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REVIEW ARTICLE

Conceptual Framework for Rational Design and Optimization of a Polyherbal NanoPhytosome

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Abstract

Multiple bioactive constituents in polyherbal formulations may be limited by poor solubility, stability, and bioavailability. This study suggests a hypothesis-driven approach to the formulation of a polyherbal nano-phytosome of *Curcuma longa*, *Aloe vera,* and *Capsicum annuum*. The proposed methodology consists of extract preparation, phytochemical screening, estimation of phenolics and flavonoids, antioxidant evaluation, development of phospholipid-based nano-phytosomes, physicochemical characterization, and *in vitro* biological evaluation. The structure is intended for the optimization of the formulation for a given set of physicochemical and biological criteria. The potential outcomes are better phytochemical preservation, formulation stability, and delivery potential than with traditional extracts. These results, however, need to be validated with experiments. The proposed framework is systematic and can be used as a basis for further laboratory studies of the development of polyherbal nano-phytosomes.

Key words: *Aloe vera*, antioxidant activity, *Capsicum annuum*, *Curcuma longa*, nano-phytosome, phytochemicals, polyherbal formulation

INTRODUCTION

Medicinal plants have remained an important part of the healthcare system in the world due to their rich phytochemical content and wide range of biological activities. It is estimated that a significant number of the world's population is using plant-based medicines for primary healthcare, and there is growing scientific evidence for the use of herbal therapeutics in modern pharmaceutical research.[1,2] Medicinal plants are important sources for the development of new therapeutic formulations due to the presence of bioactive constituents, such as phenolic compounds, flavonoids, alkaloids, terpenoids, glycosides, and carotenoids that have been widely reported for their antioxidant, antimicrobial, anti-inflammatory, and immunomodulatory properties.[3,4]

Although these benefits exist, there are still obstacles in the way of clinical translation of herbal extracts, as many phytochemicals are poorly soluble in water, have low membrane permeability, have low oral bioavailability, and are prone to chemical degradation during processing and storage. Furthermore, due to the complex composition of herbal extracts, formulation stability and therapeutic activity can vary from one batch to another. Such restrictions have led to increased research interest in the development of new drug delivery systems that would allow for the protection of the phytochemicals and enhance their absorption and biological activity.[4-7]

Nano-phytosomes are a promising platform for herbal formulations among the different nanotechnology-based delivery systems. Nano-phytosomes are expected to increase the stability of the phytochemicals, increase interaction with the membrane, and deliver the phytochemicals more efficiently than traditional herbal preparations, due to the formation of molecular complexes between the phospholipids

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and the bioactive compounds from the plants. They are gaining popularity for pharmaceutical and nutraceutical uses due to their biocompatibility, relatively easy formulation process, and suitability for plant-derived compounds.[7,8] The choice of medicinal plants is also crucial for the successful formulation development. In the present framework, the selection of *Curcuma longa*, *Aloe vera,* and *Capsicum annuum* was made due to their complementary phytochemical profile and well-established pharmacological properties. *C. longa* is a rich source of curcuminoids and phenolic compounds, which have strong antioxidant and anti-inflammatory properties. *A. vera* is rich in polysaccharides, flavonoids, and phenolic compounds, which have antioxidant, antimicrobial, and wound-healing properties, while *C. annuum* has capsaicinoids, carotenoids, and vitamin C, which also promote antioxidant and antimicrobial effects. The complementary activities of these phytochemicals give a solid scientific foundation for the investigation of a polyherbal nano-phytosome strategy for enhancing formulation quality and potential therapeutic applications.[9-14]

RESEARCH GAP

In the past decade, the use of nanotechnology in the delivery of herbal drugs has grown significantly, and many researchers have reported the preparation of nanoformulations of medicinal plant extracts. Nano-phytosomes have been gaining more and more interest among the different nanocarrier systems due to their potential to improve the stability and delivery of plant-derived bioactive compounds. Most of the reported studies have, however, concentrated on preparation and characterization of nano-phytosomes from individual medicinal plants or single phytochemicals, and comparatively less studies have been reported on the systematic development of polyherbal nanoformulations, which incorporate complementary phytochemical profile.[15]

Furthermore, previous studies have focused mainly on the preparation and physicochemical characterization of nanoparticles, and have not provided a systematic approach for the selection of the herbal formulation before nanoformulation. The formulation of polyherbal formulations is mostly empirical and has little rationale based on comparative phytochemical or biological studies. This can lead to overlooking potentially better herbal combinations and can decrease the reproducibility of formulation development between different studies.[16]

To overcome these drawbacks, the present work suggests a hypothesis-driven methodological framework that is based on a two-stage optimization strategy. The first stage involves systematic optimization of the polyherbal formulation through integrated phytochemical and antioxidant evaluation, and the second stage involves the development of nano-phytosomes based on pre-defined physicochemical quality attributes. In addition, a Quality Assessment and Decision Framework is presented that enables the formulation selection to be done in a transparent and reproducible manner using multiple complementary evaluation criteria, not just one analytical parameter.[17]

