively. Meanwhile, in Fig. 3(c) is not possible to identify the peaks related to gold due to the low concentration of the nanoparticles of the diatom as we demonstrate in Fig. 1. In Fig. 4 and 5 it can be appreciated diatoms decorates with AuNPs and graphene, respectively.

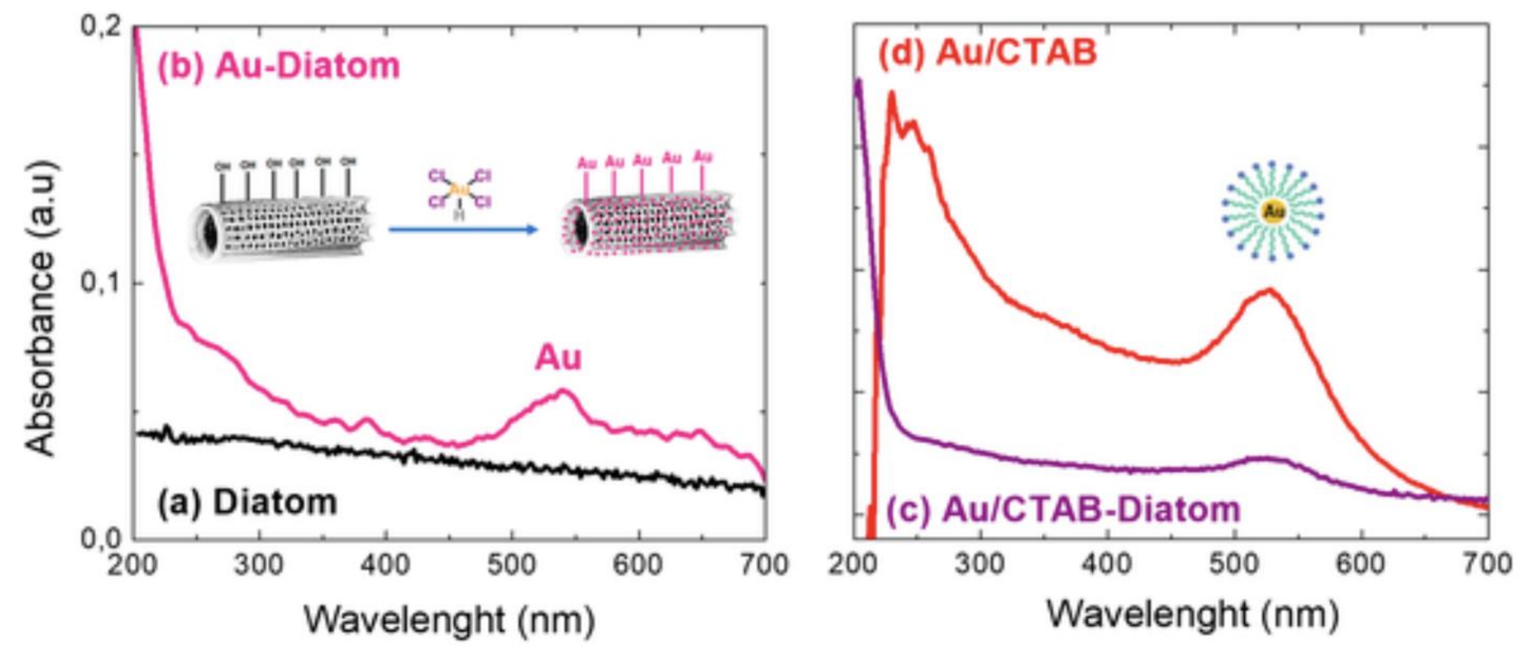

Fig. 1. Visible absorption spectra of (a) Diatoms, (b) Diatoms decorated by *In-situ* method, (c) diatoms decorated by *Ex-situ* method and (d) Au/CTAB nanoparticles

