

Surface Modification and Application of Nanomaterials in Biotechnology



Hélio Ribeiro^{1*}, Paula von Randow², Diego N Vilela³ and Lidia M Andrade⁴

¹Departamento de Química - Universidade Federal de Minas Gerais, Brazil

²Fundação Ezequiel Dias, Rua Conde Pereira Carneiro, Brazil

³Centro Universitário Barão de Mauá, R. Ramos de Azevedo, Brazil

⁴Departamento de Física, Universidade Federal de Minas Gerais, Brazil

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*Corresponding author: Hélio Ribeiro, Departamento de Química -Universidade Federal de Minas Gerais- Av. Antônio Carlos, 6627- Belo Horizonte -Brazil, email: helioribeiro@hotmail.com

Abstract

In the last years, inorganic nanostructures as carbon nanotubes, graphene, hexagonal boron nitride, and metallic nanoparticles have been applied in several biomedical and nanotechnology fields. These different types of nanomaterials also are awakened as new perspectives in prophylactic, diagnostic and therapeutic areas. However, the uses depends strongly on their chemical and physical surfaces that display an important role in their biocompatibility in different biological systems. A brief study of several types of nanomaterials, their modifications and biomedical application is the main contribution of this short communication.

Keywords: Nanotechnology; Nanomedicine; Nanomaterials; Carbon nanotubes; Graphene; Hexagonal boron nitride; Gold nanoparticles

Abbreviations: CNMs: Carbon Nanomaterials; h-BN: Hexagonal Boron Nitride; CNTs: Carbon Nanotubes; rGO: Reduced Graphene Oxide; Dox: Doxorubicin; PEG: Polyethylene Glycol; BNNTs: Boron Nitride Nanotubes; MDS: Molecular Dynamics Simulations

Introduction

Many studies about nanomaterials have been widely explored in recent decades in different scientific and technological areas. Several authors consider that the discovery of CNTs by Iijima [1] and graphene by Geim and Novoselov [2], stimulated the studies in nanotechnology. Concomitantly, the advances in probe, scanning, and transmission microscopies, it has also contributed to the discovery of new nanostructures and the understanding of others that were not yet well elucidated. It was expected exceptional physico-chemical properties and biocompatibility of nanostructures such as CNTs, graphene, h-BN, BNNTs and metallic nanoparticles, among others [3]. On the one hand, these materials have an enormous potential range of applications in nanotechnology, bioengineering and biomedicine [4,5], such as tumor markers[6], drugs delivers [7], bio-packaging [8], biosensing [9-11], adjuvant in vaccines [5-12,13], among others. However, the compatibility and dispersion of these nanoparticles in the medium of interest are fundamental to their potential applications [3]. The nanoengineering interfaces between host biological system and nanoparticles involves several challenges that need to be overcome. For instance, there-stacking or agglomeration processes of nanoparticles do not allow them to transfer their expected properties to the system, resulting in an inhomogeneous dispersion medium with minimum of biocompatibility. These undesirable processes can be overcome

by physical or chemical modification methodologies of their surfaces, such as covalent or non-covalent functionalization. Thus, our choices will depend on the nanoparticles and the biological system in study. The covalent functionalization depends on bonding between the nanoparticles and the functional groups that were chosen, according to the selectivity [3]. Based on this approach, different organic or inorganic functional groups or nanoparticles can be anchored. For instance, it can be introduced on surfaces of oxidized CNTs or graphene oxide (GO), functional groups such as alkoxy (-OR), amino (-NH₂), amine (-NHR), alkyl (-R) [14,15], heteroatom doping, metallic nanoparticles, biomolecules and biopolymers, among others. These modifications process alter significantly their interactions with the medium leading them to a large range of solubility in water, co-polymers or organic solvents [3]. On the other hand, non-covalent functionalization processes of nanoparticles are strongly dependent of their physical interaction with host system through intermolecular forces, such as van der Waals, hydrophilic, hydrophobic, hydrogen bonding and π - π interactions, among others [16]. Taking advantages of these physical interactions of molecules (conjugated, surfactants etc), they form homogeneously dispersion into different medium with their controlled physicochemical and biological properties [17].

In this context, several studies have presented different types of covalent and non-covalent functionalization of these nanostructures with great technological demands, such as: in cellulose films or fibers [18,19], chitosan [20], polyethylenimine-grafted nanoribbon (for recognition of microRNA)[11],

vinyl acetate co-polymer[17], octadecylamine [21], glucose oxidase biosensing [22], poly(ethylene glycol) [23], DNA [24], metallic nanoparticles, among others. Some examples of these modifications in CNMs can be seen in Figure 1a-1d.

