IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

Novel Herbal Drug Delivery Systems for Plumbago Zeylanica Linn. Extract: A Solubility-Focused Review

Gayatri Digambar More[1]*, Vaishnavi Sanjay Suryawanshi[1], Rutuja Randhirkumar Ghawit[1], Priyanka Bandgar[2]

[1]Department of Pharmacy, Shivlingeshwar College of Pharmacy, Almala, Latur, Maharashtra, India
[2]Assistant Professor, Department of Pharmacognosy, Shivlingeshwar College of Pharmacy, Almala, Latur,
*Corresponding author: Gayatri Digambar More
gayatridigambarmore@gmail.com

Abstract : *Plant extracts have good pharmaceutical value; however, their formulation is often hampered by problems related to poor water solubility, dissolution rate, instability, variability, and complexity of multi-component plant products [1-3]. Plumbago zeylanica Linn. (P. zeylanica) is a medicinal plant of the family Plumbaginaceae containing naphthoquinones, coumarins, flavonoids, alkaloids, tannins, saponins, steroids and phenolic compounds [4-6]. The characteristic naphthoquinone of the plant known as plumbagin is usually utilized for the purpose of chemical identification [4, 7, 8]. The current review examines critically novel drug delivery systems of herbal origin that are likely to enhance the apparent solubility, dissolution, dispersion in water, and stability of P. zeylanica extract and plumbagin [1, 9]. A structured narrative review approach was undertaken based on literature on phytochemistry, physicochemical constraints, formulation, nanocarrier characterization, stability and safety [1, 3]. Available evidence indicates that direct formulation studies using chemically standardized whole-P. zeylanica extracts remain limited, whereas comparatively stronger evidence is available for isolated plumbagin and unstandardized crude extracts [6, 10, 11Liposomes, niosomes, phytosomes, phospholipid complexes, micelles, polymeric nanoparticles and lipidbased nanoparticles represent promising but comparatively underexplored systems for standardized whole extracts [1, 12-14]. However, direct comparisons across published studies remain challenging due to variations in raw plant materials, extraction protocols, marker assays, carrier compositions, and evaluation methodologies [3, 4]. To build a reliable foundation for future work, research should prioritize rigorous botanical authentication, chromatographic fingerprinting, and marker-based standardization [3, 14]. In parallel, systematic carrier screening must be combined with validated equilibrium solubility and dissolution testing, as well as comprehensive physical, chemical, and safety assessments [3, 14]. Ultimately, developing a standardized, solubility-focused delivery system will provide a rational and reproducible framework for the pharmaceutical development of Plumbago zeylanica extract [1].*

Keywords: Plumbago zeylanica; plumbagin; herbal extract; solubility enhancement; dissolution; liposomes; niosomes

I. INTRODUCTION

Herbal extracts and plant extracts play important roles in pharmaceuticals due to the availability of medicinal plant extracts for modern drug discovery [1, 2].However , a biological or pharmacological activity of crude plant extract in screening assays cannot be considered a reproducible pharmaceutical [3, 4]. Herbal extracts represent complex

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

multiple-component matrices containing different phytoconstituents characterized by varied physicochemical properties [1, 3]. Consequently, the formulation of crude herbal extracts poses various formulation challenges including low aqueous solubility, slow dissolution rates, chemical decomposition, physical instability, and degradation of herbal formulations [3, 5]. In addition, variation in phytochemical composition or inconsistency in herbal extract preparation can affect reproducibility and quality of the product [1, 6]. Thus, the successful development of herbal formulations requires authentic sources, chemical standardization, reproducible production processes, and formulation evaluation [1, 2].

The chemical composition and pharmaceutical properties of crude extracts can greatly vary depending on the plant part, geographic origin, agricultural and environmental conditions, harvesting season, drying procedure, extraction solvent and temperature, and storage conditions [1, 2]. The variation in agricultural and processing parameters can significantly impact the yield of herbal extracts, content of marker compounds, phytochemical composition, aqueous solubility, dissolution rate, chemical degradation rates, and further formulation characteristics [1, 3]. Therefore, in order to ensure reproducibility and consistency in chemical composition, it is necessary to perform rigorous botanical authentication, preparation of vouchers, reproducible plant extraction, fingerprint analysis, and chemical standardization [1, 4]. Quality control of herbal extracts is necessary to minimize batch-to-batch variations, physical and chemical stability of extracts, and reproducible manufacture of standardized herbal products [1, 2, 4].

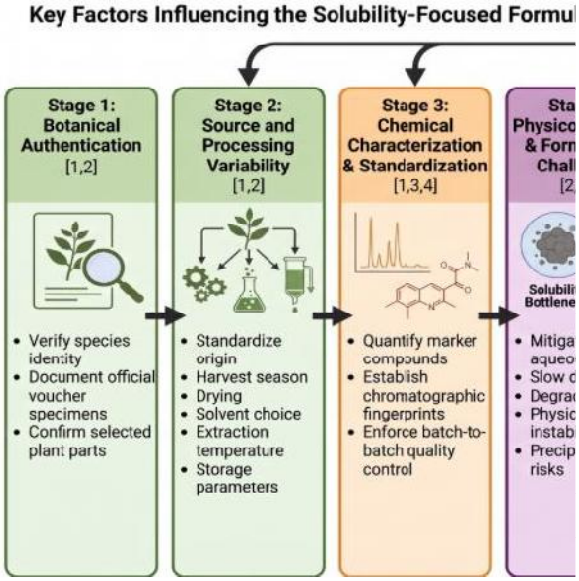

Figure 1. Factors affecting the solubility-based formulation of Plumbago zeylanica Linn. extracts. The scheme shows the linkages between botanical authentication, variation sources and processing, chemical characterization and standardization, formulation difficulties, possible delivery system screening, solubility-focused evaluation, and final formulation evaluation. The loop demonstrates the interrelationship between formulation performance, extraction, chemical standardization, and delivery system choice. This is the original illustration developed based on literature.

Plumbago zeylanica Linn. [1, 2] belongs to the family Plumbaginaceae [1, 3] and constitutes the botanically important plant with a complicated secondary metabolite composition that includes naphthoquinones, coumarins, flavonoids, alkaloids, tannins, saponins, steroids, and phenolic compounds [2, 3]. The phytochemical composition greatly differs depending on the plant organ [2, 3]. The roots and root bark of the plant are known to contain relatively more naphthoquinones, plumbagic acid, and coumarins [2, 3]. On the other hand, the leaves, stems, and aerial parts contain the different set of phytoconstituents including chitanone, plumbagic acid, sitosterol, and flavonoids [2, 3]. Formulated preparations of Plumbago zeylanica extract have been shown to exhibit anti-microbial, anti-inflammatory, anti-oxidant, anti-diabetic, hepatoprotective, anti-ulcer, and anti-fertility activities in experimental studies [1-3]. Thus, organ-specific

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

harvesting, correct processing, and chemical standardization of herbal extract are necessary to ensure reproducibility of herbal extract formulation [3, 4].

Plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone) represents the bioactive naphthoquinone isolated from Plumbago zeylanica and frequently used as a marker compound [1, 2]. Nevertheless, the plumbagin represents only one component and cannot be used for reflecting the complete chemical composition of the whole-P. zeylanica extract [3, 4]. Multicomponent extract contains numerous phytoconstituents possessing different polarities, aqueous solubilities, chemical stability, carrier affinity, and excipient interaction [4, 5]. As a result, the information on the isolated compound cannot be directly used for generalizing information about the whole-P. zeylanica extract [3, 6]. Despite the fact that the information on purified plumbagin can be useful for the preformulation work on the isolated lipophilic component, the findings cannot be generalized to the solubility, dissolution, stability, or formulation of the standardized herbal extract [4, 5].

Low-water soluble or lipophilic phytoconstituents cause various difficulties during preparation of homogeneous aqueous and dispersible herbal formulations [1, 2]. The low thermodynamic aqueous solubility results in limited maximal equilibrium concentration of the constituent present in a liquid medium in the form of molecules [1, 3]. During physical pharmacy assessments, it is necessary to strictly distinguish between the equilibrium solubility, apparent solubility, dissolution rate, molecularly dissolved substance, colloidal dispersion, particle association with carrier, precipitation, and assay content [2, 4]. An increase in total content of the marker compound or decrease in particle size in a liquid formulation is not necessarily equal to solubility enhancement [3, 5]. The physical separation of molecularly dissolved substance from suspensions, colloids, and precipitate during the evaluation of the whole-P. zeylanica extract and purified plumbagin requires the development of validated separation techniques and analytical methods [4, 5].

Novel delivery systems for herbal drugs like liposomes, niosomes, micelles, nanoemulsions, phytosomes, phospholipid complexes, polymeric nanoparticles, solid lipid nanoparticles, and nanostructured lipid carriers may serve as the promising technologies for the improvement of the aqueous solubility, dissolution rate, aqueous dispersion, chemical and physical stability of poorly water-soluble phytoconstituents [1, 2]. Such advanced nanocarrier systems may improve the physical properties of the formulation through established mechanisms like solubilization in lipid or surfactant phase, encapsulation in vesicles, complexation with phospholipids, interfacial dispersion, and entrapping in polymeric or lipid matrixes [1, 3, 4]. Nevertheless, the presence of the formulation mechanism and indirect evidence from another botanical system do not prove the existence of direct evidence for whole-P. zeylanica extract or purified plumbagin [5]. As a result, every carrier platform requires rigorous evaluation based on solubility, dissolution, dispersion, physical stability, chemical stability, and safety studies [2, 5, 6].

Direct formulation research utilizing chemically standardized whole-Plumbago zeylanica extract has remained scarce [1, 2], as majority of studies evaluate unstandardized crude extracts or isolated components [1, 3, 4]. On the contrary, comparatively stronger formulation evidence exists for the purified plumbagin [1, 3, 4]. The low-energy Capryol 90/Labrasol/Kolliphor RH40 nanoemulsions loaded with purified plumbagin exhibited high reported solubility of plumbagin in the selected excipients (94.6 mg/mL in Capryol 90; 125.0 mg/mL in Labrasol) [3], an average droplet size of 30.9 nm [3], and the stability of droplet size during 6 months at 25 °C [3]. Moreover, high-pressure homogenized oleic acid/Polysorbate 80 nanoemulsions solubilized 51.8 mg/mL of purified plumbagin [4], resulting in the average droplet size of 135 nm [4], 3-month stability at 25 °C [4], and release half-lives of 6.1 h in gastric and 7.0 h in intestinal fluids [4]. Despite the fact that the information on the isolated compound provides a rationale for preformulation [1, 4], it cannot be automatically generalized to multicomponent extract [1, 5]. Thus, formulation studies on the standardized whole-extract remain necessary [1, 2].

Direct formulation studies utilizing chemically standardized whole-P. zeylanica extract remain limited [1, 2]. Available evidence is mostly concerned with the isolated purified plumbagin, unstandardized crude extracts, unformulated preparations, or related phytoconstituents [1, 3, 4]. In addition, head-to-head comparisons among different delivery systems loaded with standardized extract have yet to be performed [1, 5]. The available studies contain great

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

methodological differences in relation to plant part used, extraction procedures, marker analysis, carrier composition, formulation technique, solubility and dissolution testing [2, 4, 6]. In addition, the data on long-term physical stability, chemical stability, and formulation-specific safety appears to be insufficient [2, 5, 7]. Such limitations make direct comparison of delivery systems impossible and emphasize the necessity for the standardized whole-extract formulation studies [1, 2].

This critical review evaluates novel herbal drug delivery systems like liposomes, niosomes, micelles, nanoemulsions, phytosomes, phospholipid complexes, polymeric nanoparticles, solid lipid nanoparticles, and nanostructured lipid carriers for whole-P. zeylanica extract, purified plumbagin, and related herbal delivery systems [1, 2, 5]. This review is strictly focused on equilibrium solubility, apparent solubility, dissolution, aqueous dispersion, precipitation, physical stability, chemical stability, formulation quality, and safety [1, 2]. Information obtained with standardized whole-P. zeylanica extract will be clearly differentiated from the data on purified plumbagin and indirect evidence from related herbal systems [1, 3, 5]. Ultimately, this review will aim to identify the formulation opportunities, evidence limitations, and priorities for future development [1, 2].

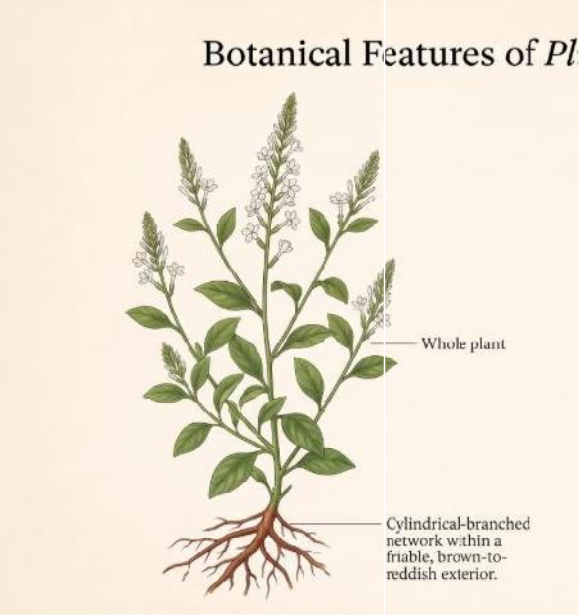

Figure 2. Botanical features of Plumbago zeylanica Linn, including the whole plant, leaves, white flowers, glandular calyx, flower spike and characteristic roots.

