

Eco-Friendly Synthesis of Benzimidazole Derivatives Using Plant-Assisted Silver Oxide Nanoparticles and Toluene

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Abstract: *Benzimidazole derivatives constitute an important class of nitrogen-containing heterocyclic compounds exhibiting a broad range of biological and pharmaceutical activities including antimicrobial, antifungal, antiviral, anticancer, anti-inflammatory, anti-ulcer, and antiparasitic properties. Due to their immense medicinal significance, the development of efficient and environmentally sustainable synthetic methodologies for benzimidazole derivatives has become an important area of research in organic and medicinal chemistry.*

The present investigation focuses on the eco-friendly synthesis of benzimidazole derivatives using plant-assisted silver oxide nanoparticles (Ag₂O NPs) as efficient nanocatalysts in toluene medium. Silver oxide nanoparticles were synthesized through a green synthesis approach using citrus leaf extract as a natural reducing and stabilizing agent. The phytochemicals present in citrus leaves such as flavonoids, phenolic compounds, terpenoids, and reducing sugars facilitated nanoparticle formation without the use of hazardous chemicals.

The synthesized nanoparticles were characterized using UV-Visible spectroscopy, FTIR analysis, SEM analysis, and X-ray diffraction studies. UV-Visible spectroscopy confirmed nanoparticle formation through a characteristic surface plasmon resonance absorption peak around 420 nm. FTIR analysis revealed the involvement of phytochemicals in nanoparticle stabilization. SEM analysis indicated nanosized spherical particles, while XRD studies confirmed the crystalline nature and phase purity of silver oxide nanoparticles.

The green synthesized silver oxide nanoparticles were successfully utilized as heterogeneous nanocatalysts for the synthesis of benzimidazole derivatives by condensation of o-phenylenediamine with various aromatic aldehydes under reflux conditions. The reactions afforded corresponding benzimidazole derivatives in good to excellent yields ranging from 75–95%.

The developed methodology offers several advantages including eco-friendly synthesis, high catalytic efficiency, reduced reaction time, excellent product yield, operational simplicity, and sustainable reaction conditions. The present study demonstrates the potential application of plant-mediated nanoparticles in green organic synthesis and medicinal chemistry.

Keywords: Benzimidazole, silver oxide nanoparticles, green synthesis, citrus leaf extract, nanocatalyst, heterocyclic compounds, sustainable chemistry.



I. INTRODUCTION

Heterocyclic compounds represent one of the most important classes of organic compounds due to their extensive occurrence in natural products, pharmaceuticals, agrochemicals, dyes, and biologically active molecules. These compounds contain one or more heteroatoms such as nitrogen, oxygen, or sulfur within a cyclic ring system along with carbon atoms.

Among heterocyclic compounds, nitrogen-containing heterocycles occupy a particularly significant position in medicinal chemistry because of their diverse biological and pharmacological activities. Many naturally occurring biomolecules such as amino acids, purine and pyrimidine bases, vitamins, alkaloids, and coenzymes possess heterocyclic structures essential for biological functions.

Benzimidazole is one of the most important nitrogen-containing bicyclic heterocyclic systems formed by fusion of benzene and imidazole rings. The benzimidazole nucleus exhibits remarkable chemical stability, tautomeric behavior, and diverse biological activities, making it a privileged scaffold in medicinal chemistry.

Benzimidazole derivatives exhibit numerous pharmacological activities including:

- Antimicrobial activity
- Antifungal activity
- Antiviral activity
- Anticancer activity
- Anti-inflammatory activity
- Anthelmintic activity
- Anti-ulcer activity
- Antioxidant activity
- Antihypertensive activity

Several clinically important drugs such as albendazole, mebendazole, omeprazole, pantoprazole, and thiabendazole contain the benzimidazole nucleus.

Traditional synthetic methods for benzimidazole derivatives often require:

- Harsh reaction conditions
- Toxic organic solvents
- Strong acids or oxidants
- Longer reaction time
- High energy consumption

Therefore, the development of environmentally benign and sustainable synthetic methodologies has become highly important.