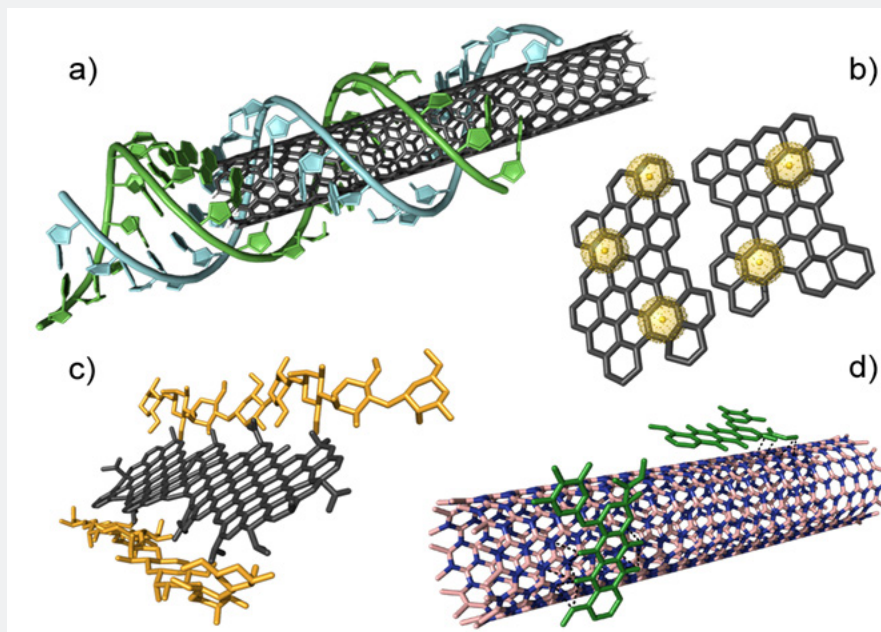


Figure 1: Different types of chemical and physical modifications surfaces of carbon nanomaterials : (a) CNTs enveloped by DNA, (b) r-GO attached with gold nanoparticles, (c) r-GO with chitosan strips, and (d) BNNTs with doxorubicin.

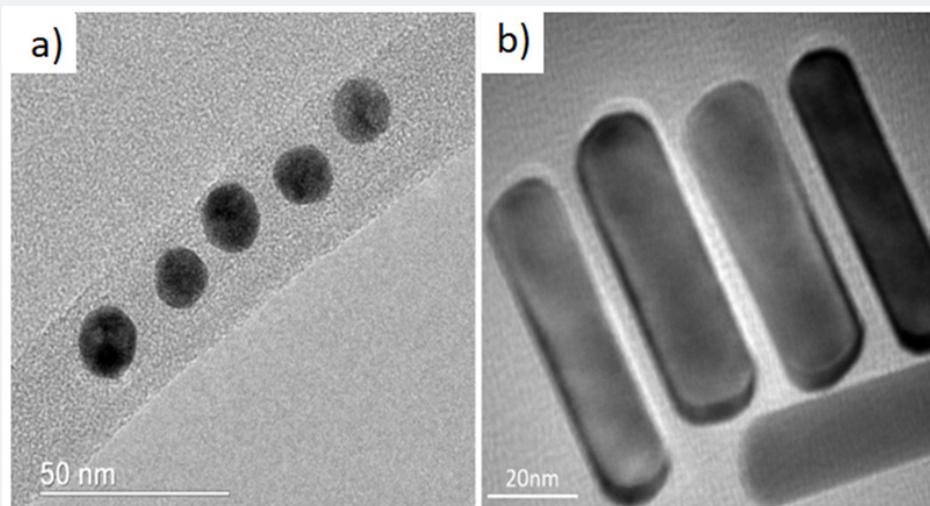


Figure 2: TEM images of gold nanoparticles with different magnitudes: (a) gold nanospheres, and (b) gold nanorods. The images were taken from Centro de Microscopia of Federal University of Minas Gerais.

