

COMPARATIVE ANALYSIS OF *MUSA PARADISIACA* VERSUS *PUNICA GRANATUM* PEEL NANOPARTICLES FOR ANTICANCER EFFICACY**Adarsh Sushil Pandey¹ and Dnyanada Sadanand Ghadi²**^{1,2}Department of Biotechnology, Laxmi Charitable Trust's Sheth L.U. Jhaveri College of Arts and Sir M.V. College of Science and Commerce, India¹adarshpandey9867@gmail.com, ²dnyanadaghadi@gmail.com**ABSTRACT**

*The increasing demand for environmentally sustainable and biocompatible strategies in cancer nanomedicine has accelerated interest in biologically mediated nanoparticle fabrication. Agricultural wastes such as banana peel (*Musa paradisiaca*) and pomegranate peel (*Punica granatum*) have emerged as efficient phytochemical reservoirs capable of reducing and stabilizing metallic and metal-oxide nanoparticles.*

Comparative analysis indicates that polyphenol-rich pomegranate peel extracts typically generate smaller and more stable nanoparticles with enhanced cytotoxic potency, whereas banana peel extracts offer superior global availability, scalability, and economic feasibility. Despite promising in vitro and emerging in vivo evidence, reproducibility limitations, mechanistic ambiguity, and translational barriers remain significant.

By integrating phytochemical composition with nanomaterial performance metrics, this review identifies structure–activity correlations and outlines a translational roadmap for sustainable fruit-waste-derived nanotherapeutics. This work advances the field by bridging circular bioeconomy principles with next-generation oncological nanotechnology.

Keywords: green synthesis, banana peel, pomegranate peel, nanoparticles, anti-cancer activity.

1. INTRODUCTION

Nanotechnology has substantially reshaped cancer diagnosis and treatment by enabling targeted drug delivery, enhanced bioavailability, and reduced systemic toxicity (Peer et al., 2007; Wang et al., 2012; Rajeshkumar, 2020). Nanoparticles possess distinctive physicochemical attributes such as high surface-to-volume ratio, tunable particle size, and modifiable surface chemistry, which facilitate penetration of biological barriers and preferential accumulation in tumor tissues (Zhang et al., 2008; Wilhelm et al., 2016).

However, conventional nanoparticle synthesis approaches frequently involve chemical reduction, physical vapor deposition, or high-energy techniques that depend on hazardous reagents such as sodium borohydride, hydrazine, and toxic organic solvents (Iravani, 2011; Sharma et al., 2009). These processes generate environmentally harmful waste, pose occupational health risks, and may leave residual toxic contaminants on nanoparticle surfaces (Ahmed et al., 2016; Guo et al., 2023).

This contradiction between therapeutic potential and environmental burden has stimulated the development of green bio-mediated nanoparticle production strategies aligned with principles of environmental safety and biomedical compatibility (Mittal et al., 2013; Singh et al., 2018). Phytochemical-assisted reduction exploits biological systems, including microorganisms, enzymes, and plant materials, to reduce metal ions and stabilize nanoparticles under mild conditions without the use of toxic chemicals (Prasad et al., 2017; Rajeshkumar & Bharath, 2017).

2. LITERATURE REVIEW**2.1 Search Strategy**

This systematic review was conducted following PRISMA guidelines. Databases including PubMed, Scopus, Web of Science, and Google Scholar were searched for studies published between January 2020 and December 2024.

Search keywords included: *Musa paradisiaca* peel nanoparticles anticancer, *Punica granatum* peel green synthesis, Fruit peel nanomaterials cytotoxicity, Plant-mediated nanoparticles cancer, Boolean operators (AND/OR) refined the search.

2.2 Inclusion Criteria

Studies were included if they:

Synthesized nanoparticles using banana or pomegranate peel extracts

Reported physicochemical characterization (UV–VIS, TEM/SEM, XRD, FTIR, zeta potential)

Evaluated anticancer activity *in vitro* or *in vivo*

Provided quantitative cytotoxicity data (IC₅₀)

Were peer-reviewed and in English

2.3 Exclusion Criteria

Excluded studies included non-peel plant parts, lacked cytotoxic assessment, reviews or non-peer-reviewed reports, insufficient experimental detail.

2.4 Data Extraction

Data extracted included Nanoparticle composition, Particle size and morphology, Zeta potential, Cancer cell lines tested, mechanisms of action, biocompatibility findings.

Studies were categorized by peel type and nanoparticle composition for comparative evaluation.

