COMPARATIVE ANALYTICAL EVALUATION OF OROXYLUM INDICUM EXTRACTS AND GREEN-SYNTHESIZED NANOPARTICLES

[1]Brijesh Kumar Singh, [2]Dr. Arvind Negi
[1]Research Scholar, [2]Supervisor
[1-2]Faculty of Pharmaceutical Science, Asian International University, Imphal West, Manipur

Abstract
Oroxylum indicum (L.) Kurz is a medicinal Bignoniaceae species rich in flavonoids, particularly baicalein/baicalin, chrysin, oroxylin A and related glycosides. Green conversion of plant extracts into metallic nanoparticles introduces a second analytical entity: a phytochemical-capped colloid whose physicochemical behavior, biological response and formulation potential may differ substantially from the parent extract. This study develops a comparative pharmaceutical-analysis framework for evaluating O. indicum extracts alongside O. indicum-mediated metallic nanoparticles, with silver nanoparticles (AgNPs) used as the principal model because recent literature directly documents their synthesis from aqueous bark extract. The comparison integrates extract standardization, chromatographic fingerprinting, UV-visible spectroscopy, FTIR, X-ray diffraction, electron microscopy, dynamic light scattering, zeta potential, antioxidant and antimicrobial screening, stability trending and formulation-oriented drug-release assessment. Published evidence is distinguished from proposed analytical experiments: for example, an O. indicum bark-mediated AgNP study reported a surface-plasmon band at 403 nm, predominantly spherical morphology and an average grain size of 24.93 nm, whereas the drug-release section of the present study is a prospective pharmaceutical framework rather than a claim of completed in vivo delivery. A decision matrix is proposed to determine when the crude or standardized extract is analytically preferable and when nano-conversion may offer advantages in colloidal handling, antimicrobial performance or controlled-delivery development. The central conclusion is that nanoformulation should not be presumed to improve every biological endpoint; instead, extract-to-nanoparticle transformation should be evaluated as a measurable change in chemical availability, surface chemistry, particle attributes and release behavior.

Keywords: Oroxylum indicum; green synthesis; silver nanoparticles; phytochemical fingerprinting; physicochemical characterization; antioxidant activity; antimicrobial activity; drug release; pharmaceutical analysis

1. Introduction

Medicinal-plant extracts are chemically complex pharmaceutical starting materials. Their activity depends not only on the identity of the plant but also on organ selected, extraction solvent, extraction energy, temperature, solid-to-liquid ratio, storage and analytical standardization. O. indicum is especially relevant because flavonoids dominate its reported phytochemistry and multiple plant parts have been used in traditional medicine. Modern reviews consistently identify baicalein, baicalin, chrysin, oroxylin A, oroxin A and oroxin B among the recurrent marker compounds [1–4].

Green nanotechnology adds a distinct formulation layer. In plant-mediated metallic nanoparticle synthesis, reducing phytochemicals convert metal ions to a nanoscale metallic phase, while other extract constituents adsorb to the nascent surface and contribute to capping and stabilization. Consequently, the final dispersion is not simply 'the extract in smaller form'. It contains a metallic core, an interfacial phytochemical corona and a residual soluble fraction. Analytical comparison therefore requires techniques that interrogate both chemistry and colloidal physics.

1.1 Rationale for a comparative Study

Many reports characterize either an herbal extract or a green nanoparticle product in isolation. Pharmaceutical development, however, requires comparative questions: Which chemical markers remain detectable after synthesis? Does the antioxidant response increase, decrease or simply change mechanism? Is antimicrobial activity associated with the extract, the metal surface, or both? Does particle size remain stable during storage? Can a phytochemical-rich fraction be associated with a carrier in a way that changes dissolution or release? These questions motivate a

paired analytical design rather than a descriptive nanoparticle-only study.

1.2 Aim and objectives

The aim is to establish a structured analytical framework for comparing O. indicum extracts with O. indicum-mediated green metallic nanoparticles. Specific objectives are to

(i) define comparable extract and nanoparticle test materials;
(ii) integrate phytochemical and physicochemical measurements;
(iii) compare antioxidant and antimicrobial endpoints without assuming nano-superiority;
(iv) establish stability-indicating attributes; and
(v) outline a pharmaceutical drug-release program suitable for future loaded or phytochemical-associated nanocarriers.

