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Review

Pharmaceutical and Biomedical Applications of Gold Nanoparticles

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Abstract

Gold nanoparticles (GNPs) have been extensively used in various applications in pharmaceuticals applications. Due to their unique characteristics such as tunable surface properties as well as surface plasmon resonance (SPR), GNPs have garnered attention in various applications exclusively in therapy and diagnostics. Gold nanoparticles (GNPs) are one of many NPs that have long been the focus of research. Due to their flexibility in synthesis and functionalization, GNPs have been profoundly used in treatments and diagnostic purpose. This article discusses and highlights therapeutic characteristics of GNPs that have been exploited in biomedical applications in recent years to improve biomedical research in various biomedical field such as nuclear medicine, molecular imaging and contrast agent, vaccine development, medical implant, diagnostics, biosensing, and lab-on-chip applications. At the forefront of modern therapeutic technology, GNPs based cancer treatment, antiviral agents and etc., have great potential which is also highlighted briefly in this article.

Keywords: Gold nanoparticles, medical implant, diagnostics, cancer treatment, antiviral agents.

INTRODUCTION

Nanotechnology is referred to the designing and application of components which occur at the nano-scale: up to 10–1,000 nm in size. Gold nanoparticles provide an outstanding material for study due to the fact that they are one of the most stable, non-toxic, and easy to synthesize nanoparticles and exhibit various fascinating properties like assembly of various types and quantum size effect. The optical behaviour of gold nanoparticles is dependent on their surface plasmon resonance (SPR), located in a wide region ranging from visible to the infrared region of the spectrum, which is determined by collective oscillation of conducting electrons. The range of the spectrum depends on various features of gold nanoparticles, including size and shape. Methods have been developed to synthesize these materials reproducibly, which can further be modified using countless chemical functional groups. Many new sensitive and specific assays are based on the gold nanoconjugates. Gold nanoparticles have emerged as an excellent candidate for the application in delivery of various payloads to the target site. These payloads range from small drug molecules including drugs to large biomolecules like DNA,

RNA, and proteins. Some drugs molecules do not require modification of a monolayer of gold nanoparticles for their delivery and can be directly conjugated with gold nanoparticles through physical absorption and ionic or covalent bonding. Whereas for the delivery of other payloads, gold nanoparticles require functionalization like PEGlyation, peptide and amino acid conjugation, or functionalization with oligonucleotides.16 Apart from that, another prerequisite for the efficient delivery of therapeutic agents is their release. Various internal stimuli (glutathione, pH and enzymes) and external stimuli (light, etc.) have been investigated for the efficient release of these payloads from gold nanoparticles. Due to the vast amount of information available and the level at which it is being renewed, we have chosen the generalized data from the past few years to present this review encompassing the most promising application of gold nanoparticles in drug delivery In the first stage the gold precursor, which is usually an aqueous gold salt solution, is reduced to gold nanoparticles using a specific reducing agent like citrate. In the second stage the stabilization of gold nanoparticles is done by a specific capping agent. The capping agents hinder the agglomeration of metallic nanoparticles.

