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Platinum Nanoparticles in Cancer Therapy: Physicochemical Properties, Synthesis, Functionalization, and Therapeutic Applications

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Abstract: Platinum nanoparticles (PtNPs) have attracted increasing attention in cancer therapy due to their controllable size, large surface area, catalytic activity, and favorable biocompatibility. These features enable PtNPs to overcome limitations of conventional therapies and provide new opportunities for precision oncology. However, a systematic overview of their properties, synthesis, functionalization, and applications remains lacking. This review summarizes the physicochemical properties of PtNPs and discusses their synthesis methods and surface functionalization strategies for regulating structure, stability, and biological performance. Recent advances in PtNP-based applications are highlighted, including drug delivery, photothermal therapy (PTT), photodynamic therapy (PDT), catalytic oxygen generation, and multimodal synergistic therapy. These approaches demonstrate the potential of PtNPs to modulate the tumor microenvironment, enhance reactive oxygen species (ROS) generation, and improve therapeutic efficacy. Overall, PtNP-based nanoplatforms represent a promising strategy for advanced cancer therapy and potential clinical translation.

1. Introduction

In recent years, cancer has remained one of the leading causes of death worldwide, and effective therapeutic strategies continue to be a major challenge in clinical oncology. Conventional chemotherapy, although widely used, suffers from poor selectivity, systemic toxicity, and multidrug resistance. Platinum-based drugs such as cisplatin, carboplatin, and oxaliplatin are commonly used for treating solid tumors, but their clinical application is limited by nonspecific distribution and dose-related side effects. Therefore, the development of more effective and targeted therapeutic strategies is urgently needed.

Advances in nanomedicine have provided new opportunities for cancer treatment. Among various nanomaterials, platinum nanoparticles (PtNPs) have attracted significant attention due to their controllable size, large specific surface area, catalytic activity, and good biocompatibility. These features enable PtNPs to function as both drug delivery carriers and active therapeutic agents, while their enzyme-like catalytic activity allows regulation of the tumor microenvironment and enhancement of therapeutic efficacy.

This review summarizes the physicochemical properties, synthesis strategies, and functionalization approaches of PtNPs, and highlights their applications in drug delivery, photothermal therapy, photodynamic therapy, catalytic oxygen generation, and multimodal synergistic therapy. The relationships among physicochemical properties, functionalization strategies, and biomedical applications are illustrated in Figure 1.

