
Available online at [www.irjpas.com](http://www.irjpas.com)

**Review Article**

**APPROACHES FOR IMPROVING THE PHARMACOLOGICAL AND PHARMACOKINETICS PROPERTIES OF HERBAL DRUGS**

Manish Mathur  
18E/564, CHB, Jodhpur

**Corresponding Author:** Manish Mathur, Email: ravi_mm2099@yahoo.com; eco5320@gmail.com

**Abstract:** Despite the world wide adaptability of herbal plants and their products, these conventional drugs suffering with many pharmacological and pharmacokinetics constraints. Major drawbacks related with these traditional drugs includes low aqueous solubility and physical stability, reduce absorption, rapid metabolism, instability under high acidic conditions and inability to cross blood-brain barriers. The present review article discussed various novel drug delivery approaches (like Liposome, Emulsion, Transfersome, Ethosome and Microspheres) that are using to combat with these constraints. Various important issues related with natural drugs carrier like their generalized mode of action, their advantages over conventional drugs and methods of their preparation are summarized.

**Keywords:** Herbal drugs, Novel Drug Delivery Approaches, Pharmacological Properties, Liposomes, Emulsion, Transfersome, Ethosome and Microspheres

**Introduction**

The herbal formulation, which is one of the major segments of traditional system of medicine, contributes immensely to the positive health of an individual. However, delivery of herbal drugs also requires modification with the purpose to achieve sustained release, to increase patient compliance etc.\(^1\). The efficacy of many herbal drugs is often limited by their potential to reach the site of therapeutic action. In most cases (conventional dosage forms), only a small amount of administered dose reaches to target site, while the majority of the drug distributes throughout the rest of the body in accordance with its physicochemical and biochemical properties such as low solubility, reduced absorption, rapid metabolism, instability in highly acidic pH conditions and excretion\(^2\). To minimize drug degradation, to reduce dose and its toxicity, increased solubility and stability and improved tissue macrophages distribution various drug delivery and novel drug delivery systems are currently under development\(^3\). Novel drug delivery system (NDDS) is advantageous in the delivering the herbal drug at predetermined rate and exhibits site specific action. In novel drug delivery technology, control of the distribution of drug is achieved by incorporating the drug in carrier system or in changing the structure of drug at molecular level\(^4\). In phyto-formulation research, developing nano dosage forms like polymeric phytosomes, nanoemulsion, ethosomes, proniosomes, floating drug delivery system, micro-emulsions have a number of advantages for herbal drugs, including enhancement of solubility, stability and bioavailability, protection from toxicity, enhancement of pharmacological activity, protection from physical and chemical degradation\(^5\). Thus the NDDS have potential to address various problems related with herbal medicine practice (HMP).

