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Review Article

Green Synthesised Metal Nanoparticles and its Anti-Inflammatory and Anticancer Activity

Sirajudheen Mukriyan Kallungal*, Nameel Ashfaque Abdulazeez Avanjipuram, Ridha Rasheed, Shamna Cheruvakatil, Sheiha Poongavanam, Muddukrishnaiah Kotakonda, Shilpa Valiyaparambil

Department of Pharmaceutics, Jamia Salfiya Pharmacy College, Pulikkal, Malappuram, Kerala, INDIA.

ABSTRACT

Background: Metallic nanoparticles have the potential to address various medical challenges including inflammation, cancer and fungal infections. **Aim:** We synthesized metal nanoparticles and evaluated their anti-inflammatory and anticancer activities. **Methodology:** This study examined the biogenic synthesis of metallic nanoparticles and their anti-inflammatory actions. It discusses the mechanisms of their action, including the suppression of the NF-B and COX-2 pathways and emphasizes the importance of stability and specific targeting. The data were uptrained from research articles from PubMed, Research Gate, Google Scholar and other sources. **Results:** Nanotechnology, with its multidisciplinary approach, has opened new avenues for innovative treatments by leveraging the unique properties of nanoparticles. Metallic nanoparticles, such as silver, gold, zinc oxide and titanium, exhibit remarkable anti-inflammatory, anti-cancer and antibacterial activities, which are attributed to their ability to scavenge Reactive Oxygen Species (ROS), inhibit NF-B and cyclooxygenase-2 pathways and induce oxidative stress in cells. Moreover, these nanoparticles hold promise as pharmaceutical carriers, enhancing the efficacy of anticancer medications and offering opportunities for immunotherapy and chemotherapy. **Conclusion:** The review highlighted the importance of metallic nanoparticles in advancing medical research and their potential impact on improving healthcare outcomes.

Keywords: Metallic nanoparticles, Green synthesis, Inflammation, Skin Cancer, Antibacterial.

Correspondence:
Dr. Sirajudheen Mukriyan Kallungal
Department of Pharmaceutics, Jamia Salfiya Pharmacy College, Pulikkal, Malappuram-673637, Kerala, INDIA.
Email: mksiraj@gmail.com

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INTRODUCTION

Nanotechnology is multidisciplinary, encompassing engineering, physics, chemistry, biology and other fields. Significant advances in science and technology brought about by the introduction of nanotechnology have opened up possibilities for the advancement of medical research and treatment of diseases in healthcare systems.[1] Nanoparticles, also known as ultrafine particles, are small particles with a size range of 1-100 nanometers (nm). Nanoparticles can be synthesized using both natural and synthetic method.[2,3] Nanoparticles have a high surface-to-volume ratio because of their high reactivity, mobility, solubility and strength. Since its formation, soil, dust, water, minerals and nanoparticles have been present on the Earth. Nanoparticles and nanomaterials are used in various industries including food, agriculture and medicine.[4] Nanoparticles are used in the food industry for food processing, preservation and packaging. Nanotechnology has made use of nonfertilizer, insecticides, herbicides and sensors in agriculture. Nanotechnology is also used for communicable and noncommunicable diseases.[5] Nanotechnology is used to detect life-threatening disorders such as cancer in the early stages.[6,7] Nanoparticles are classified into four categories based on their chemical composition: carbon-based, metal-oxide-based, bio-organic-based and composite-based.[8] There are two types of nanoparticles: inorganic and organic nanoparticles. Inorganic materials are composed of metallic nanoparticles, whereas organic nanoparticles are biodegradable. They are used as antibacterial, antifungal and antiviral agents. Nanoparticles have two approaches: top-down and bottom-up. Different physical, chemical and biological methods have been employed for nanoparticle synthesis.[9] Metallic nanoparticles (Figure 1) are eco-friendly synthesis methods that use green synthesis to avoid the formation of dangerous by-products. A good solvent system and natural resources were used to blend the biogenic nanoparticles. The incorporation of different biological components can be achieved by green manufacturing of metallic nanoparticles. On a large scale, plant extracts are important for the synthesis of metallic nanoparticles.[10]

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METHODOLOGY

In this study, we first analyzed studies that explain the biogenic synthesis of metallic nanoparticles and their anti-inflammatory actions.[11] The anti-inflammatory actions of different metal and metal oxide nanoparticles, such as gold,[12] zinc oxide, silver,[13] selenium and titanium dioxide,[14] are discussed in this review based on mechanistic studies. Preventing the expression of proinflammatory ROS and proinflammatory cytokine scavenging mechanisms is caused by the suppression of NF-B and COX-2 pathways by nanoparticles produced through green synthesis.[15] Stability and specific targeting are important factors for the efficacy of anti-inflammatory metabolic nanoparticles.

