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Review Article

Novel Herbal Drug Delivery Systems: An Overview

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ABSTRACT

The novel herbal drug delivery system (NHDDS) is an emerging approach that enhances the therapeutic potential of herbal medicines by improving their bioavailability, stability, and targeted delivery. Conventional herbal formulations often suffer from limitations such as poor solubility, low absorption, and rapid metabolism, leading to reduced therapeutic efficacy. To overcome these challenges, various novel drug delivery systems—including liposomes, niosomes, phytosomes, nanoparticles, microspheres, and ethosomes—have been developed for herbal drugs. These carriers protect bioactive phytoconstituents from degradation, facilitate controlled and sustained release, and enable site-specific drug action, thereby reducing the required dose and minimizing side effects. Recent advancements in nanotechnology and polymer sciences have further strengthened the application of NHDDS in delivering phytochemicals effectively. This overview highlights the need, design strategies, advantages, and recent progress in novel delivery systems for herbal formulations, emphasizing their role in modernizing traditional medicine and improving patient compliance.

INTRODUCTION

Novel herbal drug delivery systems are advanced methods developed to improve the effectiveness of herbal medicines by overcoming challenges like poor bioavailability and stability. Techniques such as liposomes, phytosomes and nanoparticles help deliver herbal drugs more efficiently by enhancing absorption, protecting active compounds and ensuring controlled release. Traditional herbal

medicines often face challenges such as poor solubility, low bioavailability, instability and inconsistent dosing. Novel drug delivery systems help overcome these issues by enhancing absorption protecting herbal compounds from degradation and enabling targeted and sustained release. This leads to improved therapeutic efficacy, reduced dosing frequency and better patient compliance. Modern delivery methods like liposomes, phytosomes, nanoparticles and

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transdermal patches are used to improved herbal drug delivery.

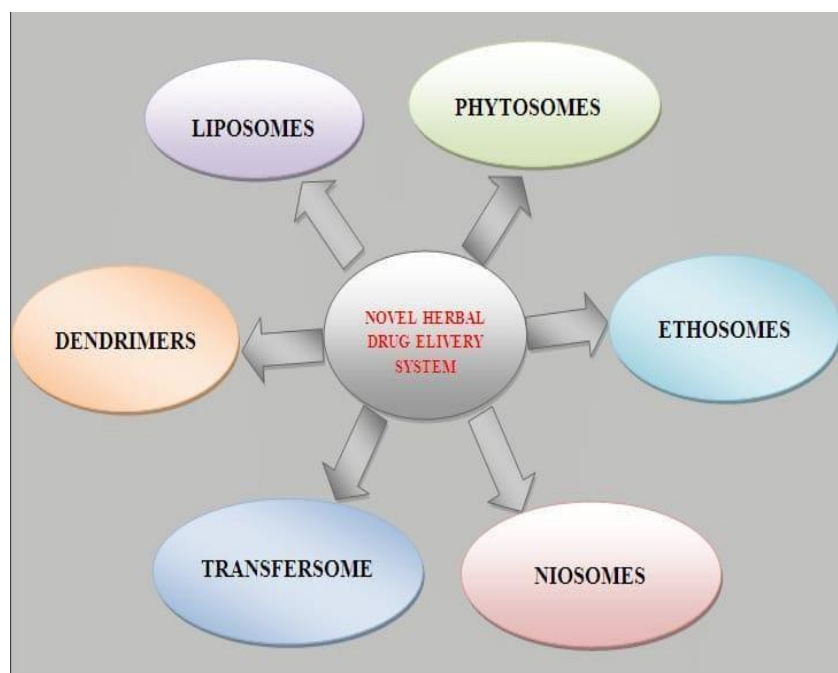
2.Current Challenges in Upgrading and

Modernization of Herbal Formulations:

Modernizing herbal formulations faces several key challenges. The lack of standardization and quality control leads to variations in efficacy and safety. Contamination, adulteration, and poor raw material quality further complicate product reliability. Regulatory differences between countries and insufficient clinical evidence limit

global acceptance. Many herbal compounds show poor solubility, stability, and bioavailability, making formulation difficult. Scaling up advanced delivery systems like nanoparticles and liposomes adds technical and cost challenges. Moreover, sustainability issues, intellectual property rights, and limited research funding hinder progress in developing consistent, safe, and effective modern herbal products.

