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PHYTOCHEMICAL AND PHARMACOKINETIC EVALUATION OF AYURVEDIC FORMULATIONS USING MODERN DRUG DELIVERY TECHNOLOGIES

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ABSTRACT
Ayurvedic formulations have gained increasing global recognition due to their therapeutic potential and holistic approach to disease management. These formulations contain diverse phytoconstituents, including polyphenols, flavonoids, alkaloids, terpenoids, and glycosides, which contribute to a broad spectrum of pharmacological activities. However, the clinical application of many Ayurvedic bioactives is often limited by poor aqueous solubility, low bioavailability, extensive first-pass metabolism, rapid elimination, and pharmacokinetic variability. Recent advancements in pharmaceutical sciences have led to the development of innovative drug delivery technologies aimed at overcoming these limitations and enhancing therapeutic performance. This review critically examines the phytochemical composition and pharmacokinetic behavior of major Ayurvedic formulations and explores the role of modern drug delivery systems in improving their efficacy. Various delivery platforms, including nanoparticles, nanoemulsions, liposomes, phytosomes, hydrogels, and controlled-release systems, have demonstrated significant potential in enhancing solubility, stability, absorption, targeted delivery, and sustained drug release. Representative case studies involving curcumin, Ashwagandha, Brahmi, and other Ayurvedic formulations highlight the successful integration of traditional medicine with advanced pharmaceutical technologies. Furthermore, challenges associated with standardization, regulatory acceptance, safety assessment, and clinical translation are discussed. The integration of modern drug delivery strategies with Ayurvedic therapeutics offers a promising pathway toward the development of scientifically validated, pharmacokinetically optimized, and globally acceptable phytopharmaceutical products.

KEYWORDS: Ayurveda, Phytochemicals, Pharmacokinetics, Drug Delivery Systems, Phytopharmaceuticals

1. INTRODUCTION
One of the oldest systems of medicine in the world, Ayurveda has been used for over 5,000 years and forms a critical part of the healthcare systems, especially those of South Asia. The principles of health, disease prevention, and person-specific treatment form the foundation of Ayurveda, which uses a wide variety of plant and mineral based, and poly-herbal formulations, to restore balance in the physiology and ensure well-being [1]. In the last few decades, with the popularity and growing interest in natural treatments and the growing awareness of the harmful effects of synthetic drugs, the world is once again turning to Ayurvedic medicines and other traditional health care systems [2]. Moreover, the synergic approach of Ayurveda to modern medicine has been seen as a potential approach to improve the patients' care, especially in the management of chronic and lifestyle-related diseases [3]. Even with this acceptance, scientific proof of the effectiveness of the Ayurvedic prescriptions is still a mandatory condition for wider acceptance in the mainstream healthcare system.
Therapeutic potential of ayurvedic formulations is mainly due to its high phytochemical constituents. The polyphenols, flavonoids, alkaloids, terpenoids, tannins, glycosides and other secondary metabolites present in these formulations are responsible for their pharmacological activities. In contrast to conventional single molecule drugs, Ayurvedic medicine may have synergistic effect of the multiple phytoconstituents that act as multiple targets. These phytochemical matrices are complex, and thus provide opportunities and challenges to understanding their biological effects as well as product quality. Incorporation of phytochemical characterization techniques has helped the identification of marker compounds and chemical fingerprints in Ayurvedic formulations, thereby enhancing the quality assurance, standardization and reproduction aspects of the formulations [4]. However, the phytochemical makeup and therapeutic effects still vary as a result of plant source, growing conditions, processing techniques and formulation practices.

However, many of the bioactive compounds found in Ayurvedic medicines have poor pharmacokinetic properties, which hinder their therapeutic use. Oral bioavailability is often low due to poor aqueous solubility, low permeability across membranes, chemical instability, rapid elimination, and variable GIT absorption. These limitations make it difficult to get optimal therapeutic levels at target sites and help to explain the variable clinical response. Further, phytochemicals can interact with drug metabolizing enzymes, transport proteins and co-administered drugs, which could affect the pharmacokinetic and pharmacodynamic profiles [5]. Advanced analytical and pharmacokinetic evaluation strategies are needed to assess the absorption, distribution, metabolism and excretion (ADME) processes inherent in polyherbal formulations.

