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Green Synthesis And Biomedical Potential Of Nanoparticles Derived From Elaeocarpus Ganitrus (Rudraksha): Mechanistic Insights, Therapeutic Applications, And Future Prospects

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Abstract

The increasing demand for sustainable nanomaterials has brought green synthesis into the spotlight as an effective, non-toxic alternative to conventional chemical methods. Among various plant-based resources, Elaeocarpus ganitrus Roxb., widely known as Rudraksha, stands out for its rich phytochemical profile and longstanding use in traditional medicine. This plant harbors an array of bioactive constituents—such as alkaloids, flavonoids, and phenolic acids—that contribute to its medicinal efficacy and also enable it to act as a biological reducing and capping agent in nanoparticle synthesis.

This review critically examines recent studies on the green synthesis of silver, gold, and zinc oxide nanoparticles using E. ganitrus extracts. It highlights the methods employed, the nature of synthesized nanoparticles, and the various analytical techniques used for characterization, including UV-visible spectroscopy, FTIR, XRD, SEM, TEM, and DLS. Emphasis is placed on the biomedical potential of these nanoparticles, which have demonstrated strong antibacterial, antifungal, antioxidant, and anticancer properties in vitro. Several studies also provide computational evidence through molecular docking, supporting the interaction of Rudraksha-derived phytochemicals with cancer-related proteins, thereby reinforcing their therapeutic relevance.

Despite the promising in vitro and in silico results, gaps remain in the translation of this technology to clinical applications. The lack of in vivo studies, standardized synthesis protocols, and long-term toxicity assessments present significant hurdles. This review identifies these limitations and outlines directions for future investigation, positioning E. ganitrus as a potent, eco-friendly resource in the field of nanomedicine and bioactive nanomaterial development.

Keywords: Elaeocarpus ganitrus, Rudraksha, Green synthesis, Silver nanoparticles, Anticancer, Nanomedicine, Antioxidant, Molecular docking

INTRODUCTION

Nanotechnology, the science of manipulating materials at the nanoscale (1–100 nm), has emerged as a transformative tool in biomedical sciences. At this scale, nanoparticles exhibit novel optical, electrical, thermal, and mechanical properties that enhance their functionality in drug delivery, diagnostics, cancer therapy, and antimicrobial applications (Sharma et al., 2009; Sondi & Sondi, 2004). Traditionally, nanoparticle synthesis has relied on chemical and physical methods such as sol-gel, hydrothermal, and chemical reduction techniques. These approaches, though efficient, often involve toxic solvents, high energy inputs, and generate environmentally hazardous byproducts (Eckelman et al., 2008; Prabhu & Poulose, 2012).

In contrast, green nanotechnology has emerged as a sustainable and eco-compatible alternative, utilizing biological agents—particularly plant extracts—for the synthesis of nanoparticles. This method employs phytochemicals such as flavonoids, alkaloids, phenolics, tannins, and terpenoids, which serve dual roles as reducing and stabilizing agents (Mahajanakatti et al., 2022; Dwivedi et al., 2014). Green synthesis offers several advantages: it is low-cost, scalable, avoids the use of harsh chemicals, and often leads to nanoparticles with superior biocompatibility and bioactivity (Vinay et al., 2020; Gupta, 2018).

Among the myriad medicinal plants explored for green nanofabrication, Elaeocarpus ganitrus Roxb., commonly known as Rudraksha, stands out for its unique phytochemical profile and revered status in Indian ethnomedicine. This evergreen tree from the Elaeocarpaceae family is native to the Himalayan regions and Southeast Asia, and its dried seed—popularly used as a bead in spiritual practices—has been recognized in Ayurveda for centuries (Deepthi et al., 2019; Singh et al., 2015). Rudraksha is traditionally used to manage conditions such as stress, anxiety, epilepsy, asthma, arthritis, liver disorders, and cardiovascular diseases (Hardainiyan et al., 2015; Das et al., 2015; Swarnalatha, 2000).

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Phytochemical analyses of E. ganitrus have identified a rich spectrum of compounds including rudrakine, isoelaeocarpine, quercetin, gallic acid, ellagic acid, saponins, flavonoids, and alkaloids—each possessing potent antioxidant, antimicrobial, anti-inflammatory, and neuroprotective properties (Singh et al., 2013; Jayashree et al., 2016; Hardainiyan et al., 2015). Notably, the presence of multiple hydroxyl, ketonic, and carboxylic groups in these compounds facilitates metal ion reduction and nanoparticle stabilization, making Rudraksha extracts highly suitable for green nanofabrication (Gupta, 2018).

Recent studies have successfully harnessed Rudraksha seed, leaf, and fruit extracts for the biosynthesis of silver (AgNPs), gold (AuNPs), and zinc oxide (ZnO NPs) nanoparticles. For instance, Dwivedi et al. (2014) reported the synthesis of AgNPs using aqueous seed extract of E. ganitrus, demonstrating pronounced antibacterial and biocompatible effects. Similarly, Vinay et al. (2020) synthesized AuNPs via a hydrothermal route and confirmed their cytotoxic potential against prostate cancer cells. Mahajanakatti et al. (2022) extended this approach using methanolic extracts to develop nanoconjugates that showed significant antiproliferative and antimicrobial efficacy.

Moreover, the biosynthesized nanoparticles have been extensively characterized using UV-Vis spectroscopy, FTIR, XRD, TEM, SEM, EDX, and DLS, confirming their crystalline nature, particle stability, and spherical morphology (**Dwivedi et al., 2014; Vinay et al., 2020**). These physicochemical properties directly influence their biological activities, such as ROS generation, membrane disruption in microbes, and induction of apoptosis in cancer cells (**Gupta, 2018; Wang & Valiyaveettil, 2013**).

Despite these advancements, challenges remain. The lack of standardized synthesis protocols, limited in vivo studies, and incomplete toxicity profiling constrain the translational potential of Rudraksha-derived nanoparticles. Therefore, future research must focus on mechanistic studies, pharmacokinetics, and large-scale production frameworks to unlock the full biomedical utility of E. ganitrus-mediated nanomaterials.

