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Comprehensive Review on Herbal Drugs as Novel Drug Delivery Systems

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Abstract: *Traditional medicine has always used herbal medicines since they contain a multitude of bioactive phytoconstituents with proven therapeutic benefits. The lack of specific activity, low bioavailability, low water-solubility, and chemical instability have complicated the introduction of them into modern pharmacotherapy. Several innovative drug delivery systems, such as nanoparticle, liposomes, phytosomes, niosomes, nanoemulsions, etc., have turned out to be coach potatoes in destroying these limitations. These delivery methods enhance stability, bioavailability and localization of herbal drugs besides reducing toxicity and enhancing compliance among patients. The review provides a detailed analysis of various herbal NDDS formula, commercial products, current challenges and even future trends.*

Keywords: Herbal medicine, Novel Drug Delivery Systems (NDDS), Phytosomes, Liposomes, Nanoparticles, Niosomes, Bioavailability, Targeted delivery, Phytoconstituents, Green nanotechnology, Cosmeceuticals, Standardization, Personalized medicine

I. INTRODUCTION

Traditional healthcare systems have relied on medicinal plants since pre-historic times and provide a great pool of bioactive phytoconstituents with established therapeutic effects. However, despite thousands of years of use and their safety profiles, most pharmacokinetic and physicochemical issues--primarily, low aqueous solubility, poor bioavailability, rapid disappearance, and inability to reach a site of action--explain the radical limitation in potential of the therapeutic uses of herbal medicines in modern medicine. Such issues are likely to produce poor treatment effects, a great deal of patient responder inconsistency, and high or frequent dosage requirement. The emergence of the Novel Drug Delivery Systems (NDDS) has become a revolution in the way the herbal medicines are formulated and made available. NDDS also utilize the use of high-tech carriers and delivery mechanisms that include nanoparticles, liposomes, phytosomes, nanoemulsions, microspheres, ethosomes, niosomes that are tailored to overcome weaknesses of traditional herbal preparations. These systems allow the targeted, controlled and extended delivery over the biological membrane, enhanced permeation into the biological membrane and stabilization of the phytoconstituents which are susceptible to degradation subsequent gastrointestinal passage and throughout the biological system. Moreover, NDDS also help with patient compliance by reducing dose rates and side effects, especially with long term care like chronic diseases. The capacity of such systems to trap both hydrophilic and lipophilic herbal constituents allows greater flexibility in the creation of the dosage forms that would be suitable to the therapeutic needs. With the increase in the demand of safer, more efficient, and scientifically proven phytomedicine, there is an increasing trend of using herbal drugs in modern drug delivery mechanism in the pharmaceutical, nutraceutical and cosmetical sectors. This review examines developments, types, commercial products, issues, and directions of herbal NDDS in an integrated manner paying close attention to its ability to bridge the gap between traditional herbal and modern pharmaceutical science. Herbal Medicines and NDDS need.

II. HERBAL MEDICINES AND THE REQUIREMENT OF NDDS

Biologically active phytoconstituents (including alkaloids, flavonoids, glycosides, and terpenoids) as sources of herbal drugs are produced as reactions products out of plant material. The drugs have enormous therapeutic potential but are normally spoiled by limited solubility in aqueous solutions, low bioavailability, chemical instability in the

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gastrointestinal tract, and non specific effects. NDDS promotes the activity of herbal drugs, improving the solubility and stability, reduces toxicity, and maintains ability of drugs

Examples:

• Curcumin (turmeric): Improved anti-inflammatory activity via liposomal or nano-based formulation.
• Silybin (milk thistle): Improved hepatoprotective activity via phytosomes (e.g., Siliphos®).
• Quercetin (apple, onion): Improved antioxidant activity via SLNs.

III. FORMULATIONS OF HERBAL NOVEL DRUG DELIVERY SYSTEMS

3.1. Nanoparticles

Nanoparticles (NPs) are colloidal carriers with a diameter of 10-200 nm, which are preferably prepared with biodegradable polymers such as PLGA, chitosan, and PCL. The systems entrap the herbal actives, prevent degradation and provide control and site-specific release of the drugs. Recent Case n Berberine-PLGA nanoparticle in diabetes and inflammation.

Example: Berberine-loaded PLGA nanoparticles for diabetes and inflammation.

3.2. Liposomes

Liposomes are vesicles of phospholipid bilayer that entrapment of the hydrophilic and lipophilic drugs. They are biocompatible and providing increased circulation time and higher cellular uptake.

Modern Example: Liposomal curcumin (Lipocurc®): Applied in cancer therapy and chronic inflammation.

