

PHYSICAL DRIVE NANOCARRIERS: A SMART ROUTE TO ENHANCED THERAPY

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ABSTRACT

Although many plant-based substances struggle to achieve full efficacy in the body due to low solubility and limited absorption, herbal medicines have long been respected for their safety and therapeutic effects. The popular medicinal plant *Ocimum sanctum*, or tulsi, contains potent bioactive compounds with antibacterial, anti-inflammatory, and antioxidant properties. However, the therapeutic effect of these natural chemicals is diminished because they often degrade rapidly or do not reach sufficient concentrations in the circulation. This problem has a contemporary answer thanks to nanotechnology. The fragile phytochemicals may be protected, stabilised, and made more bioavailable by transforming Tulsi extracts into stabiliser-based formulations. By delivering the active ingredients to the target site more effectively, these sophisticated nanocarriers may improve therapeutic outcomes at lower doses. The creation and assessment of sophisticated herbal nanocarriers based on *Ocimum sanctum* extract are the main objectives of this work. Their physicochemical characteristics, drug-loading capacity, release behaviour, and possibly the hazardous enhancement arising from them were evaluated. The results should show that Tulsi's therapeutic efficacy can be greatly increased via nanocarrier-based delivery, providing a stabilising step toward the development of more effective, scientifically supported herbal treatments.

Keywords: *Ocimum sanctum*, Herbal nanocarriers, nanotechnology, phytochemicals, bioavailability, nanoformulation, therapeutic potential, antioxidant activity, anti-inflammatory activity, herbal drug delivery, nanoparticles.

1. Introduction:

One such plant, highly praised in traditional medicine for its stabilising properties and medicinal applications, is *Ocimum tenuiflorum*. Nevertheless, many of the form ingredients do not demonstrate optimal efficacy in the human body, despite their demonstrated advantages. Herbal chemicals often exhibit poor solubility, volatility, and limited bioavailability, which contribute significantly to this restriction. They either fail to reach the target location in adequate quantity or are swiftly digested or broken down in the gastrointestinal system. High dosages are therefore required to provide therapeutic benefits, thereby reducing patient compliance and limiting clinical utility.

Nanocarrier-based delivery systems offer a possible solution to these problems, thanks to recent advances in pharmaceutical technology. Liposomes, polymeric nanoparticles, niosomes, nanoemulsions, and solid lipid nanoparticles are examples of nanocarriers that can prevent the degradation of herbal bioactives, enhance targeted or controlled distribution, and enable targeted or controlled delivery. These nanoscale carriers function as small, protective vehicles that deliver phytochemicals to the site of action more effectively and securely. Therefore, developing sophisticated herbal nanocarriers derived from *Ocimum sanctum* is an essential step toward advancing herbal medicine, strengthening its scientific validity, and ensuring that its natural compounds realise their full therapeutic potential. [1]

2. Objective of the study:

- 2.1. To use *Ocimum sanctum* leaf extract to create a green synthesis technique for nanoparticles that mimics the use of hazardous chemicals and severe reaction conditions. [2]
- 2.2. To use common methods, such as UV-visible spectroscopy, FTIR, SEM/TEM, and XRD, to characterise the size, shape, surface characteristics, and crystalline nature of the produced nanoparticles. [3]
- 2.3. To determine how Tulsi's phytochemicals augment the biological activities (such as antibacterial, antioxidant, or antimicrobial potential) of the *O. sanctum*-mediated nanoparticles.
- 2.4. To assess the nanoparticles' cytotoxicity or biosafety profile to determine if they are appropriate for use

in environmental, pharmacological, or biomedical applications. [5]

3. Scope and significance

This research encompasses therapeutic, environmental, and biomedical domains. Research has demonstrated that *O. sanctum*-synthesised nanoparticles exhibit potent antibacterial activity, particularly against multidrug-resistant bacteria such as *Acinetobacter baumannii* [6]. In a similar vein, Tulsi-mediated nanoparticles possess powerful antioxidant properties that aid in neutralising free radicals and suggest possible therapeutic uses for illnesses linked to oxidative stress [7].

Ocimum sanctum-based nanoparticles also show significant promise in cancer therapy. In MCF-7 breast cancer cells, gold nanoparticles prepared from Tulsi oil extract have been shown to induce reactive oxygen species production and mitochondrial dysfunction, suggesting strong anticancer potential [97]. In the environmental sector, Tulsi-derived nanoparticles have been used for water purification and dye degradation, offering an eco-friendly solution for removing pollutants, such as Congo red, from wastewater [8].

Tulsi's potential to promote green nanotechnology is one of its main advantages. Because the plant's natural phytochemicals do not require harsh chemicals, the synthesis is safer, less expensive, and more ecologically friendly. Tulsi-based nanoparticles are also more biocompatible, making them ideal for biomedical applications such as drug delivery systems, antibacterial agents, and anti-inflammatory compositions [9,10]

4. Plant Profile



Fig 1: *Ocimum sanctum* tulsi [102]

4.1. Taxonomy

Table 1: Taxonomy of *Ocimum sanctum*

Scientific Name	<i>Ocimum sanctum</i>
Kingdom	Plantae
Phylum	Spermatophyte
Class	Magnoliopsida
Family	Lamiaceae
Order	Lamiales
Genus	Ocimum
Species	sanctum

