



GUAVA-DERIVED GREEN NANOPARTICLES: PHYTOCHEMICAL CONTRIBUTIONS, SYNTHESIS, BIOLOGICAL MECHANISMS, AND THERAPEUTIC PROSPECTS

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Abstract *Psidium guajava* L. (Guava) is one of the most commonly utilized plant species in the synthesis of metallic nanoparticles due to the presence of polyphenols, flavonoids, tannins, terpenoids, and ascorbic acid in its leaf, fruit, peel, seeds, and bark. This review paper presents an analysis of 53 published research articles (2016-2026) where guava is employed for the synthesis of silver, gold, zinc oxide, copper oxide, iron oxide, manganese oxide, cobalt oxide, titanium dioxide, palladium, and nickel oxide nanoparticles, along with their biological applications including antibacterial, antifungal, antioxidant, anticancer, antidiabetic, neuroprotection, and agricultural protection. The guava phytochemicals can act effectively as reducing and capping agents for a large variety of metal precursors, yielding nanoparticles that display broad bioactivities both in vitro and, in some cases, in vivo. However, the research in the area is still largely descriptive, carried out in individual laboratories with inconsistent characterization of nanoparticles and insufficient testing for normal cell and in vivo safety, as well as a lack of any direct evidence of ROS-mediated damage rather than just its presumed involvement. The guava-mediated nanoparticles remain thus a promising yet essentially pre-clinical approach, awaiting the standardization of extraction and synthesis, characterization, and safety studies.

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Introduction

Nanoparticles are materials whose at least one dimension is between 1 and 100 nm and have a surface area to volume ratio, quantum confinement, and surface reactivity that are entirely different from the properties shown by bulk materials and thus have high catalytic activity, adjustable optical properties, and the ability to act on biological membranes (Antunes Filho et al., 2025). Nanoparticles of metals (silver, gold, platinum, and palladium) as well as metal oxides (zinc oxide, copper oxide, iron oxide, titanium dioxide, cobalt oxide, manganese oxide, nickel oxide) and nanocomposites are among the candidates that have been tested for their use in antimicrobial, anticancer, biosensing, catalytic, and environmental remediation applications (Begum et al., 2025). Biological activity of such nanoparticles is not a characteristic of the metals themselves but is highly dependent on their size, shape, charge, crystallinity, agglomeration state, and the chemistry of the capping agent used during their synthesis (Biswal et al., 2020). Nanoparticles can be synthesized using physical methods (laser ablation, ball milling, and sputtering) or through chemical reduction with the aid of reducing agents like sodium borohydride, hydrazine, or citrates. These methods

give effective control over the size of the NPs, but they employ hazardous reagents, produce dangerous by-products, and may cause contamination of the surface, limiting the biocompatibility of the NPs (Govindasamy et al., 2022). The green synthesis of NPs employs plant extracts as reducing and capping agents rather than chemicals. Green synthesis is affordable, does not require aseptic conditions, and operates quickly at room temperature (Trieu et al., 2025). However, green does not mean sustainable or safe: a great number of green synthesis procedures still use organic solvents and create waste that is never compared to traditional synthesis in terms of life-cycle sustainability (Mazhar et al., 2025).

Psidium guajava is a tropical Myrtaceae plant that is inexpensive, fast-growing, and grown extensively in South Asia, Southeast Asia, Africa, and Latin America, thus making its leaves, fruits, peel, seeds, and bark easily accessible raw materials. Tissues of guava have a good amount of polyphenols, flavonoids (quercetin, myricetin, kaempferol), tannins, terpenoids and ascorbic acid; the very same functional groups (phenolic hydroxyl groups, carbonyl group, carboxylic acid groups, amine groups) responsible for the traditional uses of the plant as antidiarrhoeal, antioxidant, antimicrobial and hypoglycaemic agents are involved in metal ion chelation and colloidal

stability, making it possible to produce guava extract-based nanoparticles of a wide variety of classes ([Patiño-González et al., 2025](#)). However, despite the plethora of individual studies, there is a lack of systematic arrangement of the existing guava-nanoparticle research concerning the correlation between plant chemistry, nanoparticle synthesis conditions, and biological effects ([Singh et al., 2019](#)). This review provides an integrated summary of a selected body of 53 scientific publications obtained through PubMed literature searches that combine “*Psidium guajava*” with nanoparticle synthesis, characterization, and biological activity (2016-2026), with respect to (i) phytochemicals responsible for nanoparticle synthesis by guava, (ii) synthesis methods and classes of nanoparticles produced and characterized, (iii) the mechanistic rationale behind antimicrobial, antioxidant, and anticancer activities, and (iv) safety, reproducibility, and translational challenges. Considering the diversity of designs of the selected scientific studies, a narrative and structured review is used in place of a more formal PRISMA approach, whereby a claim based on one paper is clearly indicated.

Phytochemical Basis and Green Synthesis Mechanism

Tissues of guava have an extensive range of phytochemicals that have been identified time and again as functional components of green synthesis, including phenolic acids like gallic acid, chlorogenic acid; flavonoids such as quercetin, myricetin, kaempferol, and catechin derivatives; condensed tannins; terpenoids; ascorbic acid; and carbohydrates and organic acids. Metabolomic profiling of the *Psidium* genus using UPLC-QTOF-MS revealed such a complex array of phenolic/terpenoid-type metabolites, which is associated with their hepatoprotective activity in nanoliposomal formulation ([Saber et al., 2018](#)). Leaves form the tissue used most often, owing to its high polyphenolic content and ease of aqueous extraction; the vast majority of syntheses described here, including silver ([Baruah et al., 2025](#); [Islam et al., 2023](#); [Wang et al., 2018](#)), zinc oxide ([Boopathi et al., 2024](#); [Thejashwini et al., 2024](#)), cobalt oxide ([Govindasamy et al., 2022](#)) and manganese oxide ([Karthik et al., 2024](#)) nanoparticles used leaf extracts. Gold nanorods have been particularly synthesized from fruit peel ([Patiño-González et al., 2025](#)) and chitosan nanoparticle encapsulation of peel phytochemicals ([Udappusamy et al., 2025](#)); bark, root, and flower tissues are not represented, an evidence gap rather than an indication of inactivity. The type of extraction solvent, temperature, duration of contact, use of fresh/dried samples, and variety used differ from one study to another and are rarely completely disclosed ([Rani et al., 2024](#)).

