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 4, November 2026
Impact Factor: 8.2

AI-Optimized Polyherbal Nanoformulation Combining Curcumin, Tulsi, Ginger and Piperine

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Abstract : *Background: Polyherbal formulations combine complementary medicinal plant constituents, but curcumin, a widely studied antioxidant and anti-inflammatory phytoconstituent, is limited by poor aqueous solubility, rapid metabolism and low bioavailability. Objective: This review examines the concept of an artificial intelligence (AI)-optimized polyherbal nanoformulation containing curcumin, tulsi, ginger and piperine, with emphasis on improving solubility, stability and bioavailability. Methods: Published literature on the pharmacology and physicochemical profile of the four constituents, on nanocarrier-based delivery of curcumin, and on machine-learning approaches to formulation optimization was compiled and critically analysed. Results: The reviewed literature indicates that curcumin, tulsi and ginger possess antioxidant and anti-inflammatory activity, that piperine inhibits drug-metabolizing enzymes and has been reported to markedly increase curcumin bioavailability, and that nanocarriers can improve the dispersion, protection and delivery of poorly soluble phytoconstituents. AI and machine-learning models can relate formulation variables to quality attributes such as particle size, zeta potential, entrapment efficiency and drug release, and may reduce the number of experimental trials. Conclusion: Combining these ingredients with nanotechnology and AI-guided optimization is a promising approach for herbal drug delivery; however, experimental preparation, characterization, safety, stability and biological validation remain necessary before pharmaceutical application.*

Keywords: Artificial Intelligence; Nanoformulation; Bioavailability; Solubility; Antioxidant Activity; Anti-inflammatory Activity; Drug Delivery; Machine Learning; Herbal Medicine

I. INTRODUCTION

Medicinal plants have been used for centuries as important sources of therapeutic agents. In recent pharmaceutical research, interest in plant-based medicines has increased because many herbal constituents possess multiple biological activities. However, the use of individual phytoconstituents is sometimes limited by poor water solubility, low absorption, rapid metabolism, instability, and inadequate bioavailability. Combining selected herbal constituents and incorporating them into an advanced drug-delivery system may help overcome some of these limitations.

A polyherbal formulation contains two or more medicinal plant-derived ingredients that may provide complementary pharmacological effects. Curcumin, tulsi, ginger, and piperine are promising natural compounds that can be considered for such a formulation. Curcumin is a major polyphenolic constituent obtained from *Curcuma longa* and has been widely investigated because of its antioxidant and anti-inflammatory properties.[1,2] However, its practical therapeutic application is restricted by factors such as poor aqueous solubility, limited absorption, and rapid metabolism.[3,4]

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Tulsi (*Ocimum tenuiflorum*) is a traditionally important medicinal plant containing several phytochemicals, including phenolic compounds, flavonoids, and essential-oil constituents.[5,6] Various studies have investigated tulsi for antioxidant, antimicrobial, and anti-inflammatory activities.[7–9] Ginger (*Zingiber officinale*) contains biologically active compounds such as gingerols and shogaols, which have also been associated with antioxidant and anti-inflammatory effects.[10,11] The presence of diverse phytoconstituents in tulsi and ginger makes them useful candidates for investigation in combination with other herbal ingredients.

Piperine, an alkaloid obtained mainly from *Piper nigrum*,[12,13] has attracted particular attention because of its potential influence on the absorption and metabolism of certain bioactive compounds.[14,15] Its association with curcumin has been studied as an approach to improve the systemic availability of curcumin.[16] Therefore, incorporating piperine along with curcumin, tulsi, and ginger provides an interesting basis for developing a multi-component herbal delivery system.

Nanotechnology offers a promising strategy for improving the delivery characteristics of poorly soluble herbal compounds.[17–19] Nano-sized delivery systems can alter the physicochemical behavior of active constituents and may improve dispersion, apparent solubility, protection from degradation, and interaction with biological tissues. Depending on the selected carrier and formulation technique, nanosystems may include polymeric nanoparticles, lipid-based nanoparticles, nanoemulsions, liposomes, or other suitable nanocarriers. Lipid-based and amorphous curcumin formulations, for example, have been investigated to improve oral bioavailability.[20–22] Nevertheless, the improvement obtained depends on the composition, preparation method, particle characteristics, and stability of the developed system.