4.2. Phytochemicals of *Ocimum sanctum* (Tulsi):

4.2.1. Flavonoids (Luteolin, Apigenin, Quercetin)

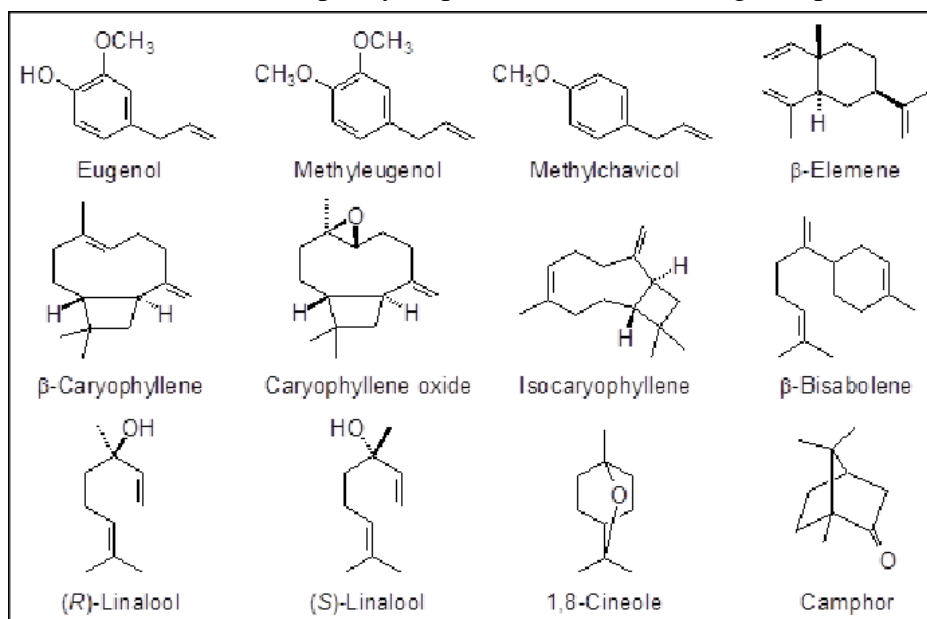
Among Tulsi's most prevalent compounds are flavonoids. Substances such as quercetin, luteolin, and apigenin offer strong anti-inflammatory and antioxidant properties. They help reduce inflammation-related illnesses, protect cells from oxidative damage, and neutralise free radicals [11,12]. Tulsi has a wide range of therapeutic potential, as these flavonoids also exhibit antibacterial and anticancer properties [13].

4.2.2. Phenolic Acids (Rosmarinic Acid, Caffeic Acid, Ferulic Acid, Chlorogenic Acid)

One of the most powerful antioxidant compounds found in tulsi is rosmarinic acid, which is abundant in phenolic acids. These substances boost immunity and lessen oxidative stress. Function and demonstrate neuroprotective benefits [11, 13]. As a natural reducing agent that aids in the formation of stable nanoparticles, rosmarinic acid is also essential to the creation of green nanoparticles [12].

4.2.3. Terpenoids (Ursolic Acid, Oleanolic Acid)

Many of the medicinal benefits of tulsi are caused by terpenoids. Strong anti-inflammatory, anti-cancer, and hepatoprotective properties are demonstrated by compounds such as ursolic acid and oleanolic acid [11,13]. These compounds also enhance Tulsi's capacity to promote wound healing and prevent the development of



certain microorganisms [13].

4.2.4. Essential Oils (Eugenol, Methyl Eugenol, Linalool, β-Caryophyllene)

Eugenol, methyl eugenol, linalool, and β-caryophyllene are among the volatile chemicals found in the 0.5–1.5% essential oil found in tulsi ves. Due to its potent therapeutic actions, eugenol is particularly significant [11,14]. Additionally, these oils serve as natural stabilising and capping agents during nanoparticle synthesis, assisting in the creation of homogeneous nanoparticles [14].

4.2.5. Tannins, Saponins, Glycosides, and Alkaloids.

Although they are less common, these secondary metabolites are crucial to Tulsi's therapeutic profile. They have immunomodulatory, adaptogenic, and antioxidant properties that support the body's ability to fight infections, adapt to stress, and maintain overall health [11,15]

5. Distribution & Habitat of Tulsi (*Ocimum sanctum*)

Fig. 2: Chemical constituents of *Ocimum sanctum* (Tulsi) [102]

The well-known medicinal plant tulsi (*Ocimum sanctum*/*Ocimum tenuiflorum*) is found across tropical climates, particularly in Asia. Because of its cultural and therapeutic significance, it is both widely grown and grows naturally.

5.1. Distribution

5.1.1. Native to the Indian subcontinent, tulsi grows widely in both lowlands and mountainous areas up to 1800 meters in the Himalayas [16].

5.1.2. It is found in several tropical and subtropical Asian nations, including China, Malaysia, India, Nepal, and Sri Lanka [17].

5.1.3. It is found in several tropical and subtropical Asian nations, including China, Malaysia, India, Nepal, and Sri Lanka [17].

5.1.4. Tulsi has been imported and grown worldwide, notably in Africa, Australia, and several regions of the Americas, due to its medical and cultural significance [16].

5.1.5. Its cultivated presence is significantly wider than its native range since it is frequently planted in farms, temples, and home gardens [17].

5.2. Habitat

5.2.1. Tulsi has high environmental adaptation, flourishing in roadsides, scrublands, wastelands, and tropical dry deciduous forests [18].

5.2.2. Although it may grow in a variety of soil types, such as loam, lateritic, and slightly alkaline soils, it favours wet, well-drained soils [19].

5.2.3. The plant prefers wet conditions, but it cannot withstand waterlogging; therefore, drainage is necessary for healthy development [19].

5.2.4. The high essential oil concentration and rapid development of tulsi are supported by full sun and warm weather [17].

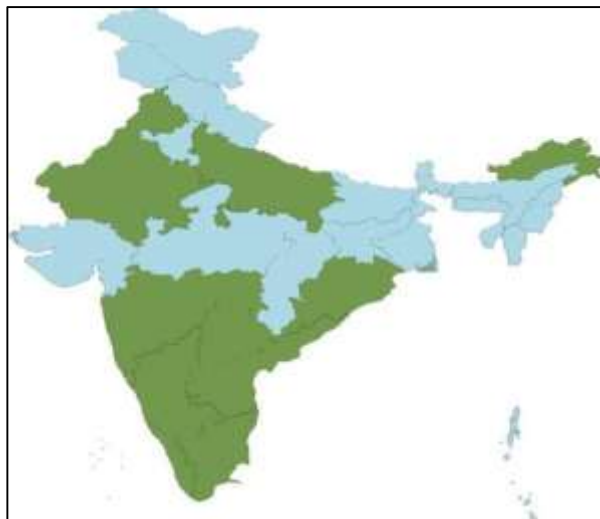


Fig 3. Natural Habitats of Tulsi

6. Morphological Characteristics of *Ocimum sanctum* (Tulsi)

6.1. **Growth Habit:** Tulsi is an upright, fragrant sub-shrub with numerous branches that usually grows to a height of 30 to 60 cm, though some accounts report heights of up to 75 cm [20,21]. Because of its frequent branching, it has a distinctively bushy look.