THERAPEUTIC APPLICATIONS OF GOLD NANOPARTICLES

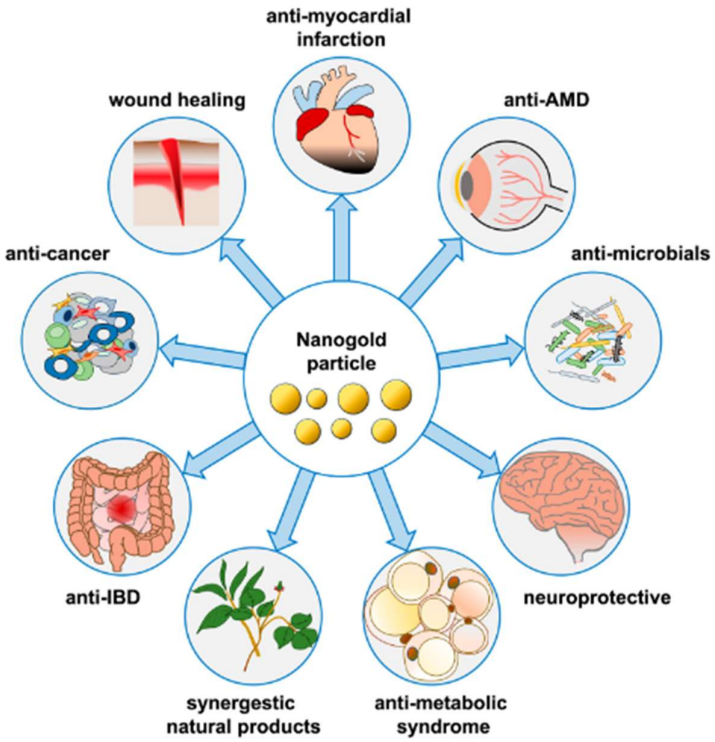


Fig 1: Therapeutic application of Gold Nanoparticles

Gold nanoparticles: promising biomaterials for osteogenic/adipogenic regulation in bone repair

Hyperlipidemia is a risk factor in the process of bone defect repair, which has a negative impact on the process of osteogenesis, increasing the difficulty of bone defect repair. Therefore, it is necessary to find materials that can promote bone defect repair under the condition of hyperlipidemia. Gold nanoparticles (AuNPs) have been applied in the fields of biology and clinical medicine for many years and developed to modulate osteogenic differentiation and adipogenic differentiation. In vitro and vivo studies displayed that they promoted bone formation and inhibited fat accumulation. Further, the metabolism and mechanisms of AuNPs acting on osteogenesis/adipogenesis were partially revealed by researchers. This review further clarifies the role of AuNPs in osteogenic/adipogenic regulation during the process of osteogenesis and bone regeneration by summarizing the related in vitro and in vivo research, discussing the advantages and challenges of AuNPs and highlighting several possible directions for future research, with the aim to provide a new strategy for dealing with bone defects in hyperlipidemic patients. Gold Nanoparticles Promote the Bone Regeneration of Periodontal Ligament Stem Cell Sheets Through Activation of Autophagy. AuNPs could enhance the osteogenesis of PDLSC sheets by activating autophagy, and 45-nm AuNPs was more effective than 13-nm AuNPs. This study determined the role of AuNPs in regulating the osteogenic differentiation and bone regeneration of PDLSC sheets, providing a new strategy for promoting the repair of alveolar bone defects.

Green Synthesis of Gold Nanoparticles for Tuberculosis

The study of green synthesis of GNPs is a quickly evolving field in nanotechnology for TB. The present review summarises exhaustive literature for plants containing phytoconstituents having antitubercular activity along with the understanding of the synthesis of GNPs not only using plant extracts but biomolecules, microorganism, and various bioreactors. A detailed study is needed to give a lucid mechanism of biosynthesis of GNPs using biomolecules; microorganism present in different plant extracts which will be valuable to improve the properties of GNPs for TB treatment.

Gold Nanoparticles in Diagnosis and Treatment of Alzheimer's Disease

Gold nanoparticles are one of the most important nanoparticles with many applications in diagnosis such as tumor markers detection, microbial pathogen detection, and many imaging techniques and therapies like gene therapy, cancer therapy, and drug delivery systems. Apart from this, these are also used in information technology and many electronic and communication technologies. Delivering of drug across the blood brain is a major problem in the neurodegenerative diseases majorly Parkinson and Alzheimer's diseases. The gold nanoparticles are golden opportunities in the treatment of neurodegenerative diseases and drug delivery in the blood-brain barriers and inducing the neuronal activities. The gold nanoparticles and its very clear applications in the blood-brain barrier hurdle to treat neurodegenerative diseases, biomarkers for Alzheimer's disease, diagnostics targeting, and inhibiting amyloid fibrils in AD and role of gold nanoparticles in the Alzheimer's disease treatment.

Gold Nanoparticle-Based Platforms for Diagnosis and Treatment of Myocardial Infarction

The NPs have been used to develop different nanobiosensors, mainly optical sensors for early detection of biomarkers as well as biomimetic/bioinspired platforms for cardiac tissue engineering (CTE). Therefore, in this Review, we presented an overview on the potential application of AuNPs as optical (surface plasmon resonance, colorimetric, fluorescence, and chemiluminescence) nanobiosensors for early diagnosis and prognosis of MI. On the other hand, we discussed the potential application of AuNPs either alone or with other NPs/polymers as promising three-dimensional (3D) scaffolds to regulate the microenvironment and mimic the morphological and electrical features of cardiac cells for potential application in CTE. Furthermore, we presented the challenges and ongoing efforts associated with the application of AuNPs in the diagnosis and treatment of MI.