The terms “green synthesis,” “plant-mediated synthesis,” and “phytofabrication” describe a common pathway: preparation of an aqueous extract,

mixing with a metal-salt precursor, reduction and nucleation of primary clusters, particle growth, capping by residual phytochemicals, and purification. The pathway (Fig. 1) is illustrated in virtually all papers discussing nanosilver preparation in the database, ranging from straightforward leaf-silver syntheses using aqueous solutions ([Islam et al., 2023](#); [Wang et al., 2018](#)) to more complex multi-component pathways involving, for example, dopamine/carboxymethyl cellulose-doped titanium ([Ganapathy et al., 2024](#)) or iron- and cobalt-doped zinc oxide produced by green co-precipitation ([Boopathi et al., 2024](#)). The Guava phytochemicals have been hypothesized to undertake four correlated roles that include binding with metal ions, electron donation, nucleation control, crystal growth control, and surface capping. The roles can be observed through ultraviolet-visible spectroscopy (surface plasmon resonance band at 430–455 nm for silver nanoparticles ([Suwan et al., 2019](#)); [Islam et al., 2023](#)) and FTIR spectra showing that plant-derived hydroxyl, carbonyl, and amine bands persist on the washed nanoparticle surface ([Karthik et al., 2024](#); [Wang et al., 2018](#)). Zeta potential of about -14 to -20 mV ([Hanna et al., 2026](#); [Karthik et al., 2024](#); [Wang et al., 2018](#)) signifies the presence of a negatively charged phytochemical corona with relatively poor electrostatic stability, which correlates with the need for extra polymer stabilization in certain formulations to prevent agglomeration ([Suwan et al., 2019](#)).

The database contains information on the unusual variety of nanoparticle types that have been synthesized from guava (Figure 2; Table 1): silver and silver-oxide nanoparticles are by far the most studied, spanning antioxidant/antimicrobial characterisation ([Wang et al., 2018](#)), antifungal micelle-coated formulations ([Suwan et al., 2019](#)), antibacterial coatings ([Islam et al., 2023](#)), in-vivo disease-resistance evaluation in fish ([Hafeez et al., 2023](#)), protein-corona interface studies ([Baruah et al., 2025](#)), neuroprotective evaluation ([Tagad et al., 2026](#)), and combined antibacterial/anticancer silver-oxide particles ([Yousef et al., 2025](#)). Optimized gold nanorods for antioxidant application from peeled sour guava extract ([Patiño-González et al., 2025](#)); ZnO, Cu/Cu-oxide, Fe-oxide, Mn-oxide, Co-oxide, Ni-oxide, TiO₂ and Pd nanoparticles have each been noted at least once about photocatalytic, antibacterial, and anticancer targets ([Govindasamy et al., 2022](#); [Hanna et al., 2026](#); [Karthikeyan et al., 2021](#); [Kaushal et al., 2023](#); [Madubuonu et al., 2019](#); [Sathiyavimal et al., 2020](#); [Singh et al., 2019](#); [Tan et al., 2026](#)). This range adds weight to the idea that the guava's phytochemistry constitutes a flexible reducing/capping system as opposed to a one-fits-all approach for any particular metal chemistry. pH, temperature, ratio of extracts to precursors, and processing after synthesis are the most consistently correlated factors with nanoparticle size and yields, such as the poloxamer-407-coated guava-based silver

nanoparticles that were shrunk to about 70nm and enhanced in their antifungal stability (Suwan et al., 2019), but very little research has been done on the variability from batch to batch or a life cycle

assessment, and so “eco-friendly” and “sustainable” should be understood as qualitative descriptions of avoided chemicals.

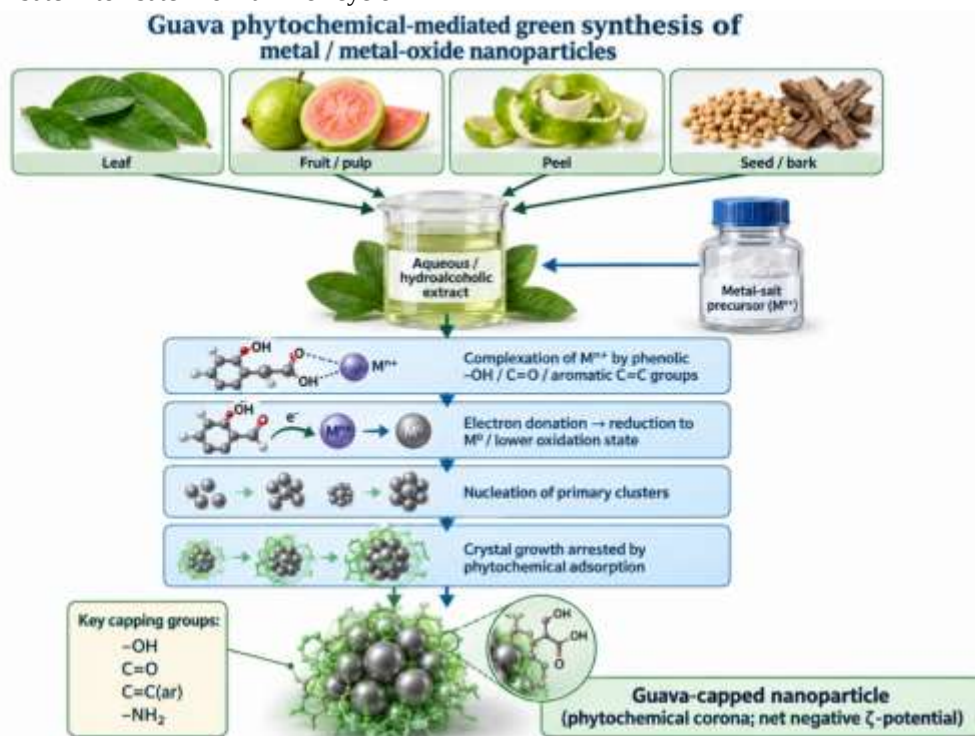


Figure 1 Schematic representation of the guava phytochemical-mediated green synthesis pathway for metal / metal-oxide nanoparticles, from plant-tissue extraction to the phytochemical-capped nanoparticle product