6.2. **Stem Characteristics:** As it ages, the hairy, gently pubescent stem turns semi-woody at the base [22]. Its quadrangular (four-angled) cross-section, characteristic of plants in the Lamiaceae family, is one of its distinguishing characteristics [20,23].

6.3. **Leaf Morphology** Depending on the cultivar, tulsi leaves can be brilliant green or purplish green, simple, and opposite (decussate) [21]. The leaf blade is elliptical, usually up to about 5 cm long, and has a border that is slightly toothed or serrated [21]. Essential oils give the petiole, which is hairy, thin, and 1.5–3 cm long, a strong perfume [23].

6.4. **Root System** Thin, wiry, branching roots make up the root system. The interior tissues may have a violet-tinged tint, although the exterior surface appears dark brown [23].

6.5. **Inflorescence:** The flowers are placed in tight whorls along the axis of the inflorescence, which is a long, upright raceme [21].

7. Floral Characteristics



Fig 4: Seeds of Tulsi [102]

7.1. **Pedicels (flower stalks) are longer than the calyx** [23].

7.2. **Calyx is ovoid/campanulate (bell-shaped), about 3–4 mm long, bilipped, and pubescent** [23].

7.3. **Corolla is around 4 mm long, hairy (pubescent), and emits a mild nectar-like aroma** [23]. Flower colour may range from **purplish white to light purple**, depending on genotype.

7.4. **Fruit and Seeds:** The fruit is a little nutlet that is pale brown to reddish in colour, subglobose to widely ellipsoid, and slightly compressed [23].

8. Morphotypes of Tulsi



Fig 5: Types of Tulsi [98]

8.1. Tulsi comes in a variety of morphotypes that may be distinguished by their chemical profile, fragrance, and leaf pigmentation:

8.2. The leaves of Rama Tulsi are light and vivid green.

8.3. The purplish-green leaves of Krishna/Shyam Tulsi

8.4. Vana Tulsi is a wild variety with bigger leaves and a stronger scent [21].

9. Medicinal Uses of *Ocimum sanctum* (Tulsi)

9.1. In Ayurveda, tulsi has long been considered a therapeutic herb, and contemporary research is beginning to validate its traditional uses. The plant's numerous medicinal benefits are attributed to its abundance of flavonoids, polyphenols, and essential oils.

9.2. **Powerful Natural Antioxidant** Compounds found in Tulsi help the body combat oxidative stress. These naturally occurring antioxidants have been shown in lab experiments to dramatically reduce oxidative markers and protect cells from free-radical-induced damage [20,24].

9.3. **Natural Anti-Inflammatory Herb Tulsi helps with anti-inflammation**, which is the root cause of many chronic and painful diseases. The body's inflammatory molecules are inhibited by substances like ursolic acid and eugenol [20,22].

9.4. **Strong Antimicrobial and Antiviral Agent** The essential oils of tulsi have the power to either kill or suppress dangerous microorganisms. Studied that the plant's extracts are active against certain viruses, fungi, and bacteria, including *Staphylococcus aureus* and *E. Coli* [22,24].

9.5. **Support for Blood Sugar Control** Tulsi can help control blood glucose levels, according to recent research. In diabetic animals, it significantly increases the body's ability to use glucose and promotes insulin function [20,24].

9.6. **Heart-Protective Benefits** by reducing cholesterol, stopping lipid oxidation, and enhancing circulation, tulsi promotes heart health. People with high blood pressure or cholesterol might benefit from it because its essential oils help relax blood vessels [23, 24].

9.7. **Protection for the Brain and Nervous System** Tulsi is well-known for its neuroprotective and soothing properties. It contains adaptogenic substances that help balance cortisol levels and support the body's stress response. Additionally, research demonstrates enhanced memory and protection against oxidative damage to brain cells [23, 21].

9.8. **Anti-cancer** Certain substances found in Tulsi, such as eugenol, have the capacity to inhibit the development of cancer cells and promote their programmed cell death. Laboratory studies provide encouraging evidence of Tulsi's anticancer potential, but further human trials are required [20,21].

9.9. **Immune-Boosting Effects** Tulsi enhances both innate and adaptive immunity, strengthening the body's defences. Tulsi has been shown to improve antibody production and enhance immune resistance when consumed regularly [24, 21].

9.10. **Support for Respiratory Health** Tulsi has long been used to treat colds and coughs by relieving airway irritation, reducing mucus production, and clearing congestion. It is helpful for conditions such as bronchitis and asthma due to its bronchodilator effects [22,24].

9.11. **Benefits for the Digestive System:** Tulsi helps protect the lining of the digestive tract and is mild on the stomach. According to studies, its anti-inflammatory and antioxidant properties can promote overall digestion and help prevent the development of stomach ulcers [20,23].

10. Pharmacological Activities of Tulsi (*Ocimum sanctum*)

Thanks to potent phytochemicals, including eugenol, ursolic acid, rosmarinic acid, and flavonoids, tulsi is well known for having a diverse pharmacological profile. Numerous advantageous biological processes have been verified by contemporary research:

10.1. **Anti-inflammatory Activity:** Tulsi has potent anti-inflammatory properties that help lessen tissue damage, discomfort, and swelling. This is mostly due to substances such as ursolic acid and eugenol, which block the production of inflammatory mediators, including prostaglandins and cytokines [25,26].

