e-ISSN:2347-7857
p-ISSN:2347-7849
RESEARCH AND REVIEWS: JOURNAL OF PHARMACEUTICS AND NANOTECHNOLOGY

Applications of Nanotechnology Based Dosage Forms for Delivery of Herbal Drugs.

Mayank Sharma*

School of Pharmacy, Devi Ahilya Vishwavidyalaya, Indore, Madhya Pradesh, India.

Review Article

Received: 05/12/2013
Revised: 26/12/2013
Accepted: 29/12/2013

*For Correspondence

School of Pharmacy, Devi Ahilya Vishwavidyalaya, Indore, Madhya Pradesh, India.

Key words: Herbal drugs, nanotechnology, novel drug delivery systems, NDDS, Nano Carriers: Emulsion, ethosome, liposome, microsphere, nanoparticles, solid lipid nanoparticle

ABSTRACT

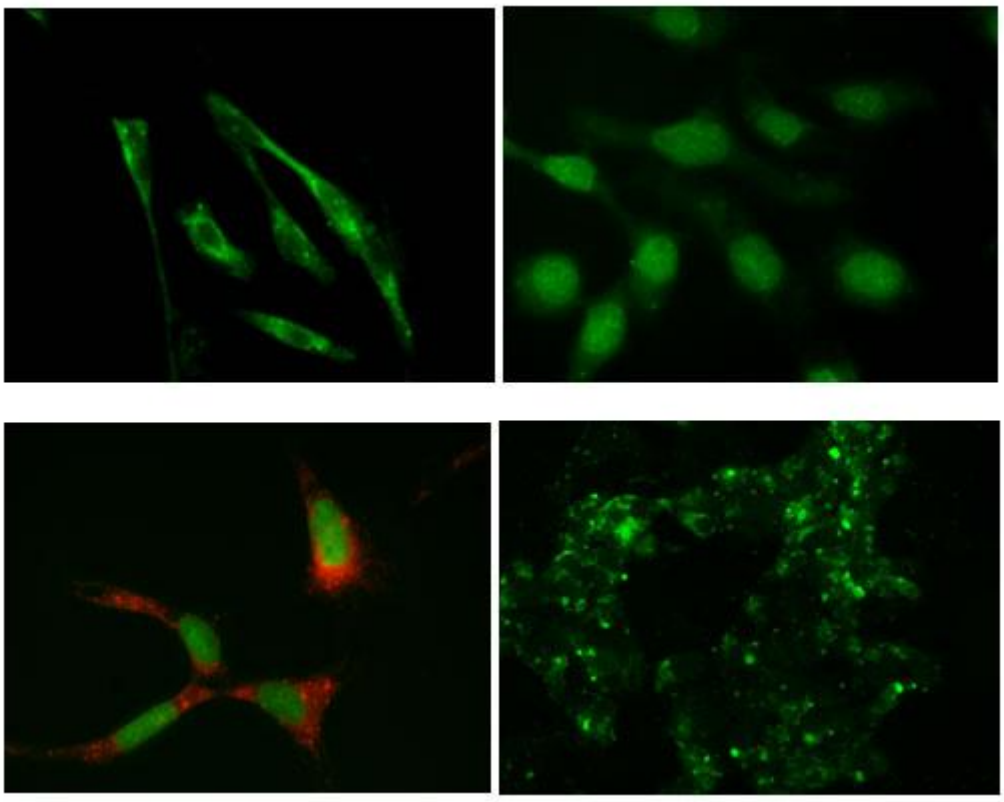
Over the past decade, major advances have been made on development of novel drug delivery systems (NDDS) form plant actives and extracts. Herbal medicines have been widely used all over the world since ancient old ages and have been recognized by physicians and patients for their better therapeutic value as they have fewer adverse effects as compared with modern medicines. Herbal therapeutics can be achieved by Drug Delivery systems. This herbal treatment helps to increase the therapeutic value by reduce the toxicity and side effects of drugs at the same time it also increase the bioavailability. The use of herbal formulations for novel drug delivery systems is more beneficial and has more advantages compared to others. The novel herbal formulations like liposomes, phytosomes, ethosomes microsphere, nanocapsules, transferosomes, polymeric nanoparticles, nanoemulsions and has been reported using bioactive and plant extracts. The main reason behind development of alternative drug delivery is to increase efficiency of drug delivery and safety in drug delivery and provide more convenience to the patient. Distribution, sustained delivery, and protection from physical and chemical degradation. The present work highlights the current status of the development of novel herbal formulations and summarizes their method of preparation, type of active ingredients, size, and entrapment efficiency, route of administration, biological activity and applications of novel formulations.