II. REVIEW METHODOLOGY

1. Review design

This systematic review evaluates the solubility, dissolution, stability, standardization, and formulation development issues associated with Plumbago zeylanica Linn. extract [1, 2]. This review combines botanical identification, phytochemical identification, screening of drug delivery systems, and formulation assessment focused on solubility [3, 4], thereby distinguishing the findings on extract from plumbagin and phytochemistry [1, 5].

2. Literature search

Relevant research articles were retrieved from different online databases such as PubMed, PubMed Central, Scopus, Web of Science, ScienceDirect, SpringerLink, Wiley Online Library, Google Scholar, and Directory of Open Access Journals [1-3]. The search was based on keywords including Plumbago zeylanica Linn., major constituents (with particular emphasis on plumbagin), solubility issues, and novel delivery systems for herbal drugs [1-3]. Principal search

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

terms included “Plumbago zeylanica phytochemistry,” “Plumbago zeylanica extract solubility,” “plumbagin solubility,” “plumbagin nanoemulsion,” “plumbagin liposome,” “herbal extract liposome,” “phytoconstituent niosome,” “micelle herbal drug delivery,” “phytosome solubility enhancement,” “Plumbago zeylanica toxicity,” and “plumbagin formulation stability” [2-7]. These terms were used seperately and in varying combinations using Boolean operators (AND, OR) to refine retrieval specificity [1, 3].

3. Eligibility criteria

The study was regarded as pertinent when it contained any of these aspects: Botanical authentication or chemical characterization of Plumbago zeylanica Linn. [1, 2, 8]; solubility/dissolution studies of plumbagin/extracts [12, 13]; development/testing of drug delivery systems such as liposomes, niosomes, micelles, nanoemulsions, phytosomes, and nanoparticles [3, 5, 6]; physical and chemical stability of herbal preparations [5, 12, 13]; safety/toxicity of P. zeylanica extracts/plumbagin [2, 10]; or quality control and standardization techniques for herbal products [1, 8]. Studies that were either unrelated to P. zeylanica/plumbagin, did not have any bearing on formulation/solubility, were duplicates, or were deficient in methodological information were not included in the review [1, 5].

4. Evidence interpretation

In order to ensure scientific accuracy, all of the literature used in observation was defined according to its evidence level and separated into three types of evidence.

(1) direct evidence, which includes research on the whole extract of Plumbago zeylanica Linn. or isolated and cleaned plumbagin;

(2) indirect evidence, which stands for research based on similar compounds or botanical extracts;

(3) formulation rationale, which works as an explanation of the possibility of using certain delivery systems on P. zeylanica in the absence of the direct evidence.

This type of classification is important because you cannot use the results of the formulation from purified plumbagin to the entire plant extract since mixed extracts contain diverse active substances that differ from one another in terms of solubility, polarity, stability, and interactions with exipients.

III. BOTANICAL PROFILE OF PLUMBAGO ZEYLANICA

1. Taxonomy and distribution

Plumbago zeylanica Linne is a perennial medicinal plant native to the Plumbaginaceae family [1, 2]. Most often found in tropical and subtropical climates, it can be found in regions of India, Sri Lanka, Southeast Asia, and other regions with mild climates [1–3]. The plant is known by several vernacular names, including chitrak, chitraka, white leadwort, and Ceylon leadwort [2–4]. From a morphological standpoint, the plant is characterized by its highly branched stem, simple alternate leaves, and inflorescence either at the tip of the stem or in its axils showcasing white flowers [1-3]. The roots possess the highest level of interest due to their traditional medical use and the presence of pharmacologically important compounds [1, 4, 5]. Moreover, other plant organs such as aerial parts, flowers, fruits, and seeds are also studied for their distinct phytochemical profiles and biological properties [1, 3, 5].

2. Plant material selection

Plant-part selection is important for formulation development. A root extract may contain a different concentration and profile of naphthoquinones compared with a leaf extract [2,8]. The extraction solvent also influences the relative recovery of polar and non-polar constituents [1,16]. Therefore, a high-quality formulation study should report:

* Botanical authentication [1,2],
* Voucher specimen number [1],
* Plant part used [2,8], *

Collection location and season [1,8],

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

* Drying conditions [1],
* Particle size of dried material [citation required],
* Extraction solvent [1,16],
* Extraction time and temperature [1],
* Drug–extract ratio [citation required],
* Extract yield [1,16], and
* Storage conditions [1,5].

Without this information, reproducibility and meaningful comparison between studies are difficult [1,8].



Figure 3. Botanical characteristics and plant materials of Plumbago zeylanica Linn.
(A) Whole plant showing characteristic habit, leaves and white flowers; (B) representative leaves and flowers; (C) roots and root bark; and (D) dried plant materials commonly used for extraction, including root, leaves, flowers, fruits and seeds.

IV. PHYTOCHEMICAL PROFILE

1. Major constituent classes

The reported phytochemical profile of Plumbago zeylanica Linn. includes naphthoquinones, coumarins, flavonoids, alkaloids, glycosides, saponins, steroids, tannins, triterpenoids, and phenolic compounds [1, 2]. The qualitative and quantitative composition varies according to the harvested plant part, extraction solvent, and analytical method [1, 3, 4].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

Table 1. Important phytochemical groups reported in P. zeylanica

Phytochemical class	Representative constituents	Solubility / stability characteristics	Implications for drug delivery	References
Coumarins	Seselin, xanthyletin, 5-methoxyseselin, suberosin, xanthoxyletin	Variable polarity; potential sensitivity to hydrolytic and photodegradation	May require carrier encapsulation to improve chemical stability and control release kinetics	[2,3]
Flavonoids	Flavonoid aglycones and glycosides (e.g., dihydroflavonols)	Co-extracted across polar to semipolar solvents; variable water and lipid solubility	May benefit from mixed-polarity carriers, phospholipid complexes (phytosomes), or polymeric nanoparticles	[1,2,8]
Phenolics	Simple phenolic acids, plumbagic acid, 4-hydroxybenzaldehyde	Water- or alcohol-soluble; susceptible to oxidation	May require antioxidant excipients or protective nanocarriers to minimize oxidative degradation	[2,3]
Alkaloids	Reported alkaloid fractions	Variable ionization and pH-dependent solubility profiles	Require analytical marker-based profiling and pH-controlled vehicle selection	[2,3]
Saponins	Surface-active glycosides	Amphiphilic structure with intrinsic surfactant properties	May aid extract self-dispersion or modify interfacial tension in lipid formulations	[2,5]
Steroids & triterpenoids	Lupeol, lupenyl acetate, β-sitosterol, stigmasterol, campesterol	Lipophilic, high melting point, and low aqueous solubility	High risk of precipitation; may require incorporation into oil phases or lipid matrices such as SLNs/NLCs	[2,3,5]
Tannins	Hydrolysable and condensed tannin fractions	High molecular weight; polyphenolic binding affinity	May cause physical incompatibility, precipitation, or cross-linking with proteinaceous/polymeric carriers	[2,3,5]

Plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone) is one of the most extensively investigated bioactive constituents associated with Plumbago zeylanica Linn. [2,3]. It is predominantly concentrated and detected in the roots and root bark, where it frequently serves as a principal chemical or analytical marker for extract standardization [1,3,4]. Structurally, plumbagin possesses a conjugated 1,4-naphthoquinone chromophore and exhibits high lipophilicity coupled with poor aqueous thermodynamic solubility (<0.1 mg/mL) [6–8]. These physicochemical properties create substantial technical challenges during extract processing, aqueous dispersion, dissolution testing, and dosage-form development [5–7]. However, the quantitative concentration of plumbagin should not serve as the sole quality-control attribute, as it does not represent the full spectrum of co-extracted phytoconstituents responsible for the overall chemical stability, matrix interactions, and biological profile of the whole extract [1,3].