10.2. **Antioxidant Activity** The herb's abundance of phenolic components helps to counteract dangerous free radicals. This promotes heart and liver function, reduces ageing, and shields tissues from oxidative stress [27, 28].

10.3. **Antimicrobial Activity** 4. Tulsi has broad-spectrum antiviral, antifungal, and antibacterial properties. Numerous fungus species, *Staphylococcus aureus*, and *E. coli* have all been demonstrated to be inhibited by its essential oils [29, 30].

10.4. **Antidiabetic Activity** Tulsi improves insulin sensitivity and lowers oxidative stress in pancreatic tissue, which helps control blood glucose levels, according to several studies[35]

10.5. **Adaptogenic / Anti-stress Activity** Tulsi is considered a natural adaptogen. It helps the body cope with physical, psychological, and metabolic stress, improving mental clarity and reducing cortisol levels [27].

10.6. **Cardioprotective Activity** Its antioxidant and lipid-lowering properties help protect cardiac tissues, improve circulation, and reduce cholesterol levels [25,28].

10.7. **Hepatoprotective Activity** Tulsi extracts protect the liver against toxins, heavy metals, and oxidative stress, and support the regeneration of liver cells [32].

10.8. **Immunomodulatory Activity** Tulsi boosts both innate and adaptive immunity. It enhances macrophage activity and strengthens natural defence systems, making the body more resistant to infections [30].

10.9. **Anti-cancer Activity** Bioactive compounds like **ursolic acid** and **carnosic acid** have shown the ability to suppress tumour growth, induce apoptosis (programmed cell death), and prevent cancer spread [28].

10.10. **Gastroprotective Activity** Tulsi reduces gastric irritation, protects stomach mucosa, and helps prevent ulcers caused by stress or medication [29].

10.11. **Neuroprotective & Cognitive-enhancing Activity** Tulsi helps improve memory, reduce neuroinflammation, and protect brain cells from oxidative damage, potentially reducing cognitive decline.

11. About Nanocarriers:

11.1. Concept of herbal nanocarriers

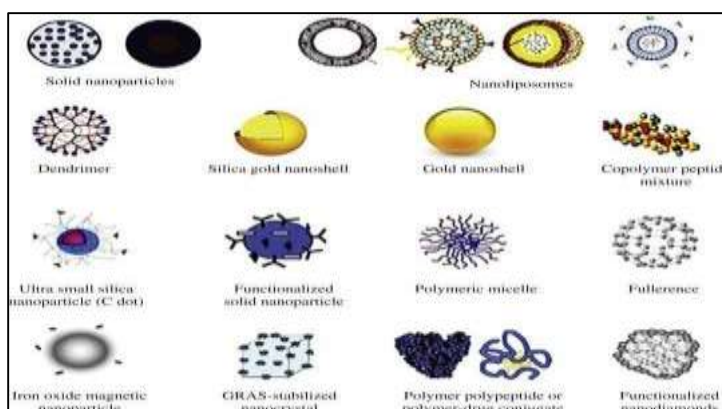


Fig 6: Types of nanocarriers [100]

Herbal nanocarriers are nano-sized drug delivery devices (1–1000 nm) intended to more effectively encapsulate, shield, and deliver bioactive compounds from medicinal plants. The medicinal efficacy of many phytochemicals is severely limited by their poor solubility, instability, fast metabolism, and low bioavailability. Herbal nanocarriers offer a modern solution by enhancing the delivery and performance of plant-derived compounds.

Loading herbal extracts into nanocarriers such as liposomes, polymeric nanoparticles, nanoemulsions, solid lipid nanoparticles, and niosomes helps protect phytochemicals from degradation, increases their solubility, improves their absorption, and allows controlled or targeted drug release. These nano-systems act as tiny protective vehicles that transport plant actives to the site of action more efficiently. [1]

The bioavailability, stability, and therapeutic potential of phytochemicals such as terpenoids, flavonoids, and polyphenols are greatly enhanced by nanocarriers. [33]

All things considered, herbal nanocarriers serve as a bridge between cutting-edge nanotechnology and conventional herbal therapy, enabling natural substances to reach their full therapeutic potential.

12. Role of Nanotechnology in Modern Drug Delivery:

Modern drug distribution has entered a new era thanks to nanotechnology, which enables more accurate and effective medication administration. Poor solubility, rapid bodily breakdown, inadequate absorption, and non-specific distribution are major issues with many conventional medications. By creating microscopic nanocarriers that can deliver medications more safely and efficiently, nanotechnology helps address these problems.

The solubility, stability, and bioavailability of several medications can be greatly improved by nanocarriers such as polymeric nanoparticles, liposomes, micelles, dendrimers, and lipid nanoparticles. Due to their small size, these systems may readily cross biological barriers and reach deeper areas that are difficult for traditional medications to reach [34].

The capacity of nanocarriers to deliver drugs in a targeted manner is one of the most significant developments. Nanotechnology significantly reduces toxicity by enabling medications to target specific cells (such as cancer cells) while sparing healthy organs. In contrast to conventional medication formulations, this selective targeting enhances treatment results and reduces adverse effects. [33]

Controlled and prolonged medication release is another important advantage. Nanocarriers can release the medication gradually over time rather than all at once, preserving therapeutic doses for extended periods. This increases patient compliance and decreases the frequency of doses. [35]

All things considered, nanotechnology is improving the effectiveness, safety, and intelligence of contemporary medications and is quickly laying the groundwork for next-generation therapeutic systems. [36]

13. Green Nanotechnology in Modern Drug Delivery:

13.1. **Green Nanotechnology** refers to the environmentally responsible design, production, and use of nanoscale materials utilising sustainable, natural means rather than hazardous chemicals or energy-intensive procedures. This method eliminates the need for harsh solvents or dangerous chemicals by using plant extracts, microbes, enzymes, or biodegradable waste products as reducing and stabilising agents to create nanoparticles. In addition to reducing environmental contamination, this process produces nanoparticles that are more biocompatible and less toxic, making them suitable for use in pharmacological, biomedical, and environmental applications [37–40].