**Liposomes**

Honeywell-Nguyen and Bouwstra\(^10\) were the first to studied liposome as an effective delivery system for the skin. Liposomes are lipid vesicles mainly composed of one or multiple lipid bi-layers composed of mixtures of phosphatidylcholines with long or short hydrocarbon chains. They have high morphological diversity as a function of hydration, temperature and composition\(^11\). A cross-section of liposome revealed the hydrophilic heads of the amphiphile orienting toward the water compartment while the lipophilic tails orient away from the water towards the center of the vesicle, thus forming a bilayer. Consequently, water soluble compounds are entrapped in the water compartment and lipid soluble compound aggregate in the lipid section. Liposome-based delivery system plays an important role owing to easy preparation, increasing the bioavailability, and also offers drug targeting and controlled release\(^12\). In addition, charged liposomes could be as carriers to enhance the permeation through the skin in the transdermal drug delivery which are administered by the percutaneous route\(^13\). Recently, it has been reported that liposomes had been employed in the field of plant polysaccharides and made encouraging successes. Liposomes possess unique physical and chemical properties, which not only improve polysaccharide stability, bioavailability, and difficulty in penetration to some cells but also enhance the pharmacodynamic action and induce the target\(^14\).
This technique is efficiently utilize for enhancing the therapeutic index of anti-cancer agents, either by increasing the drug concentration in tumor cells and/or by decreasing the exposure in normal tissues exploiting enhanced permeability and retention effect phenomenon and by utilizing targeting strategies. 15, 16 have summarized the role of liposome in liver related disorders. According to them liposomally delivered herbal drug could be taken up by Kuffer cells and provide protective effects in hepatocytes. Liposome provides following benefits enhance drug bioavailability, solubility and uptake, altered pharmacokinetics and bio-distribution and in vitro and in vivo stability and site specific action. 1 There is marked difference between phytosome and liposome; two basic differences are, in phytosome active chemical constituents molecules are anchored through chemical bonds to the polar head of the phospholipids whereas in liposome, the active principle is dissolved in the medium of the cavity or in the layers of the membrane. No chemical bonds are formed. In phytosome, phosphatidylcholine and the individual plant compound form a 1:1 or 2:1 complex depending on the substance, whereas in liposomes hundreds and thousands of phosphatidylcholine molecules surround the water soluble molecule. Various herbal liposomal formulations have been studied and they are summarized in Table 1. Essential oil from rhizome of Atractyloides macrocephala has been entrapped into liposomes by using rapid expansion supercritical solution technique (RESS). The essential oil of this plant were reported to treat various disorders related with gastro-intestinal tract and as anti-tumor. Incorporation of oil into liposomes improved the solubility and enhancing the bioavailability of this drug17. Hybrid liposomes of the silymarin extract were reported for buccal administration using cholesterol and stearyl amine for the treatment of liver disorders 18. However, lower water solubility and poor gastrointestinal absorption limits its uses, liposomal formulation of this drug were prepared by using reverse evaporation technique where interaction between the silymarin and phospholipids led to increase permeation thereby increased bioavailability 19. Film method and sonication technique were utilized for preparation of Artemisia arborescens liposome, this provide an increase stability and enhanced penetration into cytoplasmic barrier16. Extract of Tripterygium wilfordi has been incorporated into liposomes by thin film dispersion method, which led to increased stability at suitable temperature and reduced side effect 20. Quercetin (Sophora japonica) required high dose for their antioxidant and anti-inflammatory activities and due to large molecular size of drug it cannot pass through from blood brain barrier. The liposomal formulation of this drug was developed by mixture of phosphatidylcholine, quercetin and dispersion in polyethylene glycol. This provides reduction in dose amount and side effect as well as better permeability through blood brain barrier 21. Cosmotech International AG a Swiss-based company, launched liposomal powders, named Liposome Herbase. There are five extract in the current Liposome Herbase range which are standardized for specific phyto-chemicals. White and green tea are standardized for caffeine and total poly-phenols, white hibiscus for fruit acids, guarana for caffeine and Aloe vera is aloin-free product 3.

Emulsions

Emulsion is a biphasic system in which one phase is intimately dispersed in the other phase in the form of minute droplets. In emulsion, one phase is always water or aqueous phase, and the other phase is oily liquid, i.e. non-aqueous. Emulsion can be classified into ordinary emulsion (0.1-100 µm), micro-emulsion (10-100 µm) and sub-micro-emulsion (100-600 µm). Among them, the micro-emulsion is also called nano-emulsion and sub-micro-emulsion is also called lipid emulsion. Emulsion drug delivery system is targeted or distributed well due to affinity to lymph. Emulsion can release the drug for a long time because it is packed in the inner phase and makes direct contact with the body and other tissues. Apart from its targeted sustained release, producing the herbal drug into emulsion will also strengthen the stability of hydrolyzed materials, improve the penetrability of drugs to the skin and mucous and reduce the drugs stimulus to tissues. The new type, viz., Eleumem emulsion, is uses as anti-cancer drug and safer for heart and liver. Emulsion formulation for various herbal bioactive have been reported and depicted in Table 2. Emulsion of Taxus brevifolia (Docetaxel), Sophora japonica (Quercetin) and Tripterygium wilfordii (Triptolide) were prepared by homogenization method that improves the bioavailability, absorption, penetration into stratum corneum and epidermis and sustained release of these drugs 22-25. Rheum rhubarbarum (Rhubarb) uses as laxative, anti-bacterial and anti-spasmodic, the conventional dose suffering from poor solubility and require high drug concentration for desired biological activity, the emulsion prepared by micellar electro-kinetic method provides better bioavailability and good penetration ability of rhubarb26.