2. Phytochemical Basis of Oroxylum indicum

The analytical value of O. indicum derives largely from its flavonoid-rich profile. Baicalein is repeatedly described as a dominant constituent, while baicalin, chrysin, oroxylin A and glycosylated derivatives provide a broader fingerprint. The chemical profile varies by plant part and extraction conditions, making marker-based standardization preferable to relying on total extract mass alone [1–4].

2.1 Marker selection for pharmaceutical analysis

Marker / class	Analytical role	Preferred technique	Comparative question
Baicalein	Major flavone marker	HPLC-DAD/LC-MS	Retained, depleted or surface-associated after NP synthesis?
Baicalin	Polar flavonoid glycoside	HPLC-DAD/LC-MS	Does aqueous processing favor glycoside recovery?
Chrysin	Less-polar flavone	HPLC-DAD	Does solvent composition change relative abundance?
Oroxylin A	Methoxylated flavone	HPLC-DAD/LC-MS	Can it serve as a secondary identity marker?
Total phenolics	Global reducing capacity	Folin-Ciocalteu	How much phenolic material remains soluble vs particle-associated?
Total flavonoids	Class-level standardization	Colorimetric + HPLC confirmation	Does nanoparticle formation consume/immobilize flavonoids?

Table 1. Proposed marker panel for paired analysis of extract and nanoparticle preparations.

2.2 Extraction variables

Aqueous extraction is attractive for green synthesis because it avoids organic-solvent carryover into the reduction step. Hydroalcoholic extraction, however, may recover a broader flavonoid spectrum and can be analytically useful as a reference extract. A rigorous comparative design can therefore include an aqueous synthesis extract, a hydroalcoholic analytical reference extract and the final nanoparticle dispersion. This three-way comparison separates solvent effects from nano-conversion effects.

3. Comparative Study Design and Analytical Workflow

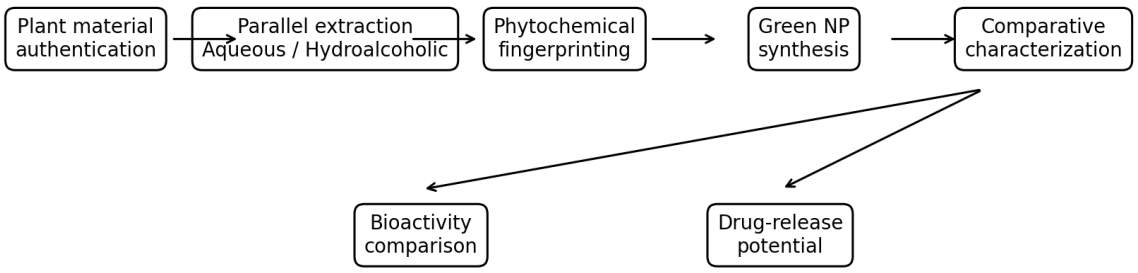

Figure 1. Comparative analytical workflow.

A paired-batch design is recommended. One homogenized plant lot should be divided into replicate extraction batches, and each extract batch should be split before metal-salt addition. One aliquot becomes the extract comparator; the other undergoes nanoparticle synthesis. This design controls botanical and extraction variability and makes subsequent chemical and biological comparisons more interpretable.

3.1 Test materials

Code	Material	Purpose
AE	Aqueous O. indicum extract	Direct precursor and biological comparator
HE	Hydroalcoholic standardized extract	Broader phytochemical reference
GNP	Green-synthesized metallic nanoparticles	Nano-converted test material
BC	Blank metal-salt control	Detects non-biogenic chemical effects
PC	Assay-specific positive control	Validates bioactivity/release method

Table 2. Comparative test-material coding scheme.

3.2 Statistical strategy

Replicate batches should be analyzed rather than relying only on replicate instrument injections. For continuous endpoints, mean ± SD should be reported and assumptions checked before parametric testing. Paired comparisons are preferred when extract and nanoparticles originate from the same batch. Multivariate analysis such as principal-component analysis may be used to visualize whether chromatographic, spectroscopic and colloidal attributes separate the extract and nanoparticle states.

4. Green Synthesis and Formation Monitoring

Aqueous bark extract has recently been reported as a reducing/capping medium for O. indicum-mediated AgNP synthesis. Formation was supported by visible color change and a UV-visible absorption maximum at 403 nm [5]. In a comparative analytical program, color change is only a preliminary indicator; the nanoparticle identity should be supported by complementary optical, structural and microscopic measurements.

