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Review

Synthesis, optical properties and applications of ultra-small luminescent gold nanoclusters

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ABSTRACT

Luminescent gold nanoclusters (AuNCs), composed of a few to about 100 gold atoms, have attracted considerable attention due to their molecule-like properties. These include the discrete electronic states and size-dependent fluorescence resulting from their size, which is comparable to the Fermi wavelength of conduction electrons. AuNCs have proved to be ideal fluorescence labels for biological applications and environmental monitoring and surveillance, thanks to an attractive set of features (e.g., ultra-small size, good biocompatibility and excellent photostability). This article covers in detail the synthesis strategies and optical properties, and highlights recent advances in analytical and biological applications of water-soluble luminescent AuNCs. We also discuss the potential challenges facing luminescent AuNCs in making breakthroughs in synthesis and biological applications.

Contents

Abbreviations: AgNC, Silver nanocluster; Apt, Aptamer; AuNC, Gold nanocluster; AuNP, Gold nanoparticle; BSA, Bovine serum albumin; CD, Circular dichroism spectroscopy; CdTe QD, CdTe quantum dot; CQD, Carbon quantum dot; DA, Dopamine; DDAB, Didodecyldimethylammonium bromide; DHLA, Dihydrolipoic acid; DLS, Dynamic light scattering; ECL, Electrochemiluminescence; EDS, Energy dispersive X-ray spectroscopy; FLIM, Fluorescence lifetime imaging; FTIR, Fourier transform infrared spectroscopy; GO, Graphene oxide; GSH, Glutathione; GST, Glutathione S-transferase; hMSC, human Mesenchymal stem cell; HOMO, Highest occupied molecular orbital; HRP, Horseradish peroxidase; HRTEM, High-resolution transmission electron microscopy; HSA, Human serum albumin; ICP-MS, Inductively-coupled plasma mass spectrometry; ISC, Intersystem crossing; ITO, Indium-tin oxide; LOD, Limit of detection; LSPR, Localized surface-plasmon resonance; LUMO, Lowest unoccupied molecular orbital; MALODI-TOF-MS, Matrix-assisted laser-desorption ionization time-of-flight mass spectrometry; MSA, Mercaptosuccinic acid; NIR, Near-infrared; PAMAM, Poly(amidoamine); PDGF AA, Platelet-derived growth factor AA; PPi, Pyrophosphate; PTMP-PMAA, Poly(methacrylic acid) functionalized with pentaerythritol tetrakis 3-mercaptopropionate; QY, Quantum yield; RNase-A, Ribonuclease A; SiNP, Silica nanoparticle; TEA, Triethylamine; TEM, Transmission electron microscopy; UV–Vis, Ultraviolet and visible spectrophotometry; VB_{12}, Vitamin B_{12}; XPS, X-ray photoelectron spectroscopy.

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1. Introduction

AuNCs are a new type of luminescent nanomaterials, usually comprising AuNPs smaller than 2 nm and typically composed of a few to about 100 gold atoms. AuNCs are distinguished from other AuNPs with strong photoluminescence, large Stokes shift and high emission rates [1]. The luminescent AuNCs provide the bridge between atomic and NP behavior in noble metals and exhibit molecule-like photophysical properties, large surface area-to-volume ratios, easy surface manipulation and color tenability. Compared with other types of luminescent materials, such as small-molecular dyes [2,3], fluorescent proteins [4], semiconductor quantum dots [5], dye-doped NPs [6], up-converting lanthanide-doped NPs [7] and carbon nanodots [8], AuNCs have many advantages, including being relatively simple to prepare, good water solubility, low toxicity, biocompatibility and surface functionalization, so they have shown great potential in theoretical studies and practical applications.

Recently, some excellent papers reviewed the approaches to synthesis, the properties, and the biological application of metallic NCs [1,9–11]. The theoretical interpretation of the luminescence spectrum of metal clusters has been introduced [12,13] and the structure, electronic, optical and magnetic properties of thiolate-protected AuNCs have been discussed [13]. Recent advances in utilizing AuNCs as optical probes for *in-vitro* and *in-vivo* fluorescence imaging were reported by Shang et al. [14].