Transfersomes

Transfersomes are made up of phospholipids supplemented with single chain surfactant with a high radius of curvature which acts as edge activators to provide vesicle elasticity and deformability 27. Transfersomes are specific deformable vesicles, which are being developed, considering the advantage of phospho-lipids vesicles, for suitable delivery of drug. These are highly elastic in nature; as such they could easily overcome the skin penetration, by squeezing themselves in a self-adapting manner. Also they possess a unique ability to get accommodated with a wide range of solubility and act as an efficient carrier for both low as well as high molecular weight drugs, e.g. analgesic, corticosteroids, hormones, anticancer drugs, insulin, proteins etc with high entrapment efficiency and a unique advantage of protection of the encapsulated drug, from metabolic degradation 28. Transfersomes could be easily prepared using various processes - suspension homogenization process, aqueous lipid suspension process, modified handshaking process and centrifugation process. Transfersomes’ inherent potential advantages are highly utilized in ‘Transdermal Immunization’, ‘Peripheral Drug Targeting’ & for ‘Transdermal Delivery’ of Insulin, NSAIDs, Heparin, Anti Cancer drugs, etc. Transfersomes are applied in a non-oculedd method to the skin, which permeate through the stratum corneum lipid lamellar regions as a result of the hydration or osmotic force in the skin. It can be applicable as drug carriers for a range of small molecules, peptides.
protein and herbal ingredients. Transfersomes can penetrate stratum corneum and supply the nutrients locally to maintain its functions resulting maintenance of skin. Zheng et al. have evaluated influences of drug properties on the encapsulation efficiency and drug release of a transfersomes. According to them high molecular weight and opposite charges to the membrane may provide transfersomes with high encapsulation efficiency. Capsaicin transfersomes were prepared by the high shear dispersion technique and the penetration of capsaicin transfersomes was found to be more resulting better topical absorption as compared to pure drug. Table 3. Colchicines and Curcumin transfersomes were prepared using hand shaking method, these formulation prevent drugs from gastro-intestinal side effect associated with oral administration and provide local, sustained and site specific delivery of colchicines and Curcumin. Transfersomes of vincristine were prepared by using lecithin and sodium deoxycholate in 70/20 ration. This formulation increases the entrapment efficiency and improved skin penetration.

Ethosomes
Ethosome are soft, malleable lipid vesicles composed mainly of phospholipids, alcoh (ethanol or isopropyl) in relatively high concentration (20-45%) and water. Ethosomes are novel lipid carriers and can be tailored for enhanced skin delivery. Ethosome, as a novel liposome, is especially suitable as a topical or trans-dermal administration carrier. It has a high deformability and entrapment efficiency and can penetrate through the skin. Compared to other liposome, the physical and chemical properties of ethosomes make the delivery of the drug through the stratum corneum into a deeper skin layer efficiently or even into the blood circulation. This property is very important as the topical drug carrier and trans-dermal delivery system. Moreover, the ethosomes carrier also provide an efficient intercellular delivery for both hydrophilic and lipophilic drugs. Ethosome are platform for the delivery of large amount of diverse group of drug and these drug is administrated in semi solid form resulting in improved patient compliance. Ethosome suspension of ammonium glycyrrhizinate (Table 4) was prepared (by solvent depression method) for the dermal administration. The glycyrrhizic ethosome increase in-vitro precutaneous permeation and significantly enhance its anti-inflammatory activity. Ethosomes of Tripterygium wilfordii (Triptolide) were prepared by controlling film hydration and ultrasonic method and evaluated in the rat model for erythma. This ethosomal formulation showed an increase in precutaneous permeability, high entrapment efficiency compared to their traditional formulation. Ethosomal of Sesbania grandifolia were developed by solvent dispersion method that enhance it trans-dermal permeation. Similarly ethosome of alkaloid of Sephora alopecuroides were prepared by transmembrane pH active loading methods that enhance drug delivery and stability.