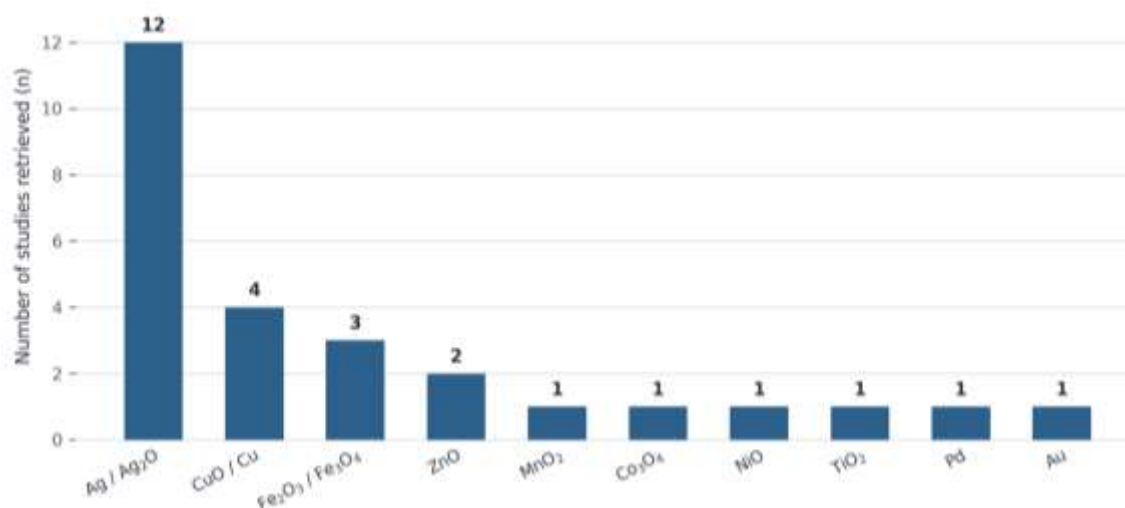


Figure 2 Number of nanoparticle synthesis papers for guava specifically obtained per nanoparticle category in the selected literature pool (comparative non-guava systems excluded)

Table 1 Master summation of guava-encouraged nanoparticle categories: feedstock used for preparation, primary biological functions, and main citations

Nanoparticle class	Guava tissue(s)	n	Principal biological activities	Key reference(s)
Ag / Ag ₂ O	Leaf (predominant)	12	Antibacterial, antifungal, antioxidant, anticancer, neuroprotective, disease resistance (fish), textile/mask coatings	(Tagad et al., 2026; Wang et al., 2018; Yousef et al., 2025)

CuO / Cu	Leaf	4	Photocatalytic dye degradation, antibacterial, anticancer, antibiotic photodegradation	(Karthikeyan et al., 2021 ; Kaushal et al., 2023 ; Singh et al., 2019)
Fe₂O₃ / Fe₃O₄	Leaf (moringa–guava composite in one study)	3	Antibacterial, photocatalytic, Cr(VI) remediation, comparative phase formation	(Begum et al., 2025 ; Madubuonu et al., 2019)
ZnO (± Fe/Co-doped)	Leaf	2	Microbicidal, antioxidant, antiproliferative, antibacterial, and anticancer (doped variants)	(Boopathi et al., 2024 ; Thejashwini et al., 2024)
MnO₂	Leaf	1	Photocatalytic activity; DNA/BSA-binding evidence	(Karthik et al., 2024)
Co₃O₄	Leaf	1	Photocatalytic, antibacterial, anticancer (MCF-7, HCT116)	(Govindasamy et al., 2022)
NiO (Ag-doped)	Leaf	1	Anticancer activity against glioma cells	(Tan et al., 2026)
TiO₂ (doped)	Leaf	1	Combined antimicrobial and anticancer activity	(Ganapathy et al., 2024)
Pd	Leaf	1	Apoptosis induction and metastasis suppression (osteosarcoma)	(Hanna et al., 2026)
Au	Peel (sour guava)	1	Antioxidant-optimised gold nanorods	(Patiño-González et al., 2025)

Characterisation and Physicochemical Properties

UV-Vis spectroscopy is always the first test conducted in almost all synthesis papers, while FTIR spectroscopy dominates the identification of the functional groups of guava responsible for interaction with nanoparticles ([Islam et al., 2023](#); [Karthik et al., 2024](#); [Wang et al., 2018](#)). X-ray diffraction confirms crystallinity and phase identity cubic silver (Islam et al., 2023), wurtzite/spinel oxide phases for zinc-, cobalt- and manganese-oxide systems ([Boopathi et al., 2024](#); [Govindasamy et al., 2022](#); [Karthik et al., 2024](#)) where TEM/SEM confirm the structure and size, which vary between 4.7 nm of palladium nanoparticles ([Hanna et al., 2026](#)) ranging from 20-35 nm for silver nanoparticles ([Wang et al., 2018](#)) and reaching ~56 nm for hydrodynamic diameter for silver doped nickel (Tan et al., 2026). Dynamic light scattering and zeta potential are only included in a part of the literature review, mainly the newer biomedical ones ([Tan et al., 2026](#); [Thejashwini et al., 2024](#)). Various methodological caveats arise. The “dry” size by TEM/SEM and the hydrodynamic diameter by DLS cannot be interchanged, while articles that include just one of them (the majority) are unable to characterise colloidal behaviour. IR shifts are in agreement with, although they do not necessarily confirm, covalent attachment of certain phytochemicals. The zeta potential determined in water is not indicative of performance in the presence of serum, something which was demonstrated through an experiment showing that the antibacterial performance of guava-capped silver nanoparticles was significantly inhibited due to the formation of the protein corona ([Baruah et al., 2025](#)). In the rare instances where the biological effects of physicochemical characteristics have been established, a smaller particle size and larger surface

area have been linked with higher antimicrobial and anticancer efficacy owing to increased ions and ROS production ([Boopathi et al., 2024](#)), and the formation of a phytochemical or protein corona can influence biological interactions that either increase or decrease the activity of the compound ([Baruah et al., 2025](#)).

Biological Activities and ROS-Mediated Mechanisms

Antimicrobial properties. In addition to plant-pathogenic organisms pertinent to agriculture, the corpus reports activity against Gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*, *Enterococcus faecalis*), Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *multidrug-resistant clinical isolates*), and fungi (*Candida albicans*, *Aspergillus niger*). The most popular assay format is disc/well diffusion; guava-derived silver nanoparticles inhibited *Alcaligenes faecalis* and *E. coli* at 100 µg/mL ([Wang et al., 2018](#)). However, minimum inhibitory/bactericidal concentrations, which enable more quantitative comparison, are reported less frequently: guava-derived silver-oxide nanoparticles demonstrated MIC values of 31.2–250 µg/mL against clinical isolates, with *Pseudomonas aeruginosa* and *Staphylococcus aureus* being the most sensitive ([Yousef et al., 2025](#)). Zinc oxide nanoparticles were assessed by MIC/MBC/MFC against five bacterial and fungal species ([Thejashwini et al., 2024](#)). The post-synthetic polymeric micelles coating provided greater antifungal activity due to reduced particle size to ~70 nm, without compromising the colloidal stability for 90 days ([Suwan et al., 2019](#)). In terms of mechanism, the field unites through a similar order: surface adherence, membrane destabilization, metal ion release, protein inhibition, ROS production, and DNA damage ([Liaqat et al., 2023](#)). In the case of iron- and

