Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol.14 , Issue 14s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Artificial Intelligence-Driven Drug Delivery Systems for Herbal Therapeutics: Computational Strategies Bridging Phytopharmaceutical Traditional and Precision Nanomedicine.

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Cite this paper as: Dr Dharmendra Singh Gurjar, Dr Balveer Singh, Dr Yash Raj Sharma, Dr Ritu Kapoor, Dr Manoj Adlakha (2025) Artificial Intelligence-Driven Drug Delivery Systems for Herbal Therapeutics: Computational Strategies Bridging Phytopharmaceutical Traditional and Precision Nanomedicine... Journal of Neonatal Surgery, 14, (13s) 951-959

ABSTRACT

Background: Herbal therapeutics possess substantial pharmacological assertion, their clinical translation is though repeatedly hindered by poor aqueous solubility, low oral bioavailability, phytochemical instability and compositional variations across batch to batch. Also, the site -specific action related data is largely absent. Artificial Intelligence (Ai) is highly positioned to solve these prolonged formulational voids.

Aim: The current review solidifies current evidence on how machine learning, Deep learning and predictive modelling are applied across phytopharmaceutical delivery pipeline from bioactive identification to nano-carrier optimisation, and to examine the points of convergence with Ayurvedic Pharmaceutical reasoning.

Methods: A non-computational conceptual literature synthesis was caried out using PubMed, ScienceDirect, Scopus and Google Scholar covering available literature from 2015 to 2026 analysing the published findings on AI-assisted phytochemical screening, nanocarrier design and herbal drug delivery alongwith classical Ayurvedic Text correlation.

Results: In the literature, quantitative structure-activity relationship modelling, graph neural networks, digital twin-based process optimisation and simulation of release functions and estimation of toxicity of nanoparticles are mentioned as examples of the ways in which AI techniques can accelerate the discovery of bioactive phytoconstituents, predict the compatibility of the drugs with the carriers, and simulate the release function and estimate the toxicity of the nanoparticles. Some improvements reported are: formulation screening is faster; encapsulation efficiency can be predicted early; problematic physicochemical interactions with the formulation can be identified early for all types of liposomal, phytosomal, polymeric and hydrogel formulations.

Conclusion: AI has the potential to revolutionize phytopharmaceutical engineering and create more standardized and personalized delivery systems for herbs, but it is a pre-clinical field that still needs to be further explored and developed. Data on the beneficial phytochemicals that they cultivate, streamlined regulatory paths and future clinical trials will be crucial to their improvement. The Rasa Panchakas are a concept suggested for material characterisation in the classical ayurvedic formulation and are tentatively proposed to be used in feature design....

Keywords: Artificial Intelligence, Herbal Therapeutics, nanocarriers, phytopharmaceuticals, drug delivery systems, Bioavailability.