INTRODUCTION

During past decades, lot of attention has been paid on the improvement of novel drug delivery systems for herbal drugs. Novel herbal drug carriers help in cure of particular disease by targeting the affected area inside a patient's body and transporting the drug to that area. Novel drug delivery system is advantageous in delivering the herbal drug at optimum rate and delivery of drug at the site of action which minimizes the toxicity and enhances bioavailability of the drugs. 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 the drug at molecular level [1]. Herbal drugs are becoming more popular in the modern world for their application to cure variety of diseases with less toxic effects and better therapeutic effects [2]. However some limitations of herbal extracts/ plant actives like instability in highly acidic pH, liver metabolism etc. led to drug levels below therapeutic concentration in the blood resulting in less or no therapeutic effect [3]. Incorporation of novel drug delivery technology to herbal or plant actives minimizes the drug degradation or pre systemic metabolism, and serious side effects by accumulation of drugs to the non targeted areas and improves the ease of administration in the paediatric and geriatric patients. Various novel drug delivery systems such as liposomes, niosomes, microspheres and phytosomes have been reported for the delivery of herbal drugs. Incorporation of herbal drugs in the delivery system also aids to increase in solubility, enhanced stability, protection from toxicity, enhanced pharmacological activity, improved tissue macrophage distribution, sustained delivery and protection from physical and chemical degradation. For example, liposomes act as potential vehicles to carry anti cancer agents by increasing amount of drug in tumour area and decrease the exposure or accumulation of drug in normal cells/tissues thereby preventing tissue toxicity effects [4]. The present article was aimed to provide insight of different types of drug delivery systems incorporating active ingredients and potential advantages of such systems.

e-ISSN:2347-7857
p-ISSN:2347-7849

Figure 1: Herbal Nanoparticle



Need For Novel Drug Delivery System for Herbal Drugs

Before reaching to the blood, many constituents of the herbal drugs will be smashed in the highly acidic pH of the stomach and other constituents might be metabolized by the liver. Resultant, the optimum quantity of the herbal drugs may not reach the blood. If the drug does not reach in the optimum amount to the infected region at "minimum effective level," then there will be no means to show the therapeutic effect of the drug. Nanocarriers applying to herbal remedies will carry optimum amount of the drug to their site of action bypassing all the barriers such as acidic pH of stomach, liver metabolism and increase the prolonged circulation of the drug into the blood due to their small size [5].

Advantages of Nanotechnology Based Dosage Forms

Nano-sized delivery system was selected because of the following reasons [5]:

- They appear to be able to deliver high concentrations of drugs to disease sites because of their unique size and high loading capacities.
- Deliver the drug in the small particle size that enhances the entire surface area of the drugs allocating quicker dissolution in the blood.
- The concentration seems to persist at the sites for the longer periods. Shows EPR (enhanced permeation and retention) effect, i.e., enhanced permeation through the barriers because of the small size and retention due to poor lymphatic drainage such in tumor.
- Exhibits passive targeting to the disease site of action without the addition of any particular ligand moiety.[5]
- Decrease in the side effects.
- Decrease in the dose of the drug formulation.

Types of Novel Herbal Drug Delivery Systems

Phytosome

Phytosomes are phospholipids-based drug delivery system has been found promising for herbal drug delivery. Complexing the polyphenolic phytoconstituents in the molar ratio with phosphatidyl choline results in a new herbal drug delivery system, known as "Phytosome". It is the phytolipids delivery system which forms a bridge between the convectional delivery system and novel delivery system. The term Phytosome relates to "phyto", which

means plant; while “some” means cell-like. Phytosomes are advanced forms of herbal products that are better absorbed, utilized to produce better results than those produced by conventional herbal extracts. Phytosomes show better pharmacokinetic and therapeutic profiles than conventional herbal extracts. Phytosomes are prepared by complexing the polyphenolic phytoconstituents in the ratio of 1:2 or 1:1 with phosphatidyl choline. Most of the phytosomal studies are focused on Silybum marianum, which contains premier liver-protectant flavonoids. The fruit of the milk thistle plant (S. marianum, family: Asteraceae) contains flavonoids known for their hepatoprotective effects [2].

The Phytosome protects herbal extract components from destruction in digestive secretions and gut bacteria by forming little cell, which is capable of being transferred from a hydrophilic environment into the lipid-friendly environment of the enterocyte cell membrane and finally reaching blood. Various Phytosome herbal formulations are shown in Table 1.