Microspheres
Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers which are biodegradable in nature and ideally having a particle size less than 200 μm. As a delivery system microspheres are advantageous because they can ingested or injected and: they can be tailored for desired release profiles and used site-specific delivery of drug and in some cases can even provide organ-targeted release. A number of plant ingredient have been micro-capsulated for various application. Microsphere of Curcuma longa oleoresin were prepared through emulsion solvent diffusion method and this formulation supports sustained drug release. Micro-encapsulation of Zeodary turmeric oil into microspheres via quasi-emulsion solvent diffusion has been used for bioavailability enhancement and sustained drug release.

Oxidised cellulose microsphere containing Camptoteteha acuminate were prepared by using evaporation method, has been successfully use for prolonged release of camptothechin drug. Similarly microsphere of sophora japonica (Quercetin) has been prepared by solvent evaporation method that significantly decreases the drug molecular size and this novel drug can easily pass through from blood barrier.

Table 1. Herbal Liposome Formulation

<table>
<thead>
<tr>
<th>Botanical Name</th>
<th>Formulation</th>
<th>Biological Activity</th>
<th>Active Ingredient</th>
<th>drawback of traditional dose</th>
<th>Application of Liposomal formulation</th>
<th>Method of preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atractylodes macrocephala</td>
<td>Essential of A. macrocephala</td>
<td>Anti-tumor and use in various gastro-intestinal diseases</td>
<td>Essential oil and oxo derivatives</td>
<td>Lower solubility and bioavailability</td>
<td>Improved solubility and enhancing bioavailability</td>
<td>Rapid expansion of supercritical solution (RESS) technique</td>
</tr>
<tr>
<td>Tripterygium wilfordii</td>
<td>Triptolide</td>
<td>Anti-inflammatory</td>
<td>Diterpene triepoxide</td>
<td>Poor water solubility and toxicity</td>
<td>Increase stability and reduce side effects</td>
<td>Thin film depression method</td>
</tr>
<tr>
<td>Sophora japonica</td>
<td>Quercetin</td>
<td>Antioxidant and anti-inflammatory and anti-cancer</td>
<td>Quercetin, 3,3',4',5'-pentahydroxy flavones</td>
<td>Required high dose, due to high particle size it cannot pass</td>
<td>Reduced dose, and side effect, enhance penetration in blood brain barrier, and bioavailability</td>
<td>By using mixture of egg phosphotydylecholine, quercetin and dispersion in polyethylene glycol</td>
</tr>
</tbody>
</table>