3.3. Phytosomes

Phytosomes are phospholipid phytosomatic ionic complexes containing actives of plants, which enhances gastrointestinal absorption and bioavailability. The lipid-phyto complex prevents enzymatic breakdown of the phytoconstituents.

Modern Example: Siliphos® (silybin + phosphatidylcholine): Marketed commercially as liver detox and hepatoprotection.

3.4. Niosomes

Niosomes- ionic surfactant vesicles similar to liposomes are chemically stable, more cost effective. They are used as a guarantee of long-term drug delivery and safe preservation of unstable herbal molecules

Recent Examples: Niosomes incorporated with glycyrrhizin for anti-inflammatory activity in oral or local administration.

IV. COMMERCIALLY AVAILABLE HERBAL NOVEL DRUG DELIVERY FORMULATIONS

The application of novel drug delivery systems (NDDS) to herbal medicine has attracted particular attention in the last few years, taking into account the fact that they have the potential to solve problems associated with low solubility, bioavailability, and stability of herbal actives. Indena and Cosmetochem are among the main industry players with commercially developed advanced delivery technologies for herbal bioactives.

Cosmetochem, a Swiss company, has developed and marketed Herbasec® technology, a series of liposomal products that include encapsulated herbal extracts whose therapeutic and cosmetic activities are well-documented. Liposomes are phospholipid bilayered vesicles capable of loading hydrophilic as well as lipophilic molecules, thereby delivering better penetration and stability to plant-derived molecules. Herbasec® line includes standardized extracts of White and Green Tea (Camellia sinensis), White Hibiscus (Hibiscus sabdariffa), Guarana (Paulliniacupana), and Aloe vera, which are primarily applied in dermal formulations for antioxidant, anti-aging, and protective activities on the skin. These formulations are increasingly being adopted in the cosmeceuticals due to improved permeation through the skin and extended activity.

In contrast, Indena, an Italian phytopharmaceutical company, has pioneered phytosome technology®—a patented delivery system that enhances the bioavailability and absorption of standardized plant extracts by forming lipid-

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compatible molecular complexes. Phytosomes are phospholipids (e.g., phosphatidylcholine) complexed with polyphenolic compounds, which are absorbed in the gastrointestinal tract and made available systemically.

Indena has launched several phytosome-based products to the global nutraceutical and pharmaceutical markets. Some of them are:

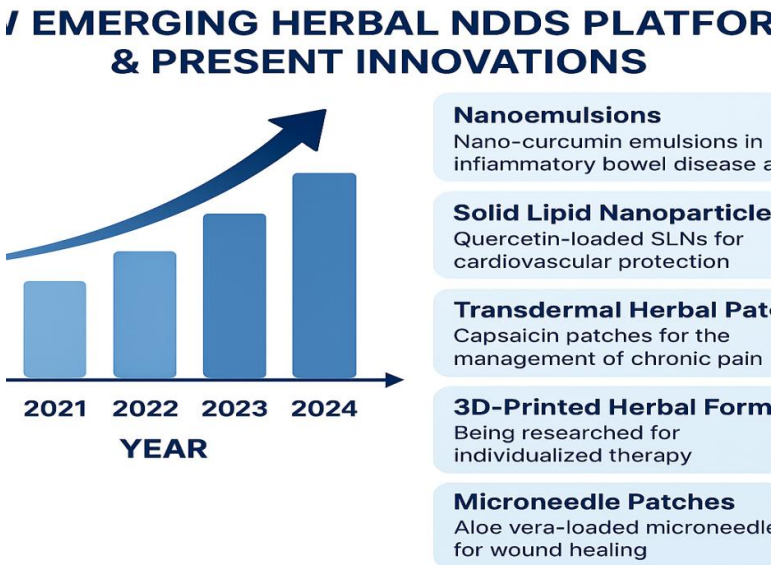
- Silybum marianum (Milk Thistle): Silymarin and silybin phytosomes with hepatoprotective activity.
- Ginkgo biloba: Ginkgoflavonglucosides, ginkgolides, and bilobalide phytosomes applied to cognitive function and peripheral vascular disorders.
- Centella asiatica: Triterpenes-enriched phytosomes applied to wound healing and microcirculatory effects.
- Glycyrrhiza glabra (Liquorice): Standardized 18ß-glycyrrhetinic acid with anti-inflammatory and skin-soothing activity.
- Ammi visnaga: Contains visnadin, a vasodilator used in angina and vascular diseases.
- Crataegus monogyna (Hawthorn): Rich in vitexin-2"-O-rhamnoside with cardiotonic and antioxidant activity.
- Aesculus hippocastanum (Horse Chestnut): Yielding escin and β-sitosterol, both of which are useful in chronic venous insufficiency.
- Terminalia sericea: Sericoside standardized with wound-healing and anti-inflammatory properties.
- Panax ginseng: Resinous ginsenosides with adaptogenic and immunomodulatory effects.
- Vitis vinifera (Grape Seed) and Camellia sinensis (Green Tea): Polyphenol-based preparations with potent antioxidant protection.