Gold Nanoparticles: Multifaceted Roles in the Management of Autoimmune Disorders

Applying NPs such as GNPs to treat inflammatory and autoimmune diseases will offer innovative solutions for efficacy improvement of current immunosuppressive treatments, which will help overcome the side effects of these therapies. It showed that colloidal GNPs could be utilized in applying nanotechnology in medicine to treat and detect ADs such as RA, T1DM, and MS.

The GNPs represent a new generation of drug delivery systems with high drug-loading capacity that can employ a wide range of materials. Furthermore, as mentioned above, GNPs are potent antioxidant and anti-inflammatory agents, resulting in quenching ROS, reducing RANKL-induced osteoclast formation and inflammatory cytokines (IL-1, IL-6, and TNF-a) VEGF, which are the main contributors to the RA pathogenesis. Therefore, GNPs can be considered as a potential novel therapeutic agent for the treatment of RA.

Moreover, hyperglycemia in diabetes could be controlled by GNPs via improving blood glucose levels, insulin resistance, and liver enzymes, reducing proinflammatory cytokines (include TNF-α, IL-6, and CRP), and enhancing the antioxidant defense enzymes. Moreover, GNPs via delivery and prolonging the insulin action could reduce the frequency of insulin injections. In MS, GNPs can increase differentiation, survival, and the growth of neuronal, anti-inflammatory, and anti-apoptotic effects, improving neurological defects. In addition, they decrease infarction volumes, eventually improving overall clinical symptoms. Moreover, GNPs, as a delivery vehicle of tolerogenic molecules, could promote the generation of Tregs by DCs cells.

Enhanced skin anti-inflammatory and moisturizing action of gold nanoparticles produced utilizing Diospyros kaki fruit extracts

The AuNPs to aid in the healing process of skin diseases. Thus, DK fruit extracts primary phytochemicals converted DK-AuNPs in an ecologically friendly plant-mediated synthesis. Several characterization techniques was performed to confirm the physicalchemical properties of the synthesized DK-AuNPs. The DK-AuNPs showed nontoxic effect in HaCaT cells until 200 μg/mL and it could inhibit ROS and Mito-SOX release in T + I-induced HaCaT cells. Moreover, we evaluated the underlying mechanism of these activities through protein expression of the MAPK/NFκB signaling pathway for anti-inflammatory and PI3K/AKT/NFκB signaling pathways for HA production. Compare to the well know and commercialy available drugs such as DEX and NAG, the synthesized DK-AuNPs could be an ecologically and cost friendly skin disease treating agent. In addition, our findings support basic data for novel nanoparticles and evaluating their activities, which may lead to the development of medicines based on DK-AuNPs.

Application of natural compounds–based gold nanoparticles for the treatment of hemolytic anemia

From time immemorial, people have tried to treat several diseases using natural compounds, including plants. Recently, researchers proposed that plants and herbal nanoparticles possess many remedial potentials. The results of this study confirmed the ability of an aqueous extract of Allium eriophyllum Boiss leaf grown under *in vitro* conditions for the biosynthesis of gold nanoparticles (AuNPs) and also revealed the anti-hemolytic anemia activity of AuNPs in an anemic rodent model. In addition, AuNPs were similar to A. eriophyllum and had a high cell viability dose dependently against the human umbilical vein endothelial cell line. In conclusion, the results of the chemical characterization confirm that the leaves of A. eriophyllum can be used to produce AuNPs with a remarkable amount of anti-hemolytic anemia property.