This manuscript does not report experimentally proven results but offers a structured framework that will be helpful for guiding future laboratory work and increasing methodological uniformity in the development of polyherbal nano-phytosome systems. The proposed approach focuses on rational formulation design and sequential optimization to provide a repeatable basis for future phytopharmaceutical research.[18-20]

SCOPE OF THE PROPOSED FRAMEWORK

The main objective of this paper is to suggest a structured methodological approach for the rational development of polyherbal nano-phytosome formulation of aqueous extracts of *C. longa, A. vera,* and *C. annuum*. The framework brings together the selection of medicinal plants, design of polyherbal formulation, phytochemical evaluation, development of nano-phytosome, physicochemical characterization, and biological evaluation in a sequential optimization strategy to enhance the methodological consistency in herbal formulation research.

This paper does not present laboratory results, but rather a scientifically sound plan for future experimental studies. The proposed framework highlights the systematic decision-making process based on multi-parameter evaluation of phytochemical, physicochemical, and biological characteristics before selection of formulations. The framework proposes a reproducible and transparent methodology that will help future research in pharmaceutical, nutraceutical, and natural product sciences and the development of standardized polyherbal nano-phytosome systems for experimental validation.

PROPOSED FRAMEWORK FOR POLYHERBAL NANO-PHYTOSOME DEVELOPMENT

Framework overview

The suggested mechanism provides a systematic approach for the rational formulation of a polyherbal nano-phytosome containing aqueous extracts of *C. longa*, *A. vera,* and *C. annuum*. The framework is developed to overcome one of the most challenging problems in the research of herbal formulation: Lack of a structured approach that combines herbal formulation optimization with the development of nanocarriers. The proposed methodology does not aim to

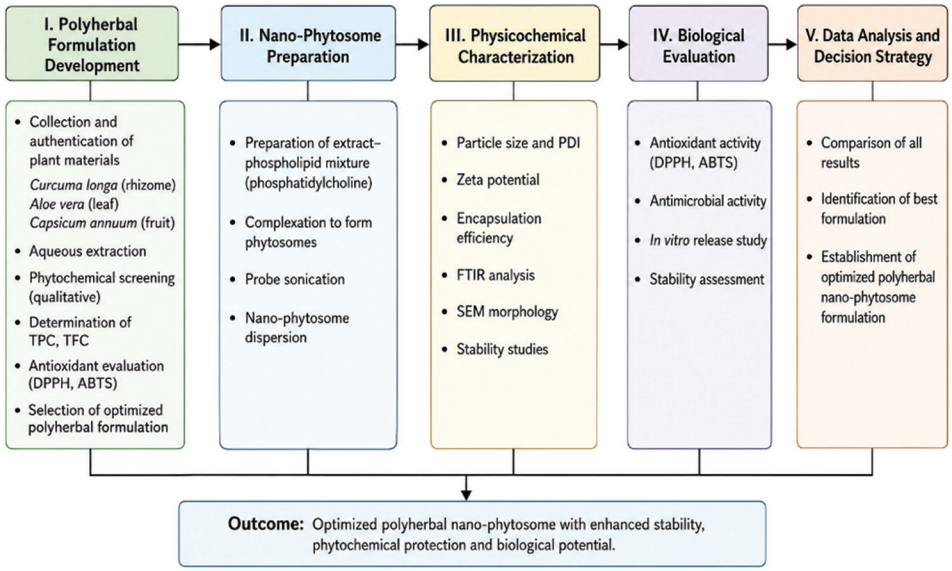


Figure 1: Conceptual overview of the proposed two-stage framework

directly transform herbal extracts into nanoformulations, but rather sequential optimization, with the aim of developing a herbal composition and the nano-phytosome system, according to pre-established scientific criteria. The aim of this strategy is to increase the methodological transparency, formulation reproducibility, and the quality of future experimental studies.[21]

The framework has two interdependent phases [Figure 1]. In Stage I, the formulation of the polyherbal formulation is developed and optimized by systematically evaluating the phytochemical composition and antioxidant potential. Various herbal combinations are suggested and comparatively evaluated by qualitative phytochemical screening, total phenolic content (TPC), total flavonoid content (TFC), and complementary antioxidant assays. This stage is designed to determine the best possible polyherbal composition before the preparation of nano-phytosome to minimize the number of empirical formulations and provide a better scientific foundation for the development process.[22]

After the optimized polyherbal formulation was identified, Stage II describes the preparation and optimization of the nano-phytosome by complexation with phospholipids. The proposed formulation is then subjected to physicochemical and biological characterization, such as particle size analysis, polydispersity index (PDI), zeta potential, encapsulation efficiency, Fourier transform infrared (FTIR) spectroscopy, scanning electron microscopy (SEM), *in vitro* release study, stability study, and antimicrobial evaluation. These analyses will give a complete formulation evaluation approach and will help validate the formulation in the future in the lab. One of the distinguishing characteristics of the proposed framework is the multi-parameter decision-making approach, which is based on the joint assessment of a range of phytochemical, physicochemical, and biological quality indicators, instead of a single analytical parameter. This sequential approach will serve as a reproducible guideline for further studies and can be modified for various medicinal plant combinations to create standardized herbal nanoformulations. The overall process of the proposed framework is shown in Figure 2.