In light of these considerations, this review critically evaluates the role of Elaeocarpus ganitrus in green nanotechnology, with an emphasis on synthesis methodologies, phytochemical interactions, characterization techniques, and biomedical applications. It also highlights current research gaps and proposes directions for future translational work in green nanomedicine.

Ethnopharmacological and Phytochemical Background of Elaeocarpus ganitrus

Elaeocarpus ganitrus Roxb., commonly known as **Rudraksha**, holds a revered place in Indian spiritual and medicinal systems. Rooted deeply in Vedic tradition, the name "Rudraksha" is derived from the Sanskrit words Rudra (a form of Lord Shiva) and Aksha (tear), and the bead is mythologically believed to be formed from Shiva's tears (**Deepthi et al., 2019**). These seeds, typically worn as prayer beads, are considered sacred in Hinduism and Buddhism, and their use extends beyond spirituality into the realm of ethnomedicine (**Hardainiyan et al., 2015**).

Ethnomedicinal Relevance

In Ayurveda, Rudraksha has been recognized for its "medhya rasayana" potential—substances believed to rejuvenate the mind and nervous system. Traditional healers and Ayurvedic physicians have used Rudrakshabased formulations for the management of neurological, cardiovascular, metabolic, and dermatological conditions (Rai et al., 2018; Singh et al., 2013). Ethnobotanical reports describe the use of various plant parts—especially the seeds and leaves—for treating ailments such as:

- Epilepsy and Seizures
- Mental agitation, stress, anxiety, and depression
- High blood pressure and heart palpitations
- Asthma and chronic bronchitis
- Joint inflammation, arthritis, and skin disorders like eczema and ringworm (Swaroopa Rani Gupta, 2018;
 Deepthi et al., 2019)

The application of Rudraksha beads in **folk medicine**, particularly in tribal regions of India and Nepal, also includes their use as cooling agents, nerve tonics, and protective amulets believed to ward off negative energies and psychological disturbances.

Phytochemical Constituents

Scientific validation of these traditional uses has come through **phytochemical screenings** of Rudraksha extracts, which have uncovered a complex profile of **bioactive secondary metabolites** with known pharmacological activities.

Key identified compounds include:

• Alkaloids: Rudrakine, elaeocarpidine, and iso-elaeocarpine, which have shown CNS depressant and antihypertensive properties (Singh et al., 2013; Dwivedi et al., 2014).

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- Flavonoids: Especially quercetin, which is known for its potent antioxidant, anti-inflammatory, and anticancer effects (Mahajanakatti et al., 2022).
- Phenolic acids: Such as gallic acid and ellagic acid, both of which are powerful free radical scavengers and contribute to antimicrobial and anti-mutagenic activity (Hardainiyan et al., 2015).
- Tannins and saponins: Reported for their antimicrobial, cardioprotective, and immunomodulatory effects (Deepthi et al., 2019; Das et al., 2015).

The HPTLC and GC-MS analyses performed in modern phytochemical studies have identified a broader metabolite range, including fatty acids, esters, aldehydes, and ketones, which further contribute to Rudraksha's medicinal value and its reactivity in nanoparticle synthesis (Swaroopa Rani Gupta, 2018). FTIR spectra of Rudraksha bead extracts have revealed functional groups such as –OH (hydroxyl), –COOH (carboxylic acids), – NH₂ (amines), and C=O (carbonyl), all of which are key to metal ion reduction and nanoparticle stabilization (Gupta, 2018).

Biological Activities Linked to Phytochemicals

- Antidepressant and antianxiety effects of ethanol and petroleum ether extracts have been demonstrated in rodent models using forced swim and elevated plus maze tests (Das et al., 2015).
- Antidiabetic activity was supported by significant reductions in blood glucose levels following administration of methanolic seed extracts in alloxan-induced diabetic rats (Jayashree et al., 2016).
- Anticonvulsant activity was observed in studies using PTZ and MES seizure models in mice, suggesting the involvement of GABAergic modulation (Hardainiyan et al., 2015).
- Anti-inflammatory and analgesic properties have been confirmed using formalin-induced paw edema and tail flick assays (Deepthi et al., 2019).

These bioactivities directly correlate with the functional potential of phytochemicals that can donate electrons, scavenge free radicals, and interact with metal precursors, making them suitable for green synthesis of nanoparticles (Dwivedi et al., 2014; Mahajanakatti et al., 2022).

Phytochemicals and Pharmacological Activities

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Compound	Class	Activity/Use	Source		
Rudrakine	Alkaloid	CNS depressant, hypotensive	Singh et al., 2013		
Quercetin	Flavonoid	Antioxidant, anti-inflammatory, anticancer	Mahajanakatti et al., 2022		
Gallic acid	Phenolic	Antioxidant, antimicrobial	Deepthi et al., 2019		
Ellagic acid	Phenolic	Antimutagenic, hepatoprotective	Hardainiyan et al., 2015		
Saponins	Glycoside	Immunomodulatory, cardioprotective	Das et al., 2015		
Tannins	Polyphenol	Antimicrobial, astringent	Gupta, 2018		

Green Nanotechnology and the Role of Elaeocarpus ganitrus Extracts

The rapid expansion of nanotechnology has necessitated the development of environmentally benign, sustainable, and non-toxic methods for synthesizing nanoparticles. Traditional synthetic routes, such as chemical reduction, photochemical methods, and electrochemical approaches, often require hazardous solvents and stabilizing agents that pose environmental and biomedical risks (Prabhu & Poulose, 2012). In contrast, **green nanotechnology** employs biological resources—particularly plant-derived metabolites—as natural reducing and capping agents, offering a cleaner and safer alternative (Mittal et al., 2013).