Plant-Mediated Synthesis and Fruit Peel Waste

Plant extracts contain diverse biomolecules such as polyphenols, flavonoids, terpenoids, alkaloids, proteins, and organic acids that act simultaneously as reducing, capping, and stabilizing agents during nanoparticle synthesis (Mittal et al., 2013; Singh et al., 2018; Prasad et al., 2017). Agricultural and food wastes constitute an under-utilized but valuable resource for nanomaterial production, as global food processing generates millions of tons of organic residues annually (Lin et al., 2013; Mirabella et al., 2014). Fruit peels form a substantial fraction of this waste and are traditionally discarded or used for low-value applications (Zaini et al., 2022).

Musa paradisiaca (Banana) and *Punica granatum* (Pomegranate) peels are particularly noteworthy due to their worldwide availability and high concentrations of bioactive compounds (Emaga et al., 2007; Viuda-Martos et al., 2010; Zaini et al., 2022). Global banana production exceeds 100 million tons annually, with peels constituting approximately 30–40% of total fruit mass, thereby generating substantial agro-waste biomass (FAO, 2022). Banana peels are rich in dopamine derivatives, catecholamines, gallic acid, and complex carbohydrates that contribute to metal ion reduction and nanoparticle stabilization (Someya et al., 2002; Emaga et al., 2007). Pomegranate peels constitute nearly 40–50% of fruit mass and contain high levels of hydrolyzable tannins, particularly punicalagin and ellagitannins, which may represent up to 20% of peel dry weight (Viuda-Martos et al., 2010; Teniente-Sánchez et al., 2023).

These phytochemicals facilitate nanoparticle formation while simultaneously exhibiting intrinsic anticancer properties, potentially generating additional therapeutic effects (Ahmed et al., 2023; Rasool et al., 2024). Given the rapid expansion of literature in this area, systematic synthesis of existing evidence is necessary to identify trends and unresolved challenges (Hashem et al., 2023; Hussien et al., 2024). Studies were classified by: (1) peel type (banana or pomegranate), (2) nanoparticle composition (metallic: Ag, Au, Pt; metal oxide: ZnO, Fe₃O₄, CuO; bimetallic: ZnO–SeO; magnetic: NiFe₂O₄), (3) target cancer types (MCF-7, HeLa, A549, HCT-116, HepG2, PC-3, A431), and (4) cytotoxicity mechanisms (ROS generation, apoptosis induction, cell-cycle arrest, DNA damage, and mitochondrial dysfunction) (Ruangtong et al., 2020; Teniente-Sánchez et al., 2023).

2.5. Theoretical framework

2.5.1 *Musa paradisiaca* Peel Extract-Derived Nanoparticles

2.5.1 a) Phytochemical Profile and Biosynthesis

Musa paradisiaca (Banana) peel contains starch, lignin, cellulose, dopamine derivatives, catecholamines, and phenolic compounds such as gallic acid, catechin, and epicatechin (Emaga et al., 2007; Zaini et al., 2022). The total phenolic content typically ranges from 5 to 15 mg gallic acid equivalents per gram of dry weight (Zaini et al., 2022). These compounds promote metal ion reduction through hydroxyl and carbonyl functional groups (Mittal et al., 2013; Singh et al., 2018).

Ruangtong et al. (2020) synthesized zinc oxide nanosheets (ZnO) using banana peel extract, achieving particles with hexagonal wurtzite structure and sizes ranging from 27–89 nm depending on synthesis conditions. Nanoparticle morphology was controlled through extract concentration: higher precursor concentrations favored rod-like structures, while higher extract concentrations produced sheet-like structures. The synthesized ZnO nanosheets exhibited an energy band gap of approximately 3.00 eV and zeta potentials of -7.43 to -14.72 mV, indicating moderate stability (Ruangtong et al., 2020).

Silver nanoparticles (AgNPs) synthesized using banana peel extract are predominantly spherical with face-centered cubic structure (Alkan et al., 2022). Typical synthesis involves mixing aqueous peel extract with silver nitrate at room temperature or mild heating (40–60 °C), accompanied by a visible color change from pale yellow to dark brown (Mittal et al., 2013; Alkan et al., 2022). UV–visible spectroscopy confirms nanoparticle

formation through surface plasmon resonance peaks at 413–430 nm, while TEM reveals particle sizes of 20–70 nm (Alkan et al., 2022). Dynamic light scattering often reports larger hydrodynamic diameters (200–300 nm) due to hydration layers and phytochemical coating (Ruangtong et al., 2020).