Large amount of nanostructures, zwitterions, supra molecular, clusters, including micelles, dendrimers, quantum dots, biopolymers CNTs, graphene, metallic nanoparticles, have been intensively investigated as biological agents in several biotechnological applications [25]. For instance, gold nanospheres and gold nanorods (Figure 2a-b), have represented

the most attractive metallic nanostructures for biological application due to their biochemical features and low related toxicity. Gold nanorods biosensing is the modality widely used especially for the development of optical and electrochemical sensing platforms. The surface plasmon resonance properties based on their sensitive spectral response in light absorption

and scattering can change in the biological environment, allowing the monitoring of light signal, for instance in cancer cells [26]. One of the most important gold nanoparticle application is in vaccine development [26]. There is a great evidence that these nanoparticles display adjuvant characteristics, promoting cell recruitment, antigen-presenting cell activation, cytokine production, and inducing a tumoral immune response [12]. Another relevant application based on physical properties of gold nanorods is their enhanced optical absorption in the visible and NIR region that has been proposed as an alternative for the localized ablation of target cancer cells without damaging other healthy cells, this technique is known as photothermal therapy [6]. Regarding the development of new strategies for cancer therapy, gold nanoparticles have shown promising perspectives to increase radiation effects mainly in tumor cells rather than in normal cells. This effect is due to the high Au atomic number that can lead to increased cross section probability under photons beams from ionizing radiation sources [27]. Nonetheless, gold nanoparticles present relative easy surface functionalization and several biological molecules currently used as immunotherapeutic, such as cetuximab and trastuzumab have demonstrated improved effects when associated with gold nanoparticles [28]. There is a plenty literature about biomedical applications of gold nanoparticles highlighting their importance and advantages to improve diagnostic and therapies for infectious and degenerative diseases as well as a 'big deal' to the pharmaceutical industry in a near future [29].

Other important class of nanomaterial with great potential application in bionanotechnology are recognized as one or bi-dimensional, such as CNTs, BNNTs, graphene, h-BN, among others. These nanostructures present exceptional physical properties, besides good chemical stability, well-tailored biocompatibility and lower cytotoxicity [21,22,30]. For example, BNNTs and CNTs are tubular nanostructures with large aspect ratio, high mechanical strengths, and they have a potential application as nanocarriers for use as cancer drugs [25]. Weng et al., [21] demonstrated that the BNNTs functionalized with hydroxyl groups loaded ~300wt% of doxorubicin (Dox), a monoclonal antibody for targeting and a fluorescence marker for visualization, with application in cancer therapy [31], this nanocomplex exhibited higher efficiency to reducing LNCaP prostate cancer cellular viability than the free drug alone [21]. CNTs also can be used as carrier for drug delivery when they are tailored at entering the cells nuclei. Researches have showed that functionalized CNTs can cross the cell membrane, without cellular recognition as harmful intruders [32]. In other studies, it was demonstrated that the Dox interacted with CNTs through π - π stacking following the functionalization with polyethylene glycol (PEG) to increase their blood circulation plasmatic half-life and to decrease their toxicity [33]. Likewise, CNTs samples, were modified with Dox, and the results showed that cancer cells efficiently took up this compound. While Dox was effectively released and accumulated in the nucleus, while CNTs remained in the cytoplasm.

This result indicates the high loading capacity of the CNTs due to its large aspect ratio and effective noncovalent interaction between them and drug molecules [25]. Gao et al. [19] showed by MDS studies that, DNA molecule in water environment can be inserted into CNTs (endohedral functionalization) through van der Waals and hydrophobic interactions. Based on their studies, they suggested that the encapsulated CNTs-DNA molecular complex can be used as DNA-modulated molecular electronics, biosensors, DNA sequencing, and gene delivery systems [32,34]. Zheng et al. [24] proposed an effective technique of dispersion of CNTs in water by their sonication process in presence of DNA. By MDS this research group suggested that DNA can binds to carbon nanotubes through π -stacking, resulting in helical wrapping in their surface [24] (Figure 1a).

Conclusion

In this short communication we highlight some experimental and theoretical works with different combinations of nanostructures and molecules, as well as metallic nanoparticles with potential bio and technological applications. However, the most important aspect for success and an optimal performance of these compounds is the choice of the best tailored functionalization process (bio-nano engineering) for each type of biological system. The physical-chemical modification is an essential step for relevant applications, leading to hybrid compounds chemically stable, tailored, well dispersed, and compatible with the biological environment of interest. Thus, it is possible to produce smart nano-systems with advanced applications in biotechnology and biomedical areas, such as ecological packaging, bio-robots, biosensors, adjutancy in vaccines and tumor markers for diagnosis and therapy.

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