2. Need for chromatographic fingerprinting

A standardized herbal formulation should combine quantitative marker analysis with chromatographic fingerprinting [1, 2]. High-performance liquid chromatography (HPLC), high-performance thin-layer chromatography (HPTLC), liquid chromatography–mass spectrometry (LC-MS), and ultraviolet-visible (UV-Vis) spectroscopy may be used according to the formulation objective and available validation [1-5].

The following parameters should be reported:

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

* Plumbagin concentration [2-4, 6],
* Total extract content [1, 5],
* Major secondary peaks and chromatographic fingerprint profile [1, 5],
* Peak-area reproducibility [1, 3],
* Method specificity [1, 3],
* Linearity [1, 3],
* Accuracy [1, 3],
* Precision [1, 3],
* Limit of detection (LOD) and limit of quantification (LOQ) [3], and
* Stability of the analyte in the formulation [1, 4, 6].

V. PHARMACOLOGICAL RELEVANCE

Extracts and bioactive constituents of Plumbago zeylanica Linn. have been investigated for antimicrobial, antifungal, anti-inflammatory, antioxidant, antidiabetic, antiulcer, hepatoprotective, wound-healing, and cytotoxic activities [1–4]. These activities provide a rationale for pharmaceutical development but do not establish a validated therapeutic indication [1, 2].

The pharmacological profile of a whole extract may result from additive, synergistic, or antagonistic interactions among several constituents [2, 3]. Consequently, replacing the whole extract with purified plumbagin may alter the biological profile [1, 4]. Similarly, incorporation into a carrier may modify release, chemical stability, and cellular exposure [5–7]. Formulation studies should therefore compare the optimized formulation with the unformulated extract and, where relevant, with purified plumbagin [2, 5, 6].

A well-designed pharmacological study should include:

• Chemically characterized extract,
• Defined formulation composition,
• Placebo or vehicle control,
• Unformulated extract control,
• Positive control,
• Dose justification,
• Appropriate statistical analysis, and
• Assessment of formulation-related toxicity [2,4,6–8].

VI. SOLUBILITY CHALLENGES

1. Solubility and dissolution

Solubility refers to the equilibrium concentration of a molecule found dissolved in a solvent [1-4]. Dissolution refers to the process of a solid dissolving into a liquid [1-4]. The two terms should not be confused with each other [1-3].

An assay may indicate high solubility values because of the presence of the molecule in the form of droplets, micelles, vesicles, or precipitate [1-3, 5, 6]. Hence preformulation and solubility studies should be carefully classified into the following types,

• Colloidal solubilization,
• Suspended or precipitated drug,
• Total formulation content, and
• Dissolved fraction after validated physical separation (e.g., membrane dialysis, ultrafiltration, or high-speed centrifugation) [1-3, 5, 6].

2. Challenges in multicomponent extracts

A whole herbal extract is not a single chemical entity [1–5]. Its constituents can differ in:

• Molecular weight,

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

• Polarity,
• Ionization,
• Melting point,
• Partition coefficient,
• Chemical stability, and
• Affinity for oils, surfactants, and polymers [1–5].

These properties influence whether a constituent remains in the aqueous phase, oil phase, interfacial layer, or carrier matrix [1–5]. As a result, a formulation optimized for plumbagin may not be optimal for hydrophilic glycosides, tannins, or flavonoid glycosides [1–5].

3. Plumbagin as a formulation model

Plumbagin is a useful model for studying the delivery of lipophilic Plumbago zeylanica Linn. constituents [1–4]. Published studies have explored nanoemulsions and self-emulsifying systems to address its limited aqueous solubility [1–3,5]. These studies support the use of lipid-based systems for purified naphthoquinones but do not establish the best carrier for the complete whole-plant extract [1,2,4,6].

4. Recommended solubility studies

A high-quality solubility study should report:

• Temperature,
• pH,
• Ionic strength,
• Equilibration time,
• Amount of excess sample,
• Mixing conditions,
• Centrifugation or filtration procedure,
• Filter compatibility,
• Analytical method,
• Calibration range,
• Recovery,
• Dissolved versus total drug,
• Replicate number, and
• Statistical analysis [1–5].

Solubility should be measured in water and relevant buffer media [1, 2]. Where appropriate, dissolution should be evaluated using a validated apparatus and sink or non-sink conditions that are clearly reported [1-3]

VII. CONVENTIONAL SOLUBILITY-ENHANCEMENT APPROACHES

1. Particle-size reduction

Micronization and nanosizing increase surface area and may accelerate dissolution [1–4]. However, particle-size reduction does not necessarily increase equilibrium solubility [1-3]. It can also enhances aggregation, surface energy, and physical instability [1, 3, 4].

2. Cosolvents

Ethanol, propylene glycol, polyethylene glycol, and cosolvents may enhance the solubility of lipophilic drug compounds [1–4]. However, their practical applicability is restricted due to potential toxicity, tissue irritation, drug precipitation on physiological dilution, and related regulations [1–4].

3. Surfactants

Surfactants can improve wetting and form micellar structures [1–4]. However, high concentrations may produce irritation, hemolysis, toxicity, or physical instability [1–5]. The critical micelle concentration (CMC) and the effect of physiological dilution should therefore be rigorously determined during preformulation development [1,2,5–7].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

4. Solid dispersions

Solid dispersions may convert a crystalline compound into an amorphous or molecularly dispersed state [1–4]. Their key limitations include potential recrystallization over time, moisture sensitivity, and difficulty in maintaining physical stability during extended storage [1–4].

5. Cyclodextrin complexation

Cyclodextrins can form inclusion complexes with selected hydrophobic molecules [1–4]. Their usefulness for a whole extract depends on the affinity of individual constituents and the possibility of competitive complexation [1–4].

6. Phospholipid complexes

Phospholipid complexes can improve the lipid affinity of selected phytoconstituents [1–5]. They should be distinguished from liposomes because a phospholipid complex is not necessarily a vesicle [1–4].