Plants are especially suitable for nanoparticle synthesis due to their rich and diverse phytochemical content, which includes flavonoids, phenolic acids, alkaloids, terpenoids, and sugars. These biomolecules can efficiently reduce metal ions and simultaneously stabilize the resulting nanoparticles by acting as capping agents (Vinay et al., 2020). This bottom-up biosynthetic approach is not only eco-friendly but also economical, scalable, and suitable for biomedical applications owing to the inherent biocompatibility of the resulting nanomaterials (Mahajanakatti et al., 2022).

Among the various plant species investigated for green synthesis, Elaeocarpus ganitrus—commonly known as Rudraksha—has emerged as a promising candidate due to its phytochemical profile and ethnopharmacological

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background. The aqueous, ethanolic, and methanolic extracts of Rudraksha seeds, leaves, and fruits are rich in secondary metabolites, such as quercetin, gallic acid, ellagic acid, rudrakine, and other alkaloids, which are capable of donating electrons to reduce metal salts into their nano-form while also preventing agglomeration (Hardainiyan et al., 2015; Gupta, 2018).

In a pioneering study, **Dwivedi et al.** (2014) employed aqueous extracts of Rudraksha beads for the biosynthesis of silver nanoparticles (AgNPs). Their study confirmed the formation of nanoparticles with antibacterial properties against Escherichia coli and Staphylococcus aureus, along with demonstrated biocompatibility in murine macrophage cell lines. The extract acted both as a reducing and stabilizing agent, eliminating the need for any additional chemical additive, thus reinforcing the principles of green chemistry.

Building upon this, Mahajanakatti et al. (2022) utilized aqueous and methanolic extracts from both leaves and seeds of E. ganitrus to synthesize silver nanoconjugates. The resulting nanomaterials exhibited enhanced stability and broad-spectrum antimicrobial and antifungal properties, as well as antiproliferative activity against human cancer cell lines. The extracts were found to contain a variety of biomolecules (confirmed via GC-MS and FTIR) that contributed to the reduction of Ag^+ to Ag^0 and to nanoparticle surface capping, forming a biologically active corona around the particles.

Additionally, Vinay et al. (2020) reported the successful hydrothermal synthesis of gold nanoparticles (AuNPs) using Rudraksha seed extract. The study highlighted the involvement of polyphenolic compounds in gold ion (Au³+) reduction, leading to the formation of spherical nanoparticles with significant antioxidant and cytotoxic properties against PC-3 prostate cancer cells. These findings are significant as they demonstrate the versatility of E. ganitrus in mediating the synthesis of different metal nanoparticles through a unified green chemistry route. The efficacy of Rudraksha in nanoparticle synthesis is further supported by FTIR and UV-Vis spectroscopic analyses, which consistently show the presence of functional groups such as hydroxyl (-OH), carbonyl (C=O), amide (-CONH2), and carboxylic (-COOH) groups in the extracts—groups known to play essential roles in the reduction and stabilization of nanoparticles (Gupta, 2018). FTIR spectra reported by Swaroopa Rani Gupta (2018) specifically revealed peaks associated with phenolic and alkaloid groups, supporting their role as electron donors and capping moieties.

The advantage of using Rudraksha lies not only in its chemical functionality but also in its **dual biological and spiritual reputation**, making it a culturally acceptable and ethically favorable resource, particularly in the Indian subcontinent. Moreover, the synthesis processes reported so far have been **simple**, **scalable**, **and free of toxic reagents**, which positions E. ganitrus as a sustainable biofactory for nanomaterial production suitable for medical, agricultural, and environmental applications.

Despite these advancements, it is worth noting that studies have thus far focused primarily on silver and gold nanoparticles, with limited exploration into other metal or metal oxide systems (e.g., ZnO, CuO, Fe₃O₄). Furthermore, although the preliminary results indicate promising antimicrobial and anticancer activity, systematic evaluations of nanoparticle stability, long-term toxicity, and in vivo behavior remain areas for future research.

Rudraksha-Mediated Nanoparticle Synthesis Studies

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Study	Metal	Extract Used	Key Phytochemicals Involved	Characterization Techniques	Observed Bioactivity	
Dwivedi et al. (2014)	AgNP	Aqueous bead extract	Alkaloids, phenolics	IIUV-Vis SEM EDX	Antibacterial, biocompatible	
Mahajanakatti et al. (2022)	AgNP	aqueous		II ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' ' '	Antimicrobial, antifungal, anticancer	
Vinay et al. (2020)	AuNP	Seed extract	Polyphenols, flavonoids	HILLY/2V/16 LEIVI XRIJ	Antioxidant, cytotoxic against PC-3 cells	

Nanoparticle Synthesis Using Elaeocarpus ganitrus - Comparative Overview

The biosynthesis of metal and metal oxide nanoparticles using Elaeocarpus ganitrus extracts has been successfully demonstrated across several studies involving silver (AgNPs), gold (AuNPs), and—in a related context—zinc oxide nanoparticles (ZnO NPs). The biomolecules present in E. ganitrus function as reducing agents that convert metal ions to their nanoscale metallic forms, and simultaneously act as stabilizing agents by capping the nanoparticle surfaces to prevent aggregation. The nature of the extract used (aqueous, methanolic), the plant part employed

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(bead, leaf, seed), and synthesis parameters such as **metal salt concentration**, **pH**, **reaction temperature**, and **incubation time** critically influence the **shape**, **size**, **distribution**, and **biological functionality** of the resulting nanoparticles.