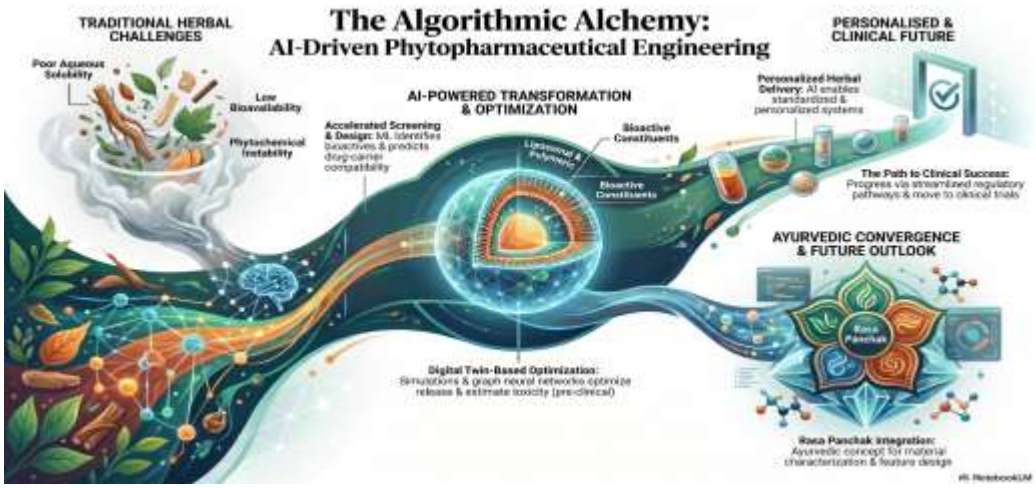

Figure 1: Graphical Representation of the Abstract

INTRODUCTION

Therapeutics of plant origin are in a unique niche in the present-day medicine. They are at the same time old and yet to come. The importance of physicochemical properties and pharmacodynamics of a *dravya* (medicinal substance) was recognised by classical *ayurvedic* pharmacology more than 2000 years ago and systematised in Charaka Samhita by the doctrine of *Rasa Panchaka* which evaluates the substance based on *Rasa* (taste), *Guna* (physical properties), *Virya* (potency), *Vipaka* (post digestive effect) and *Prabhava* (specific action) [1]. *Sushruta Samhita* also puts heavy emphasis on *Yukti* that is the application of remedy in a rational manner depending upon the situation; it also suggests that the formulation strategy is not by itself a part of therapeutic outcome but is rather a part of the therapeutic outcome [2]. Science today in medicine has reached the same conclusion, albeit by a different path - that the inherent pharmacological activity of a phytoconstituent often is lost due to unfavourable physiochemical behaviour before it reaches its biological target.

This is an issue in which the translation gap is highlighted. The therapeutic potential of polyphenols (e.g. curcumin, quercetin) is limited in vivo by their low bioavailability, first pass metabolism and aqueous insolubility. The problems of classical *dravyas*, such as terpenoids, alkaloids and glycosides, are also similar: gastrointestinal pH extremes that degrade them, they are prone to hepatic first pass conjugation, and they have variations in composition from one batch to another (caused by geographic and seasonal variations and processing variations in raw plant materials). Different carrier systems using liposomes, phytosomes, polymeric nanoparticles, solid lipid nanoparticles and hydrogels have found different applications as partial solutions to enhance solubility and/or increase the systemic residence time of the phytoconstituent in a more pharmacokinetically favourable shell [3,4]. In particular, phytosomes make use of the complexation with phospholipids for better permeation across the gut wall and across the stratum corneum, and have been compared with conventional liposomes in various pharmacokinetic studies, which yielded better results compared to conventional liposomes [5,6].

The difficulty in making progress, has been the lack of candidate carrier chemistries, not the lack of candidates. The problem has been lack of efficiency in the optimisation process. The particle size, surface charge, drug-to-lipid ratio and release rates of these particles have been fine-tuned by many cycles of trial-and-error, usually in an iterative process, which is labor intensive and difficult to scale up when the chemical diversity of the starting material (whole plant extracts) is uncontrolled. The advent of artificial intelligence (including machine learning, deep learning and related predictive modelling approaches), have started to change the nature of this problem. Instead of running each formulation sequentially, AI-based techniques can be used to learn structure-property relationships from existing experimental data and make in silico predictions regarding which carrier formulations will be most likely to work prior to the synthesis of a single batch of a particular formulation of a drug [7,8]. Each of these models – quantitative structure-activity relationship (QSAR), graph neural networks and physiologically based pharmacokinetic simulations – has shown the ability to predict the behavior of nanoparticles, their ability to interact with drug carriers and their disposition in the system with precision that is not easily achieved using empirical screening [9].

It should be mentioned here that identification of bioactive compounds is one of the important points to be highlighted before the formulation development. In the past few years, network pharmacology and machine learning techniques have played a vital part in understanding the multi-target effects of plant-derived bioactive compounds, and identified key molecular hubs such as Nrf2/KEAP1/ARE and NF-κB pathways in various phytochemicals with antioxidant and anti-inflammatory properties. In recent years, the prediction of interactions between drugs and phytoconstituents has become a trend by considering the molecular structure of the drug; this approach can be used to reduce the amount of time spent in the laboratory for drug selection. These computational techniques span the entire process of herbal medicine development, starting from

the discovery of molecules, through understanding their mechanisms, selection of suitable carriers and the eventual stage of clinical trials.