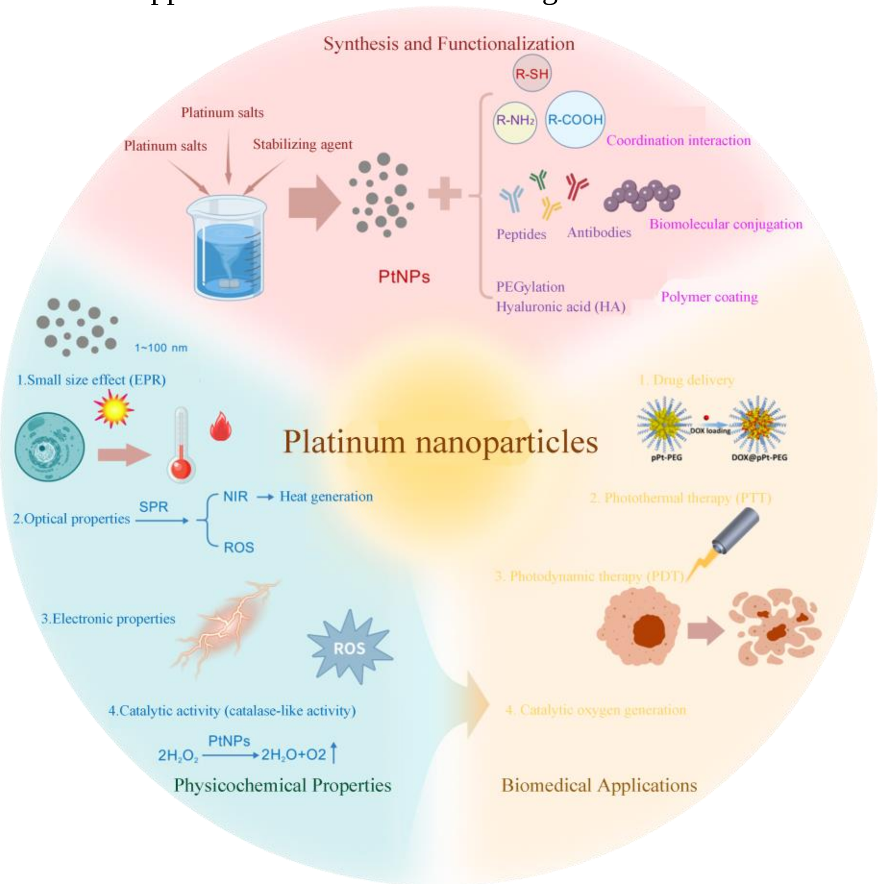

Figure 1: Schematic illustration of the physicochemical properties, functionalization strategies, and biomedical applications of platinum nanoparticles (PtNPs) in cancer therapy

PtNPs can be synthesized through reduction of platinum salts and further functionalized via coordination interactions, biomolecular conjugation, or polymer coating. Owing to their unique physicochemical properties—including small size, optical, electronic, and enzyme-like catalytic features—PtNPs can be applied in various therapeutic strategies such as drug delivery, photothermal therapy (PTT), photodynamic therapy (PDT), and catalytic oxygen generation.

2. Physicochemical Properties of Platinum Nanoparticles

Platinum nanoparticles (PtNPs) possess unique physicochemical properties, including small size, large surface area, catalytic activity, and surface functionalization capability. These properties have attracted considerable attention in biomedical applications. They influence both the biological behavior and therapeutic performance of PtNPs in tumor treatment. By regulating synthesis and surface modification strategies, their size, morphology, and surface characteristics can be precisely controlled for different applications [1].

2.1. Size and Morphological Characteristics

Particle size and morphology are key factors influencing the biological behavior and therapeutic performance of platinum nanoparticles. PtNPs typically range from 1 to 100 nm [2], and ultrasmall nanoparticles (1–10 nm) exhibit enhanced tissue penetration and tumor-targeting efficiency. In particular, ultrasmall nanoclusters can interact with cellular components and improve therapeutic outcomes while reducing systemic toxicity.

Nanoparticle size also affects tumor accumulation through the enhanced permeability and retention (EPR) effect [3], which enables nanoparticles to preferentially accumulate in tumor tissues. This property facilitates passive targeting and improves drug delivery efficiency [4].

In addition, morphology influences functional performance, as different structures exhibit varying catalytic activities. For example, hollow porous Pt nanostructures provide large surface area, enhanced drug loading capacity, and efficient catalytic decomposition of hydrogen peroxide (H_2O_2) to generate oxygen, thereby improving therapeutic efficacy [5].

2.2. Optical Properties

The optical properties of platinum nanoparticles make them promising candidates for cancer therapy. These properties are mainly attributed to the localized surface plasmon resonance (LSPR) effect, which enhances light absorption and scattering [6].

Based on these characteristics, PtNPs can absorb near-infrared (NIR) light and convert it into thermal energy or reactive oxygen species (ROS). As a result, they can be applied in photothermal therapy (PTT) and photodynamic therapy (PDT), and can also be combined with other therapeutic strategies to achieve synergistic antitumor effects [7].

2.3. Electronic Properties

Platinum nanoparticles exhibit excellent electrical conductivity and electron transfer capability, enabling their application in electrochemical-based cancer therapy [8]. In addition to drug delivery, PtNPs can regulate the electrochemical properties of the tumor microenvironment and improve therapeutic outcomes [9].

Compared with traditional electrochemical therapy, PtNPs can generate localized microcurrents under an external electric field, enhancing cytotoxic effects while minimizing damage to normal tissues. They can also promote reactive oxygen species (ROS) generation and interfere with cellular signaling pathways, thereby inhibiting tumor cell proliferation [10].

2.4. Catalytic Activity

The catalytic functions of platinum nanoparticles in tumor therapy are mainly attributed to their enzyme-like activities. By mimicking natural enzymes, PtNPs can regulate the tumor microenvironment and enhance therapeutic efficacy.