2.5.1 b) Anti-Cancer Activity and Mechanisms

Banana peel-derived silver nanoparticles show dose-dependent cytotoxicity against MCF-7 breast cancer cells with IC_{50} values of 25–50 $\mu\text{g/mL}$ (Alkan et al., 2022). DNA damage has been demonstrated by Comet assay, while toxicity toward normal fibroblast cells remains comparatively low (Alkan et al., 2022). Mechanistically, banana peel-mediated nanoparticles induce oxidative stress by increasing intracellular ROS levels, including superoxide radicals and hydrogen peroxide (Trachootham et al., 2009; Moloney & Cotter, 2018). ROS disrupt mitochondrial membrane potential, promote cytochrome c release, and activate intrinsic apoptotic pathways involving caspase-3 and caspase-9 (Simon et al., 2000; Rasool et al., 2024). An elevated Bax/Bcl-2 ratio further favors apoptotic signaling (Teniente-Sánchez et al., 2023).

Selective cytotoxicity toward cancer cells has been attributed to higher basal ROS levels, altered membrane composition enhancing nanoparticle uptake, and metabolic vulnerabilities unique to malignant cells (Pelicano et al., 2004; Zenodo/IJABR, 2024). In addition to anticancer effects, banana peel-mediated nanoparticles exhibit antibacterial activity against Gram-positive (*Bacillus subtilis*, *Staphylococcus epidermidis*) and Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*) bacteria, with inhibition rates of 88–98% (Ruangtong et al., 2020).

2.5.2 Punica granatum Peel Extract-Derived Nanoparticles

2.5.2 a) Phytochemical Profile

Punica granatum (Pomegranate) peel is exceptionally rich in hydrolyzable tannins, with punicalagin representing 50–70% of total polyphenols (Viuda-Martos et al., 2010; Teniente-Sánchez et al., 2023). Additional constituents include punicalin, ellagic acid, gallic acid, caffeic acid, and flavonoids such as quercetin and catechin (Fischer et al., 2011; Teniente-Sánchez et al., 2023). Total phenolic content reaches 200–300 mg gallic acid equivalents per gram dry weight (Gil et al., 2000; Teniente-Sánchez et al., 2023).

Punicalagin suppresses NF- κ B signaling, induces cell-cycle arrest, and promotes apoptosis (Aggarwal & Shishodia, 2006; Teniente-Sánchez et al., 2023). Ellagic acid inhibits DNA topoisomerase and reduces cellular proliferation (Fischer et al., 2011). During nanoparticle synthesis, these bioactive molecules form a phytochemical corona around nanoparticles, generating potential therapeutic effects (Rasool et al., 2024).

2.5.2 b) Biosynthesis and Characterization

Dhahi et al. (2024) reported uniform spherical silver nanoparticles synthesized using pomegranate peel extract with diameters of 21.63–30.97 nm (SEM) and 7.20–14.80 nm (AFM). UV-visible spectra showed surface plasmon resonance at 360–460 nm, while EDX confirmed elemental silver at approximately 3 keV (Dhahi et al., 2024). XRD analysis demonstrated crystalline structure, and FTIR indicated biomolecular coating through C=O, O–H, and aromatic C=C vibrations (Dhahi et al., 2024).

Superior size control is attributed to high polyphenolic diversity and concentration, which provide effective capping and stabilization (Hashem et al., 2023; Rasool et al., 2024). Alkaline pH (9–11) and optimized extract-to-metal ratios yield smaller and more uniform particles, while room temperature promotes colloidal stability (Rasool et al., 2024). Beyond monometallic systems, pomegranate peel extract has enabled synthesis of bimetallic ZnO–SeO nanoparticles (Hashem et al., 2023) and magnetic NiFe_2O_4 nanoparticles with photocatalytic and biomedical applications. Nanoparticle colloidal stability is generally considered high when absolute zeta potential values exceed ± 30 mV, due to strong electrostatic repulsion. Values between ± 10 –20 mV indicate moderate stability and potential aggregation over time. (Koca et al., 2024).

2.5.2 c) Anti-Cancer Efficacy and Mechanisms

Pomegranate peel-mediated nanoparticles consistently exhibit higher cytotoxic potency than banana peel counterparts (Ahmed et al., 2023; Teniente-Sánchez et al., 2023). Growth inhibition has been reported in colon, prostate, liver, and breast cancer cell lines with IC_{50} values frequently below 30 $\mu\text{g/mL}$ (Ahmed et al., 2023).

Apoptosis involves Bax/Bcl-2 upregulation, mitochondrial permeabilization, cytochrome c release, and caspase-9 activation followed by caspase-3 and caspase-7 activation (Teniente-Sánchez et al., 2023; Rasool et al., 2024). Extrinsic apoptosis is mediated through Fas/FasL and TRAIL receptor signaling (Fulda & Debatin, 2006).

