Biocompatible Carbon Nanodots for Functional Imaging and Cancer Therapy: Carbon Nanodots for Imaging and Cancer Therapy

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ABSTRACT

This article describes how carbon quantum dots (C-dots) are tiny carbon nanoparticles (less than 10 nm in size) being envisaged to be used in bio-sensing, bio-imaging and drug delivery nanosystems. Their low toxicity and stable chemical properties make them suitable candidates for new types of fluorescent probe, which overcome the common drawbacks of previous fluorescent probes (organic dyes and inorganic quantum dots). In addition, fluorescent C-dots possess a rather strong ability to bind with other organic and inorganic molecules due to their abundant surface groups. For that reason, fluorescent C-dots can be manipulated via series of controllable chemical treatments in order to satisfy the demands in the photocatalytic, biochemical and chemical sensing, bio-imaging, drug delivery and enhanced cell targeting. In recent studies it was described the development of carbon quantum dots with large two-photon absorption cross sections towards two-photon imaging for use in photodynamic cancer therapy. Thus, C-dots have become a rising star in biomedical research with a promising future for the application in nanomedicine.

KEYWORDS

Anticancer nanodots, Aptamers, DNA, Drug delivery, Fluorescence, Nanoprobes, Photodynamic therapy, Toxicological bio-assays

1. INTRODUCTION

The unique properties of the carbon quantum dots or carbon nanodots (C-dots) have inspired extensive studies on them due to their great potential for biotechnological and nanomedical applications. They possess tunable emission and are considered to be the next generation green nanomaterials (Baker and Baker, 2010). C-dots are promising alternatives of the semiconducting quantum dots (known as Qdots), which are composed of toxic heavy metals such as cadmium (Loukanov, 2016). Moreover, C-dots exhibit nonblinking fluorescence, excellent water solubility, and are cheaply produced. Herein, is presented a critically review of the recent studies and advantages of C-dots as imaging probes, light-powered nanoparticles and drug delivery nanosystems for cancer therapy.

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2. FABRICATION OF BIOCOMPATIBLE CARBON NANODOTS AS FUNCTIONAL IMAGING AGENTS

The fabrication methods for carbon nanodots with tunable size can generally be classified into two main approaches: bottom-up and top-down (Li, 2012; Zuo, 2015). Top-down preparations of fluorescence C-dots are the early preparation approaches, including arc-discharge method (Li, 2012; Jian, 2010;), electrochemical oxidation (Zheng, 2009; Lu, 2009; Zhou, 2007; Zhao, 2008), and laser ablation (Yang, 2009; Goncalves, 2010). Compared with the multistep preparation method of C-dots, one-step reaction processes not only simplify the preparation procedure, but also these C-dots are with better fluorescent properties. Additionally, thus created C-dots may express special fluorescent properties by using various organic reaction solution. Bottom-up approaches are based on the polymerization reaction for small molecules to the formation of nanoscale C-dots. This strategy includes hydrothermal method (Liu, 2007; Wang, 2013; Qian, 2014; Xu, 2014; Dong, 2014; Gao, 2013; Ray, 2009), microwave-assisted pyrolysis method (Tang, 2014; Zhu, 2009; Wang, 2012; Chandra, 2011; Yang, 2012), ultrasonic method (Oza, 2015), acid dehydration method (Lecroy, 2014), and pyrolysis method (Bourlinos, 2008; Zong, 2014). Among them, the most widely used are the hydrothermal method and microwave-assisted pyrolysis method, which can be realized by the one-step method for preparing fluorescent C-dots with high quantum yield (QY > 50%). Thus, nanoparticles with diameter between 1–2 nm are formed spontaneously in one-step thermal treatment from different organic materials and are sufficiently well characterized by different structural methods. The C-dot hydrophobic core is made of pure carbon (consisted of aromatic domains) that is surrounded by polar (hydroxyl, carboxyl, amino, carbonyl and epoxy) and alkyl surface groups as shown on Figure 1. The organic functional groups make the nanoparticles highly soluble in aqueous media and help their penetration through the cell membrane mainly by endocytosis.

Carbon element is the skeleton of all living cells. The full organic nanomaterials as C-dots have much lower toxicity in comparison with the widely used semiconductive inorganic nanomaterials as Qdots. Simultaneously, the nanoparticles size of C-dots is smaller (~1.5 nm as shown on Figure 1B and C) and thus, it is more convenient to enter the cell in vivo, which supposes their great potential for medical applications in respect of cancer therapy. During the past few years, scientists have shown the possibility for surface modification of these particles with other molecules such as biological affinity ligands for further use for in vivo cell research (Lim, 2015). These unique characteristics make C-dots ideal for simultaneous diagnosis and therapeutics (theranostics), which lead to advances in personalized medicine (Huang, 2012).

3. MECHANISM OF THE PHOTOACTIVATION OF C-DOTS, BIO-IMAGING AND INDUCTION OF APOPTOSIS AND NECROSIS IN THE CANCER CELLS

C-dots have strong absorption in the ultraviolet region (absorbance spectrum or Abs on Figure 2A), which can also extend to visible region (Loukanov, 2016). Absorption of light irradiation, which wavelength matches the band gap energy of the semiconductor, leads to an excitation formation. As mentioned above the surface of C-dots contains various functional groups. These groups have various energy levels, which may result in series of emissive traps (Zhu, 2015). When the light of a certain excitation wavelength illuminates the C-dots, a surface state emissive trap will dominate the emission. The most photoluminescence centers are proven to be surface states (Xu, 2004). Although the excitation may induce the band-gap absorption band, the resulting fluorescence is also controlled by the surface state emission. The oxygen-based groups on the carbon core are the primary surface state of C-dots. The surface states are the key factor in tuning the luminescence of C-dots (Bao, 2011). Red-shifted emissions is observed for C-dots with a high surface oxidation degree (photoluminescence spectrum or PL on Figure 2A). The emission can be changed from green to blue by surface reduction (Zheng, 2011). The single dots can possess multiple fluorophore units associated with their core and
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