PtNPs can improve the tumor microenvironment through catalytic reactions. In particular, their catalase-like activity enables the decomposition of hydrogen peroxide (H_2O_2) into oxygen (O_2), thereby alleviating tumor hypoxia [11]. The increased oxygen levels can enhance reactive oxygen species (ROS) generation and improve the efficacy of radiotherapy and chemotherapy.

In addition, PtNPs can regulate redox balance in the tumor microenvironment. Some modified PtNPs exhibit oxidase-like or superoxide dismutase-like activities, enabling the conversion or elimination of ROS and contributing to the regulation of oxidative stress, thereby suppressing tumor growth [11].

3. Synthesis and Functionalization of Platinum Nanoparticles

3.1. Synthesis of Platinum Nanoparticles

Various methods have been developed for the synthesis of platinum nanoparticles (PtNPs), including chemical, physical, and biological approaches. Among these, chemical reduction is the most widely used due to its simplicity and controllability [12].

In this method, platinum salts are reduced to metallic nanoparticles by different reducing agents, which influence nucleation and growth processes, thereby affecting particle size, morphology, and stability [13]. Common reducing agents include sodium borohydride, citrate, and ascorbic acid [14,15].

Stabilizing agents such as polyvinylpyrrolidone (PVP), citrate, and bovine serum albumin (BSA) are often introduced to prevent aggregation and improve dispersion stability [16,17]. Natural polymers such as chitosan can also enhance nanoparticle stability [18].

Overall, chemical reduction provides effective control over the structural and physicochemical properties of PtNPs, supporting their applications in biomedical fields.

3.2. Functionalization of Platinum Nanoparticles

Platinum nanoparticles can be functionalized through various surface modification strategies due to their high surface area and strong surface reactivity [19]. These features enable interactions with ligands, polymers, and biomolecules, thereby regulating their physicochemical properties and biological performance [20,21].

Surface functionalization can improve dispersion stability and catalytic performance by reducing surface energy and preventing aggregation [22,23]. In practical applications, chemical modification and biomolecular conjugation are widely used to enhance targeting ability, stability, and therapeutic efficacy [24]. Functional groups such as –SH, $–NH_2$, and –COOH can be introduced to regulate nanoparticle properties and enable further modification [25].

Biomolecule-based functionalization is an important strategy for targeted therapy. For example, proteins or peptides can be conjugated to improve tumor targeting and cellular uptake [26–28]. In addition, polymer coating is widely used to enhance biological performance. Hyaluronic acid (HA) enables CD44-mediated tumor targeting [29,30], while polyethylene glycol (PEG) improves circulation time and reduces immune clearance [31]. Combined PEG–HA modification further enhances targeting efficiency and therapeutic efficacy [32].

Overall, surface functionalization plays a critical role in improving the stability, biocompatibility, and targeting ability of PtNPs, thereby enhancing their antitumor therapeutic performance.

4. Applications of Platinum Nanoparticles in Tumor Therapy

Platinum nanoparticles (PtNPs) have attracted extensive attention in tumor therapy owing to their unique physicochemical properties, good biocompatibility, and tunable surface structures. By rationally designing their size, surface modification, and functional structures, PtNPs can serve as both drug delivery carriers and active therapeutic agents. PtNPs have been widely applied in various therapeutic strategies, including drug delivery, photothermal therapy (PTT), photodynamic therapy (PDT), catalytic oxygen generation, and multimodal synergistic therapy. The integration of these approaches can further enhance antitumor efficacy.

4.1. PtNPs as Drug Delivery Systems

Platinum nanoparticles (PtNPs) possess several advantages as drug delivery systems, including good biocompatibility, high drug-loading capacity, and the ability for targeted delivery and controlled release [33]. By regulating particle size, surface charge, and surface modification (e.g., polyethylene glycol, PEG), their in vivo stability and circulation time can be improved, thereby enhancing tumor accumulation [34].

Due to their large surface area, PtNPs can efficiently load therapeutic agents through various interactions, while surface modification with polymers or biomolecules further improves biocompatibility and reduces systemic toxicity [19,35,36].