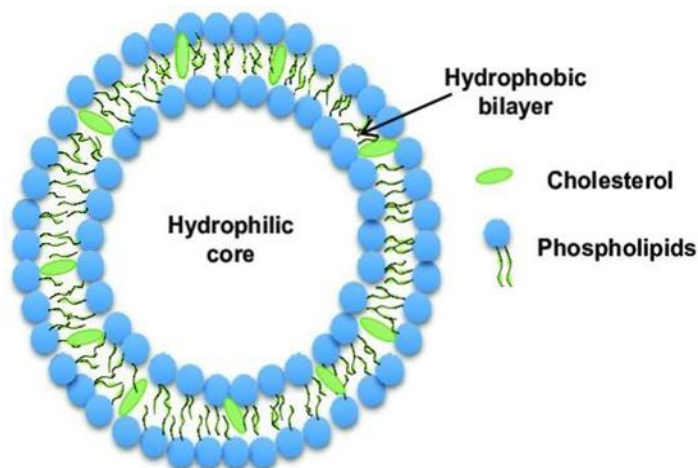
3.Different Types of Novel Herbal Formulations Currently Available in Market:



a. Liposomes:

Liposomes are microscopic vesicles made of phospholipid bilayers that can encapsulate both hydrophilic and lipophilic herbal drugs. They enhance solubility, stability, bioavailability, and therapeutic efficacy of herbal compounds. Common preparation methods include thin-film hydration, solvent injection, and reverse-phase evaporation. Liposomes protect phytoconstituents

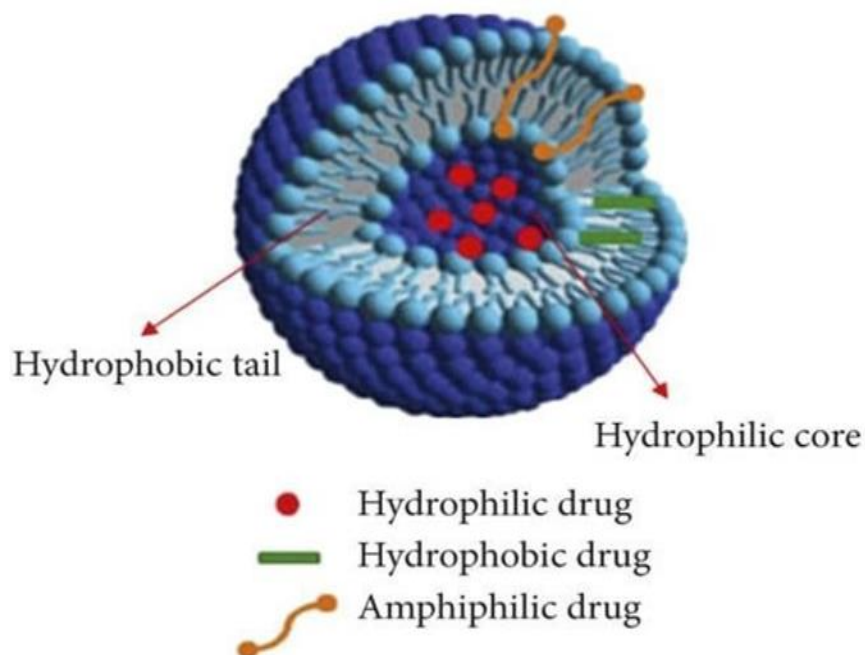
from degradation, allow controlled release, and enable targeted delivery. However, they face challenges like high production cost, stability issues, and difficulties in large-scale manufacturing. Liposomal formulations of herbal actives such as curcumin, quercetin, and silymarin have shown improved pharmacological activity and bioavailability compared to conventional forms.



b.Niosomes:

Niosomes are microscopic, bilayered vesicles made from non-ionic surfactants and cholesterol. They are similar to liposomes but more stable, cost-effective, and easy to prepare. Common preparation methods include thin-film hydration, reverse-phase evaporation, and proniosome conversion. Niosomes can encapsulate both hydrophilic and lipophilic herbal actives,

improving their solubility, stability, and bioavailability. They protect sensitive phytochemicals such as curcumin, diosgenin, and berberine from degradation and enhance pharmacological effects through sustained and targeted release. Niosomes are biocompatible, non-toxic, and suitable for oral, topical, and parenteral delivery, making them useful in novel herbal drug delivery systems.