Yet although there is a wealth of evidence, on-going literature is dispersed across various fields. Herbal medicine is rarely mentioned in nanotechnology reviews except for the use of AI as a drug delivery method. In contrast, the computational aspect of herbal/new formulations in the era of modern science is rarely addressed in ethnopharmacology reviews. Although there are some similarities between the material characterization in *Ayurveda* and the feature spaces used in many of today's computational models, few studies make an effort to link these two. This lack of research is a true hurdle, and the knowledge gained from traditional medicine can be used to enhance the accuracy of AI systems' analysis of herbal data.

Based on this background, this review attempts to consolidate the existing information related to the design of drug delivery systems with the help of artificial intelligence-based approach for herbal medicine. It aims at introducing the primary computational tools employed in screening for bioactive compounds, optimizing carriers and predicting toxicity and analyzing the overlap of these with the traditional ayurvedic principles. Particular attention will be given to the problems in the clinical development of herbal products based on in silico data.

MATERIALS AND METHODS

Study Design

This article is not computational and/or data-science based, but rather a conceptual synthesis from a domain-research perspective using an integrative approach between *Ayurvedic* and Biomedicinal Pharmacology. This work is devoid of any machine learning model, QSAR calculation, molecular docking run or any statistical re-analysis. The contribution is of an interpretative nature: a coherent pathway is organized from published results of the use of AI for the creation of phytopharmaceutical delivery and a conceptual link is made with the classical ayurvedic pharmaceutical reasoning for future studies by researchers who have the computational skills necessary to test this link.

Scope for Original Analysis

The aim of this review is to stand as an illustration of the quantitative results, description of the model performance and technical claims that have been reported in published papers regarding AI methods; the quantitative results, the description of the performance of the models, and technical claims made in this review are therefore taken verbatim from the papers cited and are not verified, recomputed or benchmarked here. Tables 1 to 4 (in this article) are organisational syntheses, rather than actual results of analysis performed by the author, based on the literature reviewed. The *Ayurveda*-AI correlation presented in Results and Discussion is not a result of computational testing, but an interpretation based on classical text study and is a proposal for testing through computation in the future. If readers are interested in implementing, modelling or formal validation of any of the AI techniques described herein, they are encouraged to read the original cited sources. The sources and search methods used to find information. Sources searching for information.

Information Sources and Search Strategy

Literature was obtained from PubMed/MEDLINE, ScienceDirect, Scopus, Web of Science and Google Scholar from January 2015 to June 2016. The three conceptual clusters identified in the search terms were: (i) AI related terms (machine learning, deep learning, neural network, QSAR, graph neural network), (ii) delivery system related terms (nanocarrier, liposome, phytosome, polymeric nanoparticle, solid lipid nanoparticle, hydrogel), and (iii) herbal terms (herbal medicine, phytochemical, phytopharmaceutical, *Ayurveda*, natural product). The lists of retrieved reviews were scanned manually for further references and the classical ayurvedic works (*Charaka Samhita, Sushruta Samhita* and *Ashtaanga Hridayam*) were referred to directly (not secondarily) to correlate with the review text used in the selected translated classical ayurvedic texts. The search structure is summarised in Table 1, but no counting of the number of screenings in PRISMA style are reported as this is a narrative and not a systematic review.

| Table 1: Search Strategy by Thematic Domain |

Thematic domain	Representative search terms	Primary databases
Bioactive phytochemical identification	phytochemical AND (machine learning OR network pharmacology OR docking)	PubMed, Scopus
Nanocarrier and formulation design	nanocarrier AND (artificial intelligence OR QSAR OR deep learning)	ScienceDirect, Web of Science
Release kinetics and pharmacokinetic simulation	drug release AND (machine learning OR digital twin OR PBPK)	PubMed, ScienceDirect
Toxicity and safety prediction	nanoparticle OR drug AND toxicity AND (deep learning OR machine learning)	PubMed, Google Scholar