13.2. Advantages of Green Nanotechnology

13.2.1. Safer Nanoparticles for Drug Delivery

Ocimum sanctum green-synthesised nanoparticles are less hazardous and more biocompatible. They are appropriate for oral, topical, and injectable drug delivery methods due to their inherent phytochemical coating [46].

13.2.2. Fast, Cost-Effective, and Scalable Synthesis

In Asia and India, *Ocimum sanctum* is extensively farmed, cheap, and abundant. Tulsi is ideal for large-scale green nanotechnology, as it enables rapid, one-pot nanoparticle production without expensive chemicals or high-energy equipment [43, 46].

13.3. Rationale for using *Ocimum sanctum* in nanoparticle synthesis:

13.3.1. Rich Phytochemical Composition Enables Green Reduction

Flavonoids, phenolics, eugenol, terpenoids, and antioxidants found in *Ocimum sanctum* leaves function as potent natural reducing agents that effectively transform metal ions (Ag^+ , Pd^{2+} , Cu^{2+}) into nanoparticles without the need for dangerous chemical reducers [47–49]. Ag^+ was effectively converted to Ag_2 in a single step by sunlight-induced synthesis employing Tulsi leaf extract [50]. Green palladium nanoparticle production has also employed tulsi extract to decrease Pd salts [51].

13.3.2. Natural Phytochemicals Act as Capping & Stabilising Agents

O. sanctum contains phenolics, polyphenols, and other plant metabolites that attach to the surfaces of nanoparticles and function as organic capping agents. This increases stability, prolongs shelf life, and stops nanoparticle aggregation [51,52]. Strong biocapping effects and outstanding colloidal stability are confirmed by numerous characterisations of Tulsi-mediated AgNPs [47,49].

13.3.3. Enhanced Biological & Therapeutic Activities

The inherent antioxidant, antibacterial, anti-inflammatory, and cytotoxic qualities of the plant are inherited and enhanced by tulsi-mediated nanoparticles. AgNPs produced using Tulsi extract had moderate cytotoxicity to human A549 cells and significant antibacterial activity against multidrug-resistant *Acinetobacter baumannii*

[48]. Tulsi-derived nanoparticles also exhibit significant antioxidant activity [47,53].

13.3.4. Eco-Friendly, Sustainable & Low-Cost Synthesis

Tulsi extract is used in accordance with green nanotechnology principles, including minimal energy use, moderate environmental impact, and the absence of hazardous chemicals. Tulsi-mediated copper nanoparticle production has been effectively applied in wastewater treatment [54], whereas sunlight-driven synthesis does not require chemical additions [50]. Production is now affordable, scalable, and environmentally safe [49,54].

13.3.5. Versatility for Catalytic & Environmental Applications

Tulsi-synthesised nanoparticles, particularly PdNPs and CuNPs, exhibit remarkable catalytic efficiency beyond medicinal applications. For instance, Pd nanoparticles made from tulsi efficiently catalysed the hydrodechlorination of 4-chlorophenol [51].

13.3.6. Improved Biocompatibility & Lower Toxicity

Compared to chemically manufactured nanoparticles, tulsi-derived nanoparticles are less harmful and more biocompatible because they are naturally capped with plant biomolecules. According to studies, Tulsi-AgNPs remain highly effective against infections but exhibit lower toxicity in human cells [28,51].

14. Materials and Methods:

14.1. Collection of *Ocimum sanctum* (Tulsi)

One of the most crucial stages before starting any scientific or pharmacological trial is the collection and accurate identification of Tulsi. Researchers use a defined process to ensure that the plant material is pure, reliable, and accurately representative of *Ocimum sanctum*.

14.2. Collection Process

Typically, clean, pesticide-free settings such as botanical gardens, herbal nurseries, or organically farmed fields are where fresh, healthy tulsi plants are sourced. Because important medicinal components, including eugenol, ursolic acid, and essential oils, are most concentrated during the blooming period, researchers prefer to harvest the plant during this time [25, 30].

Only sections free of illness are selected during collection. Depending on the research goal, leaves, stems, and even roots are collected. To remove dust and contaminants, the collected material is carefully cleaned.

Tulsi is shade-dried rather than sun-dried after cleaning. This is crucial because sensitive phytochemicals, particularly the essential oils that give Tulsi its scent and therapeutic properties, can be destroyed by direct sunlight [27, 32]. Its natural qualities are preserved by shade drying, which is important for research, including phytochemical analysis, pharmacological testing, and nanoparticle manufacturing.

14.3. Preparation of *Ocimum sanctum* Extract

For research requiring phytochemical analysis, pharmacological testing, or the creation of green nanoparticles, preparing an extract of *Ocimum sanctum* (Tulsi) is essential.

14.4. Collection and Initial Processing

The tulsi leaves are first cleaned with clean water to remove dust and contaminants after being gathered and verified. After that, the leaves are shade-dried for 5 to 7 days, or until crisp. Since direct sunlight can destroy phenolic antioxidants and volatile oils such as eugenol and caryophyllene, shade drying is recommended [30, 32].

14.5. Grinding of the Dried Leaves

A mechanical grinder is used to powder the leaves once they have dried finely. By increasing the surface area, a fine powder facilitates the extraction of additional phytochemicals, including terpenoids, rosmarinic acid, and flavonoids, by solvents [25].

Extraction Process Most reviews describe two widely used extraction methods:

14.6. Hot Solvent Extraction (Soxhlet Method) (High yield)

This is one of the most widely used laboratory techniques.

14.6.1. Depending on the desired chemicals, a solvent such as ethanol, methanol, or water is utilised to put the powdered leaves (typically 20–50 g) into a Soxhlet extractor. Eugenol and phenolics are more effectively extracted by alcohol-based solvents [29, 30].

14.6.2. After four to eight hours of continuous solvent recycling through the powder, the extract is concentrated using a rotary evaporator, leaving behind a thick, dark-green residue that is rich in bioactive chemicals [29].