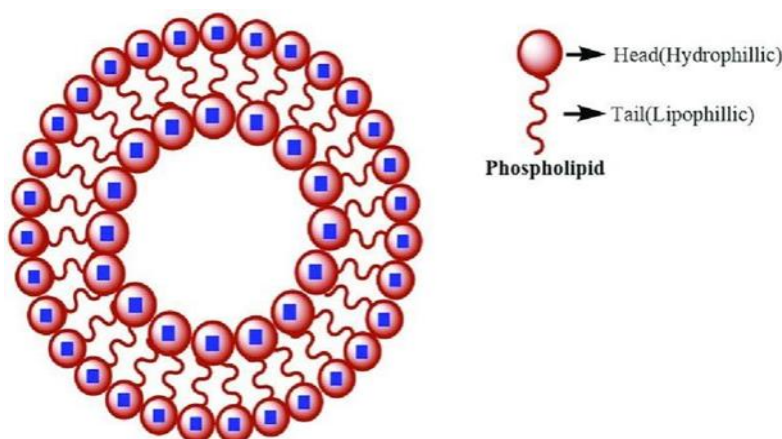


c.Phytosomes:

Phytosomes are advanced herbal formulations formed by complexing plant bioactive compounds (like flavonoids or polyphenols) with

phospholipids, usually phosphatidylcholine, to enhance their solubility and bioavailability. Unlike simple mixtures, phytosomes form a true molecular complex, allowing better absorption through biological membranes. They are commonly prepared by reacting herbal extracts with phospholipids in solvents such as ethanol or dichloromethane, followed by solvent removal.

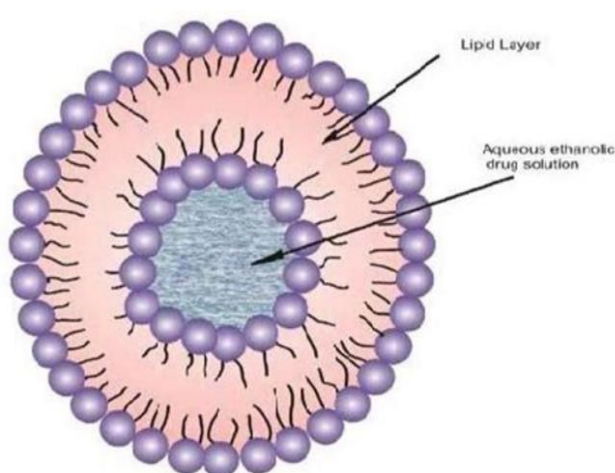
Phytosomes improve therapeutic efficacy, stability, and membrane permeability of herbal drugs, making them useful in oral and topical delivery. However, their preparation requires careful optimization, and stability issues may arise due to phospholipid oxidation. Examples include silymarin, curcumin, and ginkgo biloba phytosomes.



d.Ethosomes:

Ethosomes are soft, phospholipid vesicles containing high ethanol and water, designed to enhance skin permeability. They deliver both hydrophilic and lipophilic herbal actives through deeper skin layers by fluidizing stratum corneum lipids. Ethosomes protect phytoconstituents,

improve bioavailability, and provide better therapeutic action in topical herbal formulations. They are prepared mainly by cold or hot methods and characterized for vesicle size, entrapment, and stability. Advantages include improved penetration and stability; limitations include ethanol-induced irritation and volatility.