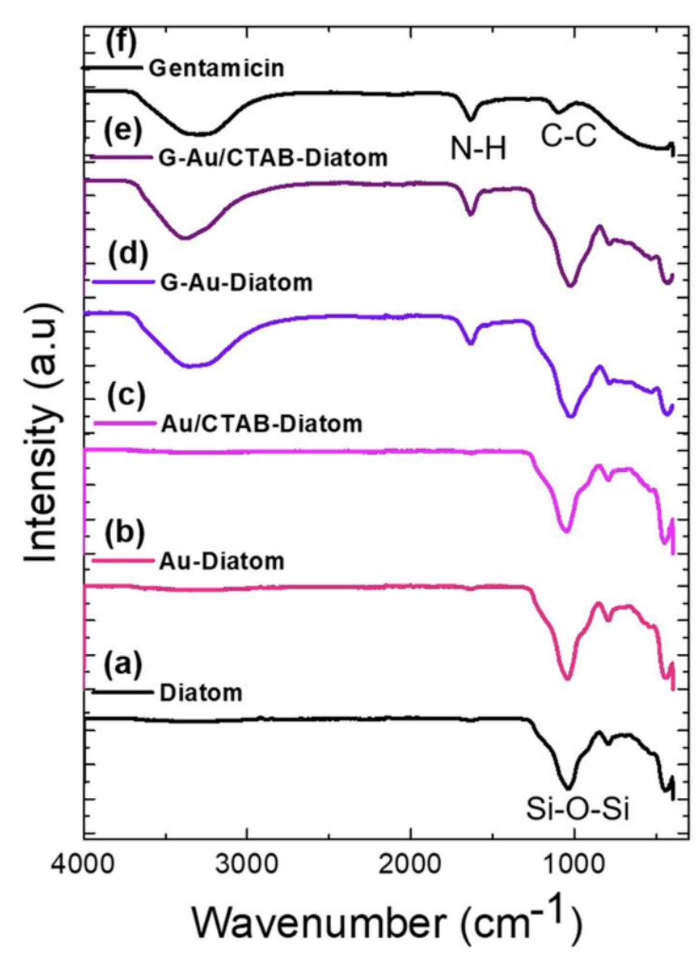

Fig. 2. FTIR spectra of (a) Diatoms, (b) Diatoms decorated by *In-situ* method (Au-Diatom), (c) Diatoms decorated by *Ex-situ* method (Au/CTAB-Diatom), (d) Au-Diatom loaded with gentamicin, (e) Au/CTAB-Diatom loaded with gentamicin, and (f) Gentamicin.

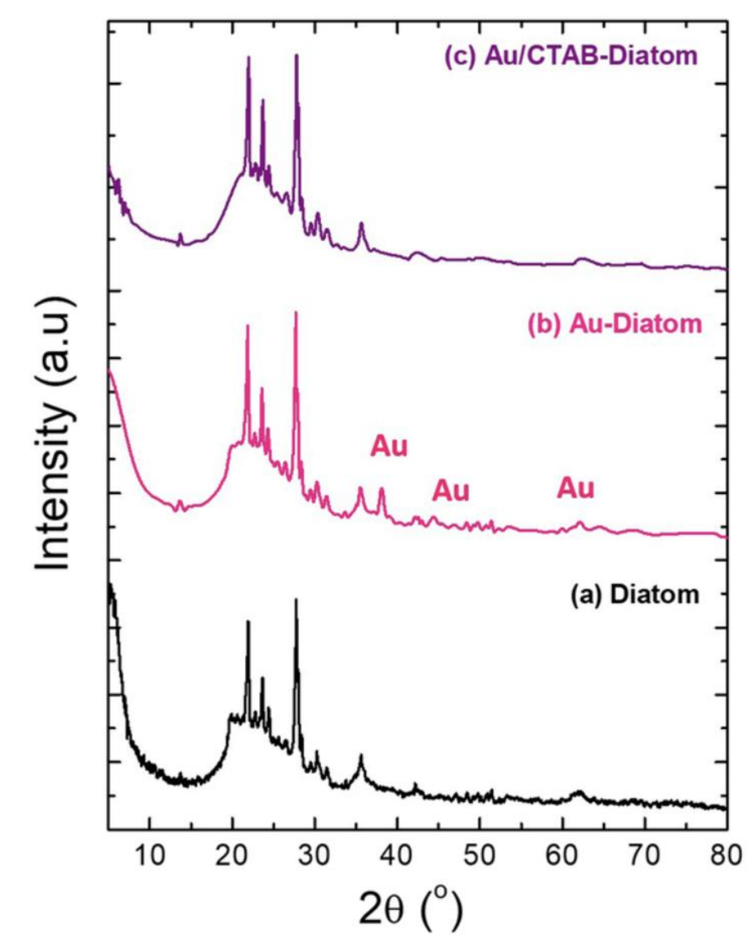

Fig. 3. XRD patterns of (a) Diatoms, (b) Diatoms decorated by *In-situ* method (Au-Diatom), (c) Diatoms decorated by *Ex-situ* method (Au/CTAB-Diatom).