4.1 Formation kinetics

Time-resolved UV-visible scans can be collected after combining extract with silver nitrate. The increase and stabilization of the surface-plasmon-resonance (SPR) band provide a rapid process fingerprint. Peak wavelength, maximum absorbance, full width at half maximum and baseline scattering can be tracked. A broadening or red shift during storage may indicate growth or aggregation, whereas an unchanged spectrum supports optical stability.

Figure 2. Schematic UV-Vis distinction between extract and AgNP dispersion

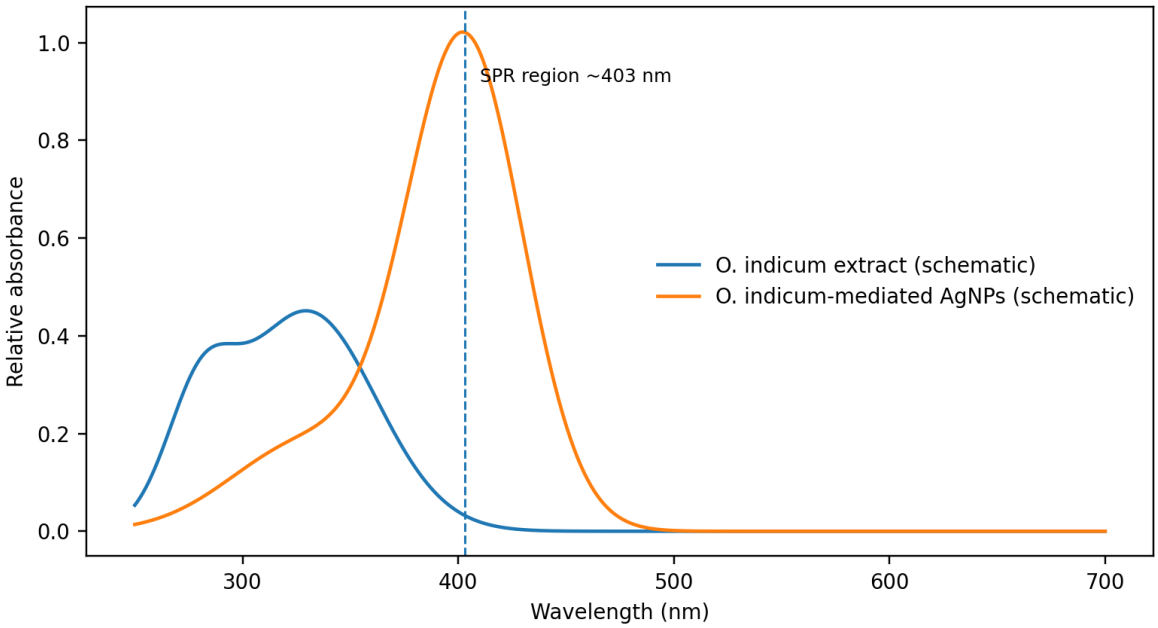

Figure 2. Schematic UV-visible comparison. The 403-nm annotation reflects a published O. indicum bark-mediated AgNP report; the curves themselves are schematic and are not presented as new experimental data.

4.2 Critical process variables

Metal-ion concentration, extract concentration, pH, temperature, mixing intensity and reaction time should be recorded as critical process parameters. Unlike an optimization-centered study, the purpose here is to hold these conditions reproducible so that downstream extract-versus-nanoparticle comparisons are not confounded by uncontrolled synthesis variation.

5. Physicochemical Characterization

5.1 FTIR and interfacial chemistry

FTIR comparison should focus on shifts or intensity changes in broad O-H stretching, carbonyl-related bands and aromatic/C-O regions. Published O. indicum AgNP work has implicated hydroxyl and carbonyl functionalities in nanoparticle formation [5]. Interpretation should remain cautious: FTIR supports functional-group involvement but does not by itself identify which individual flavonoid is bound to the particle surface.

5.2 XRD, microscopy and elemental analysis

XRD establishes crystallinity of the metallic phase and can distinguish the nanoparticle product from the amorphous/complex extract matrix. The recent bark-mediated AgNP study reported a face-centered cubic crystalline structure and an average grain size of 24.93 nm [5]. SEM or TEM should independently evaluate morphology and primary-particle dimensions, while EDX can confirm the elemental metal signal. Crystallite size from XRD and particle size from microscopy should not be treated as interchangeable.