The development of a polyherbal nanoformulation involves several formulation variables, including concentrations of active ingredients, carrier materials, surfactants, stabilizers, processing conditions, and other excipients. Changes in these factors can significantly influence important quality attributes such as particle size, polydispersity, zeta potential, entrapment efficiency, drug release, and physical stability. Conventional optimization may require a large number of experimental trials and considerable time.

Artificial intelligence (AI) and machine-learning approaches can provide an alternative strategy for systematic formulation optimization.[23–25] AI models can process experimental formulation data and identify relationships between input variables and formulation responses. Once appropriately trained and validated, such models may assist in predicting suitable combinations of formulation parameters and reducing unnecessary experimental trials. In the proposed system, AI can be used to investigate the relationship between formulation variables and critical quality attributes and to identify a formulation with desirable characteristics.

The integration of herbal pharmacology, nanotechnology, and artificial intelligence therefore provides a multidisciplinary approach for the development of an optimized polyherbal delivery system containing curcumin, tulsi, ginger, and piperine. The proposed formulation can be evaluated using physicochemical parameters such as particle size, polydispersity index, zeta potential, entrapment efficiency, drug loading, in-vitro release, and stability. Biological investigations such as antioxidant and anti-inflammatory studies may subsequently be performed to determine its potential activity.

Overall, an AI-assisted polyherbal nanoformulation represents a promising research concept that combines the advantages of naturally derived bioactive compounds with modern formulation and computational technologies. However, computational optimization alone cannot establish therapeutic effectiveness; the optimized formulation must be experimentally prepared, characterized, and appropriately validated through laboratory and, when justified, further biological studies.

Objectives:

1) To develop an AI-optimized polyherbal nanoformulation containing curcumin, tulsi, ginger, and piperine.
2) To use AI to optimize the formulation and improve its performance.
3) To enhance the solubility, stability, and bioavailability of curcumin and other herbal constituents.
4) To evaluate the antioxidant and anti-inflammatory potential of the formulation.

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5) To characterize and assess the quality, safety, and stability of the optimized nanoformulation.

II. MATERIALS AND METHODS

This review was prepared by compiling and critically analysing published literature on curcumin, tulsi (*Ocimum tenuiflorum*), ginger (*Zingiber officinale*) and piperine, on nanocarrier-based delivery systems for poorly soluble phytoconstituents, and on artificial intelligence and machine-learning approaches to formulation optimization. Information on botanical source, chemical constituents, physicochemical properties, pharmacological actions and reported bioavailability enhancement was extracted from the selected articles and organized under the headings of description, literature survey, mechanism and synergism, and constituent profiles. [Authors to add: databases searched, search keywords, period covered and inclusion/exclusion criteria.]

III. RESULTS

3.1 Description of the Formulation

The AI-optimized polyherbal nanoformulation combines curcumin, tulsi, ginger, and piperine to develop an advanced herbal drug-delivery system (Figure 1). These natural compounds have potential antioxidant, anti-inflammatory, and antimicrobial properties. Nanotechnology can help improve the delivery of poorly soluble phytoconstituents, and AI-based optimization may provide a systematic and innovative method for developing an effective polyherbal nanoformulation.

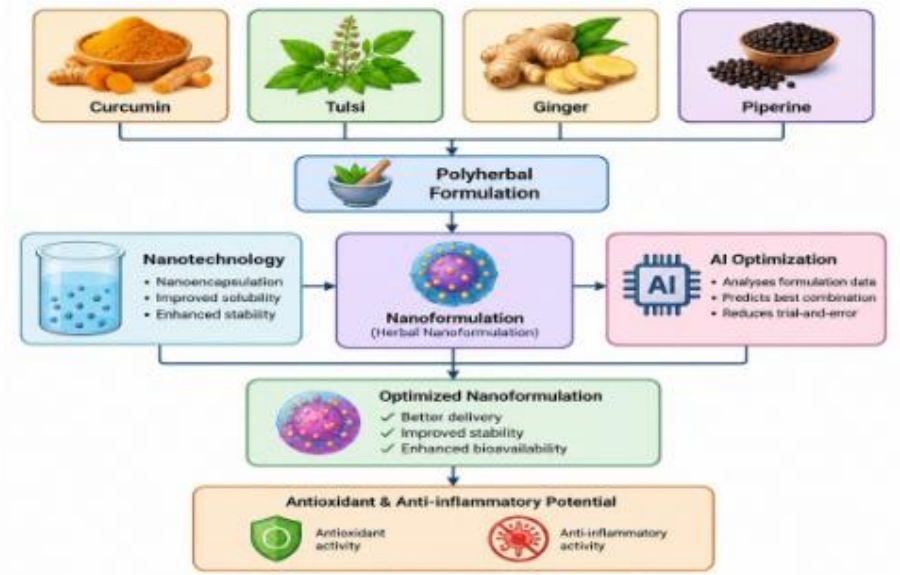


Figure 1. Schematic representation of AI-optimized polyherbal nanoformulation combining curcumin, tulsi, ginger and piperine.