Inflammation

Inflammation is the body's reaction to injury or infection and involves the immune system's protective response to remove harmful stimuli and initiate the healing process. It typically involves swelling, redness, heat and pain in affected areas. Inflammation is a protective mechanism of the human body. These originate from different sources, such as infectious agents (bacteria and viruses), Radical Oxygen Species (ROS), physical agents and metabolic stress (hypoxia). Acute respiratory distress is an example of an unfavorable reaction that can result from COVID-19. Other manifestations linked to infection include a powerful cytokine storm, viral sepsis and uncontrolled systemic inflammation. Depending on the origin of the agent, inflammation can be categorized based on whether it is an endogenous abnormal reaction or exogenous agent. Inflammation can be either acute or acute, depending on its duration.[16] The two main host defense mechanisms that mediate these responses are the innate and adaptive immune responses. The innate immune response is the initial host reaction to any foreign substance, whereas the adaptive immune response involves granulocytes, phagocytes and other cells.[17] Acute inflammation is thought to be the body's defense against infection or other injuries, whereas chronic inflammation can coexist with pathological conditions even in the absence of an illness or injury, such as obesity.[16] Tissue damage, wounds and infections cannot heal without inflammatory reaction.[17]

Prolonged inflammation may harm the body. Damaged areas require more blood because tiny artery branches supply blood to the damaged area.[17] Inflammation lasts for a specific period, depending on how much harm the infection has caused. High concentrations of cytokines and coagulation factors stimulate the production of prostaglandins and acute phase proteins, such as C-reactive protein, by hepatocytes, affecting the CNS and resulting in discomfort, fatigue and fever, which are additional systemic effects that prolonged inflammation can have. Acute inflammation, which is less severe and localized and chronic inflammation, which develops in the pathogen that causes acute inflammation and is not eradicated or destroyed, are the two categories of inflammation. The sickness can then progress

Figure 1: Different types of metal nanoparticles.

into an autoimmune condition, where healthy, normal host cells are attacked. In certain cases, chronic inflammation can lead to malignancy and the onset of pathologies such as rheumatoid arthritis. The systemic production of TNF by macrophages is characteristic of both acute and chronic inflammation; TF subsequently triggers the central innate immune response, particularly in microglial cells. Acute inflammation increases the innate immune response and leads to the production of cytotoxic inflammatory mediators, which worsen neurodegeneration in cases where chronic neurodegenerative changes have already activated microglial cells. Inflammatory mediators hasten the development of inflammation by altering endothelial permeability, neutrophil extravasation, excess plasma containing complement components and antibodies at the site of inflammation. The NF-B and COX-2 pathways are the most significant systems involved in increasing inflammation.[18-25]

Skin Cancer

The most prevalent cancer globally is skin cancer and its incidence is rising without any signs of slowing down. UVB rays cause DNA damage via an inflammatory process and UVA rays play an important role in the carcinogenesis of skin stem cells. According to estimates from the American Cancer Society, there were skin cancer-related fatalities and more than 1.6 million newly reported cases of skin cancer in 2012. Skin cancer, which is not melanoma, accounts for the Majority of Newly Diagnosed Cases (NMSC). An overview of skin cancer types, pathophysiology, normal skin design, malignant melanoma, Squamous Cell Melanoma (SCC), Basal Cell Carcinoma (BCC), risk factors and comorbidities and physiological variables are given in this article.

Types of skin cancer

Skin cancer is typically classified into two main categories: malignant melanoma and non-malignant melanoma (NMSC),

which include BCC and SCC as the key subtypes. Because instances of BCC and SCC are not compelled to be reported to national cancer registries, it is impossible to estimate the true number of NMSC cases.[26,27] The general upward trend in NMSC incidence is between 3% and 8%.[28-31] Most cases of NMSC are treatable, especially if discovered early in malignant melanoma, which is the most severe and unpredictable form of skin cancer, specifically when detected at an advanced stage.