5.3 DLS, PDI and zeta potential

Dynamic light scattering measures hydrodynamic diameter in dispersion and is therefore expected to exceed the primary metallic-core dimension when a hydrated phytochemical corona or small aggregates are present. PDI indicates breadth of the size distribution. Zeta potential is useful as a stability-trending parameter but should be interpreted together with steric capping, ionic strength and storage medium.

Attribute	Extract	Green nanoparticles	Interpretive value
UV-Vis	Molecular absorption/fingerprint	SPR + residual phytochemical bands	Formation and optical stability
FTIR	Functional-group profile	Surface/capping-related changes	Interfacial chemistry

XRD	Mostly complex/amorphous background	Crystalline metallic reflections	Phase confirmation
SEM/TEM	Not a colloidal core measurement	Primary morphology and size	Direct particle visualization
DLS/PDI	Usually not central unless extract colloids exist	Hydrodynamic size/dispersity	Dispersion quality
Zeta potential	Limited relevance for simple solution	Surface electrokinetic behavior	Stability trending

Table 3. Why the same analytical techniques have different meanings for extracts and nanoparticles.

6. Comparative Phytochemical Profiling

Chromatographic comparison is essential because nano-conversion can alter the freely measurable phytochemical pool. A practical HPLC-DAD method should quantify selected markers in the precursor extract, supernatant after nanoparticle separation and, where analytically validated, a desorbed or digested particle-associated fraction. Mass balance is more informative than simply comparing peak heights between extract and whole nanoparticle dispersion.

6.1 Proposed HPLC-DAD workflow

A reversed-phase C18 method with acidified aqueous and acetonitrile/methanol mobile phases can be developed for baicalin, baicalein, chrysin and oroxylin A. Validation should address specificity, linearity, accuracy, precision, range, detection/quantitation limits and solution stability. Because plant matrices can cause co-elution, LC-MS confirmation is desirable during method development even if routine QC ultimately uses DAD.

Fraction	**Expected information**	**Potential limitation**
Precursor extract	Initial marker concentrations	Matrix complexity
Post-reaction supernatant	Unbound/residual phytochemicals	Dilution and metal-ion interference
Washed NP pellet	Surface-associated compounds after extraction	Recovery may be incomplete
Whole dispersion	Total-system fingerprint	Scattering can complicate direct spectrophotometry

Table 4. Fraction-based phytochemical accounting after green nanoparticle synthesis.

6.2 Chemometric comparison

Peak-area ratios, total phenolic/flavonoid indices and spectroscopic descriptors can be combined using PCA or hierarchical clustering. Such analysis can reveal whether nano-conversion produces a reproducible analytical signature distinct from ordinary batch-to-batch variation. Chemometrics should supplement, not replace, validated marker quantitation.

7. Comparative Bioactivity: Antioxidant Assessment

A key analytical caution is that nanoparticle formation does not guarantee stronger antioxidant activity. In O. indicum bark study, the crude bark extract showed a DPPH IC50 of 29.91 ± 2.47 µg/mL, while the AgNP preparation showed 119.0 ± 2.07 µg/mL; quercetin was substantially more potent as the reference standard [5]. The authors interpreted the lower radical-scavenging activity of the AgNPs as potentially reflecting consumption or surface immobilization of antioxidant phytochemicals during nanoparticle formation.

Test	What it probes	Extract-related issue	Nanoparticle-related issue
DPPH	Electron/hydrogen donation	Strongly influenced by phenolics	Optical/scattering interference must be blank-corrected
ABTS	Radical-cation scavenging	Works across broader polarity	Particle absorbance can bias endpoint
FRAP	Ferric reducing capacity	Reflects reducing constituents	Metallic surfaces may contribute non-equivalent chemistry
Total antioxidant capacity	Composite reduction chemistry	Useful screening index	Not mechanism-specific

Table 5. Complementary antioxidant assays and analytical cautions.