14.7. Aqueous Extraction (Decoction or Boiling)

Because water is safe, environmentally beneficial, and capable of maintaining antioxidants, this approach is commonly employed in the manufacture of green nanoparticles.

- 14.7.1. In a beaker, the powdered leaves are combined with distilled water (e.g., 10 g in 100– 200 mL).
- 14.7.2. The mixture is heated for 15 to 30 minutes at 60 to 80 degrees Celsius.
- 14.7.3. The mixture is filtered using Whatman filter paper or muslin cloth after cooling, and the clear water extract is collected and sometimes kept at 4°C for the production of nanoparticles [30, 32].
- 14.7.4. Phenolics and flavonoids, which are abundant in water extracts, function as stabilising and reducing agents during the production of nanoparticles.
- 14.8. Filtration and Storage
- 14.8.1. To get rid of contaminants, the final extract—whether ethanolic or aqueous—is filtered. To keep extracts safe from light and oxidation, they are often kept in sealed amber bottles. Stability is preserved for later use by cold storage at 4°C [25].



Fig 7: Collection & Extraction of Tulsi

14.9. Synthesis of Silver Nanoparticles (AgNPs):

14.9.1. To create silver nanoparticles, scientists employ three primary techniques: chemical, physical, and biological (green). Every approach has its own advantages, difficulties, and style.

14.9.2. Chemical Methods (Fast but not eco-friendly)

Chemical synthesis is like a fast laboratory reaction. Silver ions (Ag^+) are reduced to silver nanoparticles by a substance like sodium borohydride. Chemists use capping agents such as citrate or PVP to keep particles stable and prevent aggregation [55].

➤ Important points:

- It is quick and frequently utilised, produces consistent, well-controlled nanoparticles, and uses hazardous chemicals, making it unsuitable for medicinal purposes. [56]

14.9.3. Physical Methods (Pure but energy-heavy)

➤ Instead of using chemicals, physical techniques depend on heat, light, or mechanical force. Examples consist of:

- Evaporation–condensation: Heating silver until it evaporates and cools to form nanoparticles [57]
- Laser ablation: Tiny nanoparticles are released into water when a laser strikes a silver plate [58].
- Crushing silver into tiny, nanoscale particles using ball milling

➤ Important points:

- Generates very pure nanoparticles
- No chemical residues
- Equipment is expensive, and energy consumption is high [59]

14.9.4. Biological / Green Synthesis (Eco-friendly & safest)

➤ Green synthesis is the most human-friendly method. Instead of harmful chemicals, it uses plants, microbes, or natural extracts. Plant extracts—like *Ocimum sanctum* (Tulsi)—contain natural phytochemicals such as flavonoids, polyphenols, and eugenol that reduce and stabilise silver nanoparticles at the same time [60].

➤ Key points:

- Safe, eco-friendly, low cost
 - No pollution
 - Produces biocompatible nanoparticles ideal for medicine
 - Tulsi-based AgNPs show extra biological activity due to natural phytochemical coating [61]
- Principle of Biological (Green) Synthesis of Nanoparticles
- Biological synthesis, often known as "green synthesis," produces nanoparticles without the use of

dangerous chemicals by utilising microorganisms, plants, or naturally occurring biomolecules. Because many biological materials naturally include substances that can decrease, stabilise, and shape nanoparticles, the procedure is effective.

- Natural phytochemicals act as reducing agents.
- Strong natural substances found in plants include terpenoids, flavonoids, polyphenols, and reducing sugars. Silver ions (Ag^+) can become metallic silver nanoparticles (Ag^0) by receiving electrons from these substances. The core of green synthesis is this straightforward "electron donation" [60].
- The same biomolecules also stabilise the nanoparticles
- The silver atoms tend to group once they are formed. However, plant molecules act as a barrier around every tiny particle. This regulates the size and shape of the particles and prevents aggregation [61].
- Plant extracts act as a complete nanofactory.
- Plant extracts serve all purposes simultaneously, in contrast to chemical procedures that call for several reagents:
 - Reducer, which transforms ions into nanoparticles
 - Capping agent, which keeps them stable
 - Growth regulator, which governs form and size
- For medicinal applications, this makes green synthesis easy, affordable, and secure [62].

14.10. **Tulsi (*Ocimum sanctum*) is especially powerful**

14.10.1. Eugenol, rosmarinic acid, ursolic acid, and phenolic antioxidants found in tulsi effectively decrease silver ions and produce stable nanoparticles with increased biological activity [63]. Tulsi is extensively studied for nanoparticle development due to its inherent synergy [64].

14.10.2. The process is eco-friendly and energy-efficient. Hazardous substances like sodium borohydride and hydrazine are avoided in biological synthesis. The technique needs modest conditions (room temperature, basic mixing), making it:

- **Safe Green**
- **Low cost**
- **Suitable for biomedical use** [65]

14.11. Characterisation of Synthesised Nanoparticles

14.11.1. Nanoparticles must be characterised to verify their formation, purity, size, shape, structure, and stability once they are created, whether by chemical, physical, or environmentally friendly means. To determine the true appearance and behaviour of the nanoparticles, scientists employ a variety of analytical techniques.

14.11.2. **UV–Visible Spectroscopy (UV–Vis)** Because silver nanoparticles exhibit a clear absorption peak due to Surface Plasmon Resonance (SPR), it is typically the first test. AgNPs' electrons vibrate collectively when light interacts with them, creating a distinctive peak at 400–450 nm [62].

14.11.3. **Fourier Transform Infrared Spectroscopy (FTIR)** Functional groups from biomolecules or plant extracts that adhere to the surface of nanoparticles can be identified using FTIR. These biomolecules prevent nanoparticles from clumping together by acting as stabilising and capping agents [63].

14.11.4. **X-Ray Diffraction (XRD)**. XRD shows the crystalline structure of nanoparticles. The diffraction peaks of silver nanoparticles usually correspond to the face-centered cubic (FCC) structure of metallic silver [64].