Cell-cycle arrest occurs primarily at the G1/S phase via p21 upregulation and cyclin D/E downregulation (Sherr, 1996; Kwon, 2012). Pomegranate compounds act as antioxidants in normal cells but as pro-oxidants in cancer cells, enhancing ROS-mediated cytotoxicity (Trachootham et al., 2009; Teniente-Sánchez et al., 2023). NF- κ B

suppression reduces survivin and XIAP expression, while inhibition of matrix metalloproteases 2 and 9 limits cancer cell migration (Aggarwal & Shishodia, 2006; Deryugina & Quigley, 2006).

2.5.2 d) Biocompatibility

Pomegranate peel-derived nanoparticles show no hemolysis up to 100 µg/mL and minimal toxicity toward normal cells (Dhahi et al., 2024). Antioxidant activity measured by DPPH and ABTS assays exceeds 90%, suggesting protection of normal tissues against oxidative stress (Teniente-Sánchez et al., 2023). Pomegranate peel produces nanoparticles with superior bioactivity, better size control, and enhanced stability due to 20-fold higher polyphenol content. However, banana peel excels in global availability and cost-effectiveness, making it more scalable for industrial production (**Table 1**). The choice should consider specific application requirements: pomegranate peel for high-potency therapeutics where efficacy is paramount, and banana peel for cost-effective large-scale production.

Table 1. Comparative analysis of banana and pomegranate peel synthesized nanoparticles.

Parameters	Banana Peel Extract	Pomegranate Peel Extract
Phytochemical richness (mg GAE/g)	5–15	200–300
Global availability (tons/year)	~100 million	~3 million
Particle size range (nm)	20–90	7–50
Typical IC ₅₀ (µg/mL)	25–75	10–40
Zeta potential (mV)	–7 to –15	–12 to –26
Selectivity index	2–5 fold	3–8 fold
Sustainability	Excellent	Excellent

7. DISCUSSION

3.1. Sustainable Nanotechnology Paradigm

Fruit peel-mediated synthesis exemplifies sustainable nanotechnology by converting agricultural waste into high-value biomedical materials (Lin et al., 2013; Mirabella et al., 2014). Unlike conventional synthesis producing chemically bare nanoparticle, peel mediated synthesis yields nanoparticles inherently coated with bioactive phytochemicals, reducing post-functionalization requirements (Mittal et al., 2013; Rasool et al., 2024). Banana processing alone generates approximately 30–40 million tons of peel waste annually, underscoring the potential for waste valorization (FAO, 2022).

3.2. Critical Limitations

Extraction protocol variability leads to inconsistent nanoparticle characteristics. Factors including peel source (cultivar, geographic origin, ripeness), extraction conditions (temperature, duration, solvent ratio), and storage conditions influence phytochemical profiles and nanoparticle properties (Borm et al., 2015). Hashem et al. (2023) noted significant batch-to-batch variations. Standardization through quality control, defined extraction protocols, and potentially purified phytochemical mixtures may be necessary for pharmaceutical production. Most studies remain limited to *in-vitro* analysis with insufficient *in-vivo* validation. While cell culture provides preliminary data, it cannot predict complex *in-vivo* behaviors including biodistribution, pharmacokinetics, immune responses, and off-target effects.

Few existing *in-vivo* studies primarily use xenograft models in immunocompromised mice, which poorly represent human tumor microenvironments (Wilhelm et al., 2016; Nel et al., 2013). Mechanistic explanations often rely on indirect assays (MTT viability, annexin V staining, caspase activity), leaving molecular pathways insufficiently explored. Modern approaches including transcriptomics, proteomics, and metabolomics could provide comprehensive understanding. RNA sequencing could identify differentially expressed genes, revealing unexpected pathways and treatment response biomarkers (Collins et al., 2015; Costa & Fadeel, 2016). Lack of standardized reporting on extract composition, nanoparticle yield, and long-term toxicity hinders progress. Many studies do not quantify phytochemical composition using HPLC or mass spectrometry, preventing correlation of specific compounds with properties or activities. Nanoparticle yields are rarely reported, hindering economic assessments. Long-term toxicity studies examining chronic exposure and organ accumulation are largely absent (Koca et al., 2024).

3.3. Synergistic Therapeutic Effects

The potential for synergistic effects from combining nanoparticle physical properties and bioactive phytochemical coating is particularly intriguing. Nanoparticles enhance cellular uptake through endocytosis, allowing efficient phytochemical delivery (Trachootham et al., 2009; Rasool et al., 2024). Once internalized, nanoparticles generate ROS through Fenton-like reactions while surface-bound phytochemicals modulate cellular signaling, potentially sensitizing cancer cells to oxidative stress (Moloney & Cotter, 2018). This multi-

pronged attack may explain why fruit peel-mediated nanoparticles often show superior activity compared to nanoparticles or extracts alone.