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3.2 Literature Survey

Key published studies relevant to the proposed formulation are summarized in Table 1.

Table 1. Summary of key literature on curcumin, piperine, ginger and nanotechnology-based delivery.

Sr. No.	Author(s) and year	Key finding	Ref.
1	Anand et al., 2007	Reviewed the problems and promises related to the bioavailability of curcumin.	[3]
2	Hewlings and Kalman, 2017	Reviewed the effects of curcumin on human health and foods.	[1]
3	Shoba et al., 1998	Reported that piperine significantly improved the bioavailability of curcumin.	[16]
4	Yallapu et al., 2012	Discussed nanotechnology as a method for improving curcumin delivery and therapeutic potential.	[17]
5	Mashhadi et al., 2013	Reviewed the antioxidant and anti-inflammatory effects of ginger.	[10]
6	Pawar et al., 2012	Developed and optimized a novel lipid-based oral formulation of curcumin.	[20]
7	Prasad et al., 2014	Reviewed the biological properties and pharmacological potential of curcumin and the limitations associated with its bioavailability.	[2]
8	Burgos-Morón et al., 2010	Discussed limitations in translating the biological activities of curcumin into therapeutic applications, emphasizing the need for appropriate formulation and careful experimental assessment.	[4]
9	Sun et al., 2012	Reviewed nanotechnology-based systems designed to improve curcumin delivery and overcome physicochemical and pharmacokinetic limitations.	[18]
10	Prasad et al., 2014	Reviewed strategies for improving curcumin absorption and bioavailability, including formulation and delivery approaches.	[26]

3.3 Mechanism and Synergism

The therapeutic core of this combination relies on distinct but overlapping pharmacological actions, as summarized in Table 2.

Table 2. Mechanism and synergism of the polyherbal components.

Sr. No.	Component	Key bioactive target	Primary role in the matrix	Therapeutic action
1	Curcumin	Downregulation of NF-κB, COX-2 and inflammatory cytokines	Core therapeutic agent	Antioxidant, anti-inflammatory, antineoplastic, neuroprotective

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Sr. No.	Component	Key bioactive target	Primary role in the matrix	Therapeutic action
2	Tulsi	Modulates humoral and cell-mediated immunity	Immunomodulatory and antimicrobial	Respiratory relief, stress adaptogen, antiviral
3	Ginger	Inhibits prostaglandin and leukotriene synthesis	Synergistic anti-inflammatory	Analgesic, gastroprotective, antiemetic
4	Piperine	Inhibits CYP3A4 and UDP-glucuronosyltransferase	Bioavailability enhancer	Increases curcumin absorption by up to 2000% [16]

3.4 Profile of the Constituents

The physicochemical and organoleptic profiles of the four constituents are given in Table 3, and their appearance is shown in Figures 2–5.

Table 3. Profile of curcumin, tulsi, ginger and piperine.

Parameter	Curcumin	Tulsi	Ginger	Piperine
Drug name	Curcumin	Tulsi / Holy basil	Ginger	Piperine
Scientific / botanical name	*Curcuma longa* L.	*Ocimum tenuiflorum*	*Zingiber officinale* Roscoe	*Piper nigrum* L.
Colour	Orange-yellow	Green	Pale yellow to light brown	Pale yellow to yellow
Odour	Odourless / faint characteristic odour	Aromatic	Characteristic, aromatic and pungent	Faint
Taste	Slightly bitter	Pungent and slightly bitter	Warm	Pungent
Chemical constituents	Curcuminoids	Eugenol, rosmarinic acid	Gingerols, shogaols	Piperine
Storage	Tightly closed container, protected from light and moisture	Protected from moisture and light	Not stated	Protected from moisture and light
pH	5–7	Approx. 5–7 (aqueous extract)	Approx. 5.5–7.0	Not stated
Density	Approx. 0.935 g/cm³	Not stated	Approx. 0.9–1.1 [unit to be confirmed]	Approx. 1.29 g/cm³

The IUPAC names of the principal constituents are as follows. Curcumin: (1*E*,6*E*)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione. 6-Gingerol (ginger): (5*S*)-5-hydroxy-1-(4-hydroxy-3-methoxyphenyl)decan-3-one. Piperine: (2*E*,4*E*)-5-(1,3-benzodioxol-5-yl)-1-(piperidin-1-yl)penta-2,4-dien-1-one.