Thematic domain	Representative search terms	Primary databases
Classical Ayurvedic pharmaceutical correlation	Rasa Panchaka; Charaka Samhita; Sushruta Samhita; Kalpana	Primary classical texts (translated editions)

Eligibility Criteria

If an application reported any one of the following information, sources were accepted: Classical texts were reported as primary; An application in *ayurvedic* herbal/natural product therapeutics involving AI/computational modelling was reported; An application involving optimisation of a nanocarrier and/or a formulation for the above application was reported; An application involving modelling of interaction between the drug and a nanocarrier was reported; An application involving simulation of release kinetics of active ingredients from the drug was reported; An application involving toxicity or safety prediction of the above application was reported. Eligible were papers that were original research papers that had been peer reviewed, and book chapters that were indexed. The conference abstracts, non-peer reviewed preprints (preprints not validated after the conference) and abstracts not published in English were not included, nor were abstracts of conference papers that were not published. If the claim is only supported by a preprint (which is not peer reviewed) this is clearly indicated in the reference to the claim, not as validated evidence.

Data Extraction and Thematic Synthesis

The following were identified, if reported, for each eligible source: the algorithm class, type of training data, approach to validation for the AI used (or computational technique); the delivery system (or class of phytochemical) studied; the main quantitative or qualitative outcome; any specification of limitation. The data that were gathered during the extraction were categorized into four thematic areas that are sequential steps in the phytopharmaceutical delivery pipeline: (a) identification and prioritisation of bioactive phytochemicals, (b) optimisation of nanocarrier and formulation design, (c) release kinetic modelling and simulation, and (d) toxicity and safety prediction and regulatory evaluation. This thematic structure is broken down, and will be used as the structure for the Results section, and is summarised in Table 2.

| Table 2: Taxonomy of AI Techniques Applied Across the Phytopharmaceutical Delivery Pipeline |

AI technique	Algorithm class	Characteristic input data	Principal pipeline application
QSAR modelling	Statistical / supervised ML	Molecular descriptors, physicochemical parameters	Bioactivity and carrier-compatibility prediction
Graph neural networks	Deep learning (graph-based)	Molecular graph structures, bond/atom features	Drug-target interaction; toxicity endpoint prediction
Transformer-based models	Deep learning (attention-based)	SMILES strings, sequence-type chemical data	Virtual screening; bioactivity classification
Physiologically based pharmacokinetic (PBPK) models	Mechanistic / hybrid ML	Physiological compartment parameters, dosing data	Systemic disposition and release kinetics simulation
Multiscale machine-learned modelling infrastructure	Hybrid multiscale ML	Nanoparticle synthesis parameters, nano-bio interaction data	Nanocarrier synthesis optimisation
Digital twin frameworks	Data-driven simulation	Real-time manufacturing/process sensor data	Continuous manufacturing and personalised dosing

Ayurvedic Textual Correlation Methodology

Correlation includes ex post facto statements of classical *ayurvedic* concepts which relate to the computational result, usually a mapping of a classical parameter (such as the *Guna* and *Virya* attribute of *Rasa Panchaka*) to a conceptually similar physicochemical parameter (such as lipophilicity) used in the AI-based modelling. This mapping is not an equivalence, but rather considered a psychological shortcut in the integrative reasoning; in this sense, it is indicated everywhere.

Quality Appraisal

Formal risk-of-bias assessment was not performed, because of the narrative design of the study. All claims of the type of AI

were confirmed by at least one independent source that had reached a similar conclusion; single-source claims were taken with a pinch of salt when discussing the results in the Discussion.