cobalt-doped zinc oxide produced by guava fruits, the combination of ROS production, particle size, oxygen vacancy concentration, and Zn^{2+} ion release was responsible for antibacterial and anticancer activity ([Boopathi et al., 2024](#)), and manganese dioxide nanoparticles from guava spectroscopically demonstrated their binding capacity to calf-thymus DNA and bovine serum albumin, providing the biomolecular interaction aspect ([Karthik et al., 2024](#)). Another unusual resistance-related example of the effects of protein corona formation is that it may decrease, not just modify, the efficacy of particles; a lysozyme corona decreased the antibacterial effectiveness of guava-polyphenol-coated silver nanoparticles against both Gram-positive and Gram-negative bacteria compared with the bare nanoparticle ([Baruah et al., 2025](#)), warning about not making a direct correlation between potency in-vitro without proteins and effectiveness in-vivo.

Antioxidant activity and redox behaviour. The most commonly used assays are DPPH and ABTS; guava-derived silver nanoparticles demonstrated IC_{50} values of $52.53 \pm 0.31 \mu\text{g/mL}$ (DPPH) and $55.10 \pm 0.29 \mu\text{g/mL}$ (ABTS $^{+}$) ([Wang et al., 2018](#)). In a rodent model, silver nanoparticles decreased lipid peroxidation and increased catalase activity, offering a biochemical rather than a cell-free readout ([Tagad et al., 2026](#)). Guava-mediated nanoparticles are often "antioxidant" in cell-free assays but "pro-oxidant" in cellular antimicrobial/anticancer assays. However, this conceptual tension is not always contradictory: intracellular ROS generation reflects metal-ion release, surface redox cycling, or mitochondrial dysfunction, while cell-free scavenging measures hydrogen-atom or electron donation to a stable synthetic radical. This balance is mainly unsettled study-by-study because very few research examine both objectives in the same system.

ROS Mechanisms. The ROS most frequently involved in these mechanisms include superoxide anion, hydrogen peroxide, and hydroxyl radicals. These can result from surface redox processes, metal ion release, and Fenton chemistry (particularly plausible for iron- and copper-containing particles ([Kaushal et al., 2023](#); [Madubuonu et al., 2019](#)), mitochondrial dysfunction, and photochemical activation. The same surface chemistry that drives photocatalytic dye degradation ([Govindasamy et al., 2022](#); [Karthik et al., 2024](#); [Kaushal et al., 2023](#)) is put forward to stimulate ROS-based biological activity. By using an explicitly structured hierarchy of evidence, which ranks direct measures of intracellular ROS levels and membrane potential at the top,

apoptotic protein expression profiles in the middle, and IC_{50} /viability values at the bottom, one finds that most of the literature here bases its claims on the latter two tiers.

Anticancer activity. Guava-based nanoparticles have been used to treat breast cancer (MCF-7, MDA-MB-231), colorectal cancer (HCT116), osteosarcoma (MG-63), and glioma cell lines. Most mechanistic details are reported for palladium nanoparticle formation by guava in osteosarcoma cells, causing S-phase cell cycle arrest and complete inhibition of colony formation (plating efficiency 0.9% versus controls), and a protein profile (increased Bax, caspase-3 and TP53; decreased Bcl-2, CDK2 and MMP-2/9) consistent with intrinsic apoptosis and suppressed invasive phenotype ([Hanna et al., 2026](#)). Guava peel-derived chitosan nanoparticles caused dose-dependent apoptosis in MDA-MB-231 cells ($IC_{50} = 50.13 \mu\text{g/mL}$), which was confirmed by molecular docking of a peel phytochemical against the anti-apoptotic protein Bcl-2 ([Udappusamy et al., 2025](#)). Similarly, guava-derived cobalt oxide nanoparticles decreased the viability of MCF-7 and HCT116 cells in a dose-dependent manner across 1.53–100 $\mu\text{g/mL}$ ([Govindasamy et al., 2022](#)). A selectivity ratio of slightly more than two is reported in the clearest example, which shows an IC_{20} of $73.93 \pm 0.49 \mu\text{g/mL}$ against HepG2 liver-cancer cells along with a less-toxic IC_{50} of $158.1 \pm 0.41 \mu\text{g/mL}$ against normal Vero cells ([Yousef et al., 2025](#)). The majority of other anticancer studies only report cancer-cell viability without a corresponding normal-cell comparator.

Integrated framework. Based on this synthesis of information, there is a reasonable causal pathway (Figure 3) between the genetic makeup of the guava, the type of plant material used, and the method of extraction, phytochemical composition, reduction/nucleation/capping kinetics, particle size, shape and surface properties, colloid behavior, ion release and biomolecular interactions, and the outcome as a result of the regulation of ROS production vs. cell membrane/mitochondrial damage. This relationship has not been described in one particular study; however, each connection has been explained in one study: the relationship between extraction parameter optimization and antioxidants' efficiency ([Nguyen et al., 2020](#); [Patiño-González et al., 2025](#)), particle size linked to antibacterial/anticancer potency ([Biswal et al., 2020](#); [Boopathi et al., 2024](#)), and protein-corona formation linked to reduced efficacy ([Baruah et al., 2025](#)).