VIII. NOVEL HERBAL DRUG DELIVERY SYSTEMS

1. Liposomes

Liposomes are vesicular nanocarriers consisting of one or more concentric phospholipid bilayers surrounding an aqueous central compartment [1–5]. Hydrophilic constituents may be incorporated into the aqueous core, whereas lipophilic constituents partition into the hydrophobic domain of the lipid bilayer [1–5].

This dual-loading capability is particularly advantageous for complex, multi-constituent herbal extracts containing both polar polyphenols and hydrophobic naphthoquinones. A liposomal Plumbago zeylanica Linn. formulation could potentially maintain both polar and non-polar constituents within a single dispersed colloidal system. Liposomal formulation can also protect bioactive compounds from damage by heat, moisture and infection, while providing controlled release over time.

Essential formulation parameters ;

To develop an effective liposomal formulation using P. zeylanica, it is essential to fulfil the following conditions:

- Selection of phospholipids (e.g. phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine),
- Cholesterol content with the ratio (this parameter plays an important role in providing the fluidity of the bilayer),
- Ratio of the extract to the lipid,
- Composition of the aqueous medium with regard to pH and ionic strength,
- Energy of treatment (e.g. sonication, high pressure homogenization, membrane extrusion),
- Conditions of storage,
- Addition of lipophilic antioxidants (e.g. α-tocopherol).

Required Analytical Characterization

To entirely characterize herbal liposomal formulations, the following are essential considerations:

• Vesicle size and polydispersity index (PDI) through dynamic light scattering,
• Vesicle surface charge and morphology (using TEM/SEM),
• Encapsulation efficiency (EE%) and extraction percentage,
• Leakage of the vesicles when in physiological incubation and long-term storage,
• Dialysis and release kinetics in vitro,
• Lipid oxidation and chemical degradation of the markers, and
• Physical and chemical stability of the formulations.

Key Limitations and Preformulation Challenges

Liposomal systems can face some chemical breakdown from oxidation of phospholipids and the hydrolysis of the esters, as well as the risks of leakages in the membranes, vesicle clumping, and vesicle fusion [1–3,5].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

Likewise, there are industrial hurdles during manufacturing, sterilizing, and storing the liposomes [1–3]. That means smaller initial vesicle size is not sufficient to guarantee successful formulating of liposomal systems because the liposomal system must meet more demanding criteria for the physical, chemical, and release stability [1–3].

2. Niosomes

Niosomes are non-ionic surfactant-based vesicular nanocarriers generally prepared using non-ionic surfactants and cholesterol [1–4]. Their bilayer structure can accommodate both hydrophilic and lipophilic constituents within central aqueous core or hydrophobic membrane domains, respectively [1–4]. They have been investigated as delivery systems for herbal bioactive compounds because of their compositional flexibility, non-immunogenic nature, and potential to provide controlled drug release [1–5].

For Plumbago zeylanica Linn., niosomes may improve the dispersion and physical stability of plumbagin-containing fractions [1-3]. The formulation may be prepared using thin-film hydration, reverse-phase evaporation, ethanol injection, or other suitable self-assembly methods [2, 4, 5].

Critical formulation variables include:

• Surfactant type and chemical structure,
• Hydrophilic–lipophilic balance (HLB) value,
• Surfactant-to-cholesterol molar ratio,
• Hydration temperature,
• Hydration duration,
• Extract/active loading capacity,
• Surface charge (ζ-potential) and charge inducers, and
• Storage conditions [2, 4, 5].

Key Limitations and Considerations

There are possible limitations which include local irritation caused by the surfactant, leaking of the vesicular membrane, physical aggregation, changes in the average size of the vesicles, and structural instability following aqueous dilution [2, 4-6]. Direct empirical evidence regarding standardized niosomes with whole-P. zeylanica extract has not yet been made available; therefore, claims should be formulated indicating the potential of the formulation and requiring experimental validation instead of claiming that it has been tested and proven in clinical practices [2,4-6].

3. Micelles

Micelles are clusters of amphiphilic molecules under the CMC [1–3]. Their hydrophobic core can hold fat-soluble components while their hydrophilic surface allows mixing with water [1-3].

Micelles are capable to enhance the effective water solubility of plumbagin and some other fat-soluble components [1-3]. Polymers in polymeric micelles can give these systems a better kinetic stability than that of micelles based on surfactants.

Evaluation requirements for micellar formulations include:

• Critical micelle concentration (CMC),
• Drug-loading capacity,
• Apparent solubility,
• Dilution stability,
• Drug precipitation,
• Micelle size,
• Polydispersity,
• Surfactant concentration,
• Chemical compatibility, and

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

• Cytotoxicity [1–5].

The major limitation is that micelles may disassemble below their critical micelle concentration after dilution, causing drug precipitation [1–3,5]. This issue should be specifically investigated during formulation development.

4. Nanoemulsions

Nanoemulsions are dispersions of oil droplets in water or water droplets in oil, stabilized by surfactants and, in some systems, cosurfactants [1, 2]. Their small droplets provide a large interfacial area and may improve the dispersion of lipophilic compounds [2-4].

A 2018 study developed a plumbagin-loaded nanoemulsion using oleic acid and high-pressure homogenization [5, 6]. A 2022 study used Capryol 90 as the oil phase with Labrasol and Kolliphor RH40 and reported an optimized formulation with a mean hydrodynamic diameter of 30.9 nm [7, 8].

Advantages

• Good suitability for lipophilic constituents [2, 3, 9].
• High interfacial area [3, 4].
• Potential for low-energy preparation [7, 8].
• Relatively straightforward liquid processing [7, 10].
• Possibility of improved apparent solubility and dissolution [2, 7, 11].

Limitations

• Kinetic rather than thermodynamic stability [2, 12].
• Droplet growth [2, 13].
• Coalescence [2, 13].
• Phase separation [2, 13, 14].
• Surfactant-related toxicity [2, 12, 15].
• Precipitation after dilution [2, 13, 16].
• Need for appropriate packaging [17-19].

Evaluation

Nanoemulsions should be evaluated for:

• Droplet size [5, 7, 17, 20].
• Polydispersity [5, 7, 17, 20].
• Zeta potential [21].
• pH [16, 22-24].
• Viscosity [1].
• Drug loading [5, 7, 8].
• Dilution stability [16, 22-24].
• Centrifugation stability [25, 26].
• Heating–cooling cycles [25].
• Freeze–thaw stability [25].
• Storage stability [16, 19, 22, 27].
• Dissolution or release [5, 28, 29].

5. Phytosomes and phospholipid complexes

Phytosomes are generally described as complexes or associations between plant constituents and phospholipids [1–4]. They should not be confused with liposomes [1-3]. Liposomes are composed of multiple lipid bilayers enclosing water,

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

whereas phytosomes are complexes formed through interactions of active substances and phospholipid molecules [1–4]. Phospholipid complexation is applicable for several kinds of phenolics, flavonoids, and naphthoquinones [1, 3, 4]. Thus, their formation must be examined by appropriate analytical methods such as Fourier-transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), X-ray diffraction (XRD), and nuclear magnetic resonance (NMR) spectroscopy where applicable [1, 4].