The challenges have been overcome by development of modern drug delivery technologies which have proven useful for improving the therapeutic performance of herbal and Ayurvedic medicines. Innovative delivery systems have been developed with the aid of recent advances in pharmaceutical science such as nanoparticles, liposomes, phytosomes, nanoemulsions, Solid Lipid Nanoparticles, Polymeric carriers, Hydrogels and targeted delivery systems. Such technologies have several benefits including better solubility, higher bioavailability, better stability of phytoconstituents, controlled drug release and targeting to a specific site [6]. The advanced drug delivery systems can help bridge the gap between traditional ayurvedic knowledge and modern pharmaceutical innovation by optimizing the pharmacokinetic behavior and enhancing the therapeutic efficacy. Therefore, phytochemical characterization coupled with the pharmacokinetic studies and modern drug delivery systems is a key approach towards evolving clinically effective and scientifically validated and accepted AYURVEDIC therapeutics in the global scenario.

OBJECTIVES OF THE REVIEW

1. To evaluate the phytochemical profiles and pharmacokinetic properties of key Ayurvedic formulations and their bioactive constituents
2. To assess the effectiveness of modern drug delivery technologies in improving the bioavailability, stability, and therapeutic performance of Ayurvedic phytoconstituents
3. To highlight current challenges and future opportunities for the development and clinical translation of advanced Ayurvedic drug delivery systems

2. Phytochemical Composition and Therapeutic Significance of Ayurvedic Formulations

Ayurvedic medicinal herbs contain many bioactive phytochemical constituents, such as polyphenols, flavonoids, alkaloids, terpenoids, glycosides, tannins, saponins and essential oils. Many biological functions, such as antioxidant, anti-inflammatory, immunomodulatory, antimicrobial, neuroprotective, anticancer activities, etc., are exhibited by phytochemicals, and these functions are considered important for the production of complete medicines using the Ayurvedic approach [7]. In particular, polyherbal formulations comprise of numerous plant-derived active chemicals that act via distinct pathways, providing a synergetic effect and enabling us to treat complex and multifactorial ailments. Phytochemical investigations have made great advances in the identification and quantitative estimation of major phytochemical compounds present in Ayurvedic preparations, thus assisting in providing scientific validation of these preparations and their incorporation into contemporary medicine practices [8].

Standardization of Ayurvedic preparations can be achieved through the identification of reliable phytochemical markers. Several methods, including HPTLC, HPLC, UPLC and mass spectroscopy, are gaining increasing acceptance in estimating marker compounds and developing fingerprints of herbal drugs for quality control. For example, simultaneous estimation of multiple bioactive markers has proven successful in the case of Ayurvedic polyherbal formulations; batch-to-batch variations have thereby been minimized and therapeutic efficiency guaranteed [9]. This is crucial in overcoming issues related to variations among sources, cultivation practices, harvesting techniques and preparation procedures.

One important feature of Ayurvedic herbal medicines is the presence of multiple synergistically interacting phytochemicals, which produce enhanced effects compared to a single constituent (see Figure 1). These synergetic interactions affect processes involved in oxidation, inflammation and immunity and confer a multi-target approach to Ayurvedic therapeutics [10]. However, a problem that arises in relation to phytochemical matrices is their solubility, stability, absorption and bioavailability. As a result, there is increased interest in the use of advanced drug delivery systems that will enhance their pharmacokinetics and therapeutic effectiveness without affecting their synergies [11,12].