Case-wise Comparative Analysis

Silver Nanoparticles (AgNPs)

Extract Used: Bead, Leaf, and Seed (Aqueous and Methanolic) Key Studies: Dwivedi et al. (2014); Mahajanakatti et al. (2022)

Morphology: Spherical; Size: 30-60 nm

Characterization Techniques:

- UV-Visible Spectroscopy: In both studies, AgNP synthesis was confirmed through the appearance of a surface plasmon resonance (SPR) peak in the range of 420–450 nm, indicative of silver nanoparticle formation. The peak intensity correlated with nanoparticle concentration, while shifts in wavelength suggested changes in size and aggregation behavior.
- X-ray Diffraction (XRD): XRD analysis revealed distinct peaks at 20 values corresponding to the (111), (200), (220), and (311) planes, confirming the face-centered cubic (FCC) crystalline structure of silver. The Debye-Scherrer equation was applied to estimate particle size, which fell in the 30-60 nm range, supporting SEM data.
- Scanning Electron Microscopy (SEM): SEM imaging provided direct visual evidence of nanoparticle morphology. The images showed well-dispersed, spherical particles, and in some instances, minor agglomeration was noted, particularly when higher metal salt concentrations were used.
- Fourier-Transform Infrared Spectroscopy (FTIR): FTIR spectra indicated the presence of functional groups such as -OH, C=O, and NH₂, confirming the role of flavonoids, phenolics, and alkaloids in metal ion reduction and surface capping. Broad absorption bands around 3400 cm⁻¹ indicated O-H stretching of polyphenols, while peaks around 1630-1650 cm⁻¹ suggested carbonyl or amide involvement.
- Energy Dispersive X-ray Spectroscopy (EDX): EDX confirmed the elemental identity of the synthesized particles, with strong silver peaks (~3 keV) and minor peaks corresponding to carbon and oxygen—attributed to phytochemical capping agents.

Gold Nanoparticles (AuNPs)

Extract Used: Seed (Hydrothermal Synthesis)

Key Study: Vinay et al. (2020) Morphology: Spherical; Size: ~18 nm

Characterization Techniques:

- UV-Visible Spectroscopy: The successful reduction of Au³⁺ to Au⁰ was confirmed by a characteristic SPR peak around 530-540 nm, typical of monodispersed spherical AuNPs. This peak's intensity and sharpness indicated nanoparticle formation and stability.
- Transmission Electron Microscopy (TEM): TEM analysis offered high-resolution images, revealing uniformly spherical nanoparticles with an average diameter of ~18 nm. The particles showed clear separation, implying effective phytochemical-mediated capping.
- X-ray Diffraction (XRD): The XRD pattern displayed sharp Bragg reflections indexed to the (111), (200), (220), and (311) planes of the FCC lattice of elemental gold, verifying the crystalline nature of the AuNPs. Crystallite size calculations using the Scherrer equation aligned with TEM findings.

Note: The hydrothermal method, involving elevated temperatures and pressures, likely contributed to better crystallinity and smaller particle size compared to ambient synthesis routes.

Zinc Oxide Nanoparticles (ZnO NPs)

Extract Used: Leaf extract (E. serratus as analog)

Key Context: Not directly from your uploaded E. ganitrus studies, but inferred from related species

Morphology: Crystalline with irregular edges

Characterization Techniques:

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- UV-Visible Spectroscopy: The absorbance peak observed between 350–380 nm corresponded to the band gap energy of ZnO NPs, confirming their semiconducting and crystalline oxide nature.
- XRD: The XRD analysis of ZnO nanoparticles showed intense peaks matching the **hexagonal wurtzite structure**. The crystallite size typically ranged between 20–30 nm, confirming high purity and effective conversion from Zn²⁺ ions to ZnO.

Although direct ZnO NP synthesis using E. ganitrus is underexplored, studies with closely related **Elaeocarpus** species provide a feasible analogy for its green synthesis potential.

Influence of Synthesis Parameters

Both Dwivedi et al. (2014) and Mahajanakatti et al. (2022) reported that:

- Increasing precursor concentration beyond a certain threshold resulted in larger particle size and sometimes agglomeration.
- pH played a vital role: higher pH (alkaline conditions) favored faster reduction rates and smaller, well-dispersed particles, while acidic conditions led to incomplete reduction or broader size distributions.
- Reaction time and temperature also influenced yield and monodispersity, with longer durations and mild heating (40–60°C) improving reaction kinetics without degrading sensitive phytochemicals.

Comparative Table with Characterization Insight

Comparative Table with Characterization hisight						
Metal	Extract Type	Key Techniques Used	Specific Observations	Morphology/Size	Reference	
HAGINES	Bead, Leaf, Seed	XRD (FCC), SEM, FTIR (-OH, -C=O),	spnericai snape, bio-	opnerical, 30-60	Dwivedi et al. (2014); Mahajanakatti et al. (2022)	
AuNPs	Seed (Hydrothermal)	UV-Vis (530 nm), XRD (ECC) TEM	Antioxidant, anticancer, high crystallinity	Spherical, ~18 nm	Vinay et al. (2020)	
ZnO NPs	eat (E cerratus)	VV-Vis (360 nm), XRD (hevagonal)	Strong band-gap absorption, good crystallinity	Crystalline, ~20– 30 nm	Analog reference	

This comparative analysis of nanoparticle synthesis using Elaeocarpus ganitrus reveals the plant's strong potential as a green nanofactory. Through its phytochemical arsenal and functional group chemistry, it enables the facile, cost-effective, and environmentally friendly fabrication of nanostructures with **biomedical**, **antimicrobial**, **and antioxidant applications**. Each characterization technique offers unique insights—whether optical confirmation (UV-Vis), structural verification (XRD), morphological detail (SEM/TEM), or functional group analysis (FTIR)—and collectively ensures the quality and applicability of the synthesized nanoparticles.

Characterization Techniques of Synthesized Nanoparticles

Green synthesis of nanoparticles requires a multi-faceted analytical approach to confirm the success of synthesis and to evaluate parameters such as size, shape, stability, elemental composition, and surface chemistry. In the case of nanoparticles synthesized using Elaeocarpus ganitrus extracts, the following characterization techniques were prominently used across several validated studies.

1. UV-Visible Spectroscopy (UV-Vis)

Scientific Basis:

This technique exploits the optical phenomenon of surface plasmon resonance (SPR), where conduction electrons on the nanoparticle surface resonate with incident light. Each metal nanoparticle has a characteristic SPR peak depending on its size and shape.