DEVELOPMENT OF THE POLYHERBAL FORMULATION

A systematic approach is needed for the development of a polyherbal formulation, taking into account the phytochemical composition of the individual medicinal plants as well as the potential complementary biological activities. In the proposed framework, *C. longa*, *A. vera,* and *C. Annuum,* were chosen due to their well-documented phytochemical diversity and reported pharmacological properties. These medicinal plants are being used together to ensure that the formulation contains the greatest possible phytochemical content, including phenolic compounds, flavonoids, curcuminoids, polysaccharides, capsaicinoids, carotenoids, and other bioactive compounds. This will likely give a wider range of biological activity than formulations made from a single plant extract and will enable the development of multifunctional phytopharmaceutical systems.[23] The framework suggests that the use of authenticated plant materials collected under standardized conditions would be used for methodological consistency. After cleaning and shade drying, the plant materials are ground to fine powders and then extracted individually with distilled water. The use of aqueous extraction was chosen as an environmentally friendly and pharmaceutically acceptable method that can be used to extract a wide range of polar phytochemicals without the use of organic solvents. The various extracts are concentrated, stored, and then mixed together to make the proposed polyherbal formulations.

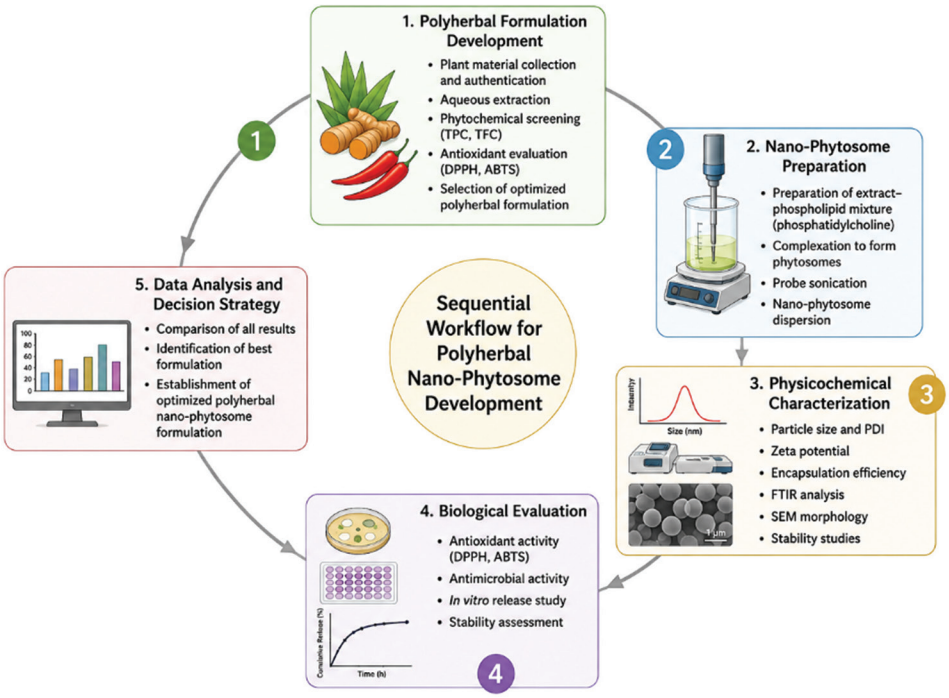


Figure 2: Overall framework for polyherbal nano-phytosome development

The framework suggests testing several polyherbal combinations to determine the most appropriate formulation ratio before the development of the nano-phytosome rather than assuming one formulation ratio [Table 1]. This approach acknowledges that different ratios of medicinal plants can affect the chemical constituents of the product and the expected biological activity of the final formulation. Thus, three representative formulations with different ratios of composition are suggested for comparison. The optimized formulation is designed to be chosen based on a structured evaluation of the phytochemical richness and antioxidant potential and not solely on "gut feeling."