Anatomy of normal skin

Clinicians need to have a fundamental understanding of the skin to properly comprehend skin cancer. The layers of the epidermis, reticular dermis, papillary dermis and subcutaneous fat constitute the normal skin (Figure 2). Four major cell types and four sub-layers were used to define the epidermis. These sublayers show the various phases of maturation that the actively divided cells or keratinocytes undergo over the course of 30 days. Keratinocytes build the stratum basale, the lowest sublayer, pushing other cells upwards.

The stratum corneum, which is composed of many laminated and loosely linked keratinized cells, is the most superficial among these sublayers. It protects the layers underneath and acts as a vital barrier. The pigment melanin, which shields the skin from UV rays, is produced by melanocytes found in the stratum basale. The dermis lies beneath the epidermis and provides support and nourishment. In addition to specialized cells such as sebaceous glands (oil glands), hair follicles, eccrine glands (sweat glands) and apocrine glands (scent glands), the dermis comprises ground substances and fibers. Blood vessels and nerves that permit touch, temperature and pain perception are also found in the dermis. Fibroblasts in this area produce collagen and elastin. Each has a different thickness of subcutaneous tissue, which is made up of nerves, connective tissue, fat and larger blood vessels. It aids in the storage of fat, control of body and skin temperature and absorption of shock.

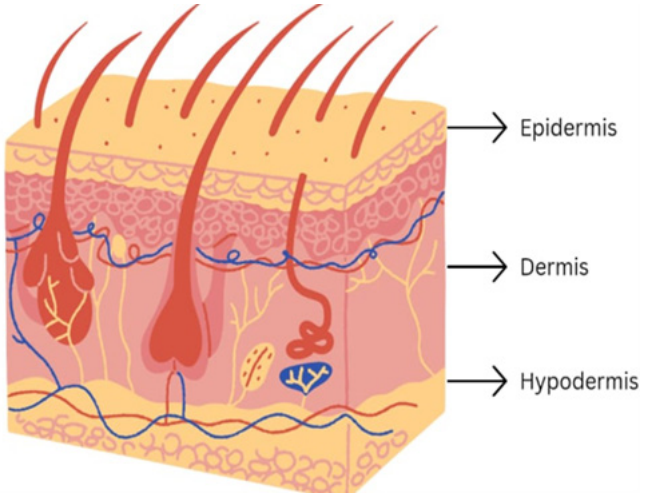

Figure 2: Anatomy of normal skin.

Skin cancer pathophysiology

Skin cancer has a multifactorial etiology. The primary causative factor for the formation of NMSC and malignant melanoma is Ultraviolet (UV) radiation from sunlight. UVA and UVB radiations are the principal subtypes of UV radiation. Compared to UVB rays, UVA can cause deeper cutaneous injuries, such as elastosis, because it can penetrate the skin more deeply. Sunburn and erythema are the main effects of UVB irradiation. UVR causes oxidative stress, immunosuppression, DNA damage, gene alterations and inflammatory reactions, all of which are critical for skin photoaging and development of skin cancer. UVB radiation directly harms the DNA. UVA photons cause indirect DNA damage, which is mediated by cellular membrane damage and production of free radicals. Research suggests a link between skin cancer growth and immunosuppression caused by UVR. UVR is a carcinogen that stimulates tumor growth. Tumorigenesis begins in addition to mutations in tumor suppressor genes. UVB rays damage DNA by inducing tumors and inflammatory responses and UV rays are a major contributor to skin stem cell carcinogenesis (Figure 3).

UV rays that reach the skin are mostly absorbed by the DNA of the epidermal keratinocytes. DNA is assumed to be the skin photoreceptor and research indicates that UVR-induced cyclobutane pyrimidine dimer synthesis is the first biochemical step leading to immune suppression. UVR-induced damage results in skin cancer owing to its intricate mechanics. UVR causes mutations in genes that suppress tumor p53, which participates in DNA repair or the death of cells with DNA damage. Consequently, p53 genes can no longer assist in DNA repair if their expression is altered. Skin cancer begins to proliferate as a result of this imbalance in apoptosis, which allows keratinocytes to divide uncontrollably. UVR-induced free radical damage is a significant cause of carcinogenesis and patients may be predisposed to skin cancer based on their genetic makeup and their capacity to metabolize free radicals. Glutathione S-transferase (GST) enzymes have antioxidant functions because of their ability to reduce the adverse effects of ROS. Skin cancer may be mediated in part by the Glutathione S-transferase Polymorphism (GSTP) enzyme, which is abundantly expressed in the dermis and epidermis of the skin. In animal experiments, deletion of the GSTP gene significantly enhanced vulnerability to the formation of skin tumors. Changes in the size, shape, color and texture of moles or other skin lesions, as well as the emergence of new skin growth, are significant clinical indicators of cutaneous cancer. A healthcare professional should be consulted if the alteration worsens over a month or more and alterations that occur over a few days are not cancerous.