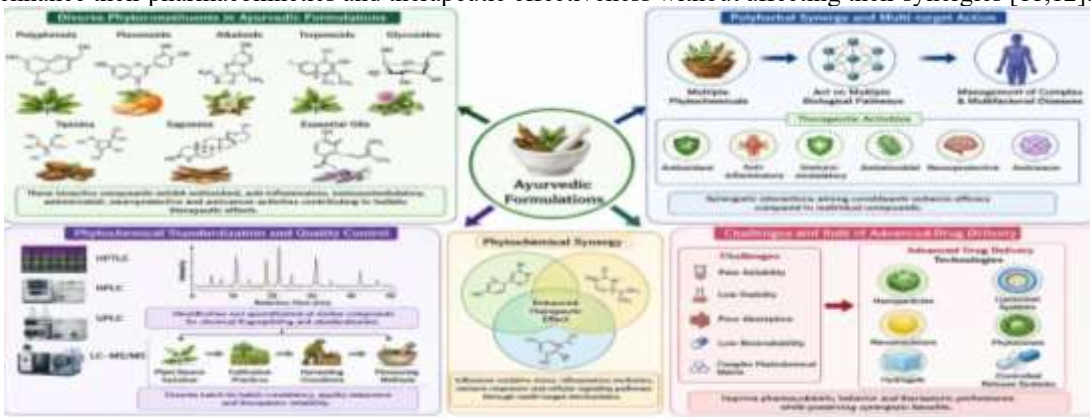

Figure 1. Phytochemical Composition, Therapeutic Significance, and Advanced Drug Delivery Strategies for Ayurvedic Formulations

This figure illustrates the major phytoconstituents present in Ayurvedic formulations, their synergistic multi-target therapeutic activities, methods for phytochemical standardization, and key pharmacokinetic challenges. It also highlights the role of advanced drug delivery technologies in enhancing bioavailability, stability, and therapeutic efficacy of herbal bioactives.

3. Pharmacokinetic Behavior of Ayurvedic Phytoconstituents

3.1 Absorption and Bioavailability Constraints

The efficacy of Ayurvedic herbal preparations depends significantly on the absorption as well as bioavailability of the active compounds. There is also the problem of poor water solubility, decreased permeability of the intestine membrane, and instability of some plant-based compounds in the gastrointestinal tract, making the absorption of such substances difficult. The interaction between the various components in the herbal mixture may also lead to a complicated mechanism of absorption. Consequently, there is often an insufficient quantity of active phytoconstituents that reaches its desired therapeutic level. Research has found that the mode of absorption may alter under diseased conditions, underscoring the importance of learning how to improve bioavailability of Ayurvedic preparations [13].

3.2 Distribution and Tissue Targeting Characteristics

Phytoconstituents are absorbed and then distributed around the body dependent upon their physicochemical properties such as molecular size, lipophilicity and plasma protein binding. It is important to ensure effective distribution of the drug to the target tissue, if the therapeutic concentration is to be reached. But several of the herbal bioactives have low tissue penetration and minimal cellular uptake making them less effective for pharmacological activity. In recent years, advances in targeted delivery technologies have been emphasizing the potential applications of carrier-mediated systems for tissue-specific localization and intracellular transport of bioactive molecules. New delivery vehicles such as vesicles and exosomes have been demonstrated to improve delivery biodistribution and therapeutic benefits [14].

3.3 Metabolism and Biotransformation Pathways

Phytoconstituents are found to be of biological activity and safety depending on their metabolism. Metabolism of most herbals includes a number of phase I and phase II metabolic reactions, mediated by cytochrome P450 enzymes, transferases and other metabolic systems. These bio-transformation reactions can be responsible for the formation of active metabolites, detoxification or decrease in pharmacological activity. Phytochemicals and their metabolites are difficult to anticipate there in vivo effects due to their complexity of metabolic pathways. Thus, knowledge of the enzymatic steps in xenobiotic metabolism is crucial to assess the therapeutic activity and safety profile of the formulations used in Ayurvedic medicine [15].

3.4 Excretion and Pharmacokinetic Variability

Phytoconstituents and metabolites are mainly eliminated via renal and biliary excretions. The rate of excretion directly affects the residence time of the drug in the system, systemic exposure, and therapeutic efficacy. There are significant inter-individual differences in the pharmacokinetics, including age, genetic differences, physiological condition, disease state and environmental factors. This variability can lead to different responses, effectiveness, and safety effects to a drug, making it difficult to standardize doses for herbal medicines [16]. All these problems highlight the need for thorough pharmacokinetic investigations of ayurvedic formulations to guarantee consistent therapeutic efficacy.

3.5 Herb–Drug Interaction Considerations

Increased use of Ayurvedic medicines along with conventional medicines has raised concerns about potential herb–drug interactions. The activity of drugs metabolism enzymes, transport proteins and receptor systems may be affected by phytochemicals, which can in turn affect the absorption, metabolism, distribution or elimination of co-administered drugs. These interactions can result in a decreased therapeutic effect, increased toxicity or unexpected side effects. Herbal constituents that affect the activity of cytochrome P450 and transporter proteins have become a major clinical issue [17]. Moreover, some interactions between herb and drugs have been linked to hepatotoxicity and metabolic disorders, making it crucial to carefully evaluate the safety and monitor patients during the use of them [18]. Hence, a comprehensive knowledge about the mechanism of herb–drug interaction is a necessity to ensure safe and effective use of Ayurvedic formulations in modern drug therapy (Table 1).