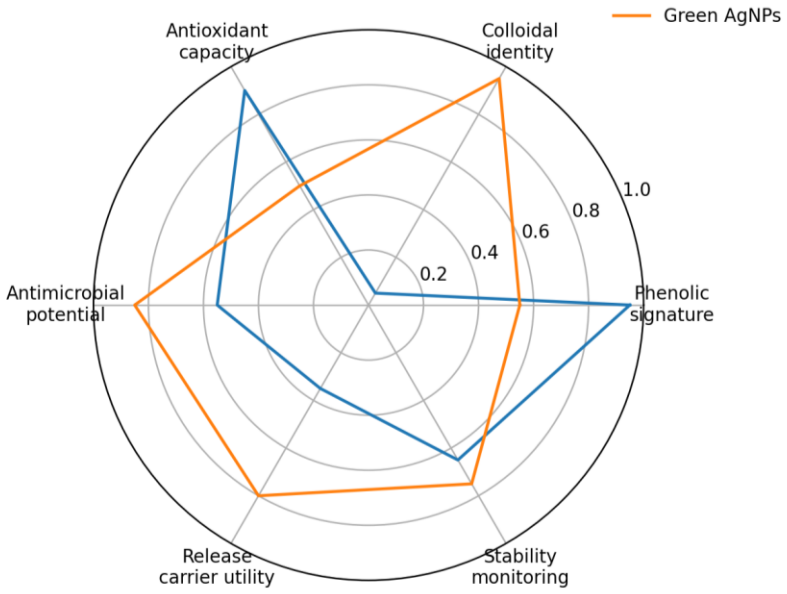

Figure 3. Conceptual normalized comparison showing that an extract can dominate phytochemical/antioxidant dimensions while a nanoparticle system may dominate colloidal and antimicrobial dimensions.

Accordingly, at least two chemically distinct antioxidant assays should be used, and nanoparticle-only blanks should be included at each test concentration. Results should be normalized consistently (mass of dried extract versus mass of nanoparticle preparation) and the normalization basis stated explicitly.

8. Comparative Bioactivity: Antimicrobial and Related Screening

Antimicrobial testing is especially relevant to silver-based systems because ionic silver release, particle-surface interactions and phytochemical capping can contribute simultaneously. The extract comparator is necessary to distinguish intrinsic plant activity from nano-enabled effects. Broth microdilution is preferable to relying only on agar diffusion, because diffusion through agar can differ greatly between soluble extract constituents and nanoparticle dispersions.

8.1 Recommended comparative endpoints

Endpoint	Extract reporting	Nanoparticle reporting	Decision use

MIC	µg extract solids/mL	µg AgNP preparation/mL and, ideally, Ag-equivalent	Potency comparison
MBC	Same mass basis as MIC	Same defined NP basis	Bactericidal assessment
Time-kill	Log CFU vs time	Log CFU vs time	Rate of action
Biofilm inhibition	% inhibition at defined concentration	% inhibition with particle blank	Surface-related potential
Cytocompatibility	Cell viability vs extract dose	Cell viability vs NP dose	Therapeutic-window context

Table 6. Comparative antimicrobial/bioactivity endpoints suitable for pharmaceutical screening.

8.2 Interpretation

A lower MIC for nanoparticles than for extract can support enhanced antimicrobial performance, but it does not prove synergy unless appropriate mixture and metal-ion controls are included. Conversely, weaker antioxidant activity and stronger antimicrobial activity can coexist because the two assays interrogate different mechanisms. A multi-endpoint interpretation is therefore more scientifically defensible than assigning a single 'bioactivity superiority' label.

8.3 Safety perspective

Any intended pharmaceutical use requires cytotoxicity, hemocompatibility and dose-exposure assessment. Plant-mediated synthesis does not automatically confer biological safety. Residual silver ions, endotoxin/bioburden, plant-derived allergens and batch variability must be controlled before translational claims are made.

9. Drug-Release Potential: Pharmaceutical Development Framework

Direct evidence for drug-release performance of O. indicum-mediated metallic nanoparticles remains much less developed than evidence for their synthesis and physicochemical/bioactivity characterization. Therefore, this section is intentionally prospective. It describes how release potential should be tested if an O. indicum marker, enriched fraction or co-loaded drug is deliberately associated with a nanoparticle-based delivery system.

9.1 Defining the released analyte

The release target must be chemically explicit. Suitable endpoints include baicalein, baicalin, a validated marker mixture or a separately loaded active pharmaceutical ingredient. 'Release of extract' is analytically ambiguous unless one or more marker compounds are quantified. HPLC or LC-MS is preferable to non-specific UV absorbance when the release medium contains multiple plant constituents.