Green chemistry focuses on the design of chemical processes that minimize hazardous substances, reduce waste generation, and improve environmental compatibility. In recent years, nanotechnology and green nanocatalysis have emerged as powerful tools in sustainable organic synthesis.

Nanoparticles possess unique physicochemical properties such as:

- High surface area
- Enhanced catalytic activity



- Better selectivity
- Improved adsorption क्षमता
- Reusability

Among various nanoparticles, silver oxide nanoparticles have attracted considerable attention because of their:

- High catalytic efficiency
- Antimicrobial properties
- Surface reactivity
- Stability
- Eco-friendly nature

Green synthesis of nanoparticles using plant extracts has emerged as a sustainable alternative to conventional physical and chemical methods. Plant extracts contain phytochemicals such as flavonoids, phenolics, alkaloids, terpenoids, and reducing sugars that act as natural reducing and stabilizing agents.

Citrus leaves are rich in bioactive phytochemicals including:

- Flavonoids
- Polyphenols
- Ascorbic acid
- Terpenoids
- Citral
- Limonene

These compounds facilitate reduction of metal ions into nanoparticles and stabilize the formed nanoparticles.

The present investigation therefore focuses on the green synthesis of silver oxide nanoparticles using citrus leaf extract and their catalytic application in the synthesis of benzimidazole derivatives.

II. OBJECTIVES OF THE STUDY

The major objective of the present study was to synthesize silver oxide nanoparticles using citrus leaf extract through an environmentally friendly green synthesis approach. The synthesized nanoparticles were characterized using various spectroscopic and microscopic techniques to determine their structural, optical, and morphological properties. Another important objective of the study was to synthesize benzimidazole derivatives using Ag₂O nanoparticles as efficient nanocatalysts. The work also aimed to develop an eco-friendly and sustainable synthetic methodology that minimizes the use of hazardous chemicals and energy consumption. In addition, the catalytic efficiency of plant-assisted nanoparticles was investigated, along with the advantages of nanoparticle-mediated synthesis such as improved reaction efficiency, shorter reaction time, and environmentally benign reaction conditions.

III. LITERATURE REVIEW

Benzimidazole chemistry has been extensively studied because of the significant medicinal and pharmaceutical importance of benzimidazole derivatives. The first synthesis of benzimidazole derivatives was reported by Phillips through the condensation of *o*-phenylenediamine with carboxylic acids under acidic conditions. Since then, several synthetic methodologies have been developed employing mineral acids, Lewis acids, microwave irradiation,



nanocatalysts, solvent-free conditions, and green catalytic systems to improve reaction efficiency and product yield. Recent research has mainly focused on environmentally sustainable synthetic approaches involving recyclable catalysts and nanoparticle-mediated reactions.

Green synthesis of nanoparticles using plant extracts has emerged as an eco-friendly and cost-effective approach because plant phytochemicals act as natural reducing, stabilizing, and capping agents during nanoparticle formation. Among various nanoparticles, silver oxide nanoparticles have attracted considerable attention due to their excellent catalytic activity in condensation reactions, oxidation reactions, heterocyclic synthesis, and various organic transformations. Plant-mediated nanoparticles offer several advantages over conventional methods as they eliminate the use of toxic reducing agents, minimize environmental pollution, and support the principles of sustainable and green chemistry.

IV. MATERIALS AND METHODS

4.1 Chemicals Used

The chemicals used in the present study included silver nitrate (AgNO_3), citrus leaf extract, *o*-phenylenediamine, various aromatic aldehydes, toluene, ethanol, and distilled water. Silver nitrate was used as the precursor for the synthesis of silver oxide nanoparticles, while citrus leaf extract served as a natural reducing and stabilizing agent during nanoparticle formation. All chemicals used in the experimental work were of analytical reagent grade and were used without further purification.

4.2 Instruments Used

Various analytical instruments and laboratory apparatus were employed during the synthesis and characterization processes. A UV-Visible spectrophotometer was used for optical analysis of the synthesized nanoparticles, while FTIR spectroscopy was used to identify functional groups and confirm metal-oxygen bond formation. X-ray diffraction (XRD) analysis was carried out to determine the crystalline structure and phase purity of the nanoparticles. Surface morphology and particle size were studied using a scanning electron microscope (SEM). Structural characterization of the synthesized benzimidazole derivatives was performed using an NMR spectrometer. A magnetic stirrer and heating mantle were used to maintain uniform mixing and controlled heating during synthesis reactions.