Manish Mathu, 2013
<table>
<thead>
<tr>
<th>Plant</th>
<th>Extract/Capsule</th>
<th>Action</th>
<th>Bioavailability/Interaction</th>
<th>Preparation Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silybum marianum</td>
<td>Silymarin extract</td>
<td>Hepatoprotective antioxidant for liver and skin</td>
<td>Low water solubility and poor absorption in gastrointestinal tract</td>
<td>Reverse evaporation technique</td>
</tr>
<tr>
<td>Artemisia arborescens</td>
<td>Artemisia</td>
<td>Antiviral</td>
<td>Increase stability, anti-herpetic activity, enhance penetration into cytoplasmatic barrier</td>
<td>Film method and sonication technique</td>
</tr>
<tr>
<td>Capsicum annua</td>
<td>Capsaicin liposome</td>
<td>Capsaicin</td>
<td>Increase in skin permeation as well as prolongation of duration of action</td>
<td>Reverse evaporation technique</td>
</tr>
<tr>
<td>Magnolia officinalis</td>
<td>Magnolol liposome</td>
<td>Anti-oxidant, Inhibiting vascular smooth muscle cell proliferation</td>
<td>Enhance therapeutic efficiency</td>
<td>Magnolol and phospholipid mixed by ultrasonic facilitation</td>
</tr>
<tr>
<td>Strychnos nux-vomica</td>
<td>Nux vomica liposome</td>
<td>Anti-tumor, Analgesic</td>
<td>High encapsulation efficiency improved stability in blood, and relative low price of phospholipids of the novel liposomes</td>
<td>Reverse evaporation technique</td>
</tr>
<tr>
<td>Diospyros montana</td>
<td>Diospyrin liposome</td>
<td>Anti-bacterial and anti-tumor</td>
<td>Enhancement of its anti-tumor effect</td>
<td>Reverse evaporation technique</td>
</tr>
<tr>
<td>Myrtus communis</td>
<td>Myrtle liposome</td>
<td>Anti-bacterial and anti-oxidant</td>
<td>Increase its activity</td>
<td>Thin film method</td>
</tr>
<tr>
<td>Radix puerariae</td>
<td>Puerarin</td>
<td>Cardio-protective and anti-arrhythmia activity</td>
<td>Modify their surface charge and membrane integrity</td>
<td>Film depression ultrasonic method</td>
</tr>
<tr>
<td>Ampelopsis grossedentata</td>
<td>Ampelopsin</td>
<td>Anti-cancer and anti-oxidant</td>
<td>Increase efficiency</td>
<td>Film ultrasound method</td>
</tr>
<tr>
<td>Taxus brevifolia</td>
<td>Paclitaxel</td>
<td>Anti-tumor</td>
<td>High entrapment efficiency (94%)</td>
<td>Thin film hydration method</td>
</tr>
<tr>
<td>Curcuma longa</td>
<td>Curcumin Liposome</td>
<td>Antioxidant and anti-cancer</td>
<td>Long circulating with high entrapment</td>
<td>Ethanol injection method</td>
</tr>
<tr>
<td>Botanical</td>
<td>Formulation</td>
<td>Biological activity</td>
<td>Active Ingredient</td>
<td>Drawback of traditional dose</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------</td>
<td>--------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td><em>Taxus brevifolia</em></td>
<td>Docetaxel</td>
<td>Anti-neoplastic agent, anti-cancer, cycle specific drug</td>
<td>Docetaxel</td>
<td>Lower bioavailability (8-9%) and absorption</td>
</tr>
<tr>
<td><em>Sophora japonica</em></td>
<td>Quercetin</td>
<td>Antioxidant and anti-inflammatory</td>
<td>Quercetin 3′, 4′, 5′-pentahydroxy flavones</td>
<td>Poor bioavailability</td>
</tr>
<tr>
<td><em>Tripterygium wilfordii</em></td>
<td>Triptolid micro-emulsion</td>
<td>Anti-inflammatory</td>
<td>Diterpene triepoxide</td>
<td>Poor water solubility and toxicity</td>
</tr>
</tbody>
</table>

**Table 2. Herbal Emulsion Formulation**
Table 3. Herbal Transferosomes Formulation

<table>
<thead>
<tr>
<th>Botanical Formulation</th>
<th>Biological Activity</th>
<th>Active Ingredient</th>
<th>Drawback of Traditional Dose</th>
<th>Application of Emulsion Formulation</th>
<th>Method of Preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsicum annuum</td>
<td>Analgesic</td>
<td>Capsaicin</td>
<td>Increase skin penetration</td>
<td></td>
<td>High Shear dispersion Method</td>
</tr>
<tr>
<td>Colchicum autumnale</td>
<td>Antigout, leuko-</td>
<td>Colchicine(s)</td>
<td>Increase skin penetration</td>
<td></td>
<td>Hand Shaking Method</td>
</tr>
<tr>
<td></td>
<td>cytolytic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>vasculitis, psoriasis, and Sweet's syndrome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curcuma longa</td>
<td>Manage Osteoarthritis, Uveitis and chronic eye inflammation and diabetic angiopathy</td>
<td>Curcumin or diferuloy lmethane (yellow polyphenol)</td>
<td>Low bioavailability due to lower absorption in gastrointestinal tract</td>
<td>Increase in permeation</td>
<td>hand shaking method using surfactant</td>
</tr>
<tr>
<td>Catharanthus roseus</td>
<td>Anti-cancer, Lymphoma, Leukemia</td>
<td>Vincristine, Cathartine, Vindoline alkaloid</td>
<td>Increase entrapment efficiency and skin penetration by improving the pre-cutaneous permeation</td>
<td>By using lecithin and sodium deoxycholate in 70/20 ratio</td>
<td>solvent dispersion method</td>
</tr>
</tbody>
</table>