After formulation, each polyherbal formulation is suggested to be subjected to preliminary phytochemical screening for the presence of major secondary metabolites, such as phenolics, flavonoids, alkaloids, tannins, terpenoids, glycosides, saponins, and carbohydrates. Qualitative phytochemical screening gives an initial idea of the chemical diversity of each formulation and helps with quantitative analyses.[24] The framework also suggests the estimation of TPC and TFC by using colorimetric methods and further antioxidant activity evaluation by free radical scavenging activity by 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) assays.[25] All of these analyses give a complete picture of the phytochemical richness and antioxidant potential. The proposed framework suggests that a multi-parameter analysis should be used, rather than a single analytical parameter, with the formulation with the most balanced performance in all the phytochemical and antioxidant evaluations being chosen for further nano-phytosome development.

A crucial aspect of the proposed methodology is this systematic optimization approach. The framework aims to reduce the subjectivity of formulation selection in the herbal formulation optimization process and provide a reproducible basis for future experimental validation. Figure 3 shows the overall workflow of Stage I.

NANO-PHYTOSOME DEVELOPMENT AND CHARACTERIZATION

The second step of the proposed framework involves developing a nano-phytosome delivery system for enhancing the physicochemical properties of bioactive compounds extracted from plants. Phytochemicals are anticipated to be more stable in the nanocarriers, interact with biological membranes more easily, and may be more effective than conventional herbal extracts in delivering phytochemicals. The proposed framework is not just a standalone process, but rather a logical extension of the optimized polyherbal formulation, where both the herbal composition and the characteristics of the nanocarriers are systematically addressed.[26]

The framework suggests the preparation of nano-phytosomes using the thin-film hydration technique, which is one of the most widely, used methods for the preparation of phospholipid-based delivery systems due to its simplicity, reproducibility, and suitability for the encapsulation of bioactive compounds of plant origin. The method involves the preparation of a thin lipid film by mixing phospholipids

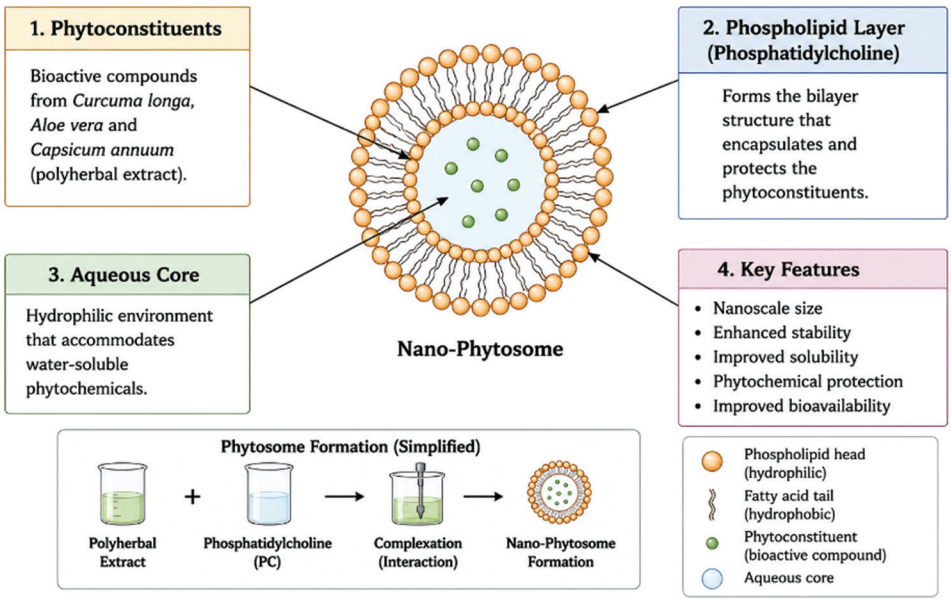


Figure 3: Stage I: Development and optimization of the polyherbal formulation

and cholesterol in a specific ratio and then adding the optimized polyherbal extract to hydrate the film. Controlled sonication is then suggested to decrease the size of the vesicles and to achieve uniform nanoscale dispersion. The formulation parameters, such as phospholipid concentration, cholesterol content, hydration conditions, and sonication time are supposed to be optimized step by step to obtain a stable and reproducible nano-phytosome system.[27] A comprehensive physicochemical characterization is a key part of the proposed framework.[28] It is recommended to perform particle size analysis to assess the average vesicle size and if the formulation is within the desired nanoscale range. The PDI is suggested to measure the uniformity of particle size, and the zeta potential measurement gives information about the electrostatic stability of the nano-phytosome dispersion. All these parameters provide a preliminary assessment of the formulation quality and are well known as key quality attributes during the development of nanopharmaceuticals.

The framework also recommends to evaluate the encapsulation efficiency to find out the percentage of encapsulated phytochemicals in the phospholipid matrix.[29] An efficient encapsulation efficiency is generally desirable as it suggests a good interaction between the bioactive components and the carrier system, which can lead to better stability and release properties. FTIR spectroscopy is the proposed investigation that would enable the evaluation of possible changes in functional groups that could accompany complex formation between the phytochemicals and phospholipids. In addition, the surface morphology and structural analysis of the developed nano-phytosomes are recommended using the SEM.