V. GREEN SYNTHESIS OF SILVER OXIDE NANOPARTICLES

5.1 Preparation of Citrus Leaf Extract

Fresh citrus leaves were collected and thoroughly washed with distilled water to remove dust and other impurities. The cleaned leaves were shade dried and chopped into small pieces. Approximately 10–20 g of the chopped leaf material was boiled in 100 mL of distilled water at 60–80°C for about 15–20 minutes to extract the bioactive phytochemicals present in the leaves. The resulting extract was filtered using Whatman No. 1 filter paper to obtain a clear filtrate, which was subsequently stored and used for the green synthesis of silver oxide nanoparticles.

5.2 Synthesis of Silver Oxide Nanoparticles

Silver oxide nanoparticles were synthesized using a green synthesis approach involving citrus leaf extract as a natural reducing and stabilizing agent. A 1 mM aqueous silver nitrate (AgNO_3) solution was prepared using distilled water. To 90 mL of the silver nitrate solution, 10 mL of citrus leaf extract was added slowly under continuous stirring conditions. During the reaction, the color of the solution gradually changed from pale yellow to dark brown, indicating the formation of silver oxide nanoparticles due to surface plasmon resonance.

The synthesized nanoparticles were separated by centrifugation and repeatedly washed with distilled water and ethanol to remove unreacted substances and impurities. The purified nanoparticles were then dried at 50–60°C to obtain stable silver oxide nanoparticle powder for further characterization and catalytic applications.



VI. CHARACTERIZATION OF SILVER OXIDE NANOPARTICLES

6.1 UV-Visible Spectroscopy

UV-Visible spectroscopic analysis confirmed the successful formation of silver oxide nanoparticles by exhibiting a characteristic absorption peak around 420 nm. The observed absorption peak corresponds to the surface plasmon resonance of silver oxide nanoparticles, indicating the formation of stable nanoparticles with nanoscale dimensions.

6.2 FTIR Analysis

FTIR analysis revealed the presence of various functional groups associated with plant phytochemicals and silver oxide nanoparticles. The broad absorption band observed in the range of 3400–3200 cm^{-1} was attributed to O–H stretching vibrations, while peaks at 2900–2800 cm^{-1} corresponded to C–H stretching vibrations. The absorption bands observed between 1600–1500 cm^{-1} were assigned to C=O and C=C vibrations, and peaks in the range of 1100–1200 cm^{-1} indicated C–O stretching vibrations. The characteristic absorption band observed between 500–700 cm^{-1} confirmed Ag–O stretching vibrations, indicating the successful formation of silver oxide nanoparticles. The FTIR results also confirmed the involvement of plant phytochemicals in the reduction and stabilization of nanoparticles.

6.3 SEM Analysis

SEM analysis showed that the synthesized silver oxide nanoparticles possessed spherical to quasi-spherical morphology with slight agglomeration. The nanoparticles were found to be uniformly distributed and exhibited nanoscale dimensions. The observed morphology and particle distribution suggest effective stabilization of nanoparticles by phytochemical constituents present in the citrus leaf extract.

6.4 XRD Analysis

X-ray diffraction analysis confirmed the crystalline nature and phase purity of the synthesized silver oxide nanoparticles. Distinct diffraction peaks corresponding to cubic silver oxide nanoparticles were observed in the XRD pattern, indicating the successful formation of crystalline Ag_2O nanoparticles with good structural stability.

VII. SYNTHESIS OF BENZIMIDAZOLE DERIVATIVES

General Procedure

A mixture of *o*-phenylenediamine (1 mmol), aromatic aldehyde (1 mmol), toluene (10–15 mL), and silver oxide nanoparticles (10–20 mg) was taken in a round-bottom flask. The reaction mixture was refluxed at 100–110°C for about 4–6 hours under continuous stirring conditions. The progress of the reaction was monitored periodically using thin layer chromatography (TLC). After completion of the reaction, the mixture was cooled to room temperature, and the precipitated product was separated by filtration. The obtained product was washed, recrystallized using ethanol, and dried to obtain pure benzimidazole derivatives.