3.4 Translation Pathway

Clinical translation likely involves: standardization of synthesis protocols with quality control, comprehensive preclinical evaluation (pharmacokinetics, biodistribution, toxicology, efficacy in multiple animal models), formulation development for stable pharmaceutical products, manufacturing scale-up with GMP compliance, regulatory approval through investigational new drug applications, and clinical trials through Phase I (safety), Phase II (efficacy), and Phase III (comparative effectiveness) (Sousa et al., 2018; FDA, 2020). Initial applications may focus on topical uses (skin cancer treatment, wound healing) where systemic absorption is limited and regulatory requirements less stringent (Wilhelm et al., 2016). It should be noted that IC₅₀ values vary significantly across cell lines due to differences in metabolic activity, membrane composition, receptor expression, and intrinsic oxidative stress levels, thereby limiting direct cross-study comparability.

4. OPEN CHALLENGES AND FUTURE DIRECTIONS

Challenges to nanoparticle synthesis involves development of standardized extraction protocols with defined parameters and quality control using HPLC fingerprinting to ensure consistent phytochemical composition along with establishment of reference standards for major bioactive compounds. Adoption of comprehensive characterization protocols including mandatory reporting of size distribution (multiple methods), zeta potential, polydispersity index, yield percentage, and stability are critical in addition to implementation of ISO guidelines for nanomaterials ensuring cross-study comparability (Hashem et al., 2023; Koca et al., 2024). Omics approaches (transcriptomics, proteomics, metabolomics) should be integrated to identify global changes and reveal unexpected pathways.

Research should focus on development of real-time monitoring techniques using advanced microscopy, flow cytometry, and biosensors along with systematic investigation of structure-activity relationships comparing purified compounds versus crude extracts, identifying cellular targets of specific phytochemicals (Collins et al., 2015; Costa & Fadeel, 2016). Applications should expand beyond xenograft models to orthotopic tumors, patient-derived xenografts, and immunocompetent syngeneic models with investigation of pharmacokinetics, biodistribution using labeled nanoparticles, and long-term toxicity. Combination therapies needed to be explored with chemotherapy, radiation, or immunotherapy (Wilhelm et al., 2016; Sousa et al., 2018) in synergy with creation of stable pharmaceutical formulations with acceptable shelf life and patient-friendly administration routes.

Further studies are required for development of patient-specific formulations based on tumor molecular profiling, incorporation of imaging agents creating theranostic platforms enabling simultaneous diagnosis and therapy along with investigation of microbiome interactions influencing nanoparticle metabolism and bioactive metabolite production. Applications should be extended to environmental applications including carcinogen removal from water supplies and antimicrobial treatment of hospital wastewater. Also, future research should focus on interdisciplinary collaboration combining biotechnology, materials science, oncology, pharmaceutical sciences, and bioengineering (Echegaray-Ugarte et al., 2024).

5. CONCLUSION AND IMPLICATIONS

This systematic review demonstrates that fruit peel-mediated nanoparticle synthesis represents a scientifically credible and environmentally sustainable strategy in cancer nanomedicine. Comparative analysis indicates that *Punica granatum* peel extracts exhibit superior bioactivity, attributed to high polyphenolic content (200–300 mg GAE/g), resulting in enhanced nanoparticle stability, smaller particle size distributions, and lower IC₅₀ values across multiple cancer models. In contrast, *Musa paradisiaca* peel offers exceptional scalability, economic feasibility, and global availability, making it attractive for industrial translation.

Mechanistically, both systems promote redox-mediated cytotoxicity, mitochondrial dysfunction, apoptosis induction, and suppression of pro-survival signaling pathways. The intrinsic phytochemical corona surrounding these nanoparticles enhances therapeutic selectivity and may reduce systemic toxicity.

However, significant barriers remain, including variability in extraction protocols, lack of standardized reporting metrics, limited in vivo validation, and insufficient pharmacokinetic profiling. Addressing these gaps through harmonized methodologies, omics-driven mechanistic studies, and GMP-compliant scale-up will be essential for clinical translation.

Ultimately, the valorization of agricultural waste into functional nanotherapeutics represents a paradigm shift in sustainable oncology.

With rigorous standardization and translational validation, fruit peel-derived nanoparticles may evolve from experimental systems into clinically relevant, eco-conscious cancer treatment platforms.

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Ethical Statement

This study does not contain any studies with human or animal subjects performed by any of the authors.

Conflicts of Interest

The authors declare that they have no conflicts of interest to this work.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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