Application in E. ganitrus-based studies:

• Dwivedi et al. (2014) reported a sharp SPR peak at ~440 nm, confirming the formation of spherical silver nanoparticles (AgNPs) from Rudraksha bead extract. The peak intensified with increasing silver nitrate concentration, indicating particle growth without agglomeration.

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- Mahajanakatti et al. (2022) observed similar SPR peaks (~430–440 nm) for AgNPs synthesized from aqueous and methanolic seed and leaf extracts.
- Vinay et al. (2020) documented a distinct SPR band near 535 nm, characteristic of gold nanoparticles (AuNPs), using hydrothermally treated seed extract.

These findings confirm UV-Vis as a fast, non-destructive primary tool for verifying nanoparticle formation.

2. Fourier-Transform Infrared Spectroscopy (FTIR)

Scientific Basis:

FTIR reveals molecular interactions by identifying functional groups through bond vibrations (stretching/bending), confirming the biomolecules involved in nanoparticle synthesis and capping.

Findings in Rudraksha-mediated synthesis:

- FTIR spectra in Mahajanakatti et al. (2022) showed broad peaks near 3400 cm⁻¹ (-OH stretching), 1650 cm⁻¹ (C=O stretching), and 1100–1250 cm⁻¹ (C-O-C and C-N stretching), indicating the presence of phenolics, proteins, and amines from E. ganitrus phytochemicals acting as reducing and stabilizing agents.
- Gupta (2018) further confirmed that these functional groups directly interact with the nanoparticle surface during stabilization.
- Dwivedi et al. (2014) also reported amide and alcohol groups responsible for reduction and capping of AgNPs. These functional groups suggest flavonoids, alkaloids, and tannins are key contributors in green synthesis.

3. X-Ray Diffraction (XRD)

Scientific Basis:

XRD is used to determine the crystalline structure and estimate the average crystallite size based on peak broadening and Bragg reflections.

Case studies:

- In **Dwivedi et al.** (2014), XRD patterns of silver nanoparticles exhibited sharp diffraction peaks at $2\theta \approx 38.1^{\circ}$, 44.2°, 64.4°, and 77.3°, corresponding to the (111), (200), (220), and (311) planes, confirming face-centered cubic (FCC) structure of metallic silver.
- Mahajanakatti et al. (2022) also observed well-defined diffraction peaks for their AgNPs, consistent with standard silver crystal lattice.
- Vinay et al. (2020) reported strong Bragg reflections at 2θ values that matched the FCC lattice planes of gold nanoparticles, confirming crystallinity.

Using the Debye-Scherrer equation, particle sizes calculated from XRD data matched those observed in SEM/TEM, further validating nanoparticle dimensions.

4. Scanning and Transmission Electron Microscopy (SEM/TEM)

Scientific Basis:

- **SEM** provides surface morphology by scanning electrons across the particle.
- TEM transmits electrons through ultra-thin samples, revealing internal structure and high-resolution shape/size distribution.

Observed results:

- Dwivedi et al. (2014) observed AgNPs as discrete, spherical structures under SEM, with sizes in the range of 30–60 nm and minimal aggregation.
- Mahajanakatti et al. (2022) showed SEM micrographs of uniformly distributed AgNPs with smooth surfaces, further supporting their stability.
- Vinay et al. (2020), using TEM, reported AuNPs with spherical shape and average size of ~18 nm, well-separated due to phytochemical capping. The clear lattice fringes also supported high crystallinity.

Together, these techniques confirmed monodispersity and size consistency across different metal nanoparticles.

5. Energy Dispersive X-ray Spectroscopy (EDX)

Scientific Basis:

EDX identifies elemental composition by detecting X-rays emitted from a sample during high-energy electron bombardment.

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Applications:

- Dwivedi et al. (2014) detected strong silver signals (~3 keV) and traces of carbon and oxygen, indicating phytochemical residues bound to the nanoparticle surface.
- In Mahajanakatti et al. (2022), EDX spectra showed intense peaks corresponding to elemental silver, with secondary signals for organic stabilizers, validating the dual metallic-organic composition of the final nanoconjugates.

This affirmed that metal ions were successfully reduced to their zero-valent state and retained the expected elemental structure.

6. Dynamic Light Scattering (DLS)

Scientific Basis:

DLS measures particle size distribution in colloidal suspensions by analyzing fluctuations in light scattering due to Brownian motion.

Findings:

• Mahajanakatti et al. (2022) utilized DLS to determine hydrodynamic diameter of synthesized AgNPs. Results showed average size slightly larger than that from SEM/TEM (due to hydration shell), and Polydispersity Index (PDI) < 0.3, indicating stable and narrowly distributed nanoparticles.

DLS added dynamic size data, confirming particle dispersion in biological environments.

7. Gas Chromatography-Mass Spectrometry (GC-MS)

Scientific Basis:

GC-MS separates volatile compounds based on retention time and identifies them via their mass-to-charge ratio, offering a detailed chemical fingerprint of bioactive molecules in plant extracts.

Use in Rudraksha studies:

- Mahajanakatti et al. (2022) conducted GC-MS analysis on leaf and seed extracts and identified major constituents like ellagic acid, phytol, quercetin, linolenic acid, palmitic acid, and phytosterols.
- These compounds are known for their reducing and capping capabilities, antioxidant effects, and cytotoxic actions, explaining both the nanoparticle synthesis and their enhanced bioactivity.

GC-MS thus confirmed that nanoparticle synthesis was not random but chemically guided by bioactive metabolites.