These phytosome preparations not only demonstrate improved pharmacokinetics but also improved therapeutic activity in preclinical and clinical studies. The market success of these products is an indicator of the vast scope of NDDS in herbal medicine and can be a benchmark for future pharmaceutical ventures into herbal pharmaceutics.[5]

V. NEW EMERGING HERBAL NDDS PLATFORMS & PRESENT INNOVATIONS

This part accounts for advanced delivery systems with examples:

- Nanoemulsions: Nano-curcumin emulsions in inflammatory bowel disease and cancer.
- Solid Lipid Nanoparticles (SLNs): Quercetin-loaded SLNs for cardiovascular protection.
- Transdermal Herbal Patches: Capsaicin patches for the management of chronic pain.
- 3D-Printed Herbal Formulations: Being researched for individualized therapy.
- Microneedle Patches: Aloe vera-loaded microneedles for wound healing.



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VI. COMMERCIALLY AVAILABLE PRODUCTS BASED ON HERBAL NDDS

Herbal Drug	Delivery Form	Commercial Product	Usage
Silymarin	Phytosome	Siliphos®	Hepatoprotection
Curcumin	Phytosome	Lipocurc®	Anti-inflammatory
Quercetin	SLN	Quercetol SLN	Antioxidant
Boswellia	Phytosome	Casperome®	Anti-inflammatory
Ashwagandha	Nanoemulsion	AshwaBoost™	Adaptogenic tonic
Resveratrol	Liposome	ResVantage®	Anti-aging

VII. CHALLENGES AND FUTURE DIRECTIONS

Though they are promising, herbal NDDS are ridden with challenges of high production cost, lack of regulatory guidelines, and lack of standardization, with limited clinic validation. Future efforts have to focus on AI-based design, personalized medicine, and global regulatory guidelines to deliver standardized and effective herbal therapeutics.
Challenges and Future Directions in Herbal Novel Drug Delivery Systems (NDDS)
with Reference to Modern Drug Delivery Examples

Challenges:

1. Standardization and Quality Control:

Unlike such strictly synthetic drugs as Paracetamol or Atorvastatin, which are chemically homogeneous and can be easily assayed, herbal extracts contain mixtures of many compounds, which vary with the growth conditions, date of harvest, and extraction procedures. With this inconsistency, it is impossible to achieve a batch-to-batch consistency of herbal NDDS, the key to regulatory approval.

2. Inadequate Solubility and Bioavailability:

Most herbal bioactives (e. g., curcumin, silymarin, quercetin) do not dissolve in water, unlike standard drugs Paclitaxel and Cyclosporine, which are also undermined by poor oral bioavailability. In traditional products, this choice included nanoparticles (for ex. Abraxane), cyclodextrin inclusion complex (e.g. Sporanox), to enhance delivery -herbal NDDS are now following suit with liposomes, solid lipid nanoparticles (SLNs) and phytosomes.

3. Limited Clinical Data

Synthetic DNDs such as liposomal doxorubicin (Doxil 8) or PEGylated interferons appeal and have a proven, rigorously clinical effectiveness with solid clinical evidence and approval of the drug by the FDA, whereas most plant-based NDDS are only supported by preclinical or pilot clinical evidence. Absence of rigorous randomized controlled clinical trials makes herbals less acceptable in clinical practice.

4. Complexity in regulation

The new drug delivery systems of this modern world are regulated, and they are organized by regulatory testing (e.g., ICH, FDA, EMA guidelines), and herbal NDDS are placed in transitional boundaries between cosmetics, dietary supplements and drugs. Another case in point is, although liposomal amphotericin B (AmBisome®) is a highly regulated drug, herbal liposomes in dermatology would be a regulated cosmetic with minimal claims and validity.5. Shelf-Life and Stability

5. Shelf-Life and Stability

Just like the first liposomal versions of insulin, which have proven to be unstable, many of the herbal NDDS particularly liposomes and nano emulsions possess issues of leakage, oxidation and aggregation over time, and need refrigerated storage or sophisticated packaging systems to maintain these inclusions.