9.2 Experimental design

Dialysis-bag, sample-and-separate or diffusion-cell approaches may be evaluated depending on particle size and formulation. Sink conditions, membrane binding, nanoparticle leakage through the membrane and marker stability must be demonstrated. Media can include pH 1.2, pH 4.5 and pH 6.8 buffers for oral-development screening, provided marker solubility and stability are adequate.

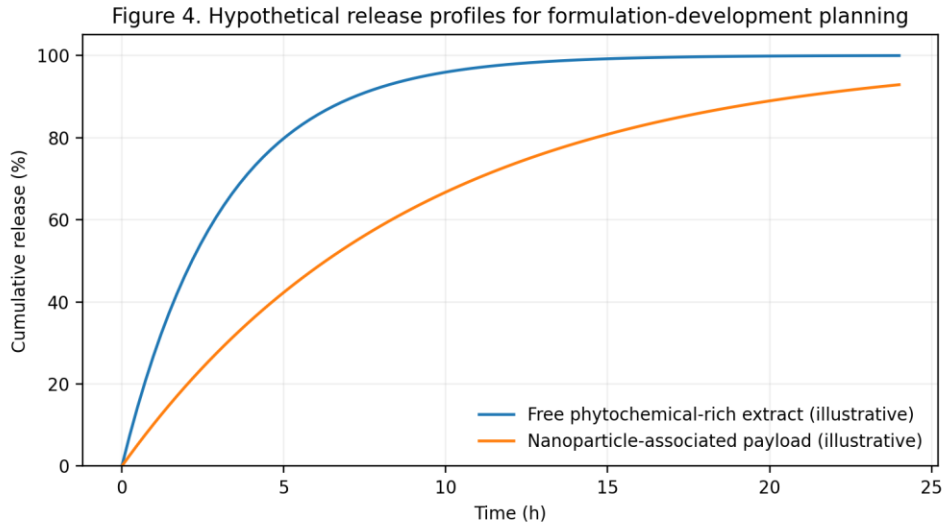

Figure 4. Hypothetical release profiles for planning purposes only. The curves the type of sustained-release hypothesis that must be experimentally tested; they are not O. indicum experimental results.

10. Release Kinetics and Comparative Modeling

Once validated cumulative-release data are obtained, both model-independent and model-dependent analyses can be used. Percentage released at predefined time points, dissolution efficiency, mean dissolution time and similarity factor f2 (where applicable to comparable profiles) provide practical summaries. Kinetic models can then be fitted to explore mechanism.

Model	Common expression	Interpretation in this context
Zero order	Qt = Q0 + k0t	Constant release; uncommon unless system is strongly controlled
First order	ln(Qremaining) vs t	Concentration-dependent release
Higuchi	Qt = kH√t	Diffusion-dominated matrix behavior
Korsmeyer-Peppas	Mt/M∞ = ktn	Empirical transport exponent for early release
Weibull	F = 1-exp[-(t/a)^b]	Flexible empirical profile comparison

Table 7. Candidate release models for future O. indicum marker-loaded formulations.

10.1 Extract versus nanoformulation comparison

The free extract should be tested under the same medium, temperature, agitation and analytical method as the nanoformulation. A slower apparent release from the nanoparticle system is meaningful only if total recovery is adequate and membrane/particle retention artifacts are excluded. Loading efficiency and association efficiency should be quantified before release testing so that the denominator for cumulative release is known.

10.2 Linking release to physicochemical attributes

Particle size, PDI, zeta potential and surface-marker loading can be correlated with burst release and later-phase release rate. A formulation with a narrow size distribution but weak marker association may still show rapid release, whereas stronger interfacial binding can reduce the initial burst. Such correlations are useful for QbD-oriented formulation development.

11. Stability Assessment and Shelf-Life-Oriented Analytics

Stability should be evaluated separately for the standardized extract and nanoparticle dispersion because their failure modes differ. Extracts may show marker degradation, oxidation, precipitation or microbial growth. Nanoparticles may additionally undergo aggregation, Ostwald ripening, surface-corona rearrangement and changes in ionic silver release.

11.1 Stability-indicating panel

Attribute	Extract acceptance concept	Nanoparticle acceptance concept

Appearance	No unexpected precipitation/color shift	No visible aggregation or irreversible sediment
Marker assay	Within predefined assay range	Total and surface-associated marker trend
UV-Vis	Fingerprint similarity	SPR wavelength/width/absorbance trend
Particle size/PDI	Not primary for true solution	Controlled change from initial value
Zeta potential	Usually secondary	Trend consistent with colloidal stability
Microbial quality	Meets intended-use limit	Meets intended-use limit
pH	Controlled within specification	Controlled because pH can alter aggregation

Table 8. Distinct stability-indicating attributes for extract and nanoparticle preparations.