Basal cell carcinoma

BCC accounts for over 80% of NMSC. Predisposing factors include intermittent UVR exposure and UVR exposure in the

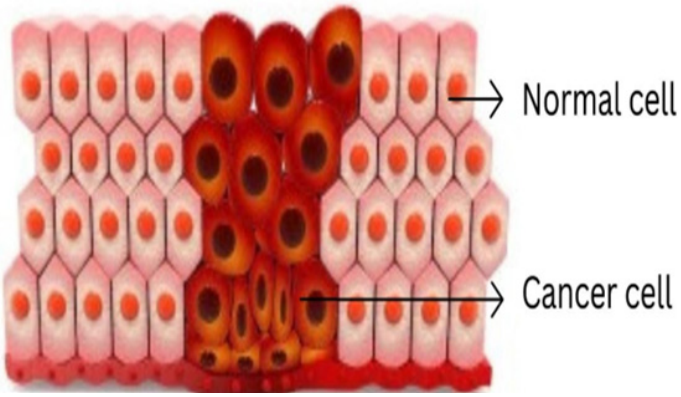

Figure 3: Cancer cell formation.

youth. The head and neck account for 80% of all BCC cases and clinical diagnosis is not difficult. BCC is a malignant tumor that originates from basal cells. In contrast to SCC, BCC typically manifests without antecedent lesions. BCC typically manifests as small papules that gradually enlarge over months or years. BCC also manifests as pearly bordered, shiny papules with a core ulcer and noticeable engorged vessels (telangiectasias) on the surface. Variants resembled scar-like, flat, yellowish-white patches. Repeated bleeding or crusting is a common occurrence. Ambiguous symptoms include sensitivity and itchiness. Clinically, BCC can be challenging to differentiate from benign growth and patients frequently confuse it for acne. BCC can occasionally involute and seem to heal, which could ease anxiety regarding the extent of the injury. Although metastasis is uncommon, local expansion can cause a great deal of harm.

Squamous cell carcinoma

Approximately 16% of skin cancer cases have SCC.[32] The incidence of SCC is highly correlated with cumulative lifetime sun exposure. SCC is a dermal invasion caused by a malignant tumor of the epidermal keratinocytes. There could be significant local tissue loss and advanced stages of metastasis through hematogenous or lymphatic dissemination are possible. Based on factors such as cancer location, underlying medical problems, cell differentiation and size, the predicted total metastasis rate ranges from 3% to 10%. SCC can manifest in a variety of ways clinically, but any lesions that do not heal after exposure to the sun should raise suspicions. Papules, nodules, plaques and smooth, erosive and hyperkeratotic (crusty) lesions are examples of clinical symptoms. The tumor may initially appear as a rough, scaly, erythematous patch or papule and may later develop into a nodule that occasionally has a plaque or warty surface. Tumor bleeding may occur without significant provocation. The tumor eventually becomes ulcerated and infiltrates the surrounding tissue. Most lesions may occasionally be located below the surrounding skin. When tiny SCC lesions are appropriately and promptly removed, prognosis is usually good. Noninvasive and invasive tumors are examples of SCC variations. The tumor first disperses locally to the skin and lymph nodes in the area and then moves to adjacent organs. SCC is more prone to spread and may require major surgery if it develops in scars, behind the ears, or along the vermilion border of the lip. Before diagnosis, almost one-third of lingual or mucosal malignancies spread.

Malignant melanoma

Although it only accounts for approximately 4% of cases, malignant melanoma is responsible for 65% of skin cancer-related deaths. Malignant melanoma can arise in any tissue that contains epidermal melanocytes, as this is where cancerous cells originate. Malignant melanoma develops as a result of several circumstances, including repression of the immune system of the skin, accelerated division of melanocyte cells, production of free radicals and damage to the DNA of melanocytes. Identification of the p16 melanoma susceptibility gene has provided insight into the genetic relationship between heredity and malignant melanoma. When p16 mutant cells are exposed to UVR, injured melanocytes proliferate unchecked. Numerous random mutations in p16 cause sporadic (non-familial) melanoma. The primary technique for the identification of malignant melanoma is eye inspection, as the majority of cases begin on the skin's surface. The clinical characteristics of malignant melanomas may vary widely. The ABCDE rule describes the clinical appearance and warning signals of most melanomas. The letter "A" and "B" denotes asymmetry (one half of the mole does not match the other half), "C" denotes diameter greater than 6 mm (roughly the size of a pencil) and "E" denotes evolution, elevation and/or enlargement of lesion. Some, but not all, of these features are present in many lesions, suggestive of melanoma. It has been observed that 2-8% of melanomas lack pigments.