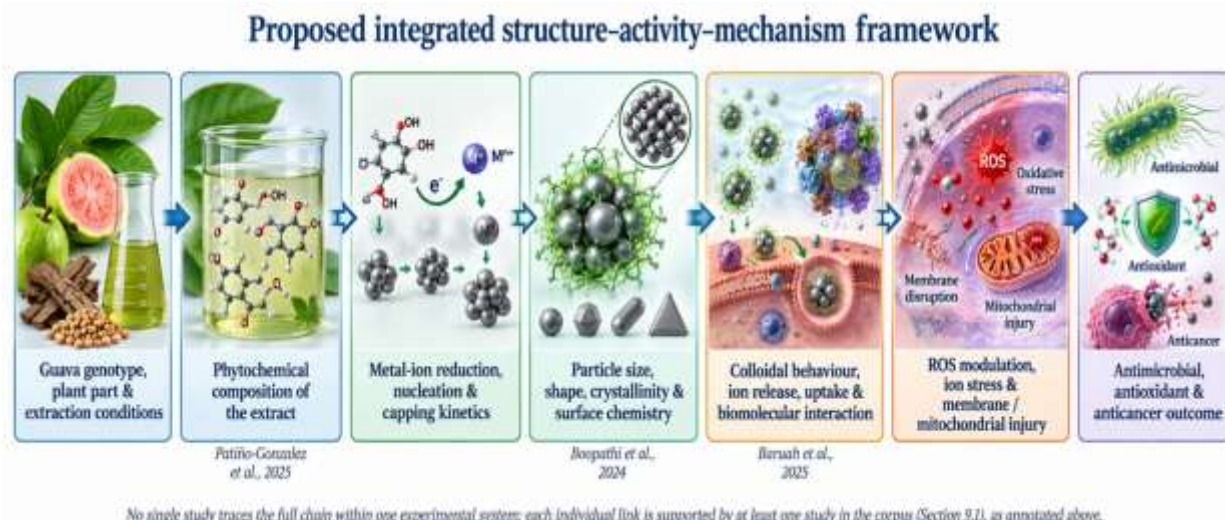


Figure 3 Proposed integrated structure–activity–mechanism framework linking guava genotype and extraction conditions through to biological outcome; each link is supported by at least one study in the corpus, though no single study traces the full chain

Table 2 Selected quantitative bioactivity benchmarks for guava-mediated nanoparticles

Nanoparticle	Assay/endpoint	Result	Reference
Ag	DPPH radical scavenging (IC ₅₀)	52.53 ± 0.31 µg/mL	(Wang et al., 2018)
Ag	ABTS• ⁺ radical scavenging (IC ₅₀)	55.10 ± 0.29 µg/mL	(Wang et al., 2018)
Ag ₂ O	MIC, clinical bacterial isolates	31.2–250 µg/mL	(Yousef et al., 2025)
Ag ₂ O	IC ₅₀ , HepG2 vs. normal Vero cells (selectivity)	73.93 vs. 158.1 µg/mL	(Yousef et al., 2025)
Pd	Colony-forming (plating efficiency)	0.9% vs. untreated control	(Hanna et al., 2026)
Co ₃ O ₄	Viability, MCF-7 / HCT116 (1.53–100 µg/mL)	90% to 52% / 82% to 37%	(Govindasamy et al., 2022)
Chitosan-NP (peel)	IC ₅₀ , MDA-MB-231	50.13 µg/mL	(Udappusamy et al., 2025)
Ag (micelle-coated)	Colloidal stability	Stable ≥ 90 days	(Suwan et al., 2019)

Therapeutic Prospects and Comparative Standing

The most obvious short-term use for the nanoparticles would be the functionalization of antimicrobial surfaces and textiles, specifically using the guava-extracted silver nanoparticles as coatings for cotton fabrics and N95 respirators (Rasheed et al., 2023), and screened against multidrug-resistant pathogens on functionalized cotton, along with a cytotoxicity study (Antunes Filho et al., 2025). Wound dressings or topical drugs have not been developed as of now, which is a translation gap in relation to the existing bacterial evidence. The cancer evidence supports palladium- and guava-mediated chitosan-encapsulated peel extract along with cobalt oxide and silver-doped nickel oxide compounds as preclinical candidates for osteosarcoma (Al-Qasmi et al., 2022), triple-negative breast cancer (Udappusamy et al., 2025), and glioma (Tan et al., 2026); there is no report of testing any of the agents in combination with the conventional cancer drug. Apart from antimicrobial and anticancer activities, there is also evidence on the use of SLN in preserving guava fruit after harvest (García-Betanzos et al., 2017), hepatoprotective

nano-liposomal delivery (Saber et al., 2018), antidiabetic application of silver nanoparticles (Nagaraja et al., 2022), neuroprotective effects in a scopolamine-induced Alzheimer's model, evidenced by improved spontaneous alternation and Morris Water Maze performance (Tagad et al., 2026), disease-resistance enhancement in aquaculture (Hafeez et al., 2023), and plant-protection applications against chilli fruit-rot disease (Mazhar et al., 2025) and organophosphorus pesticide hazards (Albadawi et al., 2024). The development of these constructs into a clinically useful application would need to have a specification for batch consistency, sterility/endotoxin screening, a complete nonclinical safety package, and classification for regulatory purposes, along with manufacturing control processes. None of these needs is met in any of the studies reviewed in the literature. The two in vivo studies with the highest translational value for safety information are those relating to fish disease resistance (Anwaar et al., 2024) and the rodent neuroprotection model (Carvalho-Silva et al., 2025); such studies have been encouraging but are still

preliminary. Comparisons, direct and matched, between the present and other plant-based methods for preparing nanoparticles have been done on only three occasions: comparing guava to *Momordica charantia* silver nanoparticles as an antifungal agent due to dissimilar capping phytochemicals (Nguyen et al., 2020); guava versus Nanoparticles of *Citrullus colocynthis* and Silver as Fish Disease Resistance Factors without any Plant Dominating (Hafeez et al., 2023); and guava versus moringa for iron-oxide phase formation (Begum et al., 2025). With this limited comparative evidence, guava ought to be seen as just one of many potential phytosynthesis substrates rather than a proven superior choice to others.

Research Gaps, Challenges and Future Directions

There are eight key evidentiary gaps that constrain the translatability of the research on guavas (Table 3). There is no study that examines guava's individual components and tests their effectiveness in reducing and capping, which means that guava-mediated treatments cannot yet be formulated. The extraction solvent, temperature, condition of the plant material, type of cultivar, and geographical source differ between studies, often leaving researchers unable to ascertain whether any differences in size, yield, or biological activity were truly due to chemistry or to experimental variability. Comprehensive characterization involving both UV–Vis, FTIR, XRD, SEM/TEM, DLS and zeta potential is performed by a subset of studies, while characterization in serum-containing environments has proven to be important based on the lysozyme corona observation is even more uncommon. The ROS-induced mechanism can only be inferred indirectly via viability or protein expression experiments rather than being directly measured via intracellular techniques or mitochondrial membrane potential. Matched normal-cell and in vivo safety data are scarce: only one study

reports a directly matched cancer-versus-normal-cell IC₅₀ comparison. In vivo tests are confined to only two biological systems: a fish infection model and a rodent neurodegeneration model, with a near-total lack of pharmacokinetic and biodistribution studies. There is not even one study about process design at reactor scale, batch-to-batch variation, or lifecycle assessment, so that “environmentally friendly” and “sustainable” can only be qualitative terms. Direct comparisons between guavas and other plant sources for nanoparticles are made in three cases only, too few to prove its superiority.