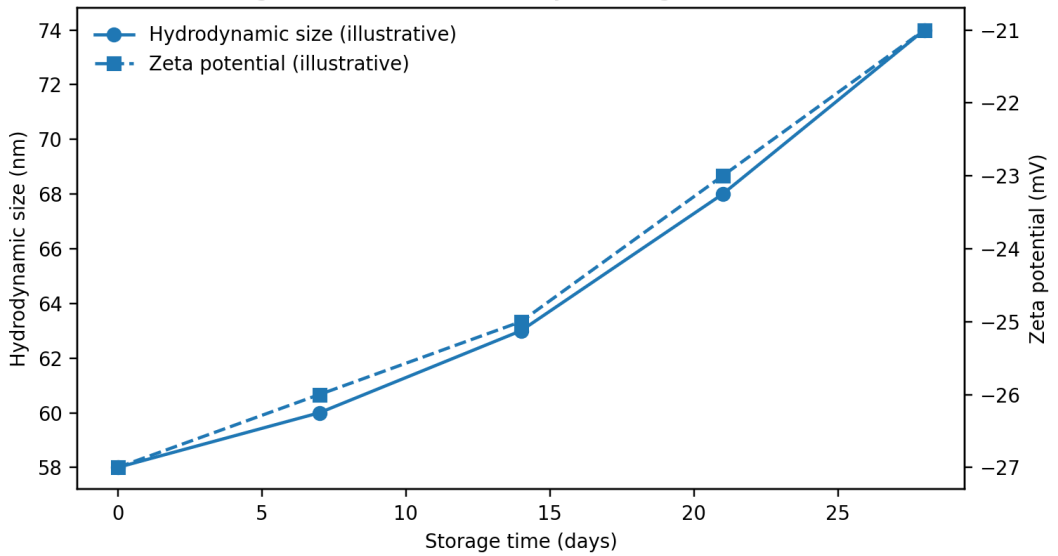

Figure 5. stability-trending framework. Numerical values are simulated solely to demonstrate how size and zeta-potential trends could be plotted.

Accelerated conditions can be useful for screening, but shelf-life assignment requires a justified protocol and validated analytical methods. Freeze-thaw and centrifugation stress tests may reveal colloidal weakness but should not be misrepresented as substitutes for real-time stability.

12. Integrated Comparative Evaluation

The comparative question is not whether nanoparticles are universally 'better' than extracts, but which material is better suited to a defined pharmaceutical objective. Extracts preserve a broader soluble phytochemical spectrum and may retain stronger radical-scavenging capacity. Green metallic nanoparticles add measurable size, surface, crystallinity and colloidal attributes and may offer enhanced antimicrobial or carrier-related functionality. Nano-conversion can simultaneously reduce the freely available concentration of some antioxidant phytochemicals.

12.1 Decision matrix

Development objective	Preferred starting material	Reason
Herbal antioxidant product	Standardized extract	Preserves soluble phenolic/flavonoid pool
Antimicrobial surface/topical research	Green AgNP system	Silver surface/ion effects may add activity
Phytochemical fingerprint QC	Extract + precursor batch	Simpler chemical interpretation
Controlled-release research	Purpose-built loaded nanocarrier	Requires defined payload and release method
Mechanistic nano-bioactivity study	Paired extract + nanoparticles	Separates botanical from nanoscale contribution
Long-term colloidal product	Nanoparticles only after stability qualification	Aggregation and metal-ion release require control

Table 9. Pharmaceutical decision matrix derived from the comparative analytical framework.

12.2 Proposed composite quality index

For research ranking, a composite score may combine normalized marker retention, particle-size control, PDI, zeta-potential stability, antimicrobial potency, cytocompatibility and release reproducibility. Such a score should be treated as a development tool, not a regulatory specification, and weights should reflect the intended dosage form.