RESULTS

Overview of Retrieved Evidence

The literature collated was synthesized around four stages of the pipeline, as listed in the Methods, with most items in the last few years (2023-2026) targeting optimisation of the nanocarriers used and prediction of their toxicity, and a smaller number of items in the same time frame dealing with bioactive phytochemical prioritisation using graph-based and transformer architectures. Table 1 provides an overview of the thematic domains, the search strategy and the yield. The taxonomy of identified and classified AI techniques is presented in Table 2, which classifies AI techniques by their algorithm and the type of characteristic of input data.

Bioactive Phytochemical Identification and Prioritisation

Indeed, direct prediction of phytochemical bioactivity has been attempted by machine-learning classification networks and reported models were able to distinguish between (anti-)oxidant, (anti-)inflammatory, immune-modulatory and (anti-)lipid metabolism activities of chemical descriptors from natural product libraries [13]. The network pharmacology techniques identified the poly-pharmacological target space of plant secondary metabolites, which is often followed by molecular docking, a procedure that results in a generally good match with the experimental validation of the effects, and converging modulation of the Nrf2/KEAP1/ARE, PI3K/AKT, MAPK, and NF-κB signalling pathways is found among the phytochemicals selected from different studies published from 2015 to 2025. This capability has been extended to prediction of drug-target interaction for phytoconstituents based on the use of graph neural networks and transformer-based models that can model and capture complex patterns in high dimensional chemical and biological data, enabling the optimization of virtual screening and prioritise compounds for pharmacological testing, prior to experimental testing [10,11,14]. Remarkably, there is little evidence of model generalisability in this literature: most of the models are trained on synthetic compound libraries, and then applied to structurally complex, sometimes stereochemically odd, phytochemical scaffolds for anticancer screening [15].

Nanocarrier and Formulation Design Optimisation

The most complete and well-defined evidence is about the design process of AI-driven nanocarriers. The use of multi-scale machine-learned modelling infrastructure, agent-based modelling, QSAR, physiologically based pharmacokinetic models and pharmacokinetic/pharmacodynamic modelling for reducing the number of “expensive and time consuming” trial and error experiments to predict the synthesis parameter and nano-bio interactions of nanoparticles was listed in the review of 2025 [9]. Generative protein design models have successfully created folded carrier-binding structures from known topological constraints using AI-assisted frameworks of nano-architectonics that integrate machine learning-assisted surface engineering with the design of carrier-binding ligand from a database. [16]. The use of machine learning, deep learning, transformer-based models and graph neural networks to optimise the selection of nanocarriers, the compatibility of nanocarriers and drugs and release profile of phytoconstituents is discussed by a dedicated review, and here precision nanotechnology (nanotechnology optimised to address patient-specific omics data) is the bridge between the phytomedicine and precision nanotechnology [17]. Also reported in the AI powered smart and sustainable drug delivery reviews, is the use of digital twin technology for continuous manufacturing, where process changes such as mixing, drying and coating can be made in real-time, and the prospect of extending to patient specific digital twins, modelling the physiological variability to enable personalised dosing [18].

There is less literature that is specifically related to the phytosome when compared to the greater literature dealing with computational aspects of the nanocarriers. But there are a number of real-world tests to which predictions by AI are being put to the test. Complexation of the standardised phytoconstituents with phospholipids (e.g. phytosomes) has been demonstrated to be more stable and have a capability to carry greater amount of phytoconstituents for therapeutic application in inflammatory disease, metabolic syndrome, osteoarthritis and some cancers [5,6]. The topical phytosome delivery reviews demonstrate its penetration ability is better than that of free phytochemical application as a result of favourable lipid-membrane compatibility [19]. The empirical studies of the past decade have confirmed these benefits in terms of bioavailability; the development of modern QSAR and machine learning models for phytosome and liposome optimisation are based on these benefits.