Required evaluation parameters for phytosomal formulations include:
• Evidence of complex formation,
• Marker content,
• Equilibrium and apparent solubility,
• Dissolution rate,
• Thermal behavior,
• Crystallinity,
• Moisture sensitivity,
• Physical stability, and
• Chemical stability [1–3].
The direct proof of the phytosomal whole-Plumbago zeylanica Linn. extract is still remains limited [3, 5]. Thus, this mode of delivery can be defined as promising, needing straight experimental proof using the well-established whole-P. zeylanica extract [1, 3, 5].

6. Polymeric nanoparticles
Polymeric nanoparticles can either encapsulate plant ingredients or serve as adsorbents through their biodegradable polymer matrix [1–4]. Selection of the polymers used such as PLGA, Chitosan, Alginate, etc. depends on the method of administration and the release requirements [1–4].
The potential advantages being offered are protection from environmental influences and enzymatic destruction as well as controlled or sustained release profile of the drug after administration. [1–5]. Key limitations include the presence of residual organic solvents from preparation processes (such as emulsification–solvent evaporation), complex multi-step manufacturing, potential polymer- or surfactant-related toxicity, scale-up challenges, and technical difficulty in accurately quantifying multiple co-extracted constituents within the polymeric matrix [1-3, 5].

7. Solid lipid nanoparticles and nanostructured lipid carriers
Solid lipid nanoparticles use a solid lipid matrix, whereas nanostructured lipid carriers combine solid and liquid lipids. These systems may accommodate lipophilic compounds and protect them from environmental degradation [1–4].
For Plumbago zeylanica Linn., such systems may be useful for plumbagin-enriched fractions [1-3]. Critical factors include lipid compatibility, loading capacity, crystallinity, polymorphic transitions, particle size, lipid digestion, and storage stability [1, 2, 4, 5].

IX. COMPARATIVE EVALUATION OF DELIVERY SYSTEMS

Table 2. Comparison of delivery systems

System	Main Solubility Mechanism	Major Advantages	Key Limitations	Current Relevance to P. zeylanica & Plumbagin	Citatio n
Nanoe mulsion s	Dissolution and molecular entrapment within submicron oil droplets (30–135 nm) dispersed in water	Direct solubilization of plumbagin up to 125 mg/mL; high interfacial surface	Thermodynamic/ kinet ic metastable instability over long-term	Strongest direct empirical preformulation and dissolution evidence for purified plumbagin	[1-3]

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

		area; reproducible high-pressure or spontaneous emulsification	storage; potential excipient load (surfactant/cosur facta nt ratio)		
Liposomes	Partitioning of hydrophobic molecules into the phospholipid bilayer or hydrophilic actives into the central aqueous core	Dual drug-loading capability; protection from enzymatic and acidic degradation; controlled release profiles	Risk of drug leakage upon storage; phospholipid oxidation; particle aggregation; complex scale-up processing	Promising exploratory platform for standardized whole extract; requires direct comparative studies	[1–3]
Phytosomes	Formation of stoichiometric chemical complexes (H-bonding) between phospholipids (phosphatidylcholin e) and phytoconstituents	Enhances lipid membrane affinity and intestinal permeation; shields polar actives in a lipophilic envelope	Requires rigorous spectroscopic proof of true chemical complex formation versus simple physical mixing	Exploratory platform for multi-constituent extract fractions and polyphenols	[1, 7–9]
Micelles	Solubilization of lipophilic phytoconstituents within the hydrophobic core of surfactant or polymeric self-assemblies	Small hydrodynamic particle size (<50 nm); substantial apparent solubility enhancement for hydrophobic fractions	Susceptible to micellar dissociation/brea kdow n upon physiological dilution; potential surfactant excipient toxicity burden	Useful for lipophilic naphthoquinone fractions; requires dilution stability screening	[1-3]
Lipid Nanoparticles (SLNs / NLCs)	Incorporation of lipophilic compounds into solid lipid or structured solid/liquid lipid core matrices	High physical protection for lipophilic actives; avoids organic solvents; sustained release capability	Lipid polymorphism during storage leading to drug expulsion; restricted drug-loading capacity	Potentially useful for lipophilic naphthoquinone s; requires loading capacity optimization	[1]
Niosomes	Entrapment of lipophilic or amphiphilic molecules within non-ionic surfactant bilayer vesicles stabilized by cholesterol	Highly flexible composition; lower raw material cost than phospholipids; vesicular delivery capability	Potential non-ionic surfactant local irritation; membrane leakage; physical instability and aggregation on	Requires direct experimental validation using standardized whole-plant extract	[1, 4]

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

			storage		
Polymeric Nanoparticles	Encapsulation, matrix entrapment, or surface adsorption of bioactives within synthetic/natural polymers	Superior protection against chemical/enzymatic degradation; tunable sustained release kinetics	Complex multi-step processing; potential residual organic solvent toxicity; polymer degradation concerns	Requires process optimization and solvent residual testing for whole extract	[1]

X. STANDARDIZATION AND QUALITY CONTROL

1. Botanical authentication

Authentication should be performed by a qualified botanist or pharmacognosist [1–5]. A voucher specimen should be deposited in a recognized herbarium [1-3]. Macroscopic and microscopic identity should be documented where appropriate [1–3,5].

2. Extract standardization

The extract should be standardized using:
Plant-part specification.
Drug–extract ratio.
Extraction solvent.
Extraction yield.
Plumbagin assay. Chromatographic fingerprint. Moisture content.
Ash values.
Residual solvent.
Microbial limits.
Heavy metals.
Pesticide residues.
Aflatoxins.

3. Analytical method validation

An analytical assay for plumbagin or other marker constituents of Plumbago zeylanica Linn. should demonstrate specificity, linearity, accuracy, precision, robustness, limit of detection (LOD), limit of quantification (LOQ), and solution stability [1–4].

4. Formulation standardization

The finished formulation should be assessed for:
Total extract content.
Marker content.
Encapsulation efficiency.
Drug loading.
Particle or droplet size.
Polydispersity. Zeta potential. pH.
Viscosity.
Appearance.
Microbial quality.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

Physical stability.
Chemical stability.

XI. PROPOSED FORMULATION DEVELOPMENT STRATEGY

To create a valid, repeatable method for formulating a nanocarrier containing Plumbago zeylanica Linn. extract, it is important to follow a defined ten-step preformulation and formulation optimization process:

Stage 1: Choosing and Gathering Plant Parts

Choose one part of the plant, preferable its roots or root bark, for the highest concentration of bioactive naphthoquinones (especially plumbagin) [1-3]. Take note of the botanical identification and keep a specimen in a herbarium. Make records regarding date and place of collection, drying conditions, and methods of storage.