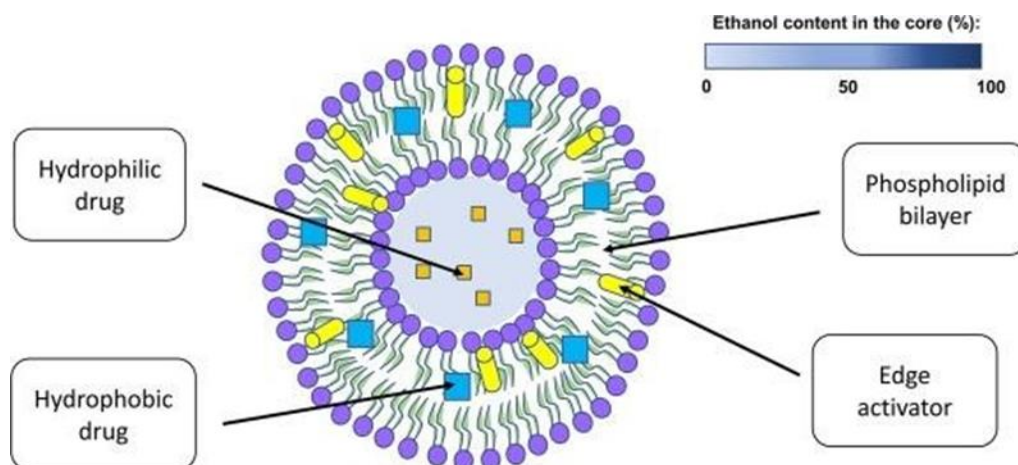


e.Transferosomes:

Transferosomes are ultra-deformable lipid vesicles composed mainly of phospholipids and

edge activators. They are designed to enhance transdermal delivery of drugs and herbal actives by easily penetrating the skin due to their elastic and flexible nature. The vesicles can carry both hydrophilic and lipophilic compounds, improving bioavailability and stability of herbal drugs. They are usually prepared by thin-film hydration or solvent injection methods and characterized for size, zeta potential, entrapment efficiency, and

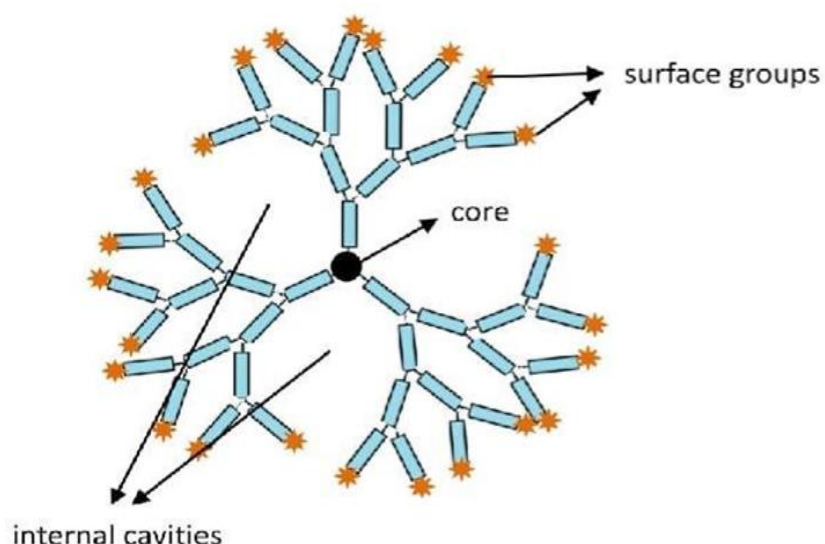
deformability. Transfersomes offer advantages like improved skin penetration, protection of phytoconstituents, and non-invasive delivery, but may face challenges such as physical instability and scale-up difficulties. Examples include transfersosomal formulations of curcumin, quercetin, and resveratrol, which show enhanced therapeutic effects in anti-inflammatory and wound-healing studies.



f. Dendrimers:

Dendrimers are highly branched, nanosized, polymeric structures with a core, interior branches, and surface functional groups. They are used as carriers in novel herbal drug delivery systems to enhance solubility, stability, and bioavailability of poorly water-soluble herbal compounds like curcumin, berberine, and ursolic acid. Drugs can

be loaded into dendrimers by encapsulation, electrostatic adsorption, or covalent bonding, allowing controlled and targeted delivery. Surface modification (e.g., PEGylation) reduces toxicity and improves compatibility. Despite their advantages, issues like cytotoxicity and high production cost limit large-scale use. Overall, dendrimers hold great promise for targeted and efficient delivery of herbal bioactive.



3. Excipients used in Novel Herbal Drug Delivery Systems:

Excipients play a vital role in improving stability, solubility, bioavailability, and targeted delivery of herbal drugs. Commonly used excipients include:

Excipients	Roles	Example
Solubilizers & Surfactant	Enhance Solubility	Tween 80
Polymers	Provide controlled release & stability	Chitosan
Lipid based	Improve permeability & Bioavailability	Phospholipid
Stabilizers & Preservatives	Protect against degradation & microbial growth	Carbopol
Penetration enhancers	Facilitates absorption through skin	Ethanol

4. Analytical Aspect of Novel Herbal Formulation:

Analytical techniques are essential to evaluate the quality, safety, and efficacy of novel herbal formulations. They help identify phytoconstituents, assess purity, determine physical and chemical stability, and ensure batch-to-batch consistency. Both spectroscopic and chromatographic methods are employed.

a. HPLC / UPLC (High / Ultra Performance Liquid Chromatography)

•Use: Separation and quantification of active compounds and markers.