Release Kinetics, Pharmacokinetic Simulation and Personalisation

Along with the development of the carrier, simulation of the drug release kinetic and biodistribution has also been developed with the help of Artificial Intelligence (AI). AI-based simulation of the interaction of biological barriers, both extracellular (nanocarrier stability, clearance by immune system, biodistribution) and intracellular (entry into cells, escape from endosomes and lysosomes, targeting of the cell nucleus) of nanocarriers has been described for difficult physiological barriers like the blood-brain barrier or the tumour microenvironment [20]. Machine learning and deep learning innovations can

predict the particle size, drug loading efficiency, and biodistribution from multidimensional information including multidimentional physicochemical characterization, pharmacokinetic data, omics profiles and preclinical outcome data, while generative algorithms are starting to suggest new chemistries of the carriers optimized for different clinical indications [21]. This ability is said to represent closing the loop between formulation design, manufacture and clinical data 18, which has been a long-held dream of formulation scientists, achieved so far by empirical means.

Toxicity, Safety and Regulatory Prediction

There is a vast and growing database of work on the toxicity prediction using AI. The rationale for using AI toxicity screening for herbal nanocarriers is that while unexpected toxicity in drug development is a well-recognised factor of failure, the evidence of this failure rate is cited from pharmaceutical drug development as a whole, and not specifically from herbal nanomedicine [22]. Deep learning and multimodal data fusion approaches are reported to transform a toxicological evaluation and graph neural network architectures are reported to outperform other architectures in toxicological molecular property prediction tasks relevant to acute and chronic toxicity endpoints [23]. The best performing machine learning toxicity models has been found to depend on the toxicity domain (hepatotoxicity, cardiotoxicity, dermal toxicity), meaning that, as yet, there is no single AI architecture that generalises across all toxicity domains that are relevant to nanocarrier encapsulated phytoconstituents [24]. This impacts directly on the realm of herbal nanomedicine, where each component of the carrier, the phytochemical and the degradation products has different toxicological profiles to be validated separately.

Synthesis Across the Pipeline

Table 3 brings together representative applications of AI in the four domains of pipelines, with the herbal delivery system context. A comparative summary of conventional nanocarrier platforms (liposomes, phytosomes, polymeric nanoparticles and hydrogels) and the main physicochemical and pharmacokinetic parameters optimized or predicted using an AI model is shown in Table 4. In this, as in all four domains, the pattern is a narrowing of the search space for experiments and the identification of likely failure modes are quicker, but the reported outcomes all have an experimental or preclinical verification step downstream before being translated. This follows in all four domains and is further elaborated in the Discussion.

| Table 3: Representative AI Applications Across the Phytopharmaceutical Delivery Pipeline |

Pipeline stage	AI application	Herbal delivery system context	Key reported benefit
Bioactive identification	Network pharmacology with ML-based virtual screening	Polyphenols, flavonoids, terpenoids	Convergent pathway hub identification (Nrf2/KEAP1, NF-κB)
Bioactive identification	Graph neural network / transformer drug-target prediction	Diverse phytoconstituent libraries	Faster candidate prioritisation before docking/assay
Carrier design	QSAR and multiscale ML modelling	Polymeric nanoparticles, lipid nanocarriers	Reduced trial-and-error synthesis cycles
Carrier design	ML-assisted surface engineering / nanoarchitectonics	Targeted nanocarriers (general nanomedicine)	High-specificity receptor-binding ligand design
Release kinetics	Digital twin / closed-loop process modelling	Continuous manufacturing of nanoformulations	Real-time process parameter adjustment
Release kinetics	PBPK and PK/PD simulation	Liposomal and phytosomal systems	Systemic disposition forecasting
Toxicity prediction	Deep learning / GNN toxicity models	Carrier-phytochemical complexes	Earlier detection of adverse physicochemical interaction

Table 4: Comparative Summary of Conventional Herbal Nanocarrier Platforms and AI-Modelled Parameters

Carrier system	Typical phytoconstituent class	Principal limitation addressed	AI-modelled parameters
Liposomes	Polyphenols, flavonoids	Poor aqueous solubility, rapid clearance	Vesicle size, lamellarity, drug-to-lipid ratio, release rate

