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Mini Review

Application of Carbon Dots in Bioimage

Sonsin FA*

Federal University of Rondônia, Brazil

Abstract

Carbon Dots (CDs) are carbon-based nanomaterials that contain excellent optical properties in addition to excellent biocompatibility. One of its many applications is bioimaging. The versatility of CDs means that it can be synthesized so that it is encompassed by specific organelles. Furthermore, its applicability can be used in the study of drug transport *in vivo*. In this work we will address some of these aspects.

***Corresponding author:** Sonsin FA, Federal University of Rondônia, Brazil

Submission: June 13, 2022
Published: September 02, 2022

Volume 4 - Issue 2

How to cite this article: Sonsin FA. Application of Carbon Dots in Bioimage. J Biotech Biores. 4(2). JBB. 000584. 2022.

Introduction

Quantum Dots (QDs) are nanomaterials used in diverse applications. Among the most studied are CdSe/CdS [1], ZnTe/ZnSe [2] (core/shell), in addition to TiO_2 [3] and carbon dots (CDs) [4]. CDs, unlike other QDs, are carbon-based nanomaterials have attracted researchers' attention because of their excellent electronic optical properties, low cost of synthesis, low cytotoxicity and excellent biocompatibility [4]. The top down and bottom-up synthesis methods used by CDs are highlighted by laser ablation, electrochemical oxidation, precursor pyrolysis and hydrothermal [5,6]. However, the hydrothermal method is the most used because it has advantages over others for obtaining good quality, maintaining control over its composition [7].

The optical properties of CDs have been extensively investigated and most works are based on Photoluminescence (PL) associated with a variety of synthesis procedures [8]. The emission spectrum of CDs can be dependent or independent of the excitation wavelength and the surface state is considered the main reason for this [9,10]. Some studies have shown a dependence of photoluminescence on the size [11], surface states [12] and heteroatoms [13] (presence of oxygen, nitrogen or sulfur) of CDs. These properties can be defined during the synthesis process or through some type of post-synthesis treatment.

The PL spectrum of CDs shows dependence on excitation, pH, solvent and temperature. Several works show the influence of temperature on the PL of post-synthesis CDs [8,10]. The temperature analysis can be explained by the fluorescence mechanism. In most cases, the PL intensity decreases with increasing temperature. In addition, a red shift is observed in the PL spectra with increasing temperature [8,9]. Numerous applications are made with CDs, however cell imaging appears as one of the main applications, because they present superior luminescent performance compared to organic and inorganic fluorophores [14,15]. In addition, its low cost, low cytotoxicity, and excellent biocompatibility make it a possible replacement for current fluorophores [14,15]. This mini review focuses on the application of CDs in bioimaging, dealing with *in vitro* and *in vivo* imaging.

Bioimaging

Organic compounds show different interactions when materials are applied for imaging studies. Cell structures can interact in a very specific way by directing materials to specific parts of cells. We will analyze *in vitro* imaging of organelles and then talk about *in vivo* imaging [4].

In Vitro Imaging

Many studies were carried out via fluorescence of several CDs in images of cells of various cell lines such as cancer cells, stem cells, neural cells, among others. In addition, they showed labeling in different cellular regions.

Nucleolus images

Cell imaging in the nucleus is crucial to reveal its morphology and its roles in cell metabolism, growth, differentiation, and heredity [4]. Barbosa CD et al. [16] It synthesized CDs from cow manure, and they were broadcast in the blue. The CDs were used for imaging breast cancer cells (MCF-7), in addition to other cell lines, where they showed subcellular selectivity and the ability to selectively stain cell nucleoli. Hua XW et al. [17] It synthesized p-phenylenediamine (pPDA) CDs showing a red emission. They used A549 lineage cells and their CDs stained the nucleoli of the cells.

Images of other organelles

In addition to the nucleus, CDs can be developed for the analysis of other organelles, such as mitochondria, lysosomes, among others. Fan Z et al. [18] Through the hydrothermal method, them synthesized CDs using (3-carboxyl) phenyl bromide phosphine (TPP), with blue emission and using the Hela cell line. These CDs showed versatility for imaging being the targeting to the nucleus or to the mitochondria. Wu X et al. [19] developed a mitochondria-targeted nanoprobe based on fluorescent CDs (TPP-CDs) for FL imaging of peroxynitrite in mitochondria. Imaging staining with nanoprobe and Mito-tracker showed that TPP-CDs had excellent mitochondria targeting capability and high image contrast in MCF-7 cells.

In Vivo Imaging

Based on *in vitro* imaging, many efforts are made to perform *in vivo* imaging, using mainly mice and zebrafish [4].

Bioimaging in mice

Malina T et al. [20] synthesized low-cost CDs using Tris(hydroxymethyl) Aminomethane (Tris) and betaine hydrochloride as precursor materials, having a large emission spectrum close to red. The use of biocompatible Quaternized CDs (QCDs) as a new stem cell tracking probe for *in vivo* fluorescence imaging of transplanted human MSCs.

Bioimaging in zebrafish

Wei X et al. [21] synthesized CDs using gynostemma as precursor material, having a blue emission spectrum. The use of CDs was made in the zebrafish embryonic process, showing that the synthesized CDs do not affect zebrafish formation.

Conclusion

he application of CDs in bioimaging proves to be very effective both *in vitro* and *in vivo*, and it may be a future replacement for current fluorophores.

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