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Review Article

A Comprehensive Review on the Nanoparticle Diversity and Synthesis Potential of Pomegranate Peel Extracts

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ABSTRACT

Pomegranate (*Punica granatum*) peel, which is usually thrown away as waste, actually contains many natural compounds that can easily convert metal salts into nanoparticles through green synthesis.¹ Among all nanoparticles, silver nanoparticles (AgNPs) made using pomegranate peel extract have been studied the most.⁵ Many studies report that these AgNPs form quickly, show clear UV-Vis absorption peaks, and have strong antimicrobial and antioxidant activities because of their stable, crystalline structure.⁵ Recent research also shows that pomegranate peel can be used to produce other nanoparticles like zinc oxide (ZnO), copper oxide (CuO), iron oxide (Fe₂O₃), and even gold nanoparticles (AuNPs).¹⁸ These nanoparticles have been confirmed through techniques such as UV-Vis spectroscopy, SEM, TEM, XRD, and FTIR, and they show promising activities in medicine, environmental purification, and antimicrobial applications.⁶ This review brings together all available information on different nanoparticles synthesized from pomegranate peel and compares their synthesis methods, percentage yields, size ranges, stability, and uses.⁹ The evidence clearly shows that pomegranate peel is not only useful for producing silver nanoparticles but is also a sustainable option for synthesizing many other types of nanoparticles.⁹ However, more comparative studies are needed to understand each nanoparticle type better and to improve their potential applications in biomedical and environmental fields.²⁰

INTRODUCTION

Nanotechnology is growing rapidly and is now used in healthcare, agriculture, food safety, and environmental protection.²⁰ Because chemical methods of making nanoparticles often involve

toxic substances, many researchers are shifting toward “green synthesis,” where plant extracts or natural materials are used to produce nanoparticles in an eco-friendly and safe way.⁶ Among plant wastes, pomegranate (*Punica granatum*) peel is one of the most useful materials because it

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contains a high amount of natural chemicals such as flavonoids, tannins, polyphenols and organic acids.²⁹ These compounds can naturally convert metal salts into stable nanoparticles without the need for harmful chemicals.⁷ As a result, pomegranate peel extract (PPE) has become a popular choice for producing silver nanoparticles (AgNPs).¹⁰ Several studies show that AgNPs synthesized from PPE exhibit strong antimicrobial, antioxidant, and anticancer properties due to their small size and stable structure.¹¹ In recent years, researchers have also started using pomegranate peel to synthesize other nanoparticles, such as zinc oxide (ZnO), copper oxide (CuO), iron oxide (Fe₂O₃), titanium dioxide (TiO₂), and gold nanoparticles (AuNPs).³ Each of these nanoparticles has unique characteristics, such as different size ranges, UV–Vis absorption peaks, and biological activities.²¹ However, a full comparison of all these nanoparticles produced from the same plant material (pomegranate peel) is still not widely available.⁹ Therefore, the purpose of this review is to bring together all the existing information on different nanoparticles synthesized from pomegranate peel. This paper compares their synthesis methods, percentage yields, characterization results, and biological applications.²⁰ By summarizing this information, the review shows that pomegranate peel is not only useful for silver nanoparticle synthesis but is a highly promising and sustainable material for producing many different types of nanoparticles through green technology.⁶

NANOTECHNOLOGY:

Nanoscience and nanotechnology have gained significant importance in pharmaceutical research and applications due to their wide-ranging potential.¹⁹ The term nanotechnology was first introduced in 1974 and refers to technologies that operate at the nanoscale and involve

multidisciplinary approaches.¹⁹ It mainly focuses on processes occurring at the molecular or nanometer level. Nanosizing offers several advantages in drug delivery, including rapid therapeutic action, reduced dose requirements, increased surface area, improved solubility, enhanced oral bioavailability, and reduced patient-to-patient variability.²⁰

Depending on the number of dimensions present at the nanoscale, nanostructures are classified into different forms. When only one dimension of a three-dimensional structure is in the nanoscale range, it is referred to as a quantum well. If two dimensions fall within the nanoscale, the structure is known as a quantum wire, while structures with all three dimensions in the nanoscale are called quantum dots.²⁰