These gaps exist on an evidentiary level, with the underlying reasons for their existence being threefold. Firstly, there is the issue of standardization because the cultivar, extraction method, and post-synthesis purification methods are rarely ever fully reported and never benchmarked between labs; there is no motivation for each group to standardize, which is perhaps the only way forward in this case. Scaling up and sustainability issues: The supply of guava leaves and peels is seasonal, and there is no scale-up process or waste management strategy available for any of the protocols in the body of work; scaling up beyond bench-top level is impossible without a pilot-scale process development. Translational and regulatory pathway: Due to a lack of data on pharmacokinetics and safety, no formulation in the corpus has been put on a regulatory pathway; the achievement of this goal will be through, first, standardisation of potency and selectivity testing, second, in vivo testing for efficacy and toxicology using additional animal models other than the two existing models, and finally, safety package development. When considered jointly rather than individually, these three obstacles comprise the practical challenge that lies between the potentially promising preclinical data described above and an actually useful guava nanoparticle system.

Table 3 The eight research gaps identified in this review

Research gap	Missing evidence	Why it matters
Active phytochemical identity	No isolation / independent testing of single constituents	“Guava-mediated” is not yet a defined, reproducible chemical formulation
Non-standardised protocols	Extraction / cultivar / plant-part conditions rarely reported in full	Cannot separate genuine chemistry from methodological variation
Incomplete characterisation	Full UV–Vis + FTIR + XRD + SEM/TEM + DLS + zeta rare; media-matched rarer still	Reported potency not reliably comparable or extrapolable to in vivo
ROS mechanism inferred	Direct intracellular ROS / mitochondrial-potential assays scarce	Magnitude and kinetics of ROS-driven bioactivity remain unknown
Missing selectivity data	Only one matched cancer-vs-normal-cell IC ₅₀ comparison	Therapeutic index cannot be estimated for most formulations
Sparse in vivo / PK data	Only two in-vivo models; no ADME or biodistribution data	Largest single gap before any translational pathway
No scale-up / life-cycle data	No reactor-scale design or formal life-cycle assessment	“Eco-friendly” / “sustainable” claims remain qualitative
Few head-to-head comparisons	Only three matched comparisons with other plant sources	Insufficient evidence that guava is superior, rather than simply capable

Conclusions

Psidium guajava is a real all-round plant that can be used in the green preparation of metallic/metal oxide

nanoparticles: its leaf, fruit and peel tissues have been used to fabricate silver, gold, zinc oxide, copper oxide, iron oxide, manganese oxide, cobalt oxide, nickel oxide, titanium dioxide and palladium nanoparticle systems, and its phenolic, flavonoid and tannin content provides a mechanistically plausible basis for metal-ion reduction, nucleation control and colloidal stabilisation supported across the corpus by consistent UV-visible and FTIR evidence. Of the many interactions between phytochemicals and nanoparticles examined herein, the most validated ones include the reducing and capping properties of guava phenolics and the influence of particle size, surface charge, and formation of biomolecular corona on biological activities. The most compelling biological effects in terms of mechanism of action are the antibacterial effect of silver nanoparticles synthesized from guava and the apoptotic anticancer effect of palladium nanoparticles synthesized using guava in osteosarcoma cells, as well as chitosan-coated peel extract in triple-negative breast cancer cells, whereas the antioxidant, antidiabetic, and neuroprotective effects are compelling but based on fewer studies. What really stops the application in therapy is the association between non-standardised synthesis and characterisation, the lack of matching data from normal cells and in vivo tests, a lack of all pharmacokinetics and biodistribution data, and finally no reproducibility, upscaling, and life cycle assessment at all. Collectively, the evidence available on green nanoparticles through the use of guavas appears to be highly encouraging in terms of its biological scope and scientific rationale, although it is mostly preclinical and heterogeneous in nature, and currently not quite ready for clinical/translation purposes.

References

- Al-Qasbi, N., Al-Gethami, W., Alhashmialameer, D., Ismail, S. H., & Sadek, A. H. (2022). Evaluation of Green-Synthesized Cuprospinel Nanoparticles as a Nanosensor for Detection of Low-Concentration Cd(II) Ion in the Aqueous Solutions by the Quartz Crystal Microbalance Method. *Materials*, **15**(18), 6240. <https://doi.org/10.3390/ma15186240>
- Albadawi, E. A., Musa, E. N. A., Ghaban, H. M., Ebrahim, N. A., Albadrani, M. S., & El-Tokhy, A. I. (2024). Eco-friendly green synthesis of silver nanoparticles from guajava leaves extract for controlling organophosphorus pesticides hazards, characterization, and in-vivo toxicity assessment. *BMC Pharmacology and Toxicology*, **25**(1), 98. <https://doi.org/10.1186/s40360-024-00826-7>
- Antunes Filho, S., Almeida, C. M., Romanos, M. T. V., Pizzorno Backx, B., & Regina Bonelli, R. (2025). Green synthesis of silver nanoparticles for functional cotton fabrics: antimicrobial efficacy against multidrug-resistant bacteria and cytotoxicity evaluation. *Artificial Cells, Nanomedicine, and Biotechnology*, **53**(1), 153–165. <https://doi.org/10.1080/21691401.2025.2485115>
- Anwaar, S., Ijaz, D. E., Anwar, T., Qureshi, H., Nazish, M., Alrefaei, A. F., Almutairi, M. H., & Alharbi, S. N. (2024). Boosting *Solanum tuberosum* resistance to *Alternaria solani* through green synthesized ferric oxide Fe₂O₃ nanoparticles. *Scientific Reports*, **14**(1), 2375. <https://doi.org/10.1038/s41598-024-52704-1>
- Baruah, K., Singh, A. K., Lyndem, S., Kumari, K., Jha, A. N., & Singha Roy, A. (2025). Fundamental Understanding of Bio-Nano Interface of Lysozyme on *Psidium guajava* Polyphenol Coated Silver Nanoparticles: Mechanistic Insights into the Effect of Protein Corona on the Antibacterial Efficacy. *Langmuir*, **41**(5), 2899–2915. <https://doi.org/10.1021/acs.langmuir.4c04832>
- Begum, S. K., Shabnam, D., Haque, N., Alam, M. J., Ferdous, J., Nur, U. J. B., Fatema, K., Shabiha, R. J., Clarke, R. J., Chowdhury, P., & Uddin, M. N. (2025). Green synthesis of magnetite Fe₃O₄ and hematite Fe₂O₃ nanoparticles using *Moringa oleifera* and *Psidium guajava* leaf extracts for sustainable applications. *Scientific Reports*, **15**(1), 36465. <https://doi.org/10.1038/s41598-025-86201-1>
- Biswal, S. K., Panigrahi, G. K., & Sahoo, S. K. (2020). Green synthesis of $\text{Fe}_2\text{O}_3\text{-Ag}$ nanocomposite using *Psidium guajava* leaf extract: An eco-friendly and recyclable adsorbent for remediation of Cr(VI) from aqueous media. *Biophysical Chemistry*, **263**, 106392. <https://doi.org/10.1016/j.bpc.2020.106392>
- Boopathi, T. S., Suksom, S., Suriyaparakash, J., Hirad, A. H., Alarfaj, A. A., & Thangavelu, I. (2024). *Psidium guajava*-mediated green synthesis of Fe-doped ZnO and Co-doped ZnO nanoparticles: a comprehensive study on characterization and biological applications. *Bioprocess and Biosystems Engineering*, **47**(8), 1271–1291. <https://doi.org/10.1007/s00449-024-03002-7>
- Carvalho-Silva, J., Araújo, A. C. V., Ferreira-Santos, P. M., Converti, A., & Porto, T. S. (2025). Pectinase immobilized on magnetic nanoparticles coated with alginate for pectin hydrolysis in guava juice assisted by a stirred electromagnetic reactor. *Preparative Biochemistry & Biotechnology*, **55**(5), 541–554. <https://doi.org/10.1080/10826068.2024.2432111>
- Ganapathy, K., Rastogi, V., Lora, C. P., Suriyaparakash, J., Alarfaj, A. A., Hirad, A. H., & Indumathi, T. (2024). Biogenic synthesis of dopamine/carboxymethyl cellulose TiO₂