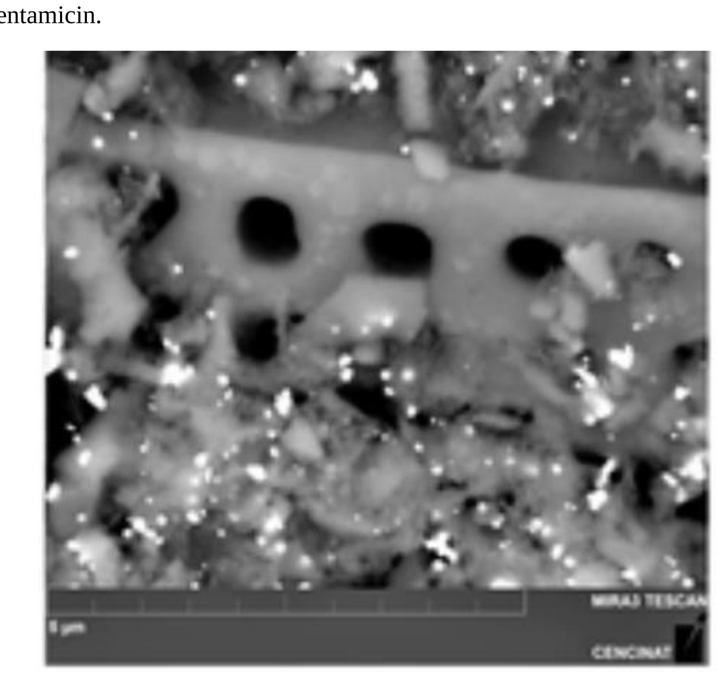

Fig. 4. TEM micrograph of Au/CTAB nanoparticles.

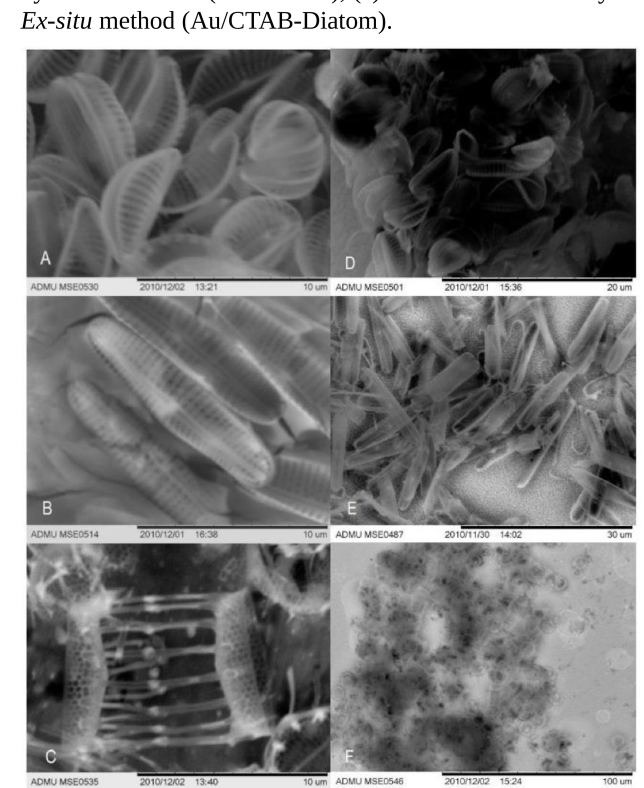

Fig. 5. (A-C) SEM images of diatoms (A) *Amphora sp.*, (B) *Navicula ramossissima*, and (C) *Skeletonema sp.* ; (D-F) SEM of diatom silica with graphene (A. *Amphora*-graphene, B. *navicula*-graphene, C. *Skeletonema*- graphene)

Discussion

In general, the drug release mechanism of diatoms is due to the diffusive transport through the silica pores shells and the fact that the silica matrix is virtually insoluble in an aqueous environment. *In-situ* samples follow a zero-order kinetic independent of the con- centration related to the gradual slow release overextending the time period, and no equilibrium conditions are achieved. This zero-order re- lease, in which the drug is released at a constant rate, offers several ad- vantages, including improved patient compliance and reduction in the frequency of drug administration. Meanwhile, in the case of the *Ex-situ* sample, the gentamicin release is fast from the initial to the final stage, this release mechanism is due to the number of gentamicin molecules adsorbed on the surface of the Au/CTAB nanoparticles combined with the gentamicin diffusion from the Au/CTAB-diatoms, this behavior fits well to the first-order model. This kinetic model offers the advantage of the release of the gentamicin immediately or at least as quickly as possible after administration and this is useful if a fast onset of action is re- quired for therapeutic reasons. For the samples of diatoms modified with graphene, there are no studies about the application of drug delivery.

Conclusion

Our findings reveal that diatom decorated with gold nanoparticles are promising candidates to control the gentamicin release in simulated body fluid. The surface area increased to 102 m2/g with the dealumination process. The decoration was confirmed by UV–vis at 540 and 526 nm respectively and SEM shows nanoparticles of 50 and 20 nm on the diatom surface. Raman spectroscopy discloses the enhancement of the fluorescence at 532 nm with the gold nanoparticles and Fluorescence microscopy demonstrates that the interaction of the nanoparticles with the gentamicin results in a fluorescence improvement. *In-situ* method promotes the gentamicin load and drug encapsulation inside the diatom, resulting in a slower release. Meanwhile, the *Ex-situ* method enhanced the release of gentamicin by using Au/CTAB nanoparticles. The advantage of the results obtained is controlling the decoration process of the diatom with gold nanoparticles it is possible to tailor the structural and optical properties for the potential application in drug delivery, bioimaging, and nanosensors. It is expected that the behavior of Diatom/graphene would be similar, to the previous mentioned samples.

Reference

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