The development of nanoparticles and nanomaterials is expanding rapidly, leading to innovative applications across various fields.¹⁹ In medicine, nanotechnology plays a crucial role in disease diagnosis, targeted drug delivery, and the development of effective treatments for numerous diseases and disorders.¹⁹ Overall, nanotechnology is considered a highly powerful and promising tool, offering immense potential for the design and development of novel pharmaceutical products, particularly in early disease detection, treatment, and prevention.²⁰

NANOPARTICLES:

Building Blocks of Nanotechnology:

Nanoparticles are defined as particles with at least one dimension in the size range of 1 to 100 nm.¹⁹ Due to their extremely small size, they exhibit unique physical, chemical, and biological properties that differ significantly from their bulk counterparts.²⁰ Nanoparticles display remarkable chemical diversity and can be composed of metals,



metal oxides, semiconductors, polymers, carbon-based materials, organic compounds, or biological molecules.^{6,7}

In addition to chemical diversity, nanoparticles also show wide morphological variation. They can exist in different shapes, including spheres, cylinders, disks, platelets, hollow structures, and tubular forms.^{6,7} These variations in composition and shape allow nanoparticles to be tailored for specific functions and applications.^{6,7}

Because of these distinctive characteristics, nanoparticles serve as the fundamental building blocks of nanotechnology.^{19,20} Their versatility enables their use in a wide range of applications, including drug delivery systems, diagnostic tools, imaging agents, environmental remediation, and antimicrobial formulations.^{19,20} The ability to design nanoparticles with controlled size, shape, and composition has made them essential components in the advancement of nanotechnology-based research and applications.^{19,20}

TYPES OF NANOPARTICLES:

Nanoparticles can be classified based on their composition, origin, and structure, each offering unique properties and applications, particularly in pharmaceuticals and biomedical research.

1. Metal Nanoparticles:

These are composed of pure metals such as silver (Ag), gold (Au), copper (Cu), and iron (Fe). They are well-known for their distinctive optical, electrical, and antimicrobial properties. Silver and gold nanoparticles, in particular, are widely applied in drug delivery, diagnostics, and imaging.^{1,10,11,12}

2. Metal Oxide Nanoparticles:

Metal oxide nanoparticles include zinc oxide (ZnO), titanium dioxide (TiO₂), iron oxide (Fe₂O₃/Fe₃O₄), and copper oxide (CuO).³ Their chemical stability and biocompatibility make them useful in pharmaceuticals, biosensors, cosmetics, and environmental applications.²

3. Polymeric Nanoparticles:

These nanoparticles are made from natural or synthetic polymers such as chitosan, alginate, PLGA, and PEG.^{6,7} They are mainly used in controlled and targeted drug delivery due to their biodegradability, safety, and ability to encapsulate therapeutic agents.

4. Lipid-Based Nanoparticles:

This group includes solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and liposomes. They enhance drug solubility, stability, and bioavailability, making them popular in pharmaceutical formulations.⁷

5. Carbon-Based Nanoparticles:

Carbon nanoparticles include carbon nanotubes, fullerenes, graphene, and carbon dots. Their exceptional mechanical strength, electrical conductivity, and large surface area make them suitable for drug delivery, biosensing, and tissue engineering.^{6,7}

6. Semiconductor Nanoparticles:

Semiconductor Nanoparticles also known as Quantum dots includes such as CdS, CdSe, and ZnS, with size-dependent optical properties. They are primarily used in bioimaging, diagnostics, and fluorescent labeling.^{6,7,8}

7. Ceramic Nanoparticles:



Ceramic nanoparticles, such as silica, alumina, and calcium phosphate, are chemically stable and biocompatible. They find applications in drug delivery, bone tissue engineering, and dental materials.^{6,7}

These nanoparticles are produced using plant extracts, microorganisms, or biomolecules. They are environmentally friendly, cost-effective, and biocompatible, and have shown promise in antimicrobial, antioxidant, and biomedical applications.^{6,7,8}