Table 4. Herbal Ethosome Formulation

<table>
<thead>
<tr>
<th>Botanical Formulation</th>
<th>Biological Activity</th>
<th>Active Ingredient</th>
<th>Drawback of Traditional Dose</th>
<th>Application of Ethosome Formulation</th>
<th>Method of Preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycyrrhiza glabra</td>
<td>Anti-inflammatory</td>
<td>Glycyrrhizic acid</td>
<td>Poor permeability</td>
<td>Increases of in vitro percutaneous permeation and significantly enhanced anti-</td>
<td>solvent dispersion method</td>
</tr>
</tbody>
</table>

Manish Mathu, 2013
**Table 5. Herbal Microspheres Formulation**

<table>
<thead>
<tr>
<th>Botanical</th>
<th>Formulation</th>
<th>Biological activity</th>
<th>Active Ingredient</th>
<th>Drawback of traditional dose</th>
<th>Application of ethosome formulation</th>
<th>Method of preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curcuma longa</td>
<td>Curcumin floating microspheres</td>
<td>Antioxidant, anti-arthritis and anti-cancer</td>
<td>Curcumin or diferuloylthane (yellow polyphenol)</td>
<td>Low bioavailability</td>
<td>Sustained drug release</td>
<td>Emulsion solvent diffusion method</td>
</tr>
<tr>
<td>Curcuma longa</td>
<td>Zeedoary oil microsphere</td>
<td>Hepatoprotective, anti-arthritis and anti-cancer</td>
<td>Curcumin or diferuloylthane (yellow polyphenol)</td>
<td>Low bioavailability</td>
<td>Sustained release and higher bioavailability</td>
<td>Quasi-emulsion- solvent diffusion method</td>
</tr>
<tr>
<td>Sophora japonica</td>
<td>Quercetin</td>
<td>Antioxidant and anti-inflammatory and anti-cancer</td>
<td>Quercetin, 3,3′,4′,5′-pentahydroxy flavones</td>
<td>Required high dose, due to high particle size it cannot pass through from blood brain barrier</td>
<td>Significantly decrease the dose size</td>
<td>Solvent evaporation</td>
</tr>
<tr>
<td>Ruta gravelons</td>
<td>Rutin-alginate-chitosan-microcapsules</td>
<td>Useful for Cadriovascular and cerebrovascular diseases</td>
<td>Flavonoid</td>
<td>Unspecific site of action</td>
<td>Targeting into cardio-vascular and cerebro-vascular region</td>
<td>Complex coacervation method</td>
</tr>
<tr>
<td>Camptotech a acuminate</td>
<td>CPT loaded microsphere</td>
<td>Anti-cancer</td>
<td>Camptothecin (CPT) is a cytotoxic quinoline alkaloid</td>
<td>Poor aqueous solubility and stability</td>
<td>Prolonged release of camptothecin</td>
<td>Oil in water evaporation method</td>
</tr>
</tbody>
</table>