6. Cost and Accessibility:

Premium NDDS, i.e. herbal systems will significantly hike up the costs of formulations. PEGylated proteins and lipidic chemotherapeutics are costly compared to generic products as an example. Similarly, formulations of any of the phytoseme or nanoparticle-based herbal compounds may prove expensive when used at large-scale public health levels in resource-deficient communities.

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Future Prospects:

1. Green Nanotechnology

This is driven by plant-based and biodegradable nanocarriers, which she moves with herbal NDDS trend in order to minimize the toxicity and environmental footprint of synthetic nanoparticle drugs such as Abraxane - launched in Canada- (paclitaxel albumin nanoparticle-bound). After a message is verified as appropriate, it gets issued as an official statement or survey.

2. Targeted and Controlled Release Systems:

When a message has undergone proper checking as being correct, it is issued in the form of an official statement or survey. Localized, controlled releases are exhibited by existing drugs such as Actisite and Gliadel wafers (tetracycline-loaded fibers and multiple of renal tumors respectively). Stimuli-responsive polymer systems or smart delivery can also be used to aid the delivery of herbal bioactives (boswellic acid or curcumin, e.g.), to support chronic ailments such as cancer or arthritis.

3. AI and In Silico Formulation Design

There is already AI-assisted optimization of formulations (e.g. in protein folding biologics) in conventional pharmaceutics. Machine learning can also allow Herbal NDDS to forecast phytoconstituent behavior, based carrier systems, and the enhancement of bioavailability.

4. Combination Therapies

Similar to regular fixed-dose combinations (e.g. Metformin + Sitagliptin), future herbal NDDS may be polyherbal nanoformulations or herb-drug hybrid nanoparticles-e.g. curcumin + doxorubicin- as to provide optimal therapeutic synergy.

5. Regulatory Frameworks and Global Harmonization

Harmonized regulatory dossaires of herbal NDDS could be precipitated by international standardisation metrics like ICH M4 requirements of identical technical documentation of pharmaceuticals facilitating marketing and approval of herbal NDDS at inter geographical levels.

6. Evidence-Based Acceptance

Just as biosimilars became acceptable following post-marketing studies and regulatory surveillance, the same should be implemented for herbal NDDS—proving traditional wisdom through multi-centric trials, real-world evidence, and pharmacovigilance systems.

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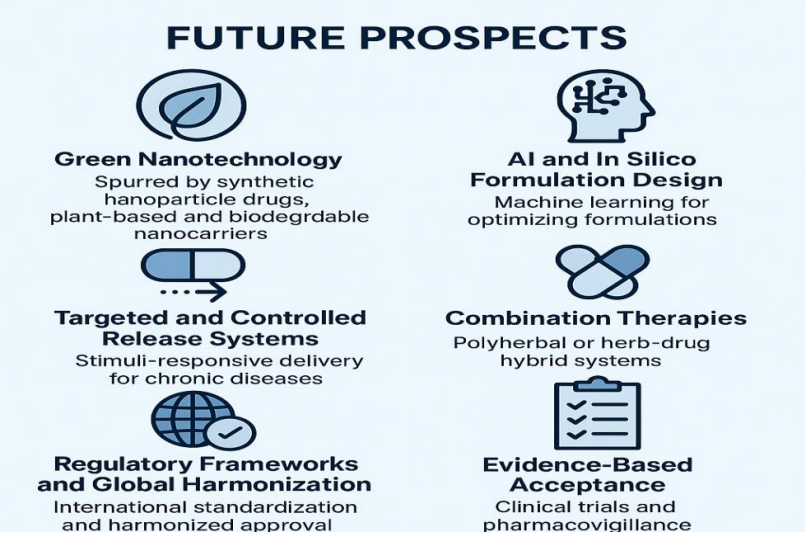

VIII. CONCLUSION

NDDS has changed a face of dimethyl through making herbal medicine more clinically effective and patient acceptable. According to Phan and Tran, nanoparticles, niosomes, phytosomes, and liposomes are the carriers that provide controlled, stable and targeted drug release (243). The research and development should continue to make it possible to use herbal NDDS in traditional medicine commonly. New drug delivery systems (NDDS) integration with herbal drug therapy is an important development to enhance the traditional limitations such as low solubility, stability and bioavailability of plant therapeutics. Such delivery systems as nanoparticles, liposomes, phytosomes, and niosomes have improved the pharmacokinetics and therapeutic action of several herbal suggestions. Although positive progress is being noted, more appropriate research, standardized clinical trials and harmonisation of regulations are required to make herbal NDDS a regular part of evidence-based medicine. The Next-generation develops promises to make traditional herbs fulfill their full clinical potential due to the contemporary science of delivery.

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