- nanoparticles using *Psidium guajava* leaf extract with enhanced antimicrobial and anticancer activities. *Bioprocess and Biosystems Engineering*, **47**(1), 131–143. <https://doi.org/10.1007/s00449-023-02954-6>
- García-Betanzos, C. I., Hernández-Sánchez, H., Bernal-Couoh, T. F., Quintanar-Guerrero, D., & Zambrano-Zaragoza, M. L. (2017). Physicochemical, total phenols and pectin methylesterase changes on quality maintenance on guava fruit (*Psidium guajava* L.) coated with candeuba wax solid lipid nanoparticles-xanthan gum. *Food Research International*, **101**, 218–227. <https://doi.org/10.1016/j.foodres.2017.08.065>
- Govindasamy, R., Raja, V., Singh, S., Govindarasu, M., Sabura, S., Rekha, K., Rajeswari, V. D., Alharthi, S. S., Vaiyapuri, M., Sudarmani, R., Jesurani, S., Venkidasamy, B., & Thiruvengadam, M. (2022). Green Synthesis and Characterization of Cobalt Oxide Nanoparticles Using *Psidium guajava* Leaves Extracts and Their Photocatalytic and Biological Activities. *Molecules*, **27**(17), 5646. <https://doi.org/10.3390/molecules27175646>
- Hafeez, R., Kanwal, Z., Raza, M. A., Rasool, S., Riaz, S., Naseem, S., Rabani, S., Haider, I., Ahmad, N., & Alomar, S. Y. (2023). Role of *Citrullus colocynthis* and *Psidium guajava* Mediated Green Synthesized Silver Nanoparticles in Disease Resistance against *Aeromonas hydrophila* Challenge in *Labeo rohita*. *Biomedicines*, **11**(9), 2349. <https://doi.org/10.3390/biomedicines11092349>
- Hanna, D. H., Taher, B. M., & El-Desouky, M. A. (2026). Synergetic anticancer activity of *Psidium guajava*-mediated palladium nanoparticles via apoptosis induction and metastasis suppression in osteosarcoma cells. *Scientific Reports*, **16**(1), 14701. <https://doi.org/10.1038/s41598-026-49913-1>
- Islam, M. J., Khatun, N., Bhuiyan, R. H., Sultana, S., Ali Shaikh, M. A., Amin Bitu, M. N., Chowdhury, F., & Islam, S. (2023). *Psidium guajava* leaf extract mediated green synthesis of silver nanoparticles and its application in antibacterial coatings. *RSC Advances*, **13**(28), 19164–19172. <https://doi.org/10.1039/D3RA03381C>
- Karthik, P., Jose, P. A., Chellakannu, A., Gurusamy, S., Ananthappan, P., Karupathevan, R., Vasantha, V. S., Rajesh, J., Ravichandran, S., & Sankarganesh, M. (2024). Green synthesis of MnO_2 nanoparticles from *Psidium guajava* leaf extract: Morphological characterization, photocatalytic and DNA/BSA interaction studies. *International Journal of Biological Macromolecules*, **258**(Pt 2), 128869. <https://doi.org/10.1016/j.ijbiomac.2023.128869>
- Karthikeyan, C., Varaprasad, K., Venugopal, S. K., Shakila, S., Venkatraman, B. R., & Sadiku, R. (2021). Biocidal (bacterial and cancer cells) activities of chitosan/CuO nanomaterial, synthesized via a green process. *Carbohydrate Polymers*, **259**, 117762. <https://doi.org/10.1016/j.carbpol.2021.117762>
- Kaushal, S., Kumar, A., Bains, H., & Singh, P. P. (2023). Photocatalytic degradation of tetracycline antibiotic and organic dyes using biogenic synthesized CuOFe₂O nanocomposite: pathways and mechanism insights. *Environmental Science and Pollution Research*, **30**(13), 37092–37104. <https://doi.org/10.1007/s11356-022-24831-2>
- Liaqat, F., Vosqa, U. T., Khan, F., Haleem, A., Shaik, M. R., Siddiqui, M. R. H., & Khan, M. (2023). Light-Driven Catalytic Activity of Green-Synthesized SnO₂ Hetero-nanostructures. *ACS Omega*, **8**(22), 20042–20055. <https://doi.org/10.1021/acsomega.3c02117>
- Madubuonu, N., Aisida, S. O., Ali, A., Ahmad, I., Zhao, T. K., Botha, S., Maaza, M., & Ezema, F. I. (2019). Biosynthesis of iron oxide nanoparticles via a composite of *Psidium guajava*-*Moringa oleifera* and their antibacterial and photocatalytic study. *Journal of Photochemistry and Photobiology B: Biology*, **199**, 111601. <https://doi.org/10.1016/j.jphotobiol.2019.111601>
- Mazhar, S., Hyder, S., Khan, B. S., Gondal, A. S., Ahmed, R., Iqra, & Iqbal, M. (2025). Green synthesis of silver nanoparticles using guava leaves: an effective strategy to control chilli fruit rot disease. *BMC Plant Biology*, **25**(1), 499. <https://doi.org/10.1186/s12870-025-06489-z>
- Nagaraja, S., Ahmed, S. S., D R, B., Goudanavar, P., M, R. K., Fattepur, S., Meravanige, G., Shariff, A., Shiroorkar, P. N., Habeebuddin, M., & Telsang, M. (2022). Green Synthesis and Characterization of Silver Nanoparticles of *Psidium guajava* Leaf Extract and Evaluation for Its Antidiabetic Activity. *Molecules*, **27**(14), 4336. <https://doi.org/10.3390/molecules27144336>
- Nguyen, D. H., Vo, T. N. N., Nguyen, N. T., Ching, Y. C., & Hoang Thi, T. T. (2020). Comparison of biogenic silver nanoparticles formed by *Momordica charantia* and *Psidium guajava* leaf extract and antifungal evaluation. *PLoS ONE*, **15**(9), e0239360. <https://doi.org/10.1371/journal.pone.0239360>
- Patiño-González, M. C., Echeverri-Cuatas, C. E., Torijano-Gutiérrez, S., Naranjo-Rios, S. M., & Agudelo, N. A. (2025). Optimization of the green synthesis of gold nanorods using aqueous extract of peeled sour guava as a source of antioxidants. *PLoS ONE*, **20**(2), e0313485. <https://doi.org/10.1371/journal.pone.0313485>