Polymeric Nanoparticle Based Diagnosis and Nanomedicine for Treatment and Development of Vaccines for Cerebral Malaria

Cerebral malaria occurs due to Plasmodium falciparum infection, which causes 228 million infections and 450,000 deaths worldwide every year. African people are mostly affected with nearly 91% cases, of which 86% are pregnant women and infants. India and Brazil are the other two countries severely suffering from malaria endemicity. Commonly used drugs have severe side effects, and unfortunately no suitable vaccine is available in the market today. In this line, this review is focused on polymeric nanomaterials and nanocapsules that can be used for the development of effective diagnostic strategies, nanomedicines, and vaccines in the management of cerebral malaria. Further, this review will help scientists and medical professionals by updating the status on the development stages of polymeric nanoparticle based diagnostics, nanomedicines, and vaccines and strategies to eradicate cerebral malaria. In addition to this, the predominant focus of this review is antimalarial agents based on polymer nanomedicines that are currently in the preclinical and clinical trial stages, and potential developments are suggested as well. This review further will have an important social and commercial impact worldwide for the development of polymeric nanomedicines and strategies for the treatment of cerebral malaria.

Applications of Gold Nanoparticles in Brain Diseases across the Blood-Brain Barrier

Brain diseases, including Alzheimer's disease (AD), brain tumors and Parkinson's disease (PD), pose heavy pressure on the public healthcare system. The main obstacle to vanquish brain diseases is the blood-brain barrier (BBB), which is a selective barrier mainly formed by brain endothelial cells. BBB prevents almost all drugs from reaching the brain, thereby hindering drug delivery. Over the past few decades, considerable signs of progress have been made in crossing the BBB and treating brain diseases. Gold nanoparticles (AuNPs) demonstrate the characteristics of adjustable size, unique optical properties, flexible surface modification, and good biocompatibility, which all contribute AuNPs as a promising candidate in biomedical fields. This article reviews the structure and properties of BBB, and discusses main transport routes through the BBB. Besides, nanoparticles, especially AuNPs applied in brain diseases as main drug delivery platforms, are systematically summarized, emphasizing several methods to modify AuNPs, including tuning particle size and surface modification, which are aimed at promoting BBB penetration or prolonging circulation time of AuNPs. In addition, AuNPs utilized in brain diseases are introduced in detail from the aspects of brain imaging, AD, brain tumors, and PD. Prospects and challenges that need to be considered in further investigations and clinical transformation of AuNPs used in brain diseases are also included, hoping to bring new insights into the applications of AuNPs in brain diseases.

A review of the application of nanoparticles in the diagnosis and treatment of chronic kidney disease

The emergence of nanoparticles has brought hope to medicine. Regarding kidney disease, early potential patients and disease progression can be identified using gas measurements and urine detection. Magnetic nanoparticles can reduce the renal fibrosis caused by iodine or gadolinium contrast agents in patients with CKD. Gold nanoparticles and silica nanoparticles are also used for renal imaging to evaluate renal inflammation and fibrosis, and may become a tool to replace renal biopsy puncture in the future. CKD is associated with vascular and renal fibrosis. Albumin nanoparticles can target degraded elastin to reverse vascular calcification. While polymer nanoparticles can package and deliver related drugs to specific parts of the kidney to improve their bioavailability and half-life and effectively treat renal fibrosis, superparamagnetic iron oxide nanoparticles can be administered intravenously to treat renal anemia and appear to be more effective than traditional oral iron agents. In addition, during dialysis treatment, the use of gold nanoparticles can improve the chemical structure of the dialysis membrane, thus reducing the adverse reactions of thrombosis and detecting the loss of amino acids in patients after dialysis. In summary, many types of nanoparticles have been used for the diagnosis and treatment of patients with CKD; however, most trials are still in the preclinical stage, and nanoparticles have not been routinely used in clinical practice. We believe that the application of nanoparticles to patients with CKD is clinically meaningful, as it may allow for more accurate and effective diagnosis and treatment of CKD in the future. Therefore, more clinical experiments on nanoparticles should be conducted so that nanotechnology can be more widely and effectively utilized in clinical settings.