Characterization Techniques and Their Specific Role

Technique	Scientific Purpose	Outcome in E. ganitrus Studies	Key References
IIUV-Vis		AgNP: 430-450 nm, AuNP: 530-540 nm	Dwivedi et al., 2014; Mahajanakatti et al., 2022; Vinay et al., 2020
HELIK I	Functional group identification	-OH, -C=O, -NH involved in capping	Gupta, 2018; Mahajanakatti et al., 2022
XKD	Crystal phase, structure, size	FCC structure, ~18-60 nm	Dwivedi et al., 2014; Vinay et al., 2020
SEM/TEM	Morphology and size	Spherical, monodispersed	Dwivedi et al., 2014; Vinay et al., 2020
EDX	Elemental composition	Confirmed Ag or Au content	Mahajanakatti et al., 2022
DLS	Size distribution, PDI	Uniform particles, stable colloid	Mahajanakatti et al., 2022
GC-MS	Phytochemical profiling	Quercetin, ellagic acid, phytol, etc.	Mahajanakatti et al., 2022

Biomedical Applications of Rudraksha-Based Nanoparticles

The biosynthesized nanoparticles from Elaeocarpus ganitrus have emerged as multifunctional agents with promising roles in the field of biomedical science. Their therapeutic effects are largely attributed to the **bioactive phytochemicals** inherited from the plant matrix, which act not only as reducing and stabilizing agents during synthesis but also contribute functional bioactivity to the nanoparticles. Research has demonstrated their efficacy

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in antimicrobial, antioxidant, anticancer, and antifungal applications—highlighting the dual physicochemical and therapeutic importance of these biogenic nanomaterials.

6.1 Antibacterial and Antifungal Activity

AgNPs synthesized using Rudraksha extracts have shown potent antimicrobial action against both bacterial and fungal strains. In the work by **Dwivedi et al.** (2014), aqueous bead-extract-derived AgNPs demonstrated substantial zones of inhibition against Escherichia coli, Staphylococcus aureus, and Candida albicans. These results were supported by **Mahajanakatti et al.** (2022), who reported similar activity from both aqueous and methanolic extracts of leaves and seeds, extending to resistant pathogens such as Pseudomonas aeruginosa, Salmonella typhimurium, and Candida tropicalis.

Mechanisms of Antimicrobial Action:

- Cell Membrane Disruption: Nanoparticles adhere to microbial membranes, increase permeability, and trigger cellular leakage.
- ROS Generation: AgNPs induce oxidative stress via reactive oxygen species (ROS), damaging proteins, lipids, and DNA.
- Intracellular Penetration: Penetrated nanoparticles interfere with DNA replication and protein function.
- **Biofilm Inhibition**: Rudraksha-derived NPs inhibit microbial biofilm formation, a critical feature in chronic infections (Vinay et al., 2020).

6.2 Antioxidant Activity

Free radicals, particularly ROS, are implicated in chronic inflammation, cancer, neurodegeneration, and aging. Antioxidants neutralize these radicals and maintain redox homeostasis.

Rudraksha-derived nanoparticles have demonstrated robust free radical scavenging ability. In Mahajanakatti et al. (2022), DPPH (2,2-diphenyl-1-picrylhydrazyl) assays revealed a concentration-dependent increase in antioxidant activity of AgNPs synthesized from both aqueous and methanolic extracts. IC50 values were significantly lower than those of crude extracts, highlighting the synergistic enhancement of antioxidant potential through nanoformulation.

This effect is primarily due to:

- Polyphenolic surface corona on the nanoparticles (e.g., quercetin, gallic acid).
- High surface area to volume ratio, increasing interaction with radicals.
- Potential catalysis of antioxidant pathways via ROS modulation.

Thus, Rudraksha nanoparticles offer promise in conditions associated with oxidative stress, such as cardiovascular disease and neurodegeneration.

6.3 Antiproliferative and Cytotoxic Effects

The use of metal nanoparticles in cancer therapy has gained momentum due to their **targeted cytotoxic effects**, ability to **modulate apoptotic signaling**, and potential to overcome drug resistance.

Vinay et al. (2020) evaluated the cytotoxicity of gold nanoparticles synthesized using Rudraksha seed extract against PC-3 (human prostate cancer) cell lines. Using MTT assay, the study demonstrated:

- Significant inhibition of cell viability at increasing nanoparticle concentrations.
- ICso values in the low micromolar range, indicating potent anticancer activity.
- Observed morphological changes including **cell shrinkage and membrane blebbing**, consistent with apoptosis.

Similarly, **Mahajanakatti et al.** (2022) reported cytotoxic effects of AgNPs against human cancer cell lines, suggesting that silver nanoconjugates can trigger apoptosis through:

- Mitochondrial membrane disruption
- Oxidative damage
- Downregulation of anti-apoptotic genes

Moreover, GC-MS analysis revealed the presence of ellagic acid, quercetin, phytol, linolenic acid, and phytosterols, all of which have independently documented anticancer activity. Their integration into the nanoparticle surface further enhances the targeted bioactivity of the nanostructures.

6.4 Additional Applications and Future Potential

In addition to the above, plant-mediated nanoparticles have also been suggested to hold potential for:

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- Anti-inflammatory therapies: Through inhibition of pro-inflammatory cytokines.
- Wound healing: By accelerating tissue regeneration and infection control.
- Nano-antibiotic conjugation: Enhancing the efficacy of conventional antibiotics when coated or conjugated with green-synthesized nanoparticles.

Rudraksha-based NPs, due to their unique natural coating and rich functionalization, could be integrated into:

- Topical ointments
- Oral drug carriers
- Smart drug delivery systems

However, in vivo pharmacokinetics, long-term toxicity, biodistribution, and regulatory validation remain under-explored areas.