Stage 2: Extract Preparation and Yield Percentage

Select the best extraction parameters in terms of solvent polarity (i.e. ethanol or hydroalcoholic solvents), extraction time, temperature, ratio of raw material to solvent, and drying process (i.e evaporation, lyophilization) [2, 3]. Determine the yield percentage of the entire extract and measure the amount of plumbagin in the extract by using tested and validated methods, either spectroscopy or chromatography [4, 5].

Stage 3: Extract Control and Characterization

Make a detailed chromatographic fingerprint of the extract using HPLC or HPTLC. Check if the extract meets the requirements for identification of the botanical [2, 3].

Stage 4: Solubility Screening of Pharmaceutical Excipient

Use thermodynamic approach to evaluate the solubility of naphthoquinones extracts in oils (e.g. oleic acid, Capryol 90), non-ionic surfactants (e.g. polysorbate 80, Labrasol), co-surfactants (e.g. Kolliphor RH40), amphiphilic fatty acids, and polymers, as well as various buffer media [5-7].

Step 5: Comparative Parallel Carrier System Creation

Make representative colloidal delivery systems—like liposomes, niosomes, polymeric micelles, and nanoemulsions—using the same extract material. Change the initial loading to keep the marker concentrations same between the different carrier systems.

Step 6: Systematic Composition Optimization (QbD / DoE)

Implement Quality-by-Design principles and pseudoternary phase diagrams and response surface methodology to optimize critical material properties (CMAs). Important parameters include lipid-to-surfactant ratio, surfactant HLB, cholesterol ratio, polymer weight, and maximum extract loading.

Step 7: Solubilization, Dissolution, and Phase Separation Analysis

Measure apparent solubility enhancement, cumulative dissolution rate across biorelevant membrane dialysis media (SGF pH 1.2 and SIF pH 6.8–7.5), and physical precipitation risks upon serial aqueous dilution [5-7]. Analytically separate molecularly dissolved bioactive fractions from colloidally entrapped, carrier-associated, and precipitated fractions.

Step 8: Extended Physical and Chemical Stability Testing

Conduct accelerated and real-time shelf-life stability monitoring under standardized temperature/humidity conditions [5, 7]. Periodically assess Z-average hydrodynamic particle size growth, polydispersity index (PDI), surface charge (ζ-potential), phase separation, chemical degradation of plumbagin, pH drift, organoleptic appearance, and microbial purity [6–8].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

Step 9: Comprehensive Finished-Formulation Toxicological Evaluation
Perform safety and biocompatibility testing directly on the final finished nanocarrier formulation rather than relying solely on raw extract toxicity data [2,7–9]. Protocols should evaluate in vitro cytotoxicity (e.g., MTS assay across target cell lines), erythrocyte hemolysis, dermal/mucosal irritation, and route-specific acute/subacute toxicity in relevant models [7–9].

Step 10: Multi-Metric Lead Formulation Selection
Select the final lead nanocarrier based on a balanced, objective matrix evaluating apparent solubility gain, dissolution kinetics, physical/chemical stability, marker retention, excipient regulatory acceptability (GRAS status), manufacturing scalability, and batch-to-batch performance reproducibility [2, 5, 7].

XII. EVALUATION PARAMETERS

1. Physicochemical characterization
Appearance.
Colour and odour.
pH.
Viscosity.
Density.
Refractive index where relevant.
Particle or droplet size.
Polydispersity index.
Zeta potential.
Morphology.
Conductivity where relevant.
2. Drug-content analysis
Total extract content.
Plumbagin concentration.
Additional marker compounds.
Encapsulation efficiency.
Drug-loading capacity.
Recovery after formulation processing.
3. Solubility and dissolution
Equilibrium solubility.
Apparent solubility.
Intrinsic solubility where applicable.
Dissolution rate.
Percentage dissolved.
Time to reach plateau.
Precipitation after dilution.
Release kinetics.
4. Stability Centrifugation.
Heating–cooling cycles.
Freeze–thaw cycles.
Accelerated stability.
Long-term stability.
Light stability.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

Oxidative stability.
Packaging compatibility.
5. Safety
In-vitro cytotoxicity.
Hemolysis.
Irritation.
Acute toxicity.
Repeated-dose toxicity.
Histopathology.
Genotoxicity where scientifically justified.

XIII. SAFETY AND TOXICITY CONSIDERATIONS

The pharmacodynamics of Plumbago zeylanica Linn. cannot be taken for granted when preparing preparations because toxicity varies based on plant part, extracting solvent, extract concentration, dosage, route of administration, and duration of exposure between the drugs [1–3].Studies on toxicity of P. zeylanica root extracts have revealed differences in organ toxicity and median lethal dose (LD50) values from using petroleum ether, acetone and hydroalcoholic solvents [1, 2].

Plumbagin is characterized by redox and cytotoxic properties [3–5]. This brings about proved therapeutic interest in the substance but requires careful choice of dose and examination of each specific formulation [2-4].

As it influences local concentration of the drug into target tissues, its chemical stability, cellular uptake, and release of the drug, it is critical to test the final formulation rather than depend solely on the safety profile of the unformulated extract.

Important safety controls for formulation testing include:

• Vehicle control,
• Empty-carrier control,
• Unformulated extract control,
• Purified plumbagin control (where relevant),
• Positive cytotoxicity reference control,
• Dose–response assessment,
• Cell-line selection appropriate to the intended administration route,
• Replicate experimental trials, and
• Independent analytical confirmation of marker concentration [2, 4, 5].

Excipients should be selected according to route of administration, required concentration, regulatory acceptability (e.g., GRAS status), and known irritation or local toxicity profiles [4, 5].

XIV. RESEARCH GAPS

The principal gaps identified in the current literature include:

1. Limited direct formulation studies evaluating standardized whole-Plumbago zeylanica Linn. extract [1–4].
2. A disproportionate research emphasis on purified plumbagin compared to the complete whole-extract matrix [2,5–7].
3. A lack of direct head-to-head comparative evaluations between liposomes, niosomes, micelles, nanoemulsions, and phytosomal systems using the same extract batch [4,8–10].
4. Inconsistent reporting of plant parts, harvesting season, extraction parameters, and baseline marker concentrations across published studies [1,3,11].
5. A lack of standardized solubility and dissolution protocols tailored to complex, multi-constituent herbal extract matrices [4,5,8].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 5, November 2026 Impact Factor: 8.2

6. Limited long-term physical and chemical stability data under real-time and accelerated storage conditions [5,6,12].
7. Insufficient toxicological data regarding formulation- and excipient-specific toxicity of novel herbal nanocarriers [2,7,12].
8. A scarcity of scale-up, industrial process validation, and Quality-by-Design (QbD) optimization studies for herbal nanomedicines [4,6,12].
9. Inadequate analytical distinction between true thermodynamic equilibrium solubility and metastable colloidal dispersion [5,6,8].
10. Limited empirical evidence connecting specific excipient/carrier compositions with extract-marker retention and entrapment efficiency [5,6,8].
11. A lack of standardized quality-control specifications and regulatory acceptance criteria for finished herbal nanoformulations [4,12].
12. Insufficient investigation of packaging compatibility, container-closure interactions, and extended storage stability for botanical nanocarriers [4,6,12].