- Rani, N., Kumar, S., & Kumar, K. (2024). Green synthesis of N-doped-carbon dots/ZnO for enhanced photocatalytic degradation of methylene blue dye: optimization of reaction parameters. *Environmental Science and Pollution Research*, **31**(42), 63408–63425. <https://doi.org/10.1007/s11356-024-35389-w>
- Rasheed, S., Amin, A., Sarwar, A., Saleem, H. G. M., & Hassan, A. (2023). Evaluation of Antimicrobial Effect of Silver Nanoparticle Based Whey Emulsions and Edible Films for the Extension of Shelf Life of Fruits and Vegetables. *Current Microbiology*, **80**(5), 158. <https://doi.org/10.1007/s00284-023-03261-2>
- Saber, F. R., Abdelbary, G. A., Salama, M. M., Saleh, D. O., Fathy, M. M., & Soliman, F. M. (2018). UPLC/QTOF/MS profiling of two *Psidium* species and the in-vivo hepatoprotective activity of their nano-formulated liposomes. *Food Research International*, **105**, 1029–1038. <https://doi.org/10.1016/j.foodres.2017.12.029>
- Sathiyavimal, S., Vasantharaj, S., Kaliannan, T., & Pugazhendhi, A. (2020). Eco-biocompatibility of chitosan coated biosynthesized copper oxide nanocomposite for enhanced industrial (Azo) dye removal from aqueous solution and antibacterial properties. *Carbohydrate Polymers*, **241**, 116243. <https://doi.org/10.1016/j.carbpol.2020.116243>
- Singh, J., Kumar, V., Kim, K. H., & Rawat, M. (2019). Biogenic synthesis of copper oxide nanoparticles using plant extract and its prodigious potential for photocatalytic degradation of dyes. *Environmental Research*, **177**, 108569. <https://doi.org/10.1016/j.envres.2019.108569>
- Suwan, T., Khongkhunthian, S., & Okonogi, S. (2019). Antifungal activity of polymeric micelles of silver nanoparticles prepared from *Psidium guajava* aqueous extract. *Drug Discoveries & Therapeutics*, **13**(2), 62–69. <https://doi.org/10.5582/ddt.2019.01018>
- Tagad, A., Galatage, S. T., Hankuntimath, N., Hugar, S., Raikar, S. R., Patil, V. P., & Manjappa, A. S. (2026). Neuroprotective potential of green-synthesized silver nanoparticles from *Psidium guajava* in a scopolamine-induced rat model of Alzheimer's disease. *Annales Pharmaceutiques Françaises*, **84**(2), 258–276. <https://doi.org/10.1016/j.pharma.2025.09.004>
- Tan, J., Tian, J., Hou, H., Alarfaj, A. A., Arulselman, P., & Fan, D. (2026). Green synthesis of silver-doped nickel oxide nanoparticles using *Psidium guajava* leaf extract and their anti-cancer potential on glioma cells. *3 Biotech*, **16**(3), 409. <https://doi.org/10.1007/s13205-026-04285-8>
- Thejashwini, P. P., Chandrika, R., Madhusudhan, M. C., Joshi, S. M., Ali, D., Alarifi, S., Jogaiah, S., & Geetha, N. (2024). *Psidium guajava*-mediated zinc oxide nanoparticles as a multifunctional, microbicidal, antioxidant and antiproliferative agent against destructive pathogens. *Bioprocess and Biosystems Engineering*, **47**(10), 1571–1584. <https://doi.org/10.1007/s00449-024-03045-8>
- Trieu, Q. A., Ai Ung, Q. N., Thai, P. N., Mai, T. M., & Nguyen, D. V. (2025). Harnessing nature for dual action: silver nanoparticles synthesized from guava leaf extract for photocatalytic degradation of methyl red and antibacterial applications. *RSC Advances*, **15**(17), 13353–13363. <https://doi.org/10.1039/D5RA01202B>
- Udappusamy, V., Thinagaran, R., Mayakrishnan, V., Balakarthikeyan, J., Kannappan, P., Al-Ghamdi, S., Alrudian, N. A., Saad Alqahtani, M., Albasheer, K., Sureka, C., El-Bidawy, M. H., Alsanousi, N., Gamil, S., & Ramesh, T. (2025). An integrated in vitro and in silico approach to assess targeted cytotoxicity against MDA-MB-231 triple-negative breast cancer cells with *Psidium guajava* peel-derived chitosan nanoparticles. *Artificial Cells, Nanomedicine, and Biotechnology*, **53**(1), 43–55. <https://doi.org/10.1080/21691401.2024.2435889>
- Wang, L., Wu, Y., Xie, J., Wu, S., & Wu, Z. (2018). Characterization, antioxidant and antimicrobial activities of green synthesized silver nanoparticles from *Psidium guajava* L. leaf aqueous extracts. *Materials Science and Engineering: C*, **86**, 1–8. <https://doi.org/10.1016/j.msec.2017.12.026>
- Yousef, A., Salem, S. S., Torayah, M. M., Saied, S. A., & Elbawab, R. H. (2025). Evaluation of antibacterial and cytotoxic effects of silver oxide nanoparticles synthesized from *Psidium guajava*. *Scientific Reports*, **15**(1), 41763. <https://doi.org/10.1038/s41598-025-98214-5>

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During the preparation of this work, the author(s) have not used any ChatGPT (OpenAI) tool.



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