These characterization techniques are not treated in isolation but rather on, an integrated evaluation approach is considered in the proposed framework. All the physicochemical parameters should be considered simultaneously to develop formulations with balanced properties, including an appropriate particle size distribution, formulation homogeneity, colloidal stability, incorporation of phytochemicals, and desirable morphological properties. This detailed assessment should help to objectively select the formulation for the next experimental study and ensure repeatability. The suggested workflow for development and characterization of the nano-phytosome is shown in Figure 4, and the suggested parameters for characterization are summarized in Table 2.

PROPOSED BIOLOGICAL EVALUATION

After physicochemical characterization, the proposed framework suggests a comprehensive biological evaluation to assess the functional performance of the optimized polyherbal nano-phytosome [Figure 5]. The purpose of these evaluations is to assess the formulation design to see if it meets the expected goals of enhanced phytochemical stability, controlled release, and biological activity. The framework is not based on a single biological assay, but uses a multi-parameter approach, covering antioxidant activity, release, formulation stability, and antimicrobial activity. All these evaluations offer complementary information about the potential pharmaceutical applicability of the proposed nano-phytosome system.[30]

It is proposed to evaluate the antioxidant potential of the optimized formulation by the radical scavenging activity of DPPH and ABTS assays. The complementary techniques are commonly used to assess the free radical scavenging activity of plant-based formulations and serve as an indirect assessment of phytochemical preservation after

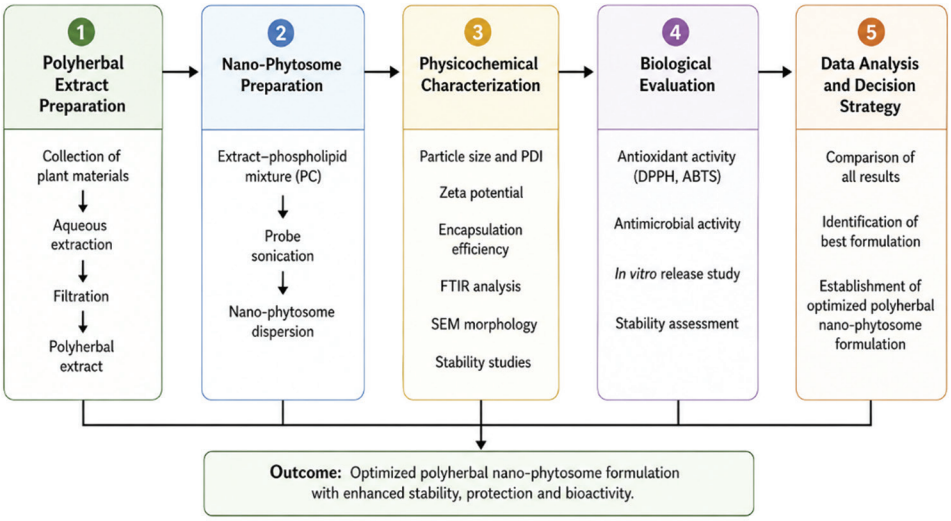


Figure 4: Proposed workflow for nano-phytosome development and characterization

Table 1: Proposed polyherbal formulations

Formulation	*Curcuma longa* (%)	*Aloe vera* (%)	*Capsicum annuum* (%)	Design rationale
PHF-1	50	25	25	Curcuma-dominant formulation emphasizing phenolic and curcuminoid content
PHF-2	40	30	30	Balanced formulation designed to maximize phytochemical diversity
PHF-3	33.3	33.3	33.3	Equal contribution from all three medicinal plants

Table 2: Proposed physicochemical characterization of the nano-phytosome

Characterization parameter	Proposed technique	Purpose
Particle size	DLS	Determine average vesicle diameter
Polydispersity index	DLS	Evaluate particle size uniformity
Zeta potential	Electrophoretic light scattering	Assess colloidal stability
Encapsulation efficiency	UV–Visible spectrophotometry/HPLC	Estimate phytochemical incorporation
FTIR spectroscopy	FTIR	Investigate phospholipid–phytochemical interactions
Surface morphology	Scanning electron microscopy	Examine vesicle shape and morphology

DLS: Dynamic light scattering, UV: Ultraviolet, HPLC: High-performance liquid chromatography, FTIR: Fourier transform infrared

Table 3: Proposed biological evaluation strategy

Evaluation	Proposed method	Purpose
Antioxidant activity	DPPH and ABTS assays	Assess free radical scavenging potential
In vitro release	Dialysis membrane diffusion method	Evaluate controlled phytochemical release
Stability assessment	Storage under pre-defined conditions	Monitor formulation stability over time
Antimicrobial activity	Agar well diffusion/Broth microdilution	Assess antimicrobial potential

DPPH: 2,2-diphenyl-1-picrylhydrazyl, ABTS: 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)

nano-phytosome formulation.[19,20] Comparative evaluation between optimized polyherbal extract and the corresponding nano-phytosome formulation is expected to give valuable insights into the effect of phospholipid encapsulation on the antioxidant activity of the formulation.