**Conclusion**

The interdisciplinary nature of NDDS technology enables diversification and development in order to improve quality of life. Novel drug delivery systems not only reduce the repeated administration to overcome non-compliance, but also help to increase the therapeutic value by reducing toxicity and increasing the bioavailability and so on. With the advancement of standardization, extraction, extraction, extraction.
identification techniques scientists now able to focuses their research for development of herbal drugs that can suit with modern system of medicine with targeted delivery, lesser amount and side effects properties. In present review it was immerged that large molecular size, lower water and lipid solubility, degradation of drug in gastro-intestinal tract, high dose requirement, slow pharmacokinetics, and toxicity problems restricted the in-vivo therapeutic activities of herbal drugs. Standardized plant extracts or mainly polar phyto-constituents like terpenoids, tannins, flavonoids when administered through novel drug delivery system show much better absorption better absorption profile which enables them to cross the biological membrane, resulting enhanced bioavailability. Hence novel drug delivery systems having a great potential to develop a site specific drugs.

Future Challenges

Beside the many advantage of these drug delivery approaches, still there are many technological challenges in developing the following techniques:

1. Nano-drug delivery systems that deliver large but highly localized quantities of drugs to specific areas to be released in controlled ways.
2. Controllable release profiles, especially in case of sensitive drugs.
3. Materials for such NDDS those are biocompatible and biodegradable.
4. Architectures/structures, such as biomimetic polymers, nanotubes, etc.
5. Technologies for self-assembly.
6. Functional improvement (active drug targeting, on-command delivery, intelligent drug release devices/bio-responsive triggered systems, self-regulated delivery systems, systems interacting with the body, smart delivery).
7. Improve devices such as implantable devices/nanochips for nanoparticle release, or Multi-reservoir drug delivery-chips.

To overcome these gaps the steps are needed to a) identify and isolate phyto-constituents which are compatible with various NDDS techniques, b) develop highly efficient and low cost NNDS techniques, c) formulate universal formulation schemes that can be used as intravenous, intramuscular or peroral drugs, d) develop better disease markers in terms of sensitivity and specificity, e) generate cell and gene targeting systems, f) device combined therapy and medical imaging, for example, nanoparticles for diagnosis and manipulation during surgery (e.g. thermotherapy with magnetic particles) and g) develop devices for detecting changes in magnetic or physical properties after specific binding of ligands on paramagnetic nanoparticles that can correlate with the amount of ligand.

References


20 Li HR, Li SF, Duan HQ. “Preparation of liposomes containing extract of Tripterygium wilfordii and evaluation of its stability”. Zhongguo Zhong Yao Za Zhi. 2007, 32 (20), 2128-2131.


34 Lu Y, Hou SX, Zhang LK, Li Y, He JY, Guo DD. “Transdermal and lymph targeting transfersomes of vincristine”. Yao Xue Xue Bao 2007, 42 (10), 1097-1101


37 Dayan N, Touitou E. “Carriers for skin delivery of trihexyphenidyl HCl, ethosomes vs. Liposomes”. Biomaterials. 2000, 21, 1879-1885
40 Chen JG, Jiang Y, Yang ZB. “Preparation of triptolide ethosomes”. AJPP 2012, 6(13), 998-1004
56 Xue KE, Yng XU, Fei Y, Neng PQ. “Preparation of wogonin liposomes and its pharmacokinetics in rat’s”. Journal of China Pharmaceutical University. 2007, 6, 502-506
60 Xu J, Fan QJ, Yin ZQ, Li XT, Du YH, Jia RY. “The preparation of neemoilmicroemulsion (Azadirachta indica) and the comparison of acaricidal time between neemoilmicroemulsion and other formulations in vitro”. *Veterinary Parasitology*. 2010, 3-4, 399-403
61 Wu SH, Ging WO. “Preparation, quality and safety evaluation of berberine nanoemulsion for oral application”. *Journal of Shanghai Jiaotong University (Agricultural Science)*. 2007, 1, 60-65
64 Yan-Yan Y, Hui ZJ, Ping FN, Ting WH, Tai ZY. “Entrapment efficiency of podophyllotoxin-encapsulated ethosome by minicolumn centrifugation-HPLC”. *Chinese Traditional and Herbal Drugs*. 2010, 10, 12-17