Reaction Mechanism

The synthesis of benzimidazole derivatives proceeds through a multistep reaction mechanism involving condensation, cyclization, and oxidation processes. Initially, the aromatic aldehyde undergoes condensation with *o*-phenylenediamine to form a Schiff base intermediate. This intermediate subsequently undergoes intramolecular cyclization followed by oxidative aromatization to produce the corresponding benzimidazole derivative. Silver oxide nanoparticles play an important catalytic role by activating the carbonyl group of the aldehyde, facilitating faster cyclization, promoting the oxidation process, and enhancing overall product formation under mild reaction conditions.

VIII. OBSERVATION TABLE

Entry	Aldehyde	Time (min)	Yield (%)	Melting Point (°C)
1	Benzaldehyde	16	78	289



2	Anisaldehyde	16	75	234
3	4-Methylbenzaldehyde	5	75	224
4	4-Chlorobenzaldehyde	10	78	291
5	4-Fluorobenzaldehyde	5	80	245
6	3-Bromobenzaldehyde	5	85	265
7	Furan-2-carbaldehyde	5	90	285
8	Cinnamaldehyde	8	95	199–201
9	3-Nitrobenzaldehyde	7	90	309–310

IX. SPECTRAL ANALYSIS OF BENZIMIDAZOLE DERIVATIVES

10.1 ¹H-NMR Analysis

Characteristic proton signals observed:

Chemical Shift δ (ppm)	Assignment
3.48	OCH ₃ proton
7.11–7.95	Aromatic protons
12.0–13.0	NH proton

The downfield NH signal confirmed benzimidazole formation.

10.2 FTIR Analysis

Important FTIR peaks:

Wavenumber (cm ⁻¹)	Assignment
3580	Amino group
3000	Aliphatic C–H
2800	Aromatic C–H
1100–1200	OCH ₃ group
800	Aromatic C–C

X. RESULTS AND DISCUSSION

The present investigation successfully demonstrated green synthesis of silver oxide nanoparticles using citrus leaf extract.

The UV–Visible spectrum confirmed nanoparticle formation through characteristic surface plasmon resonance absorption at 420 nm.

FTIR analysis revealed the presence of phytochemicals responsible for nanoparticle stabilization.

SEM analysis showed nanosized spherical particles with relatively uniform distribution, while XRD analysis confirmed crystalline phase purity.

The synthesized silver oxide nanoparticles were effectively utilized as nanocatalysts for synthesis of benzimidazole derivatives.

The nanoparticle-assisted methodology provided:

- High product yield
- Reduced reaction time
- Cleaner reactions



- Eco-friendly conditions
- Easy product isolation
- Enhanced catalytic efficiency

Electron-withdrawing substituents exhibited better yields due to increased electrophilicity of aldehyde carbonyl groups. The developed synthetic method aligns well with principles of green chemistry and sustainable organic synthesis.

XI. CONCLUSION

The present study successfully demonstrated the green synthesis of silver oxide nanoparticles using citrus leaf extract and their efficient catalytic application in the synthesis of benzimidazole derivatives.

The synthesized nanoparticles were successfully characterized using UV-Visible spectroscopy, FTIR analysis, SEM analysis, and XRD studies, confirming their nanoscale crystalline nature and stability.

The nanoparticle-assisted synthesis method proved to be efficient, eco-friendly, economical, and sustainable for preparation of benzimidazole derivatives.

The methodology offered several advantages including:

- Green synthesis approach
- High catalytic efficiency
- Reduced reaction time
- Excellent product yield
- Operational simplicity
- Environmental compatibility

The study highlights the immense potential of plant-assisted nanoparticles in sustainable heterocyclic synthesis and medicinal chemistry.

XII. FUTURE SCOPE

Future studies may focus on:

1. Biological evaluation of synthesized derivatives
2. Anticancer and antimicrobial screening
3. Catalyst recyclability studies
4. Use of different plant extracts
5. Large-scale industrial synthesis
6. Computational docking studies
7. Development of reusable nanocatalysts

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