Method for the synthesis of metallic nanoparticles

There are several methods to synthesize metallic nanoparticles, with biological and chemical methods being the most popular methods among them. The three most crucial variables for the synthesis of NPs are the eco-benign solvent, reducing agent and substance for stabilization. Chemical techniques use poisonous and hazardous chemicals and are expensive. To create nanoparticles the biosynthetic pathway uses plants and bacteria for biomedical applications. Fungi, algae, bacteria, plants and several other organisms can be used for nanoparticle synthesis. Phytochemicals are present in the extracts of plant parts such as roots, fruits, leaves and seeds, which act as stabilizing and reducing agents. Top-down and bottom-up approaches are two types of biological and chemical methods.

Top-down approach

Using this procedure, bulk materials are crushed, divided and milled to create nanoparticles using lithographic materials. The plant extract content, pH, temperature, incubation time and metal salt solution concentration all affect the stability, shape and size of the nanoparticles.

Bottom-up technique

In this method, small components such as molecules and atoms are self-assembled into new nanoparticle nuclei, which are then further developed into complete particles using various biological and chemical methods.

Metallic nanoparticle production by green synthesis

The concept of environmentally friendly green chemistry for the synthesis of metallic nanoparticles involves green synthesis. To produce clean and eco-friendly metallic nanoparticle uses, bacteria, fungi, actinomycetes and other species are used. Actinomycetes are good sources for producing nanoparticles with distinctive surface and size characteristics owing to their wide variety of secondary metabolites. Using either extracellular or intracellular methods, actinobacteria can produce metallic nanoparticles. The external production of actinomycetes is heavily reliant on polydispersity, which offers greater economic benefits than intracellular production. Fungi are widely used in the production of nanoparticles because they can produce a variety of nanoparticles with high efficiency. Organisms are green alternatives for creating nanoparticles with useful properties for the manufacturing of metallic nanoparticles. Plant extracts can be easily combined with a room-temperature metal salt solution to create nanoparticles. They require minimal maintenance and are frequently free.[33-35]

Heavy metals can be dangerous even at low concentrations. Environmental contamination can be handled by plants through increased potential for heavy metal detoxification and accumulation. The use of microbes or plant extracts for the synthesis of nanoparticles requires basic laboratory techniques to maintain microbial colonies. Plant-assisted nanoparticle synthesis has the advantage of significantly faster kinetics than other biosynthetic methods. The green synthesis of nanoparticles using plant extracts has more benefits than utilizing microorganisms because it is a one-step procedure that is nonpathogenic, affordable and generates a high number of metabolites, making it an economical and environmentally friendly method. For the formation of nanoparticles, the color of the solution begins to change after pressing and filtering, which may separate. The huge potential of the biological synthesis of nanoparticles for the safe and effective removal of poisons and contaminants from waste has attracted a lot of interest. It is an inexpensive and environmentally friendly synthesis process that does not require intermediate chemicals or specialized instruments.[36]

Characterization of nanoparticles

Size, surface area and dispersion are the three main characteristics of nanoparticles. In many applications, the homogeneity of the attributes is crucial. Numerous metallic nanoparticles created using environmentally friendly methods have been characterized using a range of techniques, including Raman spectroscopy, spectroscopy methods (UV, FT-IR), zeta sizer and zeta potential, transmission electron microscopy (SEM, Scanning Electron Microscopy) (SEM), Atomic Force Microscopy (AFM) and energy dispersion analysis of XRD (X-ray diffractometer).[37-40]

Silver nanoparticles

The biomedical industry is experiencing great success with AgNPs, primarily because of their use as antibacterial agents, medical equipment coatings and chemotherapeutic medication delivery systems. Although they have been well studied, additional work is needed to develop more bio-sustainable synthesis procedures and identify the mechanisms underlying their toxicological effects. AgNPs have applications in biotechnology, electronics, optics and environmental science. Green synthesis is one of the best techniques for producing silver nanoparticles is green synthesis.[41]