8. Biological / Green-Synthesized Nanoparticles:

TABLE 1: Examples of nanoparticles and its applications

Type of Nanoparticle	Examples	Major Applications
Metal Nanoparticles	Silver (Ag), Gold (Au), Copper (Cu), Iron (Fe)	Antimicrobial agents, drug delivery, imaging, diagnostics
Metal Oxide Nanoparticles	Zinc oxide (ZnO), Titanium dioxide (TiO ₂), Iron oxide (Fe ₃ O ₄), Copper oxide (CuO)	Drug delivery, biosensors, anticancer, cosmetics
Polymeric Nanoparticles	Chitosan NPs, PLGA NPs, Alginate NPs, PEGylated NPs	Controlled release, targeted drug delivery, gene delivery
Lipid-Based Nanoparticles	Liposomes, Solid Lipid Nanoparticles (SLNs), Nanostructured Lipid Carriers (NLCs)	Improved bioavailability, vaccine delivery, cancer therapy

SYNTHESIS AND CHARACTERIZATION OF PPE-MEDIATED NANOPARTICLES:

1. PPE-MAuNPs:

Gold nanoparticles (AuNPs) exhibit unique chemical and thermal properties, but in their native form, they are physiologically inactive. Due to their excellent biocompatibility, AuNPs have the potential to target cancer cells and exhibit antibacterial activity. PPE-mediated gold nanoparticles are synthesized using chloroauric acid reduced by aqueous pomegranate peel extract, where the phenolic compounds in the extract act as natural reducing agents. During the reaction, the

mixture changes from pale brown to dark brown, ultimately yielding a deep purple colloidal solution. The synthesized PPE-MAuNPs are characterized using dynamic light scattering (DLS) for particle size, Fourier Transform Infrared (FTIR) spectroscopy to identify functional groups, and Atomic Force Microscopy (AFM) to observe surface morphology. Transmission Electron Microscopy (TEM) further reveals that these nanoparticles are generally spherical and polydisperse. Due to their antibacterial properties, PPE-MAuNPs are considered promising candidates for medical and pharmaceutical applications.¹¹



Fig:1

2. PPE-MAgNPs:

Plant-based biosynthesis of silver nanoparticles (AgNPs) is preferred over microorganism-mediated synthesis, as it is simpler, safer, and allows better control over physicochemical and biological properties. For PPE-mediated AgNPs (PPE-MAgNPs), freshly prepared pomegranate peel extract is mixed with silver nitrate (AgNO_3) solution at room temperature. The reduction of silver ions causes a colour change from light yellow to brown and finally to dark brown.¹⁰

The nanoparticles are characterized for particle size distribution and zeta potential. Powder X-ray diffraction (XRD) using a $\text{Cu-K}\alpha$ source confirms the crystalline structure, while energy-dispersive X-ray (EDX) analysis determines the elemental composition and morphology. The green synthesis of PPE-MAgNPs provides a biocompatible and eco-friendly approach with potential applications in antibacterial and biomedical fields.

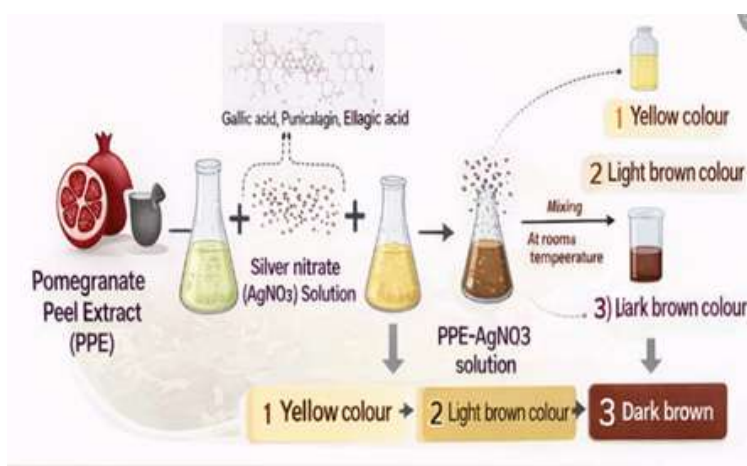


Fig:2

3. PPE-MZnONPs:

Zinc oxide nanoparticles (ZnO-NPs) are widely used in biomedical studies due to their favorable morphology, biocompatibility, and cytotoxic activity against cancer cells. PPE-mediated ZnO nanoparticles (PPE-MZnONPs) are synthesized by reducing zinc nitrate hexahydrate ($\text{Zn}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$) with phenolic compounds present in the pomegranate peel extract. The formation of PPE-MZnONPs is indicated by the appearance of a yellowish-white precipitate after