In the present work, we focus our discussions on the synthesis strategies, and the size-dependent fluorescence and electrochemiluminescence of AuNCs. We cover their applications in chemical analysis, environmental monitoring and bioimaging, and we address the outlook and the challenge of future developments in this hot field.

2. Synthesis and characterization of fluorescent gold nanoclusters

Water-soluble luminescent AuNCs of high quality and uniformity have been synthesized by various approaches. It is well known that $HAuCl_4$ solution can be readily reduced to AuNPs due to the tendency to aggregate when strong reducing agents are used. However, to synthesize small luminescent AuNCs, relatively weak reducing agents have to be used, so thiol-containing molecules are suitable reducing agents and stabilizers. A variety of techniques for synthesis can also be applied to control the reaction conditions and the preparation processes effectively.

2.1. Microwave-assisted synthesis

Microwave-assisted techniques have attracted considerable attention in enhancing nanomaterial preparations due to their distinct, fascinating advantages of uniform heating, low energy consumption, cost effectiveness, and environment-friendly features [15–17]. The driving force for speeding up chemical reactions comes from the electromagnetic field, resulting in the oscillating friction between polarized molecules, which heat up the entire solution. Hence, microwave energy is frequently utilized to shorten the reaction time and to produce uniform nanocrystals in terms of size and composition.

Under microwave irradiation for 6 h with power of 700 W, highly fluorescent AuNCs with 16 gold atoms were prepared by Yue and co-workers using BSA as the reducing agent and the stabilizer [18]. The reaction time can be shortened from several hours to ~1 h with improved approaches using microwaves. For example, Chen et al. prepared lysozyme-directed AuNCs with eight cycles of sequential microwave heating (5 min per cycle with the power of 90 W) [19]. The size of the AuNCs was estimated to be 2.3 ± 0.3 nm. The synthesis of Mannose-capped AuNCs was accelerated by seven cycles after the sample had been stirred for 10 min, so enabling the synthesis of AuNCs@Mann to be completed within 1 h [20]. The reaction time could be further shortened to several minutes by adjusting the irradiation power [21,22]. Red fluorescence was observed when the AuNCs were prepared by microwave-assisted synthesis, despite slightly different peak emissions being reported. Microwave-assisted technology provides rapid, homogeneous heating, so it can accelerate the synthesis of nanomaterials.

2.2. Sonochemical synthesis

Sonochemical synthesis is another effective strategy for preparing nanomaterials, and its advantages include being non-hazardous, rapid reaction rate, controllable reaction conditions and the ability to form NPs with uniform shapes, narrow size distribution and high purity [23–25]. The chemical effects of high-intensity ultrasound result primarily from acoustic cavitation: formation, growth, and implosive collapse of bubbles in liquids [26]. Very high temperature, pressure, and extremely rapid cooling rates can be achieved during treatment, so providing a unique platform for the growth of nanomaterials [27–29]. In their pioneer studies, Liu and co-workers [30,31] reported an easy, one-pot, sonochemical route for the preparation of BSA-AuNCs with high QY (8%). These AuNCs exhibited NIR emission at 670 nm. The composition, the size, and the emission wavelength of AuNCs may be controlled by adjusting the ultrasonic irradiation time, temperature, frequency, duty cycle, and power, and the materials obtained were applied to design multi-color molecular probes [32].

Compared with other methods of synthesis, microwave-assisted synthesis and sonochemical synthesis require short reaction times, and the particle sizes are relatively uniform due to the even distribution of heat and energy supply. However, the major limitations of sonochemical synthesis are that by-product formation and noise pollution are inevitable in many circumstances.

2.3. Photoreductive synthesis

Instead of using reducing agents, AuNCs can be prepared by irradiating the Au(III) precursors with ultraviolet light. Soejima et al. synthesized AuNCs with a mean particle size less than 3.0 nm by the photoreduction of an Au(III) complex at a UV-irradiated TiO_2 surface [33]. The preparation process consisted of two