Zinc oxide nanoparticles

ZnO nanoparticles are extensively employed in a variety of industries because of their special chemical and physical characteristics. The rubber industry uses zinc oxide nanoparticles to improve the polymer toughness and resistance, as well as to provide wear resistance and anti-aging properties of rubber composites. Zinc oxide nanoparticles are widely employed in personal care products, including sunscreens and cosmetics, owing to their strong UV-absorbing capabilities. Because of their capacity to stimulate ROS production, additional characteristics, such as antibacterial and anticancer effects, have also been investigated. ZnO nanoparticles are also good drug carriers.[42]

Gold nanoparticles

Colloidal or clustered gold nanoparticles have a gold core surrounded by an inert, biocompatible component. The ability to manipulate the size, shape and surface characteristics of these particles is one of their advantages, owing to their synthetic plasticity. Additionally, its coating can be altered to affect its stability, environmental interactions and particle solubility. Gold nanoparticle-based PA imaging has shown potential for supporting treatment procedures by offering sequential monitoring of tumor functional features, such as modification of the tumor vasculature before, during and after therapeutic procedures.[43]

Titanium nanoparticles

It has been shown that bio-mediated titanium nanoparticles have anti-inflammatory, anti-fungal, anti-microbial and other biological properties. Their biological activity is enhanced by their photo-semiconductor properties, which cause microorganisms to disintegrate.

Selenium nanoparticles

Selenium is an interesting substance mixed with anti-inflammatory medications; it is a dietary component that plays a major role in

biological systems. A trace element, selenium, is required for the continued growth and well-being of the body. Elemental selenium has drawn much interest because it is the least toxic form of the element. Selenium nanoparticles are important for anticancer and antioxidant actions, according to current research.

The anti- inflammatory action of metallic nanoparticles

A localized physical condition known as inflammation occurs when an injury or infection causes a body component to become red, painful, or swollen. In the absence of an anti-inflammatory response, infections, wounds and tissue damage cannot heal. Over the last few decades, nanoparticles have gained attention as possible drugs to reduce inflammation. Because of their extensive surface area, nanoparticles are more effective at preventing the release of inflammatory mediators, such as cytokines and enzymes, that foster inflammation. Many metal and metal oxide nanoparticles, such as gold, zinc oxide, silver, selenium, copper, titanium dioxide, zinc peroxide, nickel and iron oxide, have been reported to have anti-inflammatory properties. When a pathogen injures or attacks tissue, an inflammatory response is triggered. Based on the pattern of damage, macrophages, killer cells and stem cells are drawn into the affected tissue to aid in the response. Macrophages are important for the regulation of inflammatory responses.[44,45]

Several anti-inflammatory strategies are commonly used by nanoparticles, including scavenging ROS, suppressing NF-B and blocking proinflammatory cytokines and COX-2 pathways. One of the most important mechanisms that nanoparticles use is the suppression of proinflammatory cytokines, because cytokines enhance immune responses.

The antifungal activity of metallic nanoparticles

In the last few years, fungal contamination and emerging fungal infections have taken center stage in global safety concerns. Using the food industry as an example, fungal contamination may seriously affect public health and food safety, in addition to causing product quality degradation and financial loss.[46] The inappropriate use of antibiotics has worsened this problem, leading to a significant increase in the number of drug-resistant fungi. Therefore, researchers worldwide are working to develop a variety of strategies to stop and manage fungal infections. These strategies include the use of predatory microorganisms, antimicrobial peptides and plant essential oils. Most of these techniques have been shown to function better against fungi in the laboratory, but they also have certain drawbacks, including high costs, unstable ingredients, interference with food components and unpredictable health hazards to humans. However, in the last several years, there has been a significant increase in nanotechnology research. Numerous studies have focused on the reactivity of novel types of nanoparticles with potential uses in food science, including food processing, preservation and nutritional supplementation.[47] Nanoparticles are the most promising alternative to conventional antibiotics for the management of harmful microorganisms.

