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Review

Near-infrared light-responsive inorganic nanomaterials for photothermal therapy

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A B S T R A C T

Novel nanomaterials and advanced nanotechnologies prompt the fast development of new protocols for biomedical application. The unique light-to-heat conversion property of nanoscale materials can be utilized to produce novel and effective therapeutics for cancer treatment. In particular, near-infrared (NIR) photothermal therapy (PTT) has gained popularity and very quickly developed in recent years due to minimally invasive treatments for patients. This review summarizes the current state-of-the-art in the development of inorganic nanocomposites for photothermal cancer therapy. The current states of the design, synthesis, the cellular uptake behavior, the cellular cytotoxicity and both *in vivo* and *in vitro* nanoparticle assisted photothermal treatments of inorganic photothermal therapy agents (PTA) are described. Finally, the perspective and challenges of PTT development are presented and some proposals are suggested for its further development and exploration. This summary should provide improved understanding of cancer treatment with photothermal nanomaterials and push nanoscience and nanotechnology one step at a time toward clinical applications.

1. Introduction

Directly or indirectly, cancer affects most people's lives. Cancer is one of the leading causes of death and accounted for 8.2 million deaths worldwide in 2012 [1] and the incidence rate is increasing year by year. The main reason for this dismal picture is that even with the current state of the art of cancer diagnosis, usually this disease is detected in an advanced stage, when the primary tumor has metastasized and invaded other organs, which is beyond surgical intervention. In addition, current chemo- and radiation therapies have many well-known disadvantages, including relatively poor specificity toward malignant tissues, systemic side effects, low efficacy and drug resistance [2]. Therefore, to advance cancer therapy, therapeutic methods that should selectively eliminate only diseased cells/tissues without causing collateral damage will be expected.

As a promising alternative or supplement to conventional cancer treating approaches, photothermal therapy (PTT) has

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caused considerable attention because of its advantages including minimal invasion, few complications, and rapid recovery. PTT, also known as photothermal ablation or optical hyperthermia, employing photo-absorbers and near-infrared light energy sources, provides a precise and minimally invasive alternative for cancer treatment [3,4]. It is a procedure based on localized heating due to light absorption for selective destruction of abnormal cells. To enhance anti-cancer efficacy and optimize therapy, integration of multiple treatment strategies with synergistic effects is highly expected [5]. Among these treatment strategies, the combination of PTT with chemotherapy, termed chemo-photothermal therapy, as a minimally invasive, controllable, and highly efficient treatment method, has drawn widespread attention [6,7]. In PTT, near-infrared (NIR) light (650–900 nm) is preferred for such an application because of its easy operation, its ability to be locally focused on a specific region, and its minimal absorbance by skin and tissues to allow for noninvasive penetration of reasonably deep tissues [8]. The key component of this technique is a photothermal transducer that can efficiently absorb and convert NIR light into heat through a non-radiative mechanism.

Over the past decade, many different types of photothermal therapy agents (PTA) have been reported, including organic compounds or materials (e.g., indocyanine green [9,10] and polyaniline [11]) and inorganic nanomaterials (e.g., noble metal nanoparticles [12,13], metal chalcogenide [14,15], and carbon-based materials [16–19]). When combined with NIR light, all of them are able to generate sufficient heat to raise the local temperature and thus kill cancer cells. Organic photothermal therapy has good biocompatibility and biodegradability, and therefore can be used for nanobiotechnology. However, the low photothermal conversion efficiency, poor photothermal stability and complicated synthesis process of these materials limit their application for PTT. As an alternative, inorganic PTA have received great interest in recent years, because of their high photothermal conversion efficiency and the ease of synthesis and modification; for example, the inorganic nanoparticle size, shape and surface properties can be facilely controlled.

In the past decade, near-infrared light-responsive inorganic nanomaterials, such as gold nanoparticles, carbon nanotubes, and copper sulfide nanoparticles (Fig. 1) efficiently convert optical energy into thermal energy and enhance the efficacy of photothermal ablation therapy. Some applications are under clinical trials. In this review, we summarize the recent advances in the structural and functional evolution of inorganic nanomaterials employed in PTT. These recent progresses in materials design will lead to deeper insight of the chemistry and photonic as well as to promote the development of PTT into practical applications. The aim of this review is to arouse more attention toward inorganic photothermal nanomaterials used in cancer therapy and to encourage future work to push forward the advancement of this biomedical area.

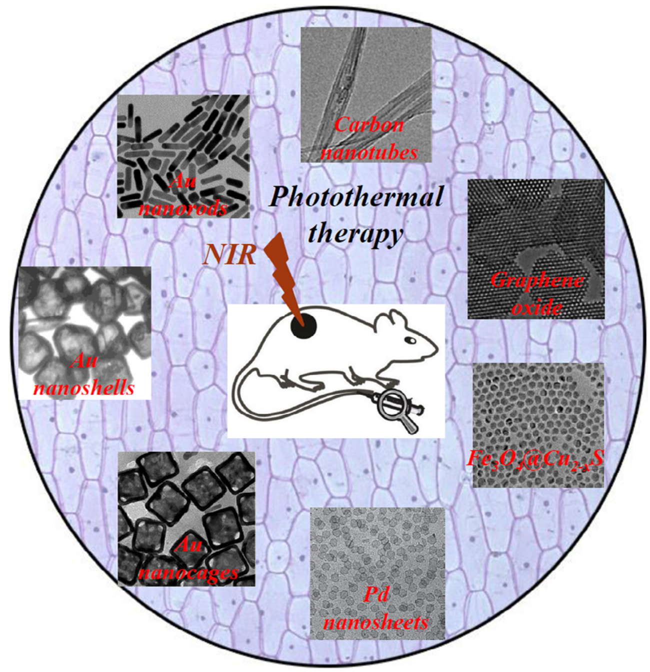

Fig. 1 – Various types of inorganic nanocomposite materials for photothermal therapy for cancer.

2. Various inorganic nanomaterials for PTT

For biomedical applications, inorganic nanomaterials, including Au-based nanomaterials, Pd nanoparticles, CuS nanoparticles, graphene, and carbon nanotubes etc., have attracted much attention in PTT. This article summarizes recent progress on various inorganic photothermal nanomaterials, including the background, synthesis, modification, cytotoxicity as well as their applications in biomedicine.

2.1. *Colloidal noble metal nanoparticles*

Noble metal nanoparticles, especially for Au and Pd nanoparticles, have been proven to show strong scattering and absorption of light in visible and near-infrared region owing to their localized surface plasmon resonances. The absorbed light is then turned into thermal energy. With pulsed light irradiation, transient thermal power generated in nanoparticles introduces abundant thermodynamic effects, such as ablation, ultrafast heating, thermal expansion, surface melting, and reshaping.

2.1.1. *Gold nanoparticles*

Localized surface plasmon resonance of gold nanocrystals endows them the capability to strongly absorb and/or scatter light at synthetically controllable resonance wavelengths, which is the underlying reason for their many applications [20–23]. A wide variety of Au nanostructures, including aggregates of colloidal particles, nanoshells, nanocages, nanorods and nanocrosses have been demonstrated for cancer photothermal therapy with NIR light. In the case of spherical gold nanoparticles, the absorption maximum exists between 400 and 600 nm. Therefore, in *in vivo* applications, very low light penetration and thus inefficient photothermal heating is generated [24]. In contrast, gold nanorods (GNRs) have attracted much interest because the absorption range of light can be finely tuned by adjusting the aspect ratio, so the heating efficiency can be maximized by using ~800 nm absorption maximum. Also, they