14.11.5. **Scanning Electron Microscopy (SEM)** SEM offers finely detailed pictures of the surface morphology of nanoparticles. It aids in identifying whether the nanoparticles are irregular, spherical, or rod-shaped [65].

14.11.6. **Transmission Electron Microscopy (TEM)** Compared to SEM, TEM provides even greater magnification. It provides accurate details regarding the internal structure, shape, and size distribution of nanoparticles [66].

14.11.7. **Dynamic Light Scattering (DLS)** DLS assesses the polydispersity index (PDI), which indicates sample homogeneity, and hydrodynamic size, or the size of particles in liquid [67].

14.11.8. **Their zeta potential indicates Zeta Potential Analysis—the surface charge of nanoparticles.** Good stability is indicated by a strong negative or positive charge, which prevents particles from clumping and repelling one another [68].

14.11.9. **Energy-Dispersive X-ray Spectroscopy (EDX / EDAX)** The elemental makeup of nanoparticles is verified using EDX. A strong signal confirms the presence of metallic silver in silver nanoparticles at around

3 keV [69].

14.12. Evaluation Parameters for Synthesised Nanoparticles

Following synthesis, nanoparticles must undergo several assessment procedures to verify their biological activity, stability, quality, and suitability for practical use. These metrics help researchers assess the efficacy and safety of the nanoparticles.

14.12.1. Particle Size and Size Distribution

Their size determines the behaviour of nanoparticles within the body; smaller particles exhibit more biological activity and penetration. To determine if the nanoparticles are tiny, uniform, and stable, methods such as DLS, TEM, and SEM are employed [70].

14.12.2. Surface Charge (Zeta Potential)

The stability of nanoparticles in suspension is reflected in zeta potential. Because they resist clumping and repel one another, highly charged particles (either + or -) remain stable for longer [71].

14.12.3. Shape and Morphology

Researchers use SEM and TEM to identify spherical, rod-shaped, or irregular nanoparticles [72]. Shape has a significant impact on cellular absorption and biological activity.

14.12.4. Crystallinity

The correct crystalline structure of nanoparticles, such as FCC for silver nanoparticles, may be determined by XRD examination [73].

14.12.5. Stability Studies

Over time, nanoparticles are monitored to verify:

- Colour changes
- Sedimentation
- Changes in size or zeta potential
- Aggregation tendencies [74]

To observe changes in size, colour, or activity, nanoparticles are subjected to various pH and temperature conditions [75].

14.12.6. Drug Loading Capacity (For Drug-Loaded NPs)

Researchers use UV-Vis or HPLC techniques to quantify the amount of medication or plant extract that is effectively loaded onto or inside nanoparticles [76].

14.12.7. Entrapment Efficiency

This measure indicates the percentage of the bioactive substance that was effectively encapsulated or bound to nanoparticles [77].

14.12.8. Antimicrobial / Antioxidant Evaluation

Antimicrobial and antioxidant studies are often performed on biologically produced nanoparticles. AgNPs derived from plants such as *Ocimum sanctum* often exhibit potent antibacterial and free-radical scavenging properties [78].

14.12.9. In-Vitro Cytotoxicity / Biocompatibility

Nanoparticles that are toxic to pathogens or cancer cells but safe for human cells are determined using cell-based tests (MTT, XTT, etc.) [79].

14.13. Applications of AgNPs:

14.13.1. Applications of Silver Nanoparticles (AgNPs)

Because of their potent antibacterial activities, large surface area, biocompatibility, and special optical and catalytic qualities, silver nanoparticles (AgNPs) are among the most commonly employed nanomaterials. They are used in environmental research, agriculture, textiles, medicine, pharmaceuticals, and food safety.

14.13.2. Antimicrobial Applications (Antibacterial, Antifungal, Antiviral) AgNPs can destroy harmful microorganisms by disrupting their cell walls, generating reactive oxygen species, and binding to DNA/proteins [80].

➤ They are used in:

- Wound dressings
- Antiseptic gels
- Antimicrobial sprays
- Hospital surfaces
- Water purification systems

14.13.3.

14.13.4. **Drug Delivery and Biomedical Applications.** Their small size and large surface area allow AgNPs to carry drugs efficiently. Biogenic AgNPs (especially plant-based) show good **biocompatibility and therapeutic activity** [81].

- Applications include:
 - Targeted drug delivery
 - Anti-inflammatory formulations
 - Anticancer research
 - Improved penetration through biological barriers

14.13.5. **Wound Healing and Tissue Regeneration** AgNPs help prevent infections while promoting faster healing by stimulating skin cell growth [82]. This is why many **wound dressings, bandages, and gels** now contain silver nanoparticles.

14.13.6. **Diagnostic and Imaging Applications** Because of their **unique optical properties**, AgNPs are used in:

- Biosensors
- Imaging probes
- Diagnostic kits [83]

They enhance the sensitivity of tests, including rapid detection of viruses and bacteria.

14.13.7. **Textile Industry** AgNPs are incorporated into fabrics to create:

- Odour-free socks
- Antimicrobial hospital linens
- Hygienic sportswear
- Long-lasting, germ-free clothing materials [84]

14.13.8. **Food Packaging and Preservation** AgNPs prevent microbial growth in food packaging films, extending the shelf life of perishable foods [85].

14.13.9. **Agriculture** AgNPs are used as:

- Nano-fungicides
- Nano-pesticides
- Plant growth stimulators [88]
- Biogenic AgNPs help control fungal and bacterial infections in crops.

14.13.10. **Water Purification** Silver nanoparticles effectively kill waterborne pathogens and are incorporated into filtration systems [87].

14.13.11. **Catalysis and Environmental Applications** AgNPs act as strong catalysts for:

- Pollutant degradation
- Reduction of dyes
- Chemical reactions used in industry [88]

15. **Conclusion:**

15.1. Summary

A common and environmentally beneficial alternative to conventional chemical and physical techniques is the green production of silver nanoparticles (AgNPs) using plant extracts. Natural phytochemicals found in plants such as *Ocimum sanctum* serve as stabilising and reducing agents, enabling the formation of nanoparticles under low-energy, safe, and gentle conditions [89,91]. These biogenic AgNPs are extremely helpful in the fields of health, the environment, and food safety because they combine the antibacterial and antioxidant properties of silver with the medicinal compounds of plants [90,91].