The framework also suggests *in vitro* release studies to examine the release behavior of phytochemicals from the nano-phytosome system in a controlled laboratory environment.[6] One of the key properties of phospholipid-based delivery systems is controlled release, which can extend

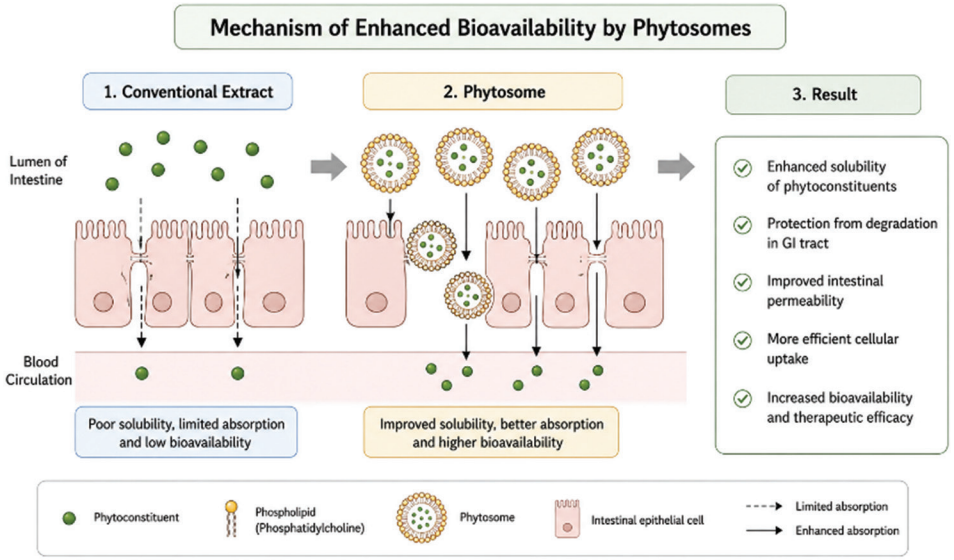


Figure 5: Proposed biological evaluation workflow

the availability of phytochemicals and enhance formulation properties. Stability studies are also recommended to determine the effect of storage conditions on critical formulation properties, such as particle size, colloidal stability, and integrity of the phytochemicals for specified observation periods in parallel. These investigations are designed to establish the storage stability of the proposed formulation in terms of its physicochemical properties.

The framework also suggests using standard microbiological procedures to evaluate the formulation for its broader biological potential against representative Gram-positive and Gram-negative bacterial strains [Table 3].[28] This would give preliminary data on the potential antimicrobial activity of the optimized nano-phytosome and would allow for comparison with the non-encapsulated polyherbal formulation. These proposed evaluations, when combined, create an overall plan for future experimental testing and a systematic framework for the evaluation of the developed formulation for pharmaceutical use.

DATA ANALYSIS AND DECISION STRATEGY

The proposed framework is a structured approach for data analysis and formulation selection [Table 4] which incorporates the parameters of phytochemical, physicochemical [Table 5], and biological evaluation [Table 6]. Formulation decisions are not supposed to be based on a single analytical result, but on the overall interpretation of several quality indicators. This multi-parameter approach aims to increase transparency, reduce subjectivity in decision-making, and increase the repeatability of future experimental investigations.

In Stage I, the proposed polyherbal formulations are comparatively evaluated by qualitative phytochemical screening, TPC, TFC, and antioxidant assays. The framework proposes that rather than choosing a formulation based on the best result from one test, the formulation with the best overall performance in all tests be selected. This can be achieved by considering that the pharmaceutical quality of a polyherbal formulation is dependent on the cumulative effect of several phytochemical and biological properties, which are not simply additive.

Similarly, the integrated assessment of the nano-phytosome formulation through physicochemical characterization and biological evaluation are highlighted in Stage II. All the above parameters should be considered together to determine the formulations with the best overall quality. This is a sequential decision-making process that gives a rational basis for formulation optimization and minimizes empirical selection.

If repeated experiments are conducted, quantitative data should be summarized by using proper descriptive statistics, such as mean and standard deviation for future experimental validation. Comparative analyses can be conducted by appropriate statistical methods (e.g., one-way analysis of variance and a suitable *post hoc* test), and statistical significance can be determined based on the study design. The statistical software and analytical methods used should depend on the experimental goals and the nature of the data.

In general, the proposed data analysis strategy is in line with the methodological approach by supporting the objective formulation selection in a systematic evaluation of multiple complementary parameters. This will help in achieving methodological consistency and reproducible development of polyherbal nano-phytosome systems in future studies in the lab.