mixing the pinkish-brown extract with the colorless zinc solution.¹⁸

Characterization of PPE-MZnONPs includes UV-Vis spectroscopy, which shows a characteristic peak at 270 nm, and FTIR spectroscopy, confirming functional group interactions. Scanning Electron Microscopy (SEM) reveals spherical agglomerated particles with an average size of 80–100 nm. These nanoparticles demonstrate antibacterial potential, though further studies are needed to fully understand their mechanisms and toxicity.

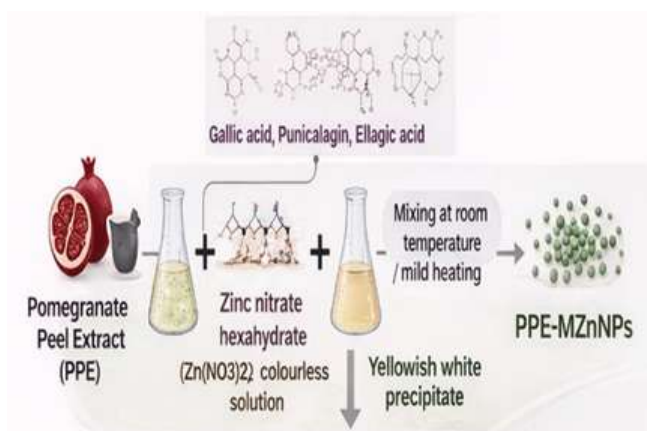


Fig:3

4. PPE-MCuNPs:

Copper nanoparticles (CuNPs) are widely recognized for their potent antibacterial activity against a variety of pathogenic microorganisms, making them valuable in clinical and biomedical applications. Copper oxide nanoparticles can penetrate microbial cell barriers, causing significant damage to nucleic acids and proteins, ultimately leading to bacterial cell death.

PPE-mediated copper nanoparticles (PPE-MCuNPs) are synthesized using pomegranate peel extract as a biological reducing and stabilizing agent, in combination with NaOH and copper chloride salts as precursors. The reaction mixture, when treated with ethanol, undergoes a colour change from brown to black, indicating the formation of CuNPs.

Characterization of PPE-MCuNPs involves several analytical techniques. UV-Visible spectroscopy confirms the surface plasmon resonance (SPR) characteristic of the nanoparticles. FTIR spectroscopy reveals interactions between CuNPs and proteins in the peel extract, with peaks at 1050 and 713 cm^{-1} indicating strong binding. Zeta potential measurements show a negative value of -56 mV , which remains stable over time, demonstrating that biomolecules in the extract act as effective stabilizing agents.

Due to their antioxidant, anti-inflammatory, and anti-apoptotic properties, PPE-MCuNPs exhibit dose-dependent therapeutic effects, including tumor suppression and potential anticancer activity. Further studies are needed to optimize dosage, minimize toxicity, and enhance their biomedical applications.^{22,23}



Fig:4

5. PPE-MPtNPs:

Platinum nanoparticles (PtNPs) are of considerable interest in biotechnology, nanomedicine, and pharmacology due to their large surface area and unique chemical properties. Biological synthesis of PtNPs can be achieved using pomegranate peel extract in a platinum chloride (PtCl_4) solution under ultrasonic conditions. A colour change from yellow to reddish-brown confirms the formation of PPE-mediated PtNPs (PPE-MPtNPs), and the final product is obtained by vacuum drying.