15.2. Advantages of Green Synthesis

15.2.1. Eco-friendly & Non-Toxic Plant-based synthesis is safer for both people and the environment since it avoids dangerous chemicals and high-temperature procedures [89].

15.2.2. Materials that are affordable and readily available even in environments with limited resources, low-cost nanoparticle manufacturing is made possible by the abundance and affordability of leaves, stems, and other plant parts [90].

15.2.3. Biocompatible Nanoparticles: Compared with chemically synthesised nanoparticles, phytochemicals naturally coat AgNPs, increasing their uptake in biological systems and reducing their toxicity [91].

15.2.4. Easy, One-Step Procedure: Plant extracts facilitate rapid one-step synthesis by acting as reducers, stabilisers, and surface modifiers simultaneously [92].

15.2.5. Sustainable and Scalable: Reviews indicate that, due to the renewable nature of plant biomass and

moderate reaction conditions, green synthesis holds great promise for large-scale manufacturing [89].

15.3. **Overall Therapeutic Potential of Herbal Nanocarriers:**

15.3.1. **Antimicrobial Power:** Because silver and plant phytochemicals work in concert, green AgNPs have potent antibacterial and antifungal action, especially against drug-resistant pathogens [94,92].

15.3.2. **Antioxidant & Wound Healing Benefits:** Plant-mediated AgNPs have superior antioxidant qualities and accelerate healing by lowering inflammation and infection [90,94].

15.3.3. **Viral and Cancer Applications:** According to several publications, plant-derived nanoparticles disrupt viral replication pathways and cause cancer cells to die [91].

15.3.4. **Better Drug Delivery:** Herbal nanocarriers improve the solubility, absorption, and long-term release of medicines produced from plants, increasing their overall effectiveness [89].

15.3.5. **Safer Nanomaterials:** Because of their natural capping molecules, plant-synthesised AgNPs exhibit lower toxicity, making them more appropriate for biomedical applications [91].

15.4. **Limitations of Present Studies:**

15.4.1. **Plant Extract Variability**

Reproducibility is challenging because the composition and quantity of phytochemicals vary with plant age, location, and season [90].

15.4.2. **Inadequate Mechanism Understanding**

Although phytochemicals reduce Ag^+ to Ag^0 , the exact chemical mechanism and reaction kinetics remain unclear [89].

15.4.3. **Difficulties with Large-Scale Production**

Scaling the process industrially is limited by inconsistent plant materials, variations in extraction, and unpredictable yields [91].

15.4.4. **Insufficient Toxicity Studies**

Most studies focus on lab-based results; long-term toxicity and in vivo effects remain under-explored [93].

15.4.5. **Lack of Standard Protocols**

There is no standardisation for extract preparation, pH, concentration, or synthesis conditions, making comparisons difficult [92].

15.4.6. **Regulatory Challenges**

Because green-synthesised nanoparticles carry biological molecules, regulatory approval for clinical use is complex and underdeveloped [89].

15.5. **Future Scope:**

15.5.1. **Advanced Pharmacological Evaluation**

Although *Ocimum sanctum*-mediated AgNPs have potent antibacterial, antioxidant, anticancer, and wound-healing properties, most research remains in vitro and preliminary. Future studies ought to incorporate: Comprehensive mechanistic research to comprehend how interactions between phytochemicals and nanoparticles improve therapeutic efficacy [6,96].

Research on pharmacokinetics and biodistribution will assist in ascertaining the movement, accumulation, and clearance of these nanoparticles throughout the body [96].

Studies comparing herbal AgNPs to chemically manufactured nanoparticles and conventional medications to confirm their actual therapeutic benefit [95].

15.5.2. **Toxicity and Safety Assessment**

The paucity of long-term safety evidence is a significant gap in the present research. The majority of research relies on restricted animal trials or short-term cell investigations. Future research ought to concentrate on:

Research on long-term toxicity, such as immunotoxicity, neurotoxicity, genotoxicity, and reproductive toxicity [93].

In vivo biocompatibility research to verify human safety [96].

Determining any organ-specific accumulation and establishing acceptable dosage levels for therapeutic uses [95,93].

For clinical translation and regulatory approval, thorough toxicology will be necessary.

15.5.3. **Scale-up and Industrial Feasibility**

Although green synthesis is cost-effective and ecologically benign, scaling it is still difficult. Future research ought to investigate:

Standardised extraction procedures to lower phytochemical content variability across batches [92].

Adjusting the pH, extract concentration, and process temperature to achieve consistent yields [95].

Continuous-flow bioreactor methods for producing plant-mediated nanoparticles on a wide scale [92]. Industrial validation of performance, stability, and shelf life under GMP conditions [96]. The commercialisation of herbal nanocarriers will be made possible by a dependable, repeatable, and industry-friendly technology.

15.6. **Prospects in Targeted & Controlled Drug Delivery**

Herbal nanocarriers have enormous promise as cutting-edge medication delivery systems. Because of their phytochemical capping, plant-based AgNPs have natural surface functions, which make them perfect for:

- 15.6.1. Ligand-based targeted delivery (e.g., using lectins, antibodies, or folate to target tumours) [96].
- 15.6.2. Systems that react to stimuli, such as pH, temperature, light, or drug release activated by an enzyme [95].
- 15.6.3. Dual-action treatments, in which the nanoparticle and plant extract have complementary biological effects (such as combination antibacterial and antioxidant activity) [90,6].
- 15.6.4. Improving solubility, bioavailability, and controlled release patterns using nano-encapsulation of unstable phytoconstituents [96].
- 15.6.5. AgNPs generated from plants may be used in tailored medication delivery and precision medicine with further engineering.

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