Carrier system	Typical phytoconstituent class	Principal limitation addressed	AI-modelled parameters
Phytosomes	Polyphenolic and flavonoid complexes	Low membrane permeability	Phospholipid-complexation efficiency, stability, permeation
Polymeric nanoparticles	Alkaloids, terpenoids	Instability, uncontrolled release	Particle size, surface charge, encapsulation efficiency
Solid lipid nanoparticles	Lipophilic terpenoids and glycosides	Variable bioavailability	Crystallinity, drug loading, biodistribution
Hydrogels	Mucilage- and polysaccharide-based extracts	Short residence time, poor controlled release	Swelling kinetics, diffusion coefficient, degradation rate

DISCUSSION

Mechanistic Basis for AI Utility in Phytopharmaceutical Delivery

What seems to be the single most desirable property of AI comes from an ability to discover latent structure-property relationships from data sets which are too high dimensional or too non-linear to be efficiently captured by traditional regression or by manual heuristics. Optimisation of nanocarriers is an interplay of the size of the particles, their zeta potential, the amount of drug they carry and their release rate, which is influenced by variables of the formulation, the processing temperature and the concentration of the surfactant, and is not always additively sumamable. To overcome this, QSAR and graph neural network models learn a continuous mapping between molecular and formulation descriptors to predicted outcome, instead of performing tests in a sequential manner [9,17]. It is akin to the physiologically based pharmacokinetic model that considers multiple physiological compartments to predict systemic exposure, but is based on a computer algorithm, rather than solely on mechanistic equations; the AI component is to fit these models to sparse, noisy data from experiments, which is more efficient than fitting solely by mechanistic equations, especially because the input phytochemical is a complex mixture instead of a single pure compound [18].

The mechanistic importance of deep learning is its ability to predict molecular initiating events, for toxicity prediction specifically, such as protein binding, mitochondrial destruction or formation of reactive metabolites, from a structural description of the molecule, without having to synthesize it first [23]. This is especially important in the case of herbal nanomedicine, where animal screening cannot afford to answer the combinatorial toxicological question of “emergent complex toxicity” – which is the toxicity of the carrier itself plus its phytochemical – for every candidate formulation.

Correlation with Classical Ayurvedic Pharmaceutical Reasoning

This cross comparison is illustrative, conceptual and has not been through a peer-reviewed process; no known study exists that quantifies the concordance between the *Ayurvedic* Guna classification and modern QSAR descriptors, so the cross comparison below is not an equivalence. *Charaka Samhita* considers five interlocking parameters of the substance; *Rasa*, *Guna, Virya, Vipaka* and *Prabhava* and uses this as a basis for evaluating a substance and determine its therapeutic behaviour by itself [1]. The modern concept of QSAR modelling is based on the same premise as that of the lipophilicity: the individual descriptors are weak predictors of the bioavailability, but when combined together in sets, as in the Lipinski type, they can be useful. Stated as an illustration only, the descriptions of the *Guna* pair *Snigdha-Ruksha* (unctuous-dry) are more or less loosely analogous to the lipophilicity axis, and of the *Guna* pair *Guru-Laghu* (heavy-light) to the absorption-rate descriptors in such models; they are suggested as conceptually parallel rather than exact matches. Another similarity is in their focus on *Kalpana* – the processing method that ultimately determines the potency of a formulation – as a key factor in a process optimised for manufacture of nanocarriers, regardless of the identity of the phytochemical [2].

If the analogy is found to be valid in testing, classical *Guna-Virya* data (as available in the structured form) could be used as additional supplementary feature inputs in machine learning models that are developed from the outcomes of nanocarriers containing herbs. This is a hypothesis that was formulated by the present synthesis rather than a discovery and should be tested in the future for practical application.