•Sample prep: Extract plant material/formulation with suitable solvent, filter (0.45/0.22 μm), dilute in mobile phase.

•Procedure:

1. Choose column (C18 common), mobile phase (gradient or isocratic), flow rate and detector (UV/PDA).

2. Equilibrate column.

3. Inject sample (5–20 μL for HPLC; smaller for UPLC).

4. Run gradient, monitor peaks, integrate and quantify against standards.

b. GC (Gas Chromatography)

•Use: Volatile phytochemicals (essential oils, terpenes) analysis.

•Sample prep: Direct injection for volatile oils or headspace/Solid Phase Microextraction (SPME) for volatiles; derivatization for less volatile compounds.

•Procedure:

1. Select capillary column and carrier gas (He/N_2).

2. Set injector and oven temperature program.

3. Inject sample (split/splitless).

4. Separate analytes; detect (FID or MS)

c. UV–Visible Spectroscopy (UV–Vis)

•Use: Quantification of chromophoric compounds (phenolics, flavonoids) and routine content assays.

•Sample prep: Dilute extract in suitable solvent, blank with solvent.

•Procedure:

1. Select wavelength (λ_{max}) or perform scan (200–800 nm).

2. Zero instrument with blank.

3. Measure absorbance; use calibration curve to quantify.

d. FTIR (Fourier Transform Infrared Spectroscopy)

•Use: Identify functional groups, excipient–drug interactions, fingerprinting.

•Sample prep: Neat (ATR), KBr pellet, or thin film depending on formulation.

•Procedure:

1. Prepare sample (ATR: place on crystal).

2. Collect spectrum ($4000\text{--}400\text{ cm}^{-1}$).

3. Interpret peaks vs reference spectra to identify functional groups and interactions.

e. NMR (Nuclear Magnetic Resonance)

•Use: Structural elucidation of isolated phytochemicals and impurity identification.

•Sample prep: Dissolve purified compound in deuterated solvent (CDCl_3 , DMSO- d_6 , etc.).

•Procedure:

1. Transfer sample to NMR tube.

2. Lock and shim instrument, acquire ^1H and ^{13}C spectra; use 2D (COSY, HSQC) if needed.

3. Interpret chemical shifts, coupling to confirm structure

f. Mass Spectrometry (MS)

•Use: Molecular weight determination, fragmentation pattern, combined with chromatography (LC–MS, GC–MS).



•Sample prep: Depends on interface (LC–MS: HPLC fractions; GC–MS: derivatized sample).

•**Procedure:**

1. Ionize analyte (ESI, APCI, EI for GC).
2. Mass analyzer separates ions (quadrupole, TOF, orbitrap).
3. Detector records m/z , generate mass spectrum for identification/quantitative

g. Dissolution Testing

•Use: In vitro release profile of actives from dosage forms (tablets, capsules, controlled-release systems).

•Sample prep: Place dosage form in dissolution medium (volume & composition per pharmacopeia).

•**Procedure:**

1. Select apparatus (USP I/II/III), medium, temperature ($37 \pm 0.5^\circ\text{C}$) and agitation RPM.
2. Start test; withdraw samples at pre-set timepoint
3. Filter, analyze by HPLC/UV to quantify released drug.

h. Particle Size Analysis (Laser Diffraction / DLS)

•Use: Characterize particle size distribution for suspensions, nanoparticles, emulsions.

•Sample prep: Dispersion in suitable medium; avoid agglomeration; sonication if needed.

•**Procedure:**

1. Choose technique: laser diffraction for broad range; DLS for nanoscale.

2. Introduce sample; measure scattering/light fluctuations.

3. Software computes size distribution (D10, D50, D90 or Z-average).

i. Zeta Potential

•Use: Surface charge of particles — predicts colloidal stability.

•Sample prep: Dilute sample in low ionic strength medium; avoid bubbles.