XV. FUTURE PERSPECTIVES

Future studies should use a quality-by-design (QbD) framework to identify critical material attributes (CMAs) and critical process parameters (CPPs) [1, 2]. The development program should begin with authenticated and chemically standardized plant material rather than an incompletely characterized extract [2, 3].

Comparative formulation studies should use the same extract batch, identical marker concentration, equivalent analytical methods, and predefined acceptance criteria [3, 4]. This design would permit a more reliable comparison of liposomes, niosomes, micelles, nanoemulsions, and phytosomal systems [4, 5].

Future work should also examine whether improved apparent solubility is maintained after dilution, during storage, and under physiologically relevant conditions [6, 7]. Stability-indicating analytical methods are necessary to detect degradation of plumbagin and other marker compounds [3, 6]. Scale-up, reproducibility, excipient safety, and packaging compatibility should be considered before claiming pharmaceutical readiness [2, 6, 7].

An ideal research design would involve a comparison of Unformulated standardized extract, Liposomal standardized extract, Niosomal standardized extract, Micellar standardized extract, Nanoemulsion standardized extract, Placebo, and Purified plumbagin formulation. The primary outcomes should be equilibrium solubility, dissolution rate, marker retention, precipitation, physical stability, and chemical stability.

XVI. CONCLUSION

Plumbago zeylanica Linn. is a medicinal plant that has varied chemical composition including plumbagin and other phytoconstituents [1, 2, 3]. The development of stable and uniform pharmaceutical formulations from this plant is hindered by its poor water solubility, slow release in water, chemical instabilities and variability of the extract [2, 4, 5].

Liposomes, niosomes, micelles, nanoemulsions, phytosomes, polymeric nanoparticles, and lipid-based nanoparticles offer plausible mechanisms for improving the apparent solubility, dispersion, dissolution, and stability of poorly water-soluble constituents [5, 6, 7]. Among these systems, the one featuring nanoemulsions is the most demonstrable when it comes to formulation, while evidence regarding standardized whole-P. zeylanica extract is limited at best [8].

A scientifically appropriate formulation approach should account for botanical authentication, reproducible extraction, chromatographic fingerprinting, marker-based standardization, appropriate selection of carriers, laboratory solubilization and dissolution studies, stability tests, and formulation-based safety tests [8]. In fact, in order to improve solubilization, particle size alone is no longer enough; thus, certain comparative research on standardized extracts is required to arrive at a suitable delivery method [4].

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

Declarations Funding
No specific funding statement is available. Authors should disclose institutional, governmental or commercial funding.

Conflict of interest
The authors should declare any financial or non-financial conflicts of interest. Author contributions
To be completed according to the contribution of each author. Data availability
No new experimental dataset was generated for this narrative review. Ethics approval
Not applicable.

REFERENCES

1. Bautista-Solano AA, Dávila-Ortiz G, Perea-Flores MJ, Martínez-Ayala AL. A comprehensive review of niosomes: composition, structure, formation, characterization, and applications in bioactive molecule delivery systems. Pharmaceutics. 2025;17(1):45.
2. Pandita A, Sharma P. Pharmacosomes: an emerging novel vesicular drug delivery system for poorly soluble synthetic and herbal drugs. ISRN Pharm. 2013;2013:348186.
3. Poli V, Motireddy SR. Antifertility potential of Plumbago zeylanica Linn.: a comprehensive review. J Med Nat Prod. 2026;3(2):100013.
4. Sumsakul W, Plengsuriyakarn T, Chaijaroenkul W, Viyanant V, Karbwang J, Na-Bangchang K. Antimalarial activity of plumbagin in vitro and in animal models. BMC Complement Altern Med. 2014;14:15.
5. Kesarwani K, Gupta R. Bioavailability enhancers of herbal origin: an overview. Asian Pac J Trop Biomed. 2013;3(4):253-266.
6. Pandey R, Bhairam M, Shukla SS, Gidwani B. Colloidal and vesicular delivery system for herbal bioactive constituents. DARU J Pharm Sci. 2021;29(2):415-438.
7. Mittal G, AP, Dhali A, Prasad R, Nurani KM, Găman MA. Plant-based therapies combined with advanced drug delivery systems for liver health: a bibliometric analysis. World J Gastrointest Pharmacol Ther. 2025;16(2):100120.
8. Chrastina A, Baron VT, Abedinpour P, Rondeau G, Welsh J, Borgström P. Plumbagin-loaded nanoemulsion drug delivery formulation and evaluation of antiproliferative effect on prostate cancer cells. BioMed Res Int. 2018;2018:9035452.
9. Chrastina A, Welsh J, Borgström P, Baron VT. Propylene glycol caprylate-based nanoemulsion formulation of plumbagin: development and characterization of anticancer activity. BioMed Res Int. 2022;2022:8315148.
10. Sumsakul W, Plengsuriyakarn T, Na-Bangchang K. Pharmacokinetics, toxicity, and cytochrome P450 modulatory effects of plumbagin in rats. BMC Pharmacol Toxicol. 2016;17(1):50.
11. Chen RP, Chavda VP, Patel AB, Chen ZS. Phytochemical delivery through transferosome (phytosome): an advanced transdermal drug delivery for complementary medicines. Front Pharmacol. 2022;13:850862.
12. Nasim N, Sandeep IS, Mohanty S. Plant-derived natural products for drug discovery: current approaches and prospects. Nucleus. 2022;65(3):399-411.
13. Chowdhury S, Shuvo JM, Mannan MA. A potential review of its traditional uses, phytochemistry, pharmacology, and toxicity of Plumbago zeylanica. J Pharmacogn Phytochem. 2023;12(5):123-131.
14. Shukla B, Saxena S, Usmani S, Kushwaha P. Phytochemistry and pharmacological studies of Plumbago zeylanica L.: a medicinal plant review. Clin Phytosci. 2021;7(1):34.
15. Pable AK, Ghotankar A. Comparative phytochemical and physicochemical study of Chitrak (Plumbago zeylanica Linn.) as Abhāva-pratinidhi Dravya for Bhallātaka (Semecarpus anacardium Linn.). J Pharmacogn Phytochem. 2025;14(5):15547.
16. Anonymous. Liposomes as nanocarriers for the delivery of phytomedicines and natural anti-cancer agents. Int J Health Sci. 2022;6(S1):1012-1025.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 5, November 2026
Impact Factor: 8.2

17. Anonymous. A mechanistic review of plumbagin effects against diabetes and related conditions. Pharm Sci Asia. 2021;48(1):1-12.
18. Sumsakul W, Plengsuriyakarn T, Na-Bangchang K. Solubility and systemic exposure challenges of plumbagin in rodent bioassays. BMC Pharmacol Toxicol. 2016;17(1):51.