Table 4: Proposed decision strategy for formulation selection

Development stage	Evaluation parameters	Decision criterion
Stage I – Polyherbal formulation	Phytochemical profile, TPC, TFC, DPPH, ABTS	Select the formulation with the most balanced phytochemical and antioxidant profile
Stage II – Nano-phytosome	Particle size, PDI, zeta potential, encapsulation efficiency, FTIR, SEM	Select the formulation with the most favorable physicochemical characteristics
Biological Evaluation	Antioxidant activity, release profile, stability, antimicrobial activity	Assess overall biological performance for future validation
Final selection	Integrated evaluation of all parameters	Choose the formulation demonstrating consistent performance across all quality indicators

TPC: Total phenolic content, TFC: Total flavonoid content, DPPH: 2,2-diphenyl-1-picrylhydrazyl, ABTS: 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid), PDI: Polydispersity index, FTIR: Fourier transform infrared, SEM: Scanning electron microscopy

Table 5: Expected physicochemical performance indicators

Parameter	Expected observation	Scientific significance
Particle size	Uniform nanoscale distribution	Improved formulation consistency
Polydispersity index	Narrow particle distribution	Homogeneous dispersion
Zeta potential	Stable colloidal system	Enhanced physical stability
Encapsulation efficiency	Efficient phytochemical incorporation	Improved phytochemical protection
Fourier transform infrared	Evidence of phospholipid–phytochemical interaction	Confirmation of complex formation
Scanning electron microscopy	Uniform vesicular morphology	Structural integrity of nano-phytosomes

Table 6: Proposed biological performance indicators

Biological parameter	Proposed evaluation	Expected significance
Antioxidant activity	DPPH and ABTS assays	Assess preservation of free radical scavenging potential
Antimicrobial activity	Standard microbiological assays	Evaluate inhibitory activity against selected microorganisms
In vitro release	Drug release studies	Determine controlled phytochemical release behavior
Stability	Short- and long-term storage studies	Assess maintenance of formulation quality

DPPH: 2,2-diphenyl-1-picrylhydrazyl, ABTS: 2,2′- azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)

SCIENTIFIC RATIONALE AND EXPECTED OUTCOMES

The proposed framework is based on the premise that the optimization of the herbal composition as well as the nanocarrier system is essential for successful herbal nanoformulation. Although a number of studies have shown that nano-phytosomes may be used for enhancing the delivery of plant-derived bioactive compounds, most of the studies have concentrated on the nanoformulation without systematically optimizing the polyherbal composition before the nanoformulation. This can affect the overall quality and reproducibility of the final formulation.[26]

The proposed two-stage approach overcomes this limitation by optimizing the polyherbal formulation through phytochemical and antioxidant evaluation and then developing the nano-phytosomes and comprehensively characterizing them. This sequential approach is designed to make sure that the nanoformulation is done with a herbal composition scientifically selected and not an extract that was empirically selected. This approach could provide a more consistent formulation and a more rational approach to future experimental studies.

In addition, the choice of *C. longa*, *A. vera,* and *C. annuum* is based on their complimentary phytochemical profile and reported biological effects.[30] The combination of these medicinal plants and phospholipid-based nano-phytosome technology offers a scientifically sound approach to the development of standardized herbal formulations. The proposed methodology is a systematic optimization approach with multi-parameter quality evaluation, which provides a repeatable methodology that can be adapted for future phytopharmaceutical research.

EXPECTED PHYSICOCHEMICAL PERFORMANCE

The suggested two-step optimization process is expected to help develop a nano-phytosome formulation with desirable physicochemical properties that can be used in the future for pharmaceutical applications. The framework involves

the preliminary phytochemical and antioxidant assessment of the polyherbal formulation before nanoformulation, which would help in building a solid base for phospholipid complexation and formulation consistency. This sequential approach will decrease the variability and help to obtain a stable nano-phytosome system.[7] After preparation of the nano-phytosomes, the formulation should have desirable physicochemical characteristics, such as uniform particle size distribution in the nano range, good colloidal stability, and efficient incorporation of phytochemicals derived from the plant.[27] The particle size analysis, PDI, zeta potential, encapsulation efficiency, FTIR spectroscopy, and SEM are suggested as the techniques to be used for the characterization of various aspects of formulation quality. All these parameters can be used to systematically assess the structural and physicochemical integrity of the nano-phytosome. In addition, the phospholipid matrix is expected to improve the protection and controlled release characteristics of the phytochemicals in comparison to conventional herbal extracts.[26] The proposed framework offers a structured approach to evaluate the formulation quality and identify critical parameters for the development of standardized polyherbal nano-phytosome systems, which are expected outcomes that must be validated in experiments.