Comparison with the Broader Nanomedicine AI Literature

The amount and maturity of the literature on AI-assisted design of synthetic drug nanocarriers are significantly larger than the parallel literature on AI-assisted design of nanocarriers for natural products, which is typical of the scaffolds of phytochemicals [15], and this mirrors the general pattern of AI models trained predominantly with synthetic compound

libraries that do poorly when applied to structurally unusual scaffolds such as those found in natural products. It's not a absurd restriction. Most of the most successful platforms for AI toxicity and ADMET prediction, such as widely-used platforms that demonstrate excellent performance on standard small molecule toxicity sets, were developed and validated with synthetic small molecule libraries; their usefulness for multi-component herbal extracts, where the active principle could be a synergistic mixture of more than one molecule, hasn't been similarly validated [22,24]. This is a real translational limit of what AI-herbal integration can do today, and is an area that has yet to be sufficiently explored.

Strengths of the AI-Integrated Approach

On the positive side, the literature reviewed does indicate real strengths, as long as the above said proviso is taken into account. Network pharmacology can be used to predict the molecular targets of phytochemicals, and these are prioritised and reported to decrease the experimental workload during phytochemical prioritisation, allowing the network pharmacology predictions to first be tested in a computational manner prior to docking or wet-laboratory screening [10,11]. A feasible way to achieve batch-to-batch consistency in herbal nano-formulations by digital twin and closed-loop optimisation frameworks has been suggested, which can overcome the compositional variability that has been a major hurdle in the standardisation of plant-based products for centuries 18. Before preclinical testing, a safety filter – the multimodal toxicity prediction – could be an added complementary tool to catch carrier-phytochemical incompatibilities that neither the carrier nor the phytochemical would do in isolation [23].

Limitations

This review does have a number of limitations associated with it due to its conceptual nature as opposed to a computational study. All results of the performed technical calculations were extracted from the literature cited and were not re-calculated or re-checked by the authors of this paper: none of the models, QSAR calculations or docking simulations were performed independently. Publication bias for positive findings is not ruled out if there is no systematic search protocol and/or if there is no risk of bias scoring. Some claims are on secondary synthesis as several sources included are reviews and book chapters. The *Rasa Panchaka* correlation is an idea and is not yet tested and should not be interpreted to be an equivalence, a formal test would require computational skills and classical knowledge in the form of structured datasets, which are not available here. AI applications in herbal research are also under-represented when compared to synthetic-drug research and there is little to no evidence of clinical-stage validation of AI-optimised herbal nano-formulations published to-date, as of the time of this review.

Future Scope

Prioritising construction of curated, standardised phytochemical and nano-carrier datasets specific to herbal and herbomineral formulations, similar to the existing synthetic compounds, in order to address the generalisation gap identified over this study. Studies comparing AI-optimised herbal nano-formulations with conventionally known counter-parts through clinical phyto-kinetic endpoints, would meaningfully address the evidence base. Regulatory frameworks for AI-assisted herbal nano-medicines also requires thorough development as current pharmacovigilance and permission pathways were neither designed for nanocarrier based products nor AI-driven formulation validations.

CONCLUSION

Artificial Intelligence is shifting phytopharmaceutical delivery designing towards predictive, more data driven bioactive screening based, nanocarrier optimisation, release pathways simulation and toxicity assessment. The gains were engaging at every stage but a clear translational ceiling persists. Herbal-specific data is scarce, and clinical stage validation is largely absent in published databases.

Classical *Ayurvedic* reasoning of multiparametric logic of *Rasa-panchaka* offers a conceptual compatible framework which assists feature selection in AI-models for herb focused data sourcing. It still remains an untested hypothesis as of now. Progress from here on largely depends on the curated phytochemical datasets, herb specific model validation and regulatory measures taken for AI-driven, nano carrier based phytopharmaceutical products.

AUTHOR CONTRIBUTION AND SCOPE STATEMENT

The article was conceived, researched and written with an *Ayurvedic* and Integrative Pharmacology point of view. It is a conceptual literature rather than a computational study, no machine learning models, QSAR analysis, molecular docking expression or statistical re-analysis was performed by the authors. All AI-related technical findings reported here were drawn from and attributed to the cited publication literature. The classical Correlation described in the Discussion section is an interpretive contribution intended to stimulate future interdisciplinary research. Readers with computational expertise are encouraged to pursue further formal validation of the hypothesis raised...

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