Electromagnetized gold nanoparticles improve neurogenesis and cognition in the aged brain

Adult neurogenesis is the lifelong process by which new neurons are generated in the dentate gyrus. However, adult neurogenesis capacity decreases with age, and this decrease is closely linked to cognitive and memory decline. Our study demonstrated that electromagnetized gold nanoparticles (AuNPs) promote adult hippocampal neurogenesis, thereby improving cognitive function and memory consolidation in aged mice. According to single-cell RNA sequencing data, the numbers of neural stem cells (NSCs) and neural progenitors were significantly increased by electromagnetized AuNPs. Additionally, electromagnetic stimulation resulted in specific activation of the histone acetyltransferase Kat2a, which led to histone H3K9 acetylation in adult NSCs. Moreover, in vivo electromagnetized AuNP stimulation efficiently increased hippocampal neurogenesis in aged and Hutchinson-Gilford progeria mouse brains, thereby alleviating the symptoms of aging. Therefore, our study provides a proof-of-concept for the in vivo stimulation of hippocampal neurogenesis using electromagnetized AuNPs as a promising therapeutic strategy for the treatment of age-related brain diseases.

The Basic Properties of Gold Nanoparticles and their Applications in Tumor Diagnosis and Treatment

Gold nanoparticles (AuNPs) have been widely studied and applied in the field of tumor diagnosis and treatment because of their special fundamental properties. In order to make AuNPs more suitable for tumor diagnosis and treatment, their natural properties and the interrelationships between these properties should be systematically and profoundly understood. The natural properties of AuNPs were discussed from two aspects: physical and chemical. Among the physical properties of AuNPs, localized surface plasmon resonance (LSPR), radioactivity and high X-ray absorption coefficient are widely used in the diagnosis and treatment of tumors. As an advantage over many other nanoparticles in chemicals, AuNPs can form stable chemical bonds with S-and N-containing groups. This allows AuNPs to attach to a wide variety of organic ligands or polymers with a specific function. These surface modifications endow AuNPs with outstanding biocompatibility, targeting and drug delivery capabilities. In this review, we systematically summarized the physicochemical properties of AuNPs and their intrinsic relationships. Then the latest research advancements and the developments of basic research and clinical trials using these properties are summarized. Further, the difficulties to be overcome and possible solutions in the process from basic laboratory research to clinical application are discussed. Finally, the possibility of applying the results to clinical trials was estimated. We hope to provide a reference for peer researchers to better utilize the excellent physicochemical properties of gold nanoparticles in oncotherapy.

Gold nanoparticle-based platforms for vaccine development

Development of prophylactic and therapeutic vaccines using nanomaterials constitutes an emerging and promising research field. Recent literature demonstrates that AuNPs, with their unique properties, represent ideal platforms towards a new era of vaccinology. Their high surface area and straightforward functionalization allow simultaneous and multivalent antigen presentation and make them excellent candidates for innovative nano-constructs in the field of vaccine development. AuNPs are readily endocytosed by APCs, affecting increased immunological responses while reducing antigen dosage. Therefore, we expect that some of these nano-formulations will be translated into clinical practice, but this can only be achieved if major challenges are addressed. First, a high level of consistency in the large-scale production, characterization, and reproducibility of engineered AuNPs must be ensured. A better comprehension of the nanoparticle interaction with the immune system and their in vivo biodistribution is pivotal to accelerate the rational design of more encouraging nanoformulations. To correctly face this issue, it is fundamental to consider the potential formation of bio-corona around AuNP surfaces. A careful evaluation of such bio-corona formation and the development of protocols or strategy to avoid such phenomenon must be considered in the future nanovaccine developments. Another critical point is the lack of representative animal models which justifies the differences from very promising results from animal tests to poorly encouraging outcomes in preliminary human trials. Finally, the fate of the nanoparticles and their biodegradability must be carefully evaluated, making nanotoxicology a growing research field in which we need to focus our attention.

Efficacy and Immune Response Elicited by Gold Nanoparticle- Based Nanovaccines against Infectious Diseases

The use of nanoparticles for developing vaccines has become a routine process for researchers and pharmaceutical companies. Gold nanoparticles (GNPs) are chemical inert, have low toxicity, and are easy to modify and functionalize, making them an attractive choice for nanovaccine development. GNPs are modified for diagnostics and detection of many pathogens. The biocompatibility and biodistribution properties of GNPs render them ideal for use in clinical settings. They have excellent immune modulatory and adjuvant properties. They have been used as the antigen carrier for the delivery system to a targeted site. Tagging them with antibodies can direct the drug or antigen-carrying GNPs to specific tissues or cells. The physicochemical properties of the GNP, together with its dynamic immune response based on its size, shape, surface charge, and optical properties, make it a suitable candidate for vaccine development. The clear outcome of modulating dendritic cells, T and B