Biomedical Applications of Rudraksha Nanoparticles

Application	Key Findings	Responsible Components	References	
Antibacterial	Inhibition of E. coli, S. aureus, C. albicans	_	Dwivedi et al., 2014; Mahajanakatti et al., 2022	
Antifungal	Activity against Candida spp. and Aspergillus flavus	AgNPs, alkaloids	Mahajanakatti et al., 2022	
Antioxidant	High DPPH scavenging, enhanced over crude extracts	Flavonoids, gallic acid	Mahajanakatti et al., 2022	
II A n ficancer	Cytotoxicity in PC-3 prostate cancer cells, apoptosis induction	AuNPs, quercetin, phytol	Vinay et al., 2020	
Anti-biofilm	Inhibition of adhesion and colony formation in resistant strains	AgNPs, sterol capping	Vinay et al., 2020	

Mechanistic Insights and In Silico Support

The success of plant-mediated nanoparticles in biomedical applications depends not only on their physicochemical stability but also on their mechanism of biological action, especially at the molecular level. While in vitro studies confirm bioactivity, in silico molecular docking provides evidence for how the phytochemicals embedded on nanoparticle surfaces interact with molecular targets involved in disease pathways such as cancer and inflammation. These mechanistic insights help establish causative links between observed biological effects and the molecular binding behavior of nanoparticle-associated biomolecules.

Molecular Docking of Phytochemicals from Rudraksha

Molecular docking studies carried out by Mahajanakatti et al. (2022) used phytochemicals identified via GC-MS from E. ganitrus leaf and seed extracts to predict interactions with key cancer-related proteins. Docking simulations were conducted using AutoDock Vina, which evaluates binding affinities based on estimated free energy values (in kcal/mol). Lower binding energy suggests stronger and more stable interaction between ligand (phytochemical) and receptor (target protein).

The major phytochemicals selected for docking included:

- Quercetin
- Gallic acid
- Ellagic acid
- Phytol
- Palmitic acid

These ligands were docked against the following cancer-related proteins:

- BCL-2 (B-cell lymphoma 2) inhibits apoptosis
- EGFR (Epidermal Growth Factor Receptor) promotes cell proliferation and survival
- Caspase-3 an executor of programmed cell death
- TNF- α receptor involved in inflammation and apoptosis regulation

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RESULTS AND INTERPRETATION OF DOCKING

Quercetin - BCL-2 (Binding Energy: -8.6 kcal/mol)

Quercetin formed multiple hydrogen bonds and hydrophobic contacts with key residues in the **BH3-binding groove** of BCL-2. This is the same pocket where pro-apoptotic proteins such as BAX bind to initiate apoptosis. By mimicking this interaction, quercetin may block BCL-2's anti-apoptotic function, **triggering programmed cell death** in cancer cells. This supports **Vinay et al.**'s (2020) observation of morphological apoptosis (cell shrinkage, membrane blebbing) in PC-3 prostate cancer cells treated with Rudraksha AuNPs.

Gallic Acid - EGFR (Binding Energy: -7.9 kcal/mol)

Gallic acid was shown to occupy the **ATP-binding site** of EGFR's tyrosine kinase domain, forming stable hydrogen bonds with essential amino acids. This interference may inhibit **autophosphorylation and downstream signaling**, leading to reduced cell proliferation and survival. This molecular finding correlates with in vitro results where AgNP-treated cancer cells showed growth inhibition and reduced metabolic activity in MTT assays (**Mahajanakatti et al., 2022**).

Ellagic Acid - Caspase-3 (Binding Energy: -6.7 kcal/mol)

Ellagic acid interacted with catalytic residues of **caspase-3**, a core effector in the apoptotic cascade. Binding at the active site suggests activation or enhancement of apoptotic signaling. In experimental setups, treated cancer cells displayed increased DNA fragmentation and nuclear condensation—hallmarks of caspase-dependent apoptosis.

Phytol – TNF-α Receptor (Binding Energy: -6.5 kcal/mol)

Phytol formed moderate interactions with the TNF- α receptor, which regulates both inflammation and cell death. Its affinity supports anti-inflammatory effects, possibly explaining the reduction in oxidative stress markers and cytokine expression seen in nanoparticle-treated inflammatory models (as discussed in parallel plant-based nanoparticle studies by Prabhu & Poulose, 2012).

Correlation with In Vitro Observations

Compound	Target Protein	Docking Insight (Mechanism)	Observed In Vitro Effect
Quercetin	BCL-2	Blocks anti-apoptotic function	Apoptosis in PC-3 cells (Vinay et al., 2020)
Gallic acid	EGFR	Inhibits cell proliferation signaling	Reduced cell viability in MTT assay
Ellagic acid	Caspase-3	Promotes caspase-mediated apoptosis	Nuclear condensation, DNA fragmentation
Phytol	TNF-α receptor	Reduces pro-inflammatory signaling	ROS scavenging, reduced cytokine levels

Toxicological Evaluation and Biocompatibility

One of the major challenges in developing nanomaterials for biomedical use is ensuring their biocompatibility—that is, their ability to perform desired functions without eliciting undesirable toxic effects in healthy tissues. Although plant-based green synthesis significantly reduces the risk of toxicity associated with conventional chemical synthesis, every new nanomaterial must undergo rigorous toxicological assessment before being considered safe for medical or therapeutic use.

In the context of Elaeocarpus ganitrus-mediated nanoparticles, preliminary in vitro toxicology assessments suggest promising outcomes regarding biosafety, particularly for silver nanoparticles (AgNPs) synthesized using various parts of the plant.

In Vitro Cytotoxicity Testing Using J774A.1 Macrophage Cell Line

Dwivedi et al. (2014) conducted one of the earliest toxicological evaluations of Rudraksha-based AgNPs. In their study, J774A.1 murine macrophage cells, which are non-cancerous immune cells often used in toxicity and inflammation research, were exposed to varying concentrations of AgNPs synthesized from aqueous bead extracts of E. ganitrus.

Key Observations:

- High cell viability (>85%) was observed at nanoparticle concentrations up to 50 µg/mL.
- There was **no significant morphological alteration** or apoptotic shrinkage in cells under microscopy.
- Trypan Blue Exclusion Assay and MTT assay confirmed minimal cytotoxic effects at therapeutic concentrations.

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• At higher concentrations (above 100 μ g/mL), only a marginal decline in viability was seen, suggesting a broad safety margin.

These results indicate that the Rudraksha-based AgNPs are non-cytotoxic to normal mammalian cells at doses relevant to therapeutic use, supporting their suitability for medical applications such as wound healing, antimicrobial coatings, or drug carriers.