Targeted delivery can be achieved through both passive and active mechanisms. The enhanced permeability and retention (EPR) effect enables passive accumulation in tumor tissues [37], while surface conjugation with ligands such as antibodies or peptides allows active targeting to specific tumor cells [38]. In addition, stimuli-responsive systems can enable controlled drug release within the tumor microenvironment [39].

PtNPs also exhibit intrinsic antitumor activity by inducing oxidative stress and interfering with cellular processes, which can further enhance therapeutic efficacy when combined with drug delivery [40,41].

Representative studies have demonstrated the effectiveness of PtNP-based delivery systems in improving drug accumulation, controlled release, and antitumor efficacy [42,43].

4.2. Photothermal Therapy

Photothermal therapy (PTT) utilizes photothermal agents to absorb near-infrared (NIR) light and convert it into heat, thereby inducing tumor cell death. Due to their favorable optical properties and biocompatibility, PtNPs have been widely investigated as effective photothermal agents [44,45].

PtNP-based nanoplatforms can achieve efficient photothermal conversion and targeted therapy. For example, mitochondrial-targeted systems have demonstrated enhanced therapeutic efficacy and reduced systemic toxicity [46]. In addition, PtNPs can be integrated with other materials to construct multifunctional nanoplatforms, enabling synergistic therapeutic effects such as combined PTT and photodynamic therapy (PDT) [47].

4.3. Photodynamic Therapy

Photodynamic therapy (PDT) relies on photosensitizers to generate reactive oxygen species (ROS) under light irradiation to kill tumor cells [48]. However, tumor hypoxia significantly limits ROS production and reduces PDT efficiency [49].

PtNPs can alleviate hypoxia through their catalase-like activity by decomposing hydrogen peroxide (H_2O_2) into oxygen (O_2), thereby enhancing ROS generation and improving PDT efficacy [50].

In addition, PtNP-based systems can enhance PDT performance by stabilizing photosensitizers and facilitating electron transfer. For example, Pt-modified nanoplatforms and composite systems have been reported to increase ROS production and improve therapeutic outcomes [50–52].

4.4. Catalytic Oxygen Generation

Platinum nanoparticles (PtNPs) exhibit catalase-like activity, enabling the decomposition of hydrogen peroxide (H_2O_2) into oxygen (O_2), thereby alleviating tumor hypoxia and enhancing therapeutic efficacy.

PtNP-based systems can achieve efficient oxygen generation through catalytic or cascade reactions, further improving the tumor microenvironment. In addition, surface modification can enhance nanoparticle stability and catalytic performance [53–55].

4.5. Multimodal Synergistic Therapy

In recent years, PtNPs have been widely applied in multimodal therapeutic systems due to their photothermal properties, catalytic activity, and excellent surface modifiability. They can simultaneously participate in photothermal therapy (PTT), photodynamic therapy (PDT), and catalytic therapy, enabling synergistic antitumor effects.

PtNP-based nanoplatforms can integrate multiple therapeutic mechanisms, such as oxygen generation, reactive oxygen species (ROS) production, and photothermal conversion, thereby improving treatment outcomes [47,56].

5. Conclusions

Platinum nanoparticles (PtNPs) have shown great potential in cancer therapy owing to their controllable size, large surface area, high catalytic activity, and favorable biocompatibility. Recent studies indicate that PtNP-based nanoplatforms can function both as drug delivery carriers and active therapeutic agents. Through rational structural design and surface functionalization, PtNPs have been successfully applied in drug delivery systems, photothermal therapy, photodynamic therapy, catalytic oxygen generation, and multimodal synergistic therapy, thereby improving antitumor efficacy. Despite these advances, several challenges still hinder their clinical translation. These include the lack of scalable synthesis methods with precise control of nanoparticle structure, limited understanding of long-term biosafety and metabolic behavior in vivo, and insufficient tumor-targeting specificity. Future research should focus on developing stimuli-responsive PtNP-based systems and integrating them with emerging therapeutic strategies such as immunotherapy and gene therapy. With continued advances in nanotechnology and biomedical research, PtNPs are expected to provide promising opportunities for precision cancer therapy and potential clinical applications.

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