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Figure 2. Curcumin (*Curcuma longa* L.).



Figure 3. Tulsi (*Ocimum tenuiflorum*).



Figure 4. Ginger (*Zingiber officinale* Roscoe).

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DOI: 10.48175/568

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Figure 5. Piperine source (*Piper nigrum* L.).

IV. DISCUSSION

The AI-optimized polyherbal nanoformulation combines curcumin, tulsi, ginger, and piperine to develop an advanced herbal drug-delivery system. Nanotechnology may improve the solubility, stability, and bioavailability of poorly soluble herbal constituents, while AI can help optimize formulation variables and reduce unnecessary experimental trials. The selected ingredients possess reported antioxidant and anti-inflammatory potential, with piperine being investigated as a bioavailability enhancer for curcumin.[15,16] Overall, this approach combines herbal medicine, nanotechnology, and artificial intelligence and requires further experimental, safety, stability, and biological evaluation before pharmaceutical application.

4.1 Potential Benefits and Advantages

- **Improved bioavailability** – Nano-sized delivery may improve the absorption of poorly soluble phytoconstituents such as curcumin.
- **Enhanced solubility and dispersion –** Nanotechnology can improve the dispersion of herbal compounds in the formulation.
- **Combined herbal effects –** Curcumin, tulsi, ginger, and piperine provide different bioactive constituents that may complement each other in a single formulation.
- **Antioxidant potential –** The selected ingredients contain compounds with reported antioxidant activity.
- **Anti-inflammatory potential –** Curcumin, ginger, and tulsi have been investigated for their anti-inflammatory properties.
- **Better formulation optimization** – AI can analyze formulation data and identify suitable combinations of ingredients and processing variables, enabling faster and more systematic optimization.
- **Reduced trial-and-error –** AI-based prediction may reduce the number of experimental batches required during formulation development.
- **Improved stability and controlled delivery –** An appropriately designed nanosystem may help protect active constituents and regulate their release.
- **Modern herbal drug delivery** – It combines traditional medicinal plants with nanotechnology and AI, providing an innovative research approach.
- **Potential for further pharmaceutical development** – The optimized formulation can be subjected to physicochemical, biological, stability, and safety studies.

4.2 Limitations

Despite these potential benefits, the approach has limitations. The use of advanced technology leads to a high formulation cost, and the manufacturing process is complex. Specialized equipment and expertise are required, and

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nanoformulations may show stability problems. In addition, computational optimization alone cannot establish therapeutic effectiveness.

4.3 Future Perspectives

The AI-optimized polyherbal nanoformulation containing curcumin, tulsi, ginger, and piperine has potential for further development as an advanced herbal drug-delivery system. Future research can focus on improving the formulation through AI-based prediction and optimization of particle size, stability, drug loading, and release characteristics. Advanced nanocarriers may be investigated to enhance the solubility, protection, and bioavailability of herbal constituents. Further in-vitro, in-vivo, toxicity, pharmacokinetic, and long-term stability studies are required to establish its safety and biological effectiveness. AI and machine-learning models can also be expanded using larger experimental datasets to improve formulation prediction and reduce development time. With appropriate experimental validation and standardization, this approach may support the future development of reproducible and scientifically evaluated polyherbal nanoformulations.

V. CONCLUSION

The AI-optimized polyherbal nanoformulation combines curcumin, tulsi, ginger, and piperine to improve herbal drug delivery. Nanotechnology may enhance solubility, stability, and bioavailability, while AI supports efficient formulation optimization. Further studies are needed to confirm its safety, stability, and therapeutic potential.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ACKNOWLEDGEMENT

The authors are thankful to the management of Shri Goraksh College of Pharmacy and Research Center, Khamgaon, for their support and for providing the necessary facilities.

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