lymphocytes, which trigger cytokine release in the host, indicates GNPs' efficiency in combating pathogens. The high titer of IgG and IgA antibody subtypes and their enhanced capacity to neutralize pathogens are reported in multiple studies on GNP-based vaccine development. The major focus of this review is to illustrate the role of GNPs in developing nanovaccines against multiple infectious agents, ranging from viruses to bacteria and parasites. Although the use of GNPs has its shortcomings and a low but detectable level of toxicity, their benefits warrant investing more thought and energy into the development of novel vaccine strategies.

Gold nanoparticles as a promising treatment for diabetes and its complications

The gold nanoparticles were green synthesized using the aqueous extract of Citrus reticulata. The synthesized NPs were characterized using chemical techniques such as FT-IR, TEM, and UV–vis. The results revealed a spherical morphology for AuNPs in the range size of 11.14 to 32.76 nm. The viability of malignant bone cell lines reduced dose-dependently in the presence of AuNPs. The IC50s of AuNPs were 166, 242, 174, and 215 µg/mL against A-673, CADO-ES1, MG-63 and CH-3573.

Biofunctionalized Chrysin-conjugated gold nanoparticles neutralize Leishmania parasites with high efficacy

Current treatments for leishmaniasis involve various drugs, including miltefosine and amphotericin B, which are associated with several side effects and high costs. Long-term use of these drugs may lead to the development of resistance, thereby reducing their efficiency. Chrysin (CHY) is a well-known, non-toxic flavonoid with antioxidant, antiviral, anti-inflammatory, anti-cancer, hepatoprotective, and neuroprotective properties. Recently we have shown that CHY targets the MAP kinase 3 enzyme of Leishmania and neutralizes the parasite rapidly. However, CHY is associated with low bioavailability, poor absorption, and rapid excretion issues, limiting its usage. In this study, we developed and tested a novel CHY-gold nanoformulation with improved efficacy against the parasites. The reducing power of CHY was utilized to reduce and conjugate with gold nanoparticles. Gold nanoparticles, which are already known for their anti-leishmanial properties, along with conjugated CHY, exhibited a decreased parasite burden in mammalian macrophages. Our findings showed that this biofunctionalized nanoformulation could be used as a potential therapeutic tool against leishmaniasis.

Metformin encapsulated gold nanoparticles (MTF-GNPs): A promising antiglycation agent

The generation of advanced glycation end products (AGEs) through nonenzymatic protein glycation contributes to the pathogenesis of long-lived diabetic problems. Metformin (MTF) is the very first drug having antihyperglycemic effects on type II diabetes mellitus which also possess interaction with dicarbonyl compounds and blocks the formation of AGEs. In the current study, MTF is bioconjugated with glycation-derived synthesized gold nanoparticles (GNPs) of significant size. Additionally, using various biophysical and biochemical approaches, we investigated the antiglycating capacity MTF-GNPs in contrast to MTF against d-ribose-derived glycation of bovine serum albumin. Our key findings via utilizing various assays demonstrated that MTF-GNPs were able to inhibit AGEs development by reducing hyperchromicity, early glycation products, carbonyl content, hydxoxymethylfurfural content, production of fluorescent AGEs, normalizing the loss of secondary structure (i.e., α-helix and β-sheets) of proteins, elevating the levels of free lysine and free arginine more efficiently compared to pure MTF. Based on these results, we concluded that MTF-GNPs possess a considerable antiglycation property and may be developed as an outstanding anti-AGEs treatment drug. Further in vivo and clinical research are necessary to determine the therapeutic effects of MTF-GNPs against AGE-related and metabolic disorders.