Silver nanoparticles and graphene materials, as well as single and several walls of carbon nanotubes, are among the many nanoparticles that exhibit strong antibacterial activity. A variety of medical products and therapeutic medications currently use many nano-sized antibacterial agents that contain silver nanoparticles. Silver nanoparticle-based antifungal compounds may not be used in foods because of their high cost, ease of aggregation in tissues and biological adverse effects. Owing to the special characteristics of zinc oxide nanoparticles, they are currently considered to be the most effective antibacterial nanoscale agents. Zinc oxide in nanoscale form is more biocompatible than other nanoparticles. Current scientific data indicate that there is little to no risk to public health when using ZnO nanoparticles.

Antifungal action of zinc oxide nanoparticles

Zinc ions (Zn2+) are present in the medium and nanosized ZnO exhibits improved photocatalytic performance compared to inorganic photocatalysts. Thus, the two main processes by which ZnO oxide nanoparticles exhibit antifungal action are the production of ROS by photons and toxicity caused by the release of Zn2+.

ROS-dependent antifungal activity

Studies by Hirota *et al*. and Xu *et al.* indicated that the antibacterial properties of zinc oxide nanoparticles frequently depend on the presence of hydrogen peroxide or oxygen radicals on their surface via oxygen defect sites.[48] Particularly, when light is present, oxidative stress resulting from the production of ROS may be the main source of physiological effects.

Metal-containing particle-mediated antifungal effect

The exact mechanism of zinc oxide nanoparticles antifungal action in the absence of light is yet unknown. Zinc oxide and other metallic compounds, such as copper and silver oxide, are soluble, which could be the key factor in determining the physiochemical characteristics that affect the effectiveness of metal-containing nanoparticles as antimicrobials.[49] They can dissolve in aqueous solutions to some degree. Therefore, zinc oxide nanoparticles have a restricted source of zinc ions, which could be the cause of the fungitoxic effect of nanoparticles. Researchers have discovered that the toxicity of zinc ions produced by metal oxides causes antibiological action in dark environments.[50]

Anticancer activity of metallic nanoparticles

Cancer is one of the greatest global causes of death and a primary barrier to accelerating anticipation. It is acknowledged on a global scale that it is extremely difficult to handle. Despite

rapid advancements in medicine, certain types of cancer cannot be properly treated with current medications. The adverse effects of traditional treatment methods are one of the main problems associated with malignant growth treatment. One option to consider when investigating novel approaches to cancer treatment is the use of nanomaterials. Nanomaterials have been used as pharmaceutical carriers to increase the *in vivo* anticancer activity of medications for over 30 years. The earliest research, conducted in the 1970s, employed liposomes, which are nanoscale drug carriers that contain anticancer medications. In the clinical setting, metallic nanoparticles have demonstrated innovative uses for diagnosing and treating a range of cancerous growth and other retroviral disorders. Unique and modified bio-based nanoparticles were designed to address hazardous materials without interfering with normal cells. Gold was first utilized for pollution thousands of years in ancient China and India and its application has increased dramatically with the development of nanotechnology. AuNPs are strong candidates for immunotherapy and chemotherapy in the treatment of diseases because of their high surface-to-volume ratio, strength and low cytotoxicity. Nevertheless, many researchers worldwide are engaged in the field of phyto-nanotechnology.

Anticancer activity of zinc oxide nanoparticles

Being a broad bandgap semiconductor, ZnO nanoparticles may easily absorb UV light. This characteristic makes ZnO nanoparticles helpful for a wide range of applications, including biomedical, cosmetic and facial products. ZnO nanoparticles are currently the subject of extensive research because of their potential to prevent cancer. The biocompatibility of ZnO nanoparticles was excellent. Zinc is biocompatible because it is an important co-factor in several cellular processes and maintains cellular homeostasis. The supplied ZnO has the ability to readily biodegrade or participate in the body's active nutritional cycle. Compared to other nanoparticles, ZnO nanoparticles exhibit inherent selective cytotoxicity against malignant cells *in vitro*. One of the distinctive properties of ZnO nanoparticles' cytotoxicity towards cancer cells has been shown to be their capacity to cause oxidative stress in these cells. This characteristic is a result of the semiconducting nature of ZnO. Oxidative stress is induced by the generation of ROS, by ZnO and, when the cell's antioxidant capacity is surpassed, cell death occurs.

Antibacterial activity of metal nanoparticles

The ongoing rise in bacterial resistance has put the scientific community under pressure to develop new antibiotic treatments. Metal nanoparticles are among the most promising of these new antibiotic agents and a wide range of studies have demonstrated their potent antibacterial action. Even when new medications are introduced into the market, antibiotic-resistant bacteria typically emerge within a comparatively short amount of time. However, because nanoparticles target numerous biomolecules simultaneously, preventing the development of resistant strains, it is hypothesized that nanoparticles with antibacterial activity have the potential to minimize or eliminate the creation of increasingly resistant bacteria.