Table 1: Herbal phytosome formulation

Active ingredients	Biological activity	Applications of phytosome formulations	References
Quercetin	Antioxidant activity	Enhanced therapeutic efficacy	[5]
Oxymatrine	Anti-viral	Improvement of bioavailability	[6]
Ginkgo biloba	Cardioprotective, anti-asthmatic and anti-diabetic	Induced hepatoprotective effect	[7]
Marsupium	Anti-viral	Increase in bioavailability	[8]
Embelin	Antibacterial and anti-fertility activities	Increase in solubility	[9]
Naringenin	Anti-inflammatory, anti-carcinogenic and anti-tumour effects	Increase in bioavailability; prolong the duration of action	[10]
Silybin	Hepatoprotective and antioxidant	Increase in therapeutic effect	[11]

Advantages of phytosome formulation

- It is able to permeate the hydrophilic botanical extract to be better absorbed in intestinal lumen.
- Phytosome increases the absorption of active constituents, so its dose size required is small.
- There is appreciable drug entrapment and improvement in the solubility of bile to herbal constituents, and it can target the liver.
- In Phytosome, chemical bonds are formed between phosphatidylcholine molecules, so it shows good stability.
- Phytosome improves the percutaneous absorption of herbal phytoconstituents [3,4].

Liposomes

Liposomes are concentric bi-layered vesicles in which aqueous volume is entirely enclosed by a membranous lipid bi-layer mainly composed of natural or synthetic phospholipids. The liposomes are spherical particles that encapsulate the solvents which are freely floating in the interior. Liposomes are constructed of phospholipids, which are amphipathic molecules as they have both hydrophobic tail and hydrophilic polar head as shown in Figure 1. [12] The polar end is composed of molecules, is phosphoric atom-bound to a water soluble molecule.

Liposomes can encapsulate both hydrophilic and lipophilic materials. Liposome has properties that enable it to enhance the ingredient solubility, bioavailability, bio-distribution, altered pharmacokinetics and in vitro and in vivo stability. Liposome drug delivery systems can enhance the therapeutic efficacy of drugs[13] — in this connection, to improve the bioavailability of silymarin through its incorporation in a stable liposomal buccal dosage form, using commercially available soybean lecithin. A variety of herbal liposomal formulations have been studied, which are summarized in Table 2.

Advantages of liposome formulation

- Liposome is used for drug delivery systems due to its unique structural properties.
- Liposome can carry both the hydrophobic and hydrophilic drug. Therefore, liposome as a drug carrier can indiscriminately deliver drugs through the cell membrane.
- Liposome herbal therapy acts as a carrier for small cytotoxic molecules and as vehicle for macromolecules as gene.
- Liposome formulation can produce sustained and controlled release of formulation and enhances the drug solubility.

e-ISSN:2347-7857
p-ISSN:2347-7849

Table 2: Herbal liposomal formulations

Active ingredients	Biological activity	Applications of liposome formulations	References
Magnolol	Inhibiting vascular smooth muscle cells (VSMCs) proliferation	Enhance the therapeutic efficacy	[14]
Nux vomica	Anti-tumour, analgesic and anti-inflammatory	Activities Increase stability of formulations	[15]
Quercetin	Antioxidant activity	Enhance therapeutic efficacy	[16]
Diospyrin	Anti-cancer activity	Enhancement of its anti-tumour effect	[17]
Myrtus communis	Antioxidant and antimicrobial activity	Increase in its activities	[18]
Artemisia arborescens	Antiviral activity	Increase in antiviral activity and stability	[19]
Puerarin	Anti-arrhythmia Activity	These formulations modify their surface charge and membrane integrity	[20]

Nanoparticles

Nanoparticles are nano- or sub–nano-sized structures composed of synthetic or semi-synthetic polymers. In recent times, nanoparticles of herbal medicines have attracted much attention. Nanoparticles are colloidal systems with particles varying in size from 10 nm to 1000 nm. It is an effective system as the formulation is encapsulated in it easily and can easily reach the effective site. The nanospheres are the solid-core spherical particulates which are nano-metric in size. They contain drug embedded in the matrix or absorbed onto the surface; and the nanocapsules have a vesicular system, in which the drug is essentially encapsulated within the central volume surrounded by embryonic continuous polymeric sheath [21]. The nanoparticulate system of formulation shows advantage, as its solubility is increased and the drug can reach the target site, as compared to other systems. Microencapsulation of herbal extract in nanopaticulate is an effective way used to protect drug or food ingredients against deterioration, volatile losses, or premature interaction with other ingredients. The advantages of the nanoparticle are that it improves the absorbency of the herbal formulation, reduces the dose of formulation and increases its solubility.[22] Various nanoparticle herbal formulations are summarized in Table 3.

Advantages of herbal nanoparticle delivery system

- Nanoparticulate system delivers the herbal formulation directly to the site of action.
- Encapsulating drugs within nanoparticles can improve the solubility and pharmacokinetics of drugs.
- Nanoparticles can also reach the choice of formulations, promote the drugs through the biological barriers and increase the bioavailability of drugs.
- It can take the drug directly to the site of action without destroying surrounding environment.