Gold nanoparticles application to the treatment of brain dysfunctions related to metabolic diseases: evidence from experimental studies

Nanotechnology is an emerging and expanding technology worldwide. The manipulation of materials on a nanometric scale generates new products with unique properties called nanomaterials. Due to its significant expansion, nanotechnology has been applied in several fields of study, including developing materials for biomedical applications, i.e., nanomedicine. The use of nanomaterials, including nanoparticles, in nanomedicine, is promising and has been associated with pharmacokinetics, bioavailability, and therapeutic advantages. In this regard, it is worth mentioning the Gold Nanoparticles (AuNPs). AuNPs' biomedical application is extensively investigated due to their high biocompatibility, simple preparation, catalytic, and redox properties. Experimental studies have pointed out critical therapeutic actions related to AuNPs in different pathophysiological contexts, mainly due to their anti-inflammatory and antioxidant effects. Thus, in this review, we will discuss the main experimental findings related to the therapeutic properties of AuNPs in metabolic, neurodegenerative diseases, and ultimately brain dysfunctions related to metabolic diseases.

Exploring the potential anti-inflammatory effect of biosynthesized gold nanoparticles using Isodon excisus leaf tissue in human keratinocytes.

In this study, IE-AuNPs were synthesized and characterized and their potential for treating inflammatory skin disorders was investigated. TEM and EDX imaging confirmed that the synthesized IE-AuNPs were polygonal, triangular, and hexagonal in shape, and were primarily composed of Au. XRD and SAED analyses revealed that the IEAuNPs were crystalline. IE-AuNPs did not cause cytotoxicity in HaCaT cells and exhibited a reliable duration of cell penetration after 3 h. Furthermore, IE-AuNPs inhibited the formation of ROS, MitoSOX, and mitochondrial dysfunction indicators, such as PINK1 and PARKIN, in HaCaT cells. Treatment with IE-AuNPs resulted in the suppression of anti-inflammatory cytokines and chemokines expression, along with the activation of autophagy biomarkers. These effects were observed through the downregulation of the PI3K/AKT/ mTORC1 signaling pathway. The promising therapeutic potential of IE-AuNPs for the prevention and treatment of various skin-related disorders is highlighted by these results. However, further research is needed to explore the interactions between different cell types and structures within the complex organ of the skin, which consists of multiple layers and distinct cell types. Additionally, there is a need to Fig. 6 The mechanism of IE-AuNPs in suppressing pro-inflammatory mediators and inducing autophagy through the PI3K/AKT signaling pathway. (A) shows the protein expression of PI3K, p-PI3K, AKT, p-AKT, p70SK6, and p-p70SK6 analyzed using immunoblotting, and all their bands were analyzed and standardized to b-actin. (B) shows the effect of IE-AuNPs on the PI3K/AKT signaling pathway in HaCaT cells with the application of the PI3K activator 740Y-P (30 lM). The negative control (NC) was treated with medium alone, and the inflammation-induced control (T + I) was treated with T + I alone. The crosshatch marks indicate significant differences between NC and T + I, and asterisks indicate significant differences between T + I and each group. # and * $p < 0.05$; ## and ** $p < 0.01$; and *** $p < 0.001$. Exploring the potential anti-inflammatory effect of biosynthesized gold nanoparticles 11 investigate the potential therapeutic applications of IE-AuNPs in diverse skin conditions. By pursuing these future research directions, the field can continue to advance and innovative strategies for managing skin inflammation and developing dermatological therapeutics can be developed.

CONCLUSION

AuNPs demonstrate great potential in cancer therapy and drug delivery, as well as biodiagnostic and imaging. In spite of these advancements, the properties of AuNPs, such as long-term toxicity, stability, and immune response effects, high surface-to-volume ratio, surface versatility, low inherent toxicity, biocompatibility, optical properties, and ability to easily functionalize with biomolecules to achieve the desired selectivity, deserve further exploration. Moreover, AuNPs offer tremendous antiviral therapeutic potential by overwhelming the challenges of therapy resistance, low solubility, excellent intrinsic properties release, and short retention time of drugs in the plasm, etc. It would also be crucial to balance the contradicting elements of generating more effective acid-responsive AuNPs, such as expected targeting delivery versus undesirable nonspecific protein adsorption, to build a more effective acid-responsive AuNPs system. Many in vitro and in vivo investigations have identified the promising toxicity of AuNPs, including the loss of AuNPs' ability to co-operate with the target receptor, which can be facilitated by adorning the surface of AuNPs with target binding sites, nonbiodegradability, and toxicity. As a result, more research is needed to resolve toxicity concerns by defining the most appropriate combination with AuNPs properties for therapeutic agents.

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