Characterization of the synthesized PPE-MPtNPs involves several analytical techniques. TEM

images reveal spherical particles ranging from 16 to 23 nm in size, while X-ray diffraction (XRD) patterns confirm the crystalline nature of the powder with predominant orientation planes. FTIR spectra show peaks at 3424 cm^{-1} and 3439 cm^{-1} , indicating the presence of phenolic groups from the peel extract, which are crucial for nanoparticle stability and reduction. The average size of the synthesized nanoparticles was found to be 20.12 nm with a spherical morphology. PPE-MPtNPs have demonstrated antibacterial, antioxidant, and anticancer properties, making them promising candidates for both industrial and biomedical applications.^{24,25}

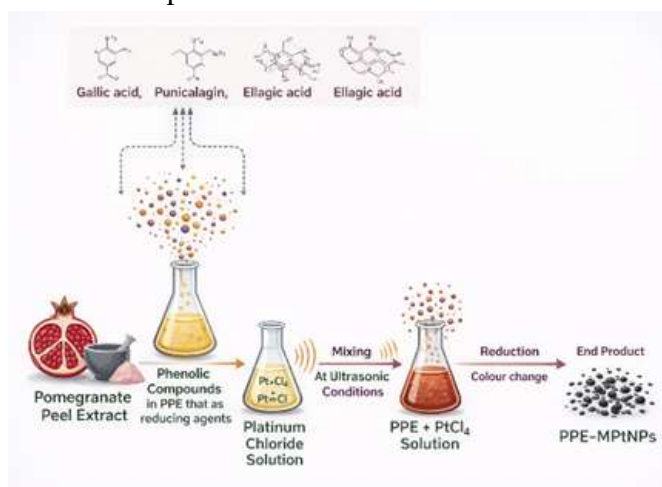


Fig:5

6. PPE-MFeNPs:

Iron nanoparticles (FeNPs) are notable for their high dispersion, magnetic susceptibility, and catalytic activity, which makes them suitable for cancer therapy and radiation oncology. Pomegranate peel extract acts as a reducing and stabilizing agent in the synthesis of FeNPs, enhancing their efficiency and biocompatibility. FeNPs are synthesized by mixing PPE with an Fe^{3+} ion solution, with additional reducing agents or surfactants to stabilize the nanoparticles. The formation of FeNPs is indicated by a colour change from brown to intense black, and the final

product is obtained through ethanol washing and vacuum drying. FTIR analysis extract, while cyclic voltammetry on a glassy carbon electrode demonstrates the electrochemical behaviour of PPE, producing a cathodic peak in the range of 120–400 mV. The progress of nanoparticle formation is monitored by a decrease in UV–Vis absorbance at 372 nm.

PPE-MFeNPs exhibit selective anticancer activity against cancer cells. However, further studies are needed to clarify their mechanism of action and assess their safety for biomedical applications.^{26,27}



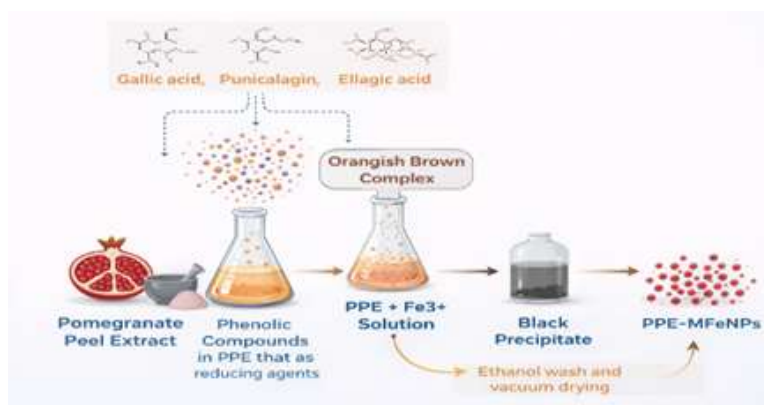


Fig:6

COMPARSION OF NANOPARTICLES:

TABLE:2 key characteristics of various nanoparticles

Nanoparticle	Precursor & Reducing Agent	Colour Change	Characterization Techniques	Particle Size / Morphology	Biomedical Applications
PPE-MAuNPs	Chloroauric acid (HAuCl ₄) + pomegranate peel extract	Pale brown → Dark brown → Deep purple	DLS, FTIR, AFM, TEM	Spherical, polydisperse	Antibacterial, anticancer, drug delivery
PPE-MAgNPs	Silver nitrate (AgNO ₃) + pomegranate peel extract	Light yellow → Brown → Dark brown	UV-Vis, XRD, EDX, Zeta potential	Polydisperse; ~10–80 nm	Antimicrobial, catalytic, biomedical applications
PPE-MZnONPs	Zinc nitrate hexahydrate + pomegranate peel extract	Colourless → Yellowish-white precipitate	UV-Vis, FTIR, SEM	Spherical, agglomerated; 80–100 nm	Antibacterial, anticancer, biomedical applications
PPE-MCuNPs	Copper chloride + NaOH + pomegranate peel extract	Brown → Black	UV-Vis, FTIR, Zeta potential	Spherical; zeta potential –56 mV	Antibacterial, antioxidant, anti-inflammatory, anticancer
PPE-MPtNPs	Platinum chloride (PtCl ₄) + pomegranate peel extract (ultrasonic)	Yellow → Reddish-brown	TEM, XRD, FTIR	Spherical; 16–23 nm, average 20.12 nm	Antibacterial, antioxidant, anticancer, diagnostics
PPE-MFeNPs	Fe ³⁺ ion solution + pomegranate peel extract + stabilizers	Brown → Intense black	UV-Vis, FTIR, Cyclic voltammetry	Spherical; size not specified	Anticancer, magnetic therapy, drug delivery

BIOLOGICAL FUNCTIONS:

Antimicrobial Activity:

The antimicrobial properties of pomegranate (*Punica granatum*) have been widely reported against a broad spectrum of bacteria. Most studies determine antibacterial activity using standard

methods such as minimum inhibitory concentration (MIC) assays or disc diffusion techniques. Methanol extracts of pomegranate exhibit enhanced antibacterial activity due to their high content of hydrolysable tannins, ellagic acid, and gallic acid.^{1,10,22}

Biosynthesized PPE-MCuNPs have demonstrated higher antimicrobial activity against various bacterial strains compared to standard antibiotics. This enhanced activity is attributed to the strong affinity of CuNPs for bacterial surface-active groups, resulting in potent bactericidal effects. Therefore, PPE-MCuNPs produced using pomegranate peel extract represent a promising alternative to conventional antibiotics.

Similarly, silver nanoparticles synthesized using pomegranate peel (PPE-MAgNPs) exhibit significant antibacterial activity. Techniques such as agar well diffusion reveal that PPE-MAgNPs are more effective against Gram-negative bacteria than Gram-positive bacteria due to their larger inhibition zones.^{12,30,31} The bactericidal effect is thought to arise from electrostatic interactions between the negatively charged bacterial cell walls and positively charged nanoparticles. PPE-MAgNPs also display synergistic activity with low doses of conventional antibiotics and anticandidal drugs.

While there is limited evidence regarding the antifungal activity of PPE-mediated nanoparticles, some studies suggest that pomegranate peel nanoparticles possess pesticidal properties that may be useful in agriculture for controlling plant pathogens. Specifically, PPE-derived AgNPs have been shown to effectively control early tomato blight caused by *Alternaria solani* at low concentrations of AgNO₃. Further in vitro and in vivo studies are needed to confirm their antifungal potential.^{32,33}

Anti-Diabetic Activity:

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia due to absolute or relative insulin deficiency, leading to end-organ damage affecting the retina, kidney, heart, nervous system, and blood vessels. According to the International Diabetes Federation (IDF), approximately 366 million people had diabetes in 2011, with projections rising to 552 million. Pomegranate, a natural antioxidant, has long been used as a hypoglycemic agent, and its nanoparticle formulations enhance its therapeutic efficacy. One mechanism involves inhibiting carbohydrate-digesting enzymes such as α -glucosidase and α -amylase to reduce hyperglycemia. Studies have shown that PPE-MAgNPs inhibit these enzymes in a dose-dependent manner.^{28,34,43}