Table 1. Key Pharmacokinetic Considerations of Ayurvedic Phytoconstituents

Pharmacokinetic Aspect	Major Limitation	Clinical Implication	Key Reference
Absorption	Poor solubility and intestinal permeability	Reduced oral bioavailability	[13]
Distribution	Limited tissue penetration and cellular uptake	Lower target-site drug concentration	[14]
Metabolism	Extensive CYP450-mediated biotransformation	Altered efficacy and metabolite formation	[15]
Excretion	Rapid renal and biliary elimination	Shortened therapeutic duration	[16]
Pharmacokinetic Variability	Genetic, physiological, and disease-related differences	Variable drug response among patients	[16]

Herb–Drug Interactions	Modulation of metabolic enzymes and transporters	Reduced efficacy or increased toxicity	[17,18]

4. Modern Drug Delivery Technologies for Ayurvedic Formulations

4.1 Nanoparticle-Based Delivery Systems

Nanoparticle based delivery systems are emerging which are able to improve the therapeutic activity of Ayurvedic phytoconstituents. This is because of their nanoscale size that enhances solubility, stability, cellular uptake and bioavailability of poorly absorbed herbal compounds. Nanoparticles also prevent early degradation of the phytochemicals, and help release the drugs in a controlled manner, improving therapeutic efficacy and minimizing dose-dependent toxicity. In recent years, research in the field of nanotechnology has shown potential in the use of polymeric, metallic and lipid nanoparticles to carry bioactive molecules for targeted delivery and to enhance their pharmacokinetic characteristics [19]. Nanoparticle based systems in ayurvedic formulations provide attractive options for the development of scientifically optimized therapeutic products from traditional ayurvedic formulations [20].

4.2 Lipid-Based Carriers and Nanoemulsions

Solid lipid nanoparticles, nanostructured lipid carriers and nanoemulsions are pharmaceutical delivery systems of lipids which have been widely studied for enhancing the delivery of lipophilic phytoconstituents. These systems promote the dissolution, intestinal absorption and systemic bioavailability of the drugs by enabling the transport of the drug molecules across the biological membranes. In particular, nanoemulsions increase the surface area and dispersion of poorly water-soluble compounds which leads to better therapeutic effects. Such platforms are getting more and more attention for the delivery of Ayurvedic phytochemicals that have a low bioavailability when taken orally [20].

4.3 Vesicular Systems: Liposomes, Niosomes, and Phytosomes

Vesicular delivery systems can be used for the encapsulation and delivery of phytochemicals. The use of liposomes and niosomes increases the stability of the drugs and penetration of tissues, while phytosomes increase the complexation of plant constituents with phospholipids, increasing drug absorption and bioavailability. Such systems are especially useful for these sensitive herbal compounds (20) and can be used to deliver these to specific tissues.

4.4 Polymeric and Hydrogel-Based Systems

The use of polymeric carriers and hydrogel-based systems can ensure controlled and sustained release of phytoconstituents which can maintain the therapeutic concentration for long periods. In addition to the above-mentioned properties, hydrogels are highly biocompatible, have a high water retention capacity, and can be optimized for various release profiles, making them promising candidates for various drug delivery applications, such as the oral, transdermal, and localized delivery of drugs. They have also been developed to be used in responsive and site-specific drug delivery systems recently [21].

4.5 Controlled and Targeted Drug Delivery Platforms

Controlled and targeted drug delivery technologies aim at achieving optimized therapeutic effects by targeting drug delivery to specific tissues with minimum systemic exposure (Table 2). The platforms offer extended or targeted drug delivery, minimize toxicity and improve the efficiency of drug treatment using sustained or site-specific release. Advanced targeting strategies and the incorporation of ayurvedic formulations is a step towards precision phytopharmaceutical development and better clinical translation of traditional medicines [20].