EXPECTED BIOLOGICAL PERFORMANCE

It is expected that the proposed framework will help to develop a polyherbal nano-phytosome with enhanced biological performance, due to the synergistic effect of complementary phytochemicals and phospholipid delivery. The blend of *C. longa*, *A. vera*, and *C. annuum* is intended to provide a synergistic effect of phytochemicals[9-16,30] that complement each other. The framework aims to preserve the phytochemical diversity and to give a better basis for the following biological evaluation, optimizing the herbal composition before the formulation of nano-phytosomes. The nano-phytosome encapsulation is also expected to further increase the stability and bioavailability of phytochemicals, as they will not be degraded early and will be released in a controlled manner.[4] Therefore, more experimental research can be done to assess the effect of the optimized nano-phytosome on the biological activity of the polyherbal extract as compared to the non-encapsulated polyherbal extract in terms of antioxidant activity, antimicrobial activity, and formulation stability. It is hoped that this comparative evaluation will give a better understanding of the functional benefits of the nano-phytosome-based herbal delivery system. While these expected results need to be tested experimentally, the proposed framework provides a systematic means for assessing biological performance, not just a single endpoint, with complementary assays. The integrated evaluation strategy has been developed to improve the reliability of further investigations and to help formulate standardized and scientifically validated polyherbal nano-phytosomes.

POTENTIAL IMPACT AND FUTURE APPLICATIONS

The proposed framework offers a systematic methodology for the rational development of polyherbal nano-phytosome formulation, which combines herbal formulation design, preparation of nano-phytosomes, and comprehensive quality assessment into a single workflow. The present formulation framework focuses on the optimization of the polyherbal composition before the nanoformulation, as compared to the conventional formulation approaches, which are mainly focused on the preparation of nanocarriers. This sequential approach is thought to enhance methodological consistency and facilitate more reproducible formulation development.

In addition to the medicinal plants listed, the framework is flexible enough to accommodate other combinations of herbs that have complementary phytochemical profiles. The step-by-step process can help researchers to plan formulation studies, choose the right parameters for evaluation, and develop clear decision-making criteria before laboratory experiments. The framework could therefore be applied to pharmaceutical, nutraceutical, and natural product development, where standardized development strategies are becoming more and more demanded. The presented methodology, although still experimental, provides a practical basis for future studies with polyherbal nano-phytosome systems. The framework could help advance the development of more reliable herbal nanoformulations and aid in the translation of laboratory research into pharmaceutical products in the future, by encouraging systematic optimization and reproducible evaluation.

LIMITATIONS AND FUTURE RESEARCH

The proposed framework is designed to give a structured methodology for the development of polyherbal nano-phytosome formulations and should be used as a conceptual and methodological study. The framework is based on well-known principles of pharmaceutical science and literature, but has not yet been tested experimentally. Therefore, the expected physicochemical and biological performance described in this manuscript should be considered as scientifically informed expectations that need to be substantiated by well-designed laboratory investigations. One of the drawbacks is that the framework has been designed with the specific plants of *C. longa, A. vera,* and *C. annuum*. The methodology can be adapted for other medicinal plants; however, formulation parameters, extraction procedures, and characterization strategies might need to be adjusted based on the phytochemical composition of the medicinal plants selected. Similarly, the criteria for optimization can differ from one pharmaceutical application to another and from one herbal extract to another, due to the different physicochemical properties.

Further studies are needed to confirm the proposed framework with experimental studies, including formulation optimization, physicochemical characterization, and biological evaluation. Further research should involve advanced phytochemical profiling, *in vitro* and *in vivo* efficacy testing, pharmacokinetic studies, long-term stability testing, toxicity testing, and scale-up feasibility. These investigations will be crucial to determine the feasibility of the framework and facilitate its implementation in pharmaceutical and nutraceutical product development.

CONCLUSION

A structured framework for the rational development of polyherbal nano-phytosome formulation based on aqueous extracts of *C. longa*, *A. vera,* and *C. annuum* is presented in this paper. The proposed methodology consists of two stages of optimization, namely, formulation design of the polyherbal formulation, development of nano-phytosomes, physicochemical characterization, biological evaluation, and systematic data analysis. The framework focuses on the optimization of the herbal formulation before nano-phytosome preparation, which is more systematic and reproducible than conventional formulation strategies mainly focusing on the preparation of the nanocarriers.

The framework also encourages multi-parameter decision-making by incorporating phytochemical, physicochemical, and biological evaluation in a single method for formulation selection. This systematic approach aims to increase the methodological consistency and facilitate the development of standardized herbal nanoformulations for future pharmaceutical and nutraceutical research. The framework is not validated by experiments, yet it provides a scientifically sound direction for future research on polyherbal nano-phytosome systems. The proposed methodology is anticipated to help researchers in the formulation studies, which will be transparent, reproducible, and evidence-based, as well as provide a basis for the future development of plant-derived nanotherapeutic delivery systems.

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