13. Limitations, Quality-by-Design Considerations and Future Work

13.1 Evidence limitations

Published O. indicum literature strongly supports the plant's flavonoid-rich chemistry and diverse preclinical bioactivities, while direct evidence for O. indicum-mediated AgNP synthesis and characterization is emerging [1–5]. However, there is not yet an equally mature evidence base for pharmaceutical drug delivery using these exact green metallic nanoparticles. For that reason, release figures and stability trend values in this study are explicitly rather than fabricated experimental findings.

13.2 QbD perspective

A future QbD program should define a quality target product profile according to route of administration. Critical material attributes may include plant-part identity, marker content, metal precursor purity and extract solids. Critical process parameters include extract-to-metal ratio, pH, temperature and reaction time. Critical quality attributes include marker retention, metal content, primary and hydrodynamic size, PDI, surface charge, residual ionic metal, microbial quality, potency and release behavior.

13.3 Future experimental priorities

Priority studies include validated mass-balance analysis of phytochemicals before and after synthesis; direct comparison of aqueous and hydroalcoholic precursor extracts; orthogonal sizing by TEM and DLS; quantitation of residual ionic silver; antimicrobial testing with metal-ion and extract controls; cytocompatibility at pharmacologically relevant concentrations; and development of a chemically specific release assay for baicalein/baicalin or a deliberately loaded API.

Advanced work could examine lyophilized nanoparticles with cryoprotectants, polymer-coated green nanoparticles, incorporation into gels or films, and non-metallic nanocarriers that use O. indicum phytochemicals as the payload rather than as the reducing reagent. These approaches may be more suitable when the therapeutic goal is sustained delivery of plant flavonoids rather than exploitation of the metal surface itself.

14. Conclusion

Comparative analytical evaluation provides a more informative pharmaceutical perspective than characterizing O. indicum extracts and green nanoparticles separately. The extract is primarily a chemically complex phytopharmaceutical material requiring marker-based identity, assay and bioactivity standardization. The green metallic nanoparticle is a hybrid colloidal material requiring those chemical measurements plus confirmation of metallic phase, particle morphology, hydrodynamic behavior, surface charge and stability. Published evidence demonstrates that O. indicum bark can mediate AgNP formation and that nano-conversion does not necessarily enhance antioxidant performance. Accordingly, claims of improved activity should be endpoint-specific and supported by matched extract controls. Drug-release potential is promising as a research direction only when the released analyte, loading/association efficiency, release method and mass balance are analytically defined. A paired-batch framework combining HPLC/LC-MS, UV-Vis, FTIR, XRD, microscopy, DLS, zeta potential, bioactivity testing and stability-indicating measurements offers a defensible pathway for translating O. indicum from traditional phytochemistry into reproducible nanopharmaceutical research.

References

1. Dinda B, et al. Oroxylum indicum: A Review. Pharmacognosy Journal. 2010;2(9):304-310. doi:10.1016/S0975-3575(10)80121-X.
2. Tan ML, et al. The Biological Activities and Therapeutic Potentials of Baicalein Extracted from Oroxylum indicum: A Systematic Review. Molecules. 2020;25(23):5677. doi:10.3390/molecules25235677.
3. Sharma KG, Devi TL, Singh OM, Singh TP. Oroxylum indicum Vent.: A Review on its Phytochemical and Pharmacological Profile. Asian Journal of Chemistry. 2022;34(3). doi:10.14233/ajchem.2022.23479.
4. Recent systematic review: Evidence-Based Health Benefits of Oroxylum indicum and Its Functional Food Potential. Foods. 2024;14(20):3465.
5. Kandel et al. Green Synthesis of Silver Nanoparticles Using Biomass of Oroxylum indicum for Its Application in Dye Degradation, Metal Sensing, and Radical Scavenging Activity. Journal of Chemistry. 2024. doi:10.1155/joch/8690950.
6. ICH Q2(R2). Validation of Analytical Procedures. International Council for Harmonisation.
7. ICH Q1A(R2). Stability Testing of New Drug Substances and Products. International Council for Harmonisation.
8. Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of release of solid drugs dispersed in solid matrices. Journal of Pharmaceutical Sciences. 1963;52:1145-1149.
9. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. International Journal of Pharmaceutics. 1983;15:25-35.
10. Peppas NA, Sahlin JJ. A simple equation for the description of solute release. International Journal of Pharmaceutics. 1989;57:169-172.
11. ISO 22412. Particle size analysis - Dynamic light scattering.
12. ICH Q8(R2). Pharmaceutical Development. International Council for Harmonisation.