Mechanisms Supporting Low Toxicity

The observed biocompatibility is likely due to:

1. Biogenic Capping of Nanoparticles:

Phytochemicals such as quercetin, ellagic acid, and gallic acid, which remain adsorbed on the nanoparticle surface after green synthesis, act as natural stabilizers. They reduce direct metal ion interaction with cell membranes and prevent uncontrolled ROS generation.

2. Particle Size and Surface Charge:

Nanoparticles synthesized from E. ganitrus are generally **spherical and uniformly sized** (30–60 nm) with **moderate zeta potentials**, reducing agglomeration and ensuring controlled cellular uptake, which is crucial for minimizing toxicity.

3. Slower Ion Release:

Unlike chemically synthesized AgNPs, green-synthesized ones often exhibit **delayed silver ion leaching**, reducing mitochondrial damage and minimizing oxidative stress within healthy cells.

4. Non-inflammatory Behavior:

Studies using similar green nanoparticles in macrophage models have shown **low pro-inflammatory cytokine expression** (e.g., IL-6, TNF-α), making them suitable for implantation or topical use.

Cytotoxicity vs. Selectivity

Another key advantage observed in related studies (Vinay et al., 2020; Mahajanakatti et al., 2022) is the selective cytotoxicity of Rudraksha-derived nanoparticles. While normal cell lines like J774A.1 remained largely unaffected, cancerous cell lines such as PC-3 (prostate cancer) and HeLa (cervical cancer) showed high sensitivity x and underwent apoptotic death at the same or lower nanoparticle concentrations.

This selectivity can be attributed to:

- Higher nanoparticle uptake in cancer cells due to enhanced permeability and retention (EPR) effect.
- Greater vulnerability of cancerous mitochondria to oxidative stress.
- Activation of intrinsic apoptotic pathways (as evidenced by increased caspase activity and nuclear condensation in vitro).

Future Recommendations for Toxicological Validation

Although these in vitro studies are highly encouraging, further validation is essential before clinical translation:

1. In Vivo Studies:

Studies in animal models (e.g., zebrafish embryos, rodents) are necessary to understand biodistribution, metabolism, and long-term effects.

2. Hematological and Histopathological Analysis:

Evaluation of blood markers and organ tissues post-treatment will help determine systemic toxicity and organspecific accumulation.

3. Genotoxicity and Immunotoxicity:

To ensure safety, it is critical to assess whether Rudraksha-derived nanoparticles alter genetic material or immune function over extended periods.

Comparative Studies:

Comparing E. ganitrus-based nanoparticles with both chemically synthesized and other green-synthesized NPs (e.g., from neem, tulsi, or aloe vera) would help standardize biocompatibility profiles.

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Toxicological Findings

Study	Cell Line/Model	Observation	Safe Concentration Range	Reference
		>85% viability, no morphological toxicity	 \ \ \ \ \	Dwivedi et al., 2014
Mahajanakatti et al. (2022)	Hala Varo calle		• •	Mahajanakatti et al., 2022
Vinav et al (2020)		Dose-dependent apoptosis in cancer cells	IC50 ~30 μg/mL	Vinay et al., 2020

Based on what we know so far, Rudraksha-based nanoparticles appear to be safe and gentle on healthy cells when used at the right dose.

CONCLUSION

The convergence of nanotechnology and phytochemistry has paved the way for environmentally sustainable and biologically potent nanomaterials, and Elaeocarpus ganitrus (Rudraksha) stands out as a remarkably efficient candidate for this endeavor. As evidenced throughout this review, E. ganitrus not only fulfills the criteria of a green bioreactor but also offers a rich repertoire of phytochemicals—such as flavonoids, alkaloids, and phenolic acids—that actively participate in the bioreduction, capping, and stabilization of nanoparticles.

The plant-mediated synthesis of silver and gold nanoparticles using extracts from various Rudraksha tissues (seeds, leaves, and beads) has yielded nanostructures with well-defined morphology, crystalline architecture, and surface functionality. These nanoparticles, characterized by UV–Vis, FTIR, XRD, SEM/TEM, EDX, DLS, and GC-MS, display not only physical stability but also profound biological activity.

In particular, Rudraksha-derived nanoparticles have demonstrated potent antibacterial, antifungal, antioxidant, and anticancer effects across a spectrum of in vitro studies. The antibacterial properties have been linked to mechanisms such as membrane rupture, reactive oxygen species (ROS) generation, and inhibition of microbial DNA. Meanwhile, their anticancer efficacy is supported by both experimental cytotoxicity data and molecular docking studies, which highlight strong binding affinities of key phytochemicals (quercetin, gallic acid, ellagic acid) to critical oncogenic targets such as BCL-2 and EGFR. These dual layers of evidence—experimental and in silico—strongly suggest that E. ganitrus-based nanoparticles function through multi-modal mechanisms that affect both microbial viability and tumor cell survival.

Toxicological evaluations further underscore the biocompatibility of these nanomaterials. In vitro assays on normal mammalian cells have shown high cell viability at therapeutic concentrations, indicating a favorable safety profile that sets the stage for biomedical applications.

Despite these promising outcomes, this field remains in a nascent stage. The current literature lacks sufficient in vivo data, pharmacokinetic profiling, and long-term toxicity studies. In addition, standardization of extraction protocols, nanoparticle synthesis conditions, and bioactivity assays will be essential for translating laboratory findings into clinical-grade formulations.

Moving forward, Rudraksha-derived nanoparticles hold substantial promise in the design of **next-generation therapeutics**, particularly in addressing antibiotic resistance, oxidative stress-related disorders, and targeted cancer therapy. With a solid foundation rooted in ethnomedicine and a growing body of scientific validation, Elaeocarpus ganitrus has the potential to bridge traditional knowledge with modern nanomedicine. Future research should focus on scaling production, exploring combinatorial delivery systems, and validating therapeutic efficacy through preclinical and clinical trials.

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