Antibacterial activity of zinc oxide nanoparticles

It has been demonstrated that ZnO nanoparticles change the cell membrane and induce ROS generation. Therefore, when coming into contact with ZnO oxide nanoparticles, bacterial cells absorb Zn+, which then suppresses the function of respiratory enzymes, creates ROS and releases free radicals, thus inducing oxidative stress. Bacterial membranes and DNA are irreversibly damaged by ROS, causing bacterial cells to die.

Mechanism of action of ZnO oxide nanoparticles

ROS are produced in response to ZnO NPs. ROS causes DNA damage, which causes the mitochondrial membrane to release apoptogenic components. Apoptogenic factors cause apoptosomes to develop, which, in turn, causes apoptosis. Primarily bound oxygen atoms on the ZnO surface give them a negative charge. A reduced pH causes protons from the surrounding air to be absorbed by the particle surface, resulting in a positively charged $ZnOH^{2+}$ surface. The particles are absorbed by the cell as a result of the interaction between these positive particles and the negative phospholipids on the outer membrane. Zn+ was released when the ZnO NPs broke down in the acidic lysosomes, preventing respiratory enzymes from carrying out their function and causing the cells to die.

Side effects of ZnO nanoparticles

Because of their high surface area and small size, ZnO nanoparticles have been linked in studies to a number of harmful consequences, including oxidative stress, genotoxicity and cytotoxicity. ZnO nanoparticle inhalation or dermal exposure has been linked to irritation of the respiratory tract, skin irritation and inflammation. Furthermore, the fact that they can cross biological barriers prompts worries about possible systemic effects when they build up in tissues and organs. Furthermore, ZnO nanoparticles have been linked to environmental toxicity, which has an impact on aquatic habitats and creatures. ZnO nanoparticles exhibit intriguing capabilities; nonetheless, due diligence in assessing possible side effects is necessary to guarantee the safe and responsible use of these particles in diverse applications.

Stability and storage of the nanoparticles

The performance and usability of nanoparticles are significantly influenced by their stability and storage. To keep nanoparticles stable and stop agglomeration or degradation over time, proper storage conditions are crucial. These parameters include temperature, humidity and radiation exposure. Nanoparticles are generally kept at regulated temperatures in dry, dark conditions

to reduce chemical reactions and maintain their physical characteristics. To further improve stability during storage, appropriate packing materials may also be used, such as inert gases or specialty coatings. To guarantee the long-term stability and effectiveness of nanoparticles for a variety of applications, from the biomedical to the environmental domains, regular monitoring of storage conditions and the use of suitable handling techniques are essential.

CONCLUSION

This work provides a thorough and concise overview of the anti-inflammatory, anti-cancer and anti-fungal effects of several metallic nanoparticles. The relationship between cells and nanoparticles has also been discussed. Commonly employed tactics for anti-inflammatory effects include scavenging Reactive Oxygen Species (ROS) and inhibiting the NF-B and cyclooxygenase-2 pathways. Inhibiting proinflammatory cytokines is one of the most significant strategies employed by nearly all nanoparticles, as they improve the immune response. Nanomaterials have been utilized as pharmaceutical carriers to increase the *in vivo* anticancer activity of drugs. Gold was first utilized for pollution and is a strong candidate for immunotherapy and chemotherapy in the treatment of diseases because of its strength, high surface-to-volume ratio and low cytotoxicity. Compared with other nanoparticles, ZnO nanoparticles are more biocompatible. Zinc oxide nanoparticles exert antifungal action through two main mechanisms: the formation of ROS by photons and the release of zinc oxide ions, which cause poisoning.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

NPs: Nanoparticles; **GST:** Glutathione S-transferase; **AgNPs:** Silver nanoparticles; **ZnO:** Zinc oxide; **AuNPs:** Gold nanoparticles; **MIC:** Minimum Inhibitory concentration; **FESEM:** Field emission scaning electronic microscope; **HRTEM:** High Resolution transmission electronic microscope; **ROS:** Reactive oxygen species; **DNA:** Deoxy ribose Nucleic acid; **SCC:** Squamous cell melanoma; **BCC:** Basal cell carcinoma; **NMSC:** Non-malignant melanoma.

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