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Review article

Anisotropic noble metal nanoparticles: Synthesis, surface functionalization and applications in biosensing, bioimaging, drug delivery and theranostics

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ABSTRACT

Anisotropic nanoparticles have fascinated scientists and engineering communities for over a century because of their unique physical and chemical properties. In recent years, continuous advances in design and fabrication of anisotropic nanoparticles have opened new avenues for application in various areas of biology, chemistry and physics. Anisotropic nanoparticles have the plasmon absorption in the visible as well as near-infrared (NIR) region, which enables them to be used for crucial applications such as biological imaging, medical diagnostics and therapy ("theranostics"). Here, we describe the progress in anisotropic nanoparticles achieved since the millennium in the area of preparation including various shapes and modification of the particle surface, and in areas of application by providing examples of applications in biosensing, bio-imaging, drug delivery and theranostics. Furthermore, we also explain various mechanisms involved in cellular uptake of anisotropic nanoparticles, and conclude with our opinion on various obstacles that limit their applications in biomedical field.

Statement of Significance

Anisotropy at the molecular level has always fascinated scientists and engineering communities for over a century, however, the research on novel methods through which shape and size of nanoparticles can be precisely controlled has opened new avenues for anisotropic nanoparticles in various areas of biology, chemistry and physics. In this manuscript, we describe progress achieved since the millennium in the areas of preparation of various shapes of anisotropic nanoparticles, investigate various methods involved in modifying the surface of these NPs, and provide examples of applications in biosensing and bio-imaging, drug delivery and theranostics. We also present mechanisms involved in cellular uptake of nanoparticles, describe different methods of preparation of anisotropic nanoparticles including biomimetic and photochemical synthesis, and conclude with our opinion on various obstacles that limit their applications in biomedical field.

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1. Introduction

In recent years, anisotropic noble metal nanoparticles (ANPs) hold great promise in a wide variety of applications because of their unique physical and chemical properties such as enhanced optical absorption in the NIR range, large extinction cross sections, enhanced photothermal heating capacity, chemical stability, and biocompatibility. ANPs refer to the shapes that are different from symmetrical spheres made of noble metals such as gold, silver, platinum and palladium. Common shapes obtained are nanorods (NRs), nanoprisms (NPrs), nanocubes (NCs), nanostars (NSs) and dendritic nanostructures [1,2]. ANPs have different mechanical, electronic, optical, magnetic and thermodynamic properties when compared to those of either the bulk or single molecule. According to Mie's theory, metallic isotropic NPs have single plasmon bands and their extinction spectra are largely dependent on factors such as diameter, composition, and the surrounding dielectric environment. Due to difference in surface energies and strains on their crystal faces, ANPs result in two distinct plasmon bands at longitudinal and transverse directions. In other words, the reduced symmetry of anisotropic NPs results in multiple plasmonic bands as a function of the number of symmetric planes present in it [3]. As a result, anisotropy at the nanoscale is a critical factor in determining the final mechanical, optical, electronic, and magnetic properties of ANPs. For instance, the magnetic volume susceptibility of gold nanorods (AuNRs) increases with decreasing rod size or increasing aspect ratio when compared to bulk gold [4]. Due to these unique properties, ANPs have received greater research interest in the field of biomedicine as photothermal agents, contrasting agents, drug delivery carriers, and theranostics [5].

In general, there are two approaches to fabricate NPs: a) top down, and b) bottom up. The Top down method involves size reduction by mechanical means followed by stabilization with surface active agents [6]. The bottom up approach involves chemical reduction of metal ions to metal NPs by various means such as chemical, electrochemical or controlled decomposition of metastable organometallic compounds. Among these two approaches, bottom up approach is most often used to synthesize ANPs as it provides better control on particle size and growth. The properties such as strong surface plasmon resonance (SPR), biocompatibility, and other surface properties, made ANPs good candidate for various biological applications [7]. For instance, surface modified ANPs showed good contrast enhancement in sensitive detections, and played an important role in nano-biotechnology tool kits by replacing conventional organic and molecular fluorescent probes [8]. Furthermore, gold ANP based sensors were able to detect pregnancy [9], ovulation [10] and HIV (Human immunodeficiency virus) at very early stages [11]. Acticoat has also launched silver NP based wound dressings that have built in antimicrobial properties [12]. Recently, it is reported that Verigene detector was able to identify nucleic acid present in certain bacteria associated with bloodstream infections [13]. The absorption of hollow nanospheres in biological window ranged between 650 and 900 nm enabled them to be used for attenuated non-invasive *in vivo* imaging [14]. Alternatively, the electromagnetic window between 800 and 1300 nm can be used for drug delivery, medicinal diagnostics and photothermal therapy ("theranostics") [15] using other ANPs such as NRs [16], NPrs [17], NCs [18], and NSs [19].

2. General aspects and perspectives of ANPs

The final shape of NPs is determined by growth kinetics of nuclei during the synthesis process. As a result, NP growth can happen either in a thermodynamically controlled or kinetically controlled regime. In general, under thermodynamically control regime isotropic growth of nanocrystals results in spheres, whereas under kinetically controlled regime anisotropic growth of nanocrystals results in ANPs of various shapes. In other words, ANPs are formed under conditions that are far from thermodynamic equilibrium. In practice, ANP synthesis was performed by substantially slowing down the rate of precursor decomposition or reduction. When crystal growth occurs away from the thermodynamic equilibrium, a small change in reaction conditions substantially amplifies the changes in surface free energies at different facets, and hence, it results in anisotropic growth at different facets. Under such cases, the adsorption of capping molecules on specific facets can further change the difference in surface free energy, which may hinder or enhance the growth at these facets [20]. The process parameters such as concentration of the metal precursors, seed NPs, reducing agents, stabilizers, presence of external salts, and reaction conditions (e.g. pH, temperature and time), also play a significant role in the formation of specific ANPs. However, the influence of these parameters on ANPs