•**Procedure:**

1. Place sample in zeta cell.
2. Apply electric field; measure electrophoretic mobility.
3. Convert to zeta potential using Smoluchowski or Henry equation.

j. Microbial Tests (Total Viable Count, Specific Pathogens)

•Use: Ensure microbiological quality and safety of herbal products.

•Sample prep: Prepare dilutions in sterile diluent; neutralize preservatives if present.

•**Procedure:**

1. Plate counts: inoculate media (PCA, SDA) for bacteria/yeast & molds, incubate 24–72 h.
2. Pathogen tests: enrichment then selective plating (Salmonella, E. coli, S. aureus, Pseudomonas).
3. Report CFU/g or presence/absence per pharmacopeial limits.



k. DSC / TGA (Differential Scanning Calorimetry / Thermogravimetric Analysis)

•Use: Thermal behavior, melting point, polymorphism (DSC) and weight loss / moisture / decomposition (TGA).

•Sample prep: Small amount (mg scale), placed in suitable pan (sealed or open).

•Procedure (short):

1. Load sample and reference (for DSC) or empty pan (TGA).
2. Set temperature program (heating rate °C/min).
3. Record endotherms/exotherms (DSC) and mass change vs temperature (TGA).

l. Karl Fischer Titration

•Use: Accurate moisture (water) content determination in raw herbs, extracts, and finished formulations.

•Sample prep: Sample dissolved or weighed; method chosen (volumetric/ coulometric) based on water content range.

•Procedure:

1. Choose KF mode: coulometric (trace water) or volumetric (higher water).
2. Prepare cell/reagents and titrate until endpoint (electrochemical detection).
3. Calculate % water from titre and sample mass.

5.Application of Novel Herbal Drug Delivery Systems:

Poor water solubility, low oral bioavailability, rapid metabolism and off-target distribution limit the clinical utility of many phytoconstituents. Nanocarriers and other novel delivery systems (phytosomes, liposomes, polymeric nanoparticles, nanoemulsions, hydrogels, solid lipid nanoparticles) can improve solubility, protect labile compounds, enable controlled release and permit targeted delivery — collectively increasing therapeutic efficacy and reducing required dose and systemic toxicity.

<u>Disease/Condition</u>	<u>Novel Herbal Drug Delivery System Examples</u>	<u>Active Herbal Constituents/Extracts</u>	<u>Benefits/Application [Source]</u>
Diabetes	Phytosomes, Nanoparticles	Ginkgo biloba, Grape Seed extracts	Improved efficacy, targeted delivery to specific organs (e.g., lungs, eyes), enhanced bioavailability
Hepatoprotective (Liver Protection)	Phytosomes (Siliphos), Solid Lipid Nanocarriers (NLC)	Silymarin (Milk thistle extract), Phosphatidylcholine	Enhanced absorption and bioavailability, improved liver targeting, reduced toxicity, clinical use in hepatic diseases
Antioxidant	Liposomes, Phytosomes	Curcumin, Myrtus communis, Puerarin	Activity enhancement, improved efficacy, enhanced stability and bioavailability, reduced side effects
Cardiovascular Disorder	Phytosomes, Nanoparticles, Emulsions	Ginkgo biloba, Hawthorn (Crataegus species), Puerarin, Garlicin	Improved efficacy, cardioprotective effects, enhanced absorption, improved stability, reduced organ damage
Cancer	Liposomes, Nanoparticles, Microemulsion, Phytosomes	Curcumin, Paclitaxel, Ampelopsin, Wogonin, Green Tea extracts	Increased drug concentration in tumor area, reduced toxicity to normal cells, enhanced efficacy, long systemic residence time, improved therapeutic outcomes

6. Targeted Herbal Drug Delivery Systems:

Targeted herbal drug delivery aims to deliver phytoconstituents precisely to the desired site, improving bioavailability, reducing dose, and minimizing side effects. It utilizes carriers like liposomes, phytosomes, polymeric nanoparticles, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), and dendrimers, which can be modified for site-specific delivery.

•Types of targeting:

- Passive targeting: Accumulation in diseased tissues (e.g., tumor via EPR effect).
- Active targeting: Use of ligands such as folate, transferrin, antibodies, or peptides to bind specific receptors.
- Stimuli-responsive targeting: Drug release triggered by pH, enzymes, or temperature changes.

•Advantages:

Improved stability and absorption of herbal actives, reduced toxicity, enhanced therapeutic efficacy, and controlled release.

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