Table 2. Modern Drug Delivery Technologies for Ayurvedic Phytoconstituents

Delivery System	Key Features	Pharmacokinetic Advantages	Representative Reference
Nanoparticles	Polymeric, lipid, or metallic nanocarriers	Improved solubility, stability, bioavailability, and targeted delivery	[19,20]
Lipid-Based Carriers	Solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs)	Enhanced dissolution, intestinal absorption, and systemic exposure	[20]
Nanoemulsions	Nanosized oil–water dispersions	Increased surface area and improved bioavailability of lipophilic phytochemicals	19,20]
Liposomes	Phospholipid vesicles	Enhanced stability, tissue penetration, and controlled release	[20]
Niosomes/Phytosomes	Non-ionic surfactant vesicles and phospholipid complexes	Improved absorption and protection of phytoconstituents	[20]
Polymeric Systems	Biodegradable polymer-based carriers	Sustained drug release and prolonged therapeutic effect	21]
Hydrogels	Three-dimensional hydrophilic networks	Controlled, localized, and responsive drug delivery	[20,21]

Targeted Delivery Platforms	Ligand-mediated and site-specific systems	Reduced off-target effects and enhanced therapeutic efficacy	[20,21]

5. Pharmacokinetic Enhancement through Advanced Delivery Systems

Advanced drug delivery systems have been able to overcome the limitations of the poor solubility, low permeability, large first pass metabolism, and fast elimination of phytoconstituents found in Ayurvedic formulations (Figure 2), thereby enhancing the pharmacokinetic performance of the formulations. Numerous natural chemical compounds, called bioactives, found in herbals have poor water solubility, leading to poor bioavailability and therapeutic efficacy. Modern delivery systems such as nanoparticles, lipid-based delivery systems, and nanoemulsions increase the solubility and dissolution rate, thus increasing systemic bioavailability [22]. Moreover, these systems provide better permeability and cellular uptake, improving and leading to better drug absorption and distribution [23]. Protection from chemical degradation and metabolic inactivation in gastrointestinal transit is also a benefit of encapsulation technologies for phytochemicals, decreasing first-pass metabolic losses [24]. Furthermore, targeted and controlled-release systems allow for site-specific drug delivery and sustained drug action, which enhances the treatment efficacy and reduces the side effects [25].

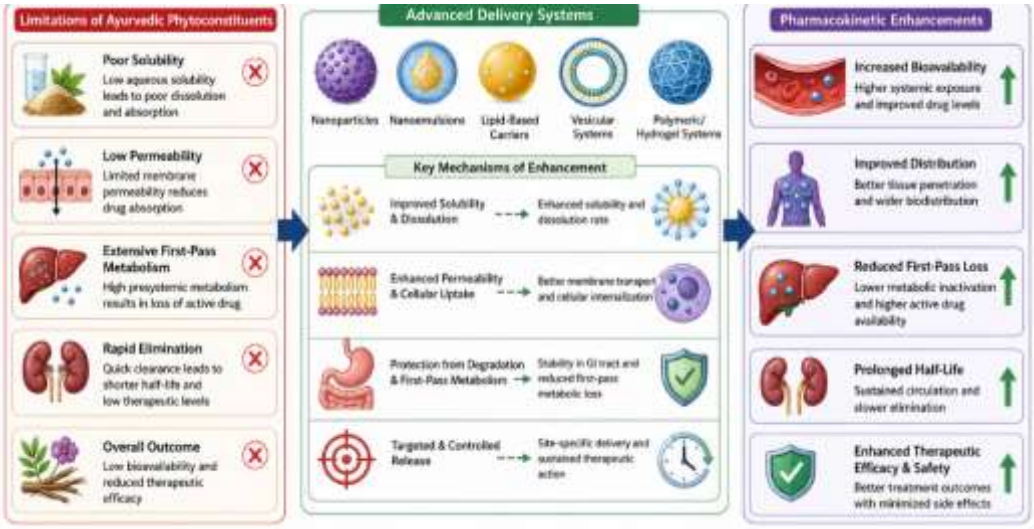

Figure 2. Pharmacokinetic Enhancement of Ayurvedic Phytoconstituents through Advanced Drug Delivery Systems

This figure illustrates how advanced drug delivery systems, including nanoparticles, nanoemulsions, vesicular carriers, and hydrogels, overcome pharmacokinetic limitations of Ayurvedic phytoconstituents by enhancing solubility, permeability, stability, and targeted delivery, resulting in improved bioavailability, prolonged circulation, and therapeutic efficacy.