Additionally, PPE-mediated nanoparticles have demonstrated protective effects on liver function in type 1 diabetic animal models. Histological studies indicate that treatment with PPE-MNPs reduces degenerative and necrotic changes in the liver, suggesting a moderate therapeutic impact against diabetes-induced hepatic abnormalities.^{35,36,37}

Anti-Cancer Activity:

Punica granatum exhibits considerable anticancer potential and has been reported to inhibit the growth of various cancer cell lines, including cervical (HeLa), bladder (T24), breast, prostate, colon, and thyroid cancer cells. Nanoparticle-based drug delivery systems provide enhanced delivery of therapeutic agents to cancerous tissues, improving diagnostic and treatment efficacy compared to conventional therapies.

Biosynthesized PPE-MAgNPs have shown the ability to reduce cancer cell viability and induce apoptosis. DNA fragmentation assays confirm that

PPE-MAgNPs trigger programmed cell death by fragmenting DNA, indicating their potential as anticancer agents. These findings suggest that aqueous pomegranate peel extract, especially in nanoparticle form, may serve as a promising therapeutic agent and drug delivery platform for various clinical applications.^{37,38,39}

Anti-Oxidant Activity:

Nanoparticles have been extensively used to enhance antioxidant activity by covalently linking, entrapping, or encapsulating antioxidants within various nanomaterials, improving their biocompatibility, controlled release, and targeted delivery.^{28,34} Encapsulation of pomegranate peel extract (PPE) within chitosan-coated nanoparticles using ionic gelation has proven to be an efficient method for protecting and delivering the delicate PPE compounds.^{44,47}

This protective coating allows PPE to function as a potent antioxidant, preventing oxidation and degradation of sensitive molecules. Furthermore, encapsulation of polyphenols in nanoparticles facilitates a gradual release when incorporated into biopolymer matrices, such as antimicrobial packaging materials. Studies have also shown that PPE exhibits strong antibacterial activity against various foodborne pathogens.^{15,16,17}

The integration of PPE into chitosan-based or zein-coated nanoparticle films creates materials with excellent antioxidant properties, suitable for applications in food preservation and medicine. PPE-mediated nanoparticles (PPE-MNPs) therefore hold significant potential both as therapeutic agents and as functional materials in the food industry.^{40,41,42}

Anti-Viral Activity:

The antiviral potential of pomegranate peels and their sonicated nanoparticles has been evaluated using *Datura* plants infected with tobacco mosaic virus (TMV). The number of local lesions on treated versus control plants served as a measure of antiviral efficacy.^{4,13,14}

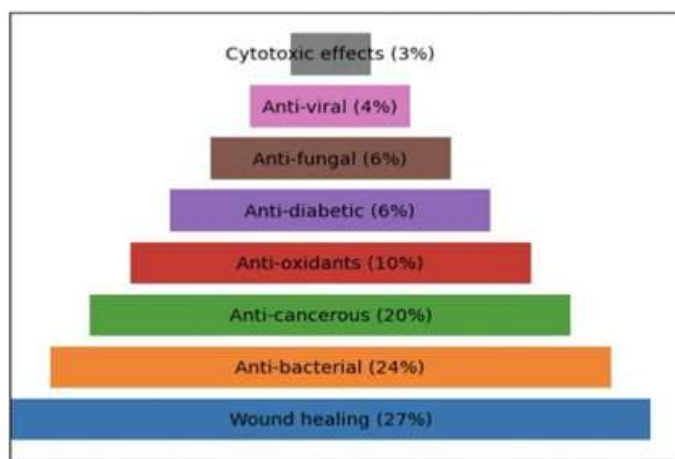
The antiviral effect is primarily attributed to the high polyphenol content of PPE, including compounds such as catechin, kaempferol, quercetin, and their glycosidic derivatives. These phenolic compounds inhibit viral replication and prevent infection, highlighting the potential of PPE-MNPs as safe and effective agents for controlling plant viruses.^{45,46}

Wound Healing:

Wound healing involves the restoration of tissue functionality through coordinated cellular and molecular processes. Natural compounds with anti-inflammatory, antibacterial, and cell-proliferative properties can significantly enhance this process. Key factors in wound healing include infection control, biofilm reduction, inflammation modulation, and the proliferation of fibroblasts and keratinocytes leading to re-epithelialization.^{43,44,45}

Nanoparticle-based formulations, particularly those containing silver nanoparticles (AgNPs), have demonstrated significant wound healing potential in vitro. PPE-MAgNPs showed enhanced wound closure after 7 days of treatment, and when combined with PPE sprays, they significantly accelerated healing over 14 days compared to conventional therapies. These findings suggest that PPE-MNPs can stimulate wound closure through controlled antibacterial and pro-inflammatory responses, offering a promising alternative to traditional wound care materials.^{48,49,50}





CURRENT LIMITATIONS:

Despite the promising biological activities and wide-ranging applications of pomegranate peel extract-mediated nanoparticles (PPE-MNPs), several limitations need to be addressed:

1. Limited In Vivo Studies

Most research on PPE-MNPs is restricted to in vitro studies. There is a lack of comprehensive in vivo studies to fully evaluate their pharmacokinetics, biodistribution, metabolism, and long-term safety. Without these studies, translating lab-scale results to clinical or commercial applications remains challenging.^{15,16}

2. Toxicity Concerns

Although PPE-MNPs are generally considered biocompatible, their cytotoxicity depends on factors such as size, shape, surface charge, and concentration. High doses or prolonged exposure may induce oxidative stress, inflammatory responses, or organ-specific toxicity, which are not fully understood.

3. Standardization of Synthesis

Green synthesis methods using pomegranate peel extract often yield nanoparticles with varying size,

shape, and stability due to differences in plant extract composition, solvent, temperature, pH, and reaction time. This lack of standardization makes reproducibility difficult and limits scalability.

4. Incomplete Mechanistic Understanding

The exact molecular mechanisms behind many biological activities, such as anticancer, antiviral, and wound healing effects, are still not fully elucidated. Understanding these mechanisms is crucial for optimizing their therapeutic potential and minimizing side effects.

5. Limited Comparative Studies

Few studies compare PPE-MNPs with chemically synthesized nanoparticles or conventional drugs. Comparative studies are necessary to validate their advantages in efficacy, stability, and safety.

6. Stability and Storage Issues

Some PPE-MNPs may aggregate or lose activity over time due to environmental factors such as light, temperature, and pH. Developing suitable storage and stabilization methods is essential for long-term applications.

7. Regulatory and Commercial Challenges



Nanoparticle-based products face stringent regulatory requirements for safety, quality, and efficacy. Limited clinical trials, lack of standardized protocols, and cost-intensive production restrict the commercialization of PPE-MNPs.^{1,6,7,19,20,26}

CONCLUSION:

Pomegranate peel extract-mediated nanoparticles (PPE-MNPs) represent a promising and sustainable approach for the synthesis of diverse nanomaterials, including silver, gold, zinc oxide, copper, platinum, and iron nanoparticles. These biogenic nanoparticles exhibit a wide range of biological activities, such as antimicrobial, anticancer, anti-diabetic, antioxidant, antiviral, and wound healing properties, highlighting their potential in biomedical, pharmaceutical, and food applications.

The green synthesis approach using PPE is eco-friendly, cost-effective, and leverages the abundant polyphenolic compounds in the peel to act as reducing and stabilizing agents. However, despite significant *in vitro* evidence of their efficacy, several challenges remain, including limited *in vivo* studies, toxicity concerns, lack of standardization, incomplete mechanistic understanding, and stability issues. Addressing these limitations through systematic research, comparative studies, and clinical trials will be crucial to fully harness the therapeutic potential of PPE-MNPs.

Overall, PPE-mediated nanoparticles offer a versatile platform for developing novel nanotherapeutics and functional materials. Their integration into medicine, agriculture, and food technology demonstrates that plant-derived nanoparticles could play a key role in advancing sustainable nanotechnology solutions for human health and industry.

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