6. Case Studies of Engineered Ayurvedic Formulations

The recent advancements in the field of pharmaceutical technologies can help develop a more engineered form of an Ayurvedic formulation that is highly efficacious in terms of both pharmacokinetics and therapeutics. As this compound possesses poor solubility and bioavailability, the various delivery system methods that have been developed for curcumin include nanoparticles, nanoemulsions, and co-delivery systems, which have been shown to increase stability, absorbability, and therapeutic effects [26]. Additionally, there have been advances in Ashwagandha formulations involving nanotechnology such as the electrospun nanofibers and nano-encapsulation technology that have aided in enhancing the delivery and bioactivity of withanolides while preserving their pharmacological properties [27]. Moreover, formulations including polyherbals such as Triphala formulations have been developed by delivering them in an advanced system, resulting in an increased stability and pharmacokinetics of the formulation [28]. Furthermore, the Brahmi formulations have shown high prospects for application in neuroprotective cases, especially in Alzheimer's disease owing to enhanced bioavailability and targeted delivery of bacosides [29].

7. Challenges in Translation, Standardization, and Regulatory Acceptance

In spite of the rapid advance in the use of the innovative drug delivery technologies in the development of Ayurvedic formulations, several issues should be solved in order to assure the successful introduction of these drugs into the routine clinical practice and gain global recognition. One of the biggest problems to be addressed includes quality control and phytochemical standardization. In particular, since the chemical composition of natural components may differ depending on numerous factors such as geographical location, cultivation techniques, harvesting conditions, plant processing and storage conditions, the efficacy and safety of ayurvedic therapy cannot be guaranteed unless strict quality parameters are established.

In addition to these issues, scale-up and manufacturing can pose a major challenge when introducing Ayurvedic therapies into practical application. While the majority of proposed carrier formulations and delivery strategies have been proven effective in laboratory settings, it is necessary to consider the issues such as the optimization of production processes,

batch-to-batch reproducibility, cost-effective approaches, appropriate equipment characteristics and long-term storage in the context of industrial production. In addition, it is essential to preserve the physicochemical properties of carriers during scale-up in order to maintain their beneficial effects.

It is important to conduct a thorough safety and toxicological evaluation of herbal therapies due to the application of new carrier systems and technologies. It has been mentioned before that herbs used in Ayurveda are considered safe and effective; however, nanotechnologies may change the distribution and uptake characteristics of these herbs and thus induce potential adverse effects. Therefore, in-depth toxicological evaluations are required in order to ensure safety and minimize risks for patients.

The problem with regulatory acceptance is another serious issue to be considered. In many countries, different criteria are applied when regulating traditional medicinal products and nano pharmaceuticals. Such difference in requirements results in problems related to product registration, quality assurance, and market approval. In addition, there are currently no standardized guidelines for evaluating and assessing the quality of herbal nanoformulations which makes the worldwide commercialization of these products rather difficult. Clinical trial results are rather limited as well as pharmacokinetics data which complicates the process even more.

8. Future Perspectives and Conclusions

The future of Ayurvedic drug delivery is seen in the integration of the knowledge gained through traditional medicine with evolving technology in the pharmaceutical industry and even with new technologies associated with artificial intelligence (AI). AI can contribute to faster development of more effective herbal formulations by predicting their behavior, interaction of the drug with the excipients and its therapeutic efficacy. Another approach for creating innovative formulations lies in the development of individually customized treatment strategies based on genetic, physiological and metabolic peculiarities of the patients.

This kind of individualized therapy may not only increase efficiency but decrease variability in treatment. In addition, integration of pharmacokinetic modelling, systems pharmacology, metabolomics, genomics and other omics technologies may give more information on how phytoconstituents are absorbed, distributed, metabolized and eliminated from the body, thus enabling evidence-based optimization of Ayurvedic formulations. While many achievements have already been attained, at present there is a range of challenges that should be solved, among which are validation, safety, regulatory and manufacturing issues. Further studies may be done in order to obtain more pharmacokinetic and clinical data to ensure formulation optimization and create quality systems for herbal delivery systems.

Overall, integration of innovative drug delivery systems with traditional medicine such as Ayurveda opens promising ways for creation of innovative formulations that can be scientifically validated, approved and used worldwide.

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