Table 3: Herbal nanoparticulate formulations

Active ingredients	Biological activity	Applications of nanostructure formulations	References
Berberine	Anti-neoplastic activity	*H. pylori* growth inhibition	[23]
Quercitrin	Antioxidant	Better therapeutic for intestinal anti-inflammatory	[24]
Hypocrellins	Antiviral activity	Improved performance in both stability and hydrophilicity	[25]
Silybin	Anti-hepatotoxic activity	Shows sustained release and targeting system	[26]
Ginseng	Antioxidant activity	Improvement in stability and improvement in its action	[27]
Radix salvia miltiorrhiza	Anti-angina activity	Improve bioavailability	[28]
Paclitaxel	Anti-tumour activity	Show sustained release	[29]

Emulsions

Emulsion is a biphasic system in which one phase is intimately dispersed in the other phase in the form of minute droplets ranging in diameter from 0.1 µm to 100 µm. In emulsion, one phase is always water or aqueous phase, and the other phase is oily liquid, i.e., non-aqueous. Among them, the micro-emulsion is also called nanoemulsion, and the sub–micro-emulsion is also called lipid emulsion. Emulsion drug delivery system is targeted or distributed well due to affinity to lymph. Micro-emulsions are solutions containing nanometre-sized droplets of an immiscible liquid dispersed in an aqueous buffer. The droplets are coated with a surfactant to reduce the surface tension between the two liquid layers. Micro-emulsion (ME) is a clear, thermodynamically stable, isotropic mixture of oil, water and surfactant, frequently in combination with a co-surfactant.

e-ISSN:2347-7857
p-ISSN:2347-7849

In addition, emulsions produce targeted sustained release, improve the penetrability of drugs into the skin and mucous and reduce the drugs' stimulus to tissues. Various emulsionbased herbal formulations are shown in Table 4.

Table 4: Herbal emulsion formulations

Active ingredients	Biological activity	Applications of emulsion formulations	References
Azadirachta indica	Acaricidal, anti-fungal, antibacterial activities	The formulation has low toxicity	[31]
Matrine	Antibacterial, anti-, inflammatory anti-viral	Sustained-release formulation	[32]
Berberine	Anti-neoplastic activity	Sustained-release formulation	[33]
Rhubarb	Cathartic and laxative activity	Analysis of nine anthraquinones and bianthrones in rhubarb	[34]
Docetaxel	Anti-cancer activity	Increase in the residence time	[35]
Quercetin	Antioxidant	Enhance penetration into stratum corneum and epidermis	[36]
Silybin	Hepatoprotective	Sustained-release formulation	[37]

Advantages of emulsion-based formulations

- It 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.
- As a result of the lipophilic drugs being made into o/w/o emulsion, the droplets of oil are phagocytosised by macrophages and increase its concentration in liver, spleen and kidney.
- As the emulsion contains herbal formulation, it will increase the stability of hydrolyzed formulated material and improve the penetrability of drug into skin and mucous. The new type, viz., Elemenum emulsion, is used as an anti-cancer drug and causes no harm to the heart and liver [30].

Microsphere

Microsphere comprises of small spherical particles, with diameters in the micrometer range, typically 1 μm to 1000 μm (1 mm). Microspheres are sometimes referred to as micro-particles. Microspheres can be manufactured from various natural and synthetic materials. Glass microspheres, polymer microspheres and ceramic microspheres are commercially available. Microspheres are classified as biodegradable or non-biodegradable. Biodegradable microspheres include albumin microspheres, modified starch microspheres, gelatine microspheres, polypropylene dextranmicrospheres, polylactic acid microspheres, etc. According to the current literature reports on non-biodegradable microspheres, polylactic acid is the only polymer approved to be used by people, and it is used as a controlled-release agent. Solid and hollow microspheres vary widely in density and therefore are used for different applications. Hollow microspheres are typically used as additives to lower the density of a material. In addition, reports on immune microsphere and magnetic microsphere are also common in recent years. Immune microsphere possesses the immune competence as a result of the antibody and antigen being coated or adsorbed on the polymer microspheres [38]. Various herbal microsphere formulations are shown in Table 5.

Table 5: Microsphere herbal formulations

Active ingredients	Biological activity	Application of microsphere formulations	References
Ginsenoside	Anti-cancer activity	To enhance solubility and stability	[39]
Quercetin	Antioxidant and anti-inflammatory activities	Enhancing its bioavailability and sustain release theformulation	[40]
Zedoary oil	Hepatoprotective	Sustained-release and higher bioavailability	[41]
Rutin	Cardiovascular and cerebrovascular diseases	Targeting into cardiovascular and cerebrovascular regions	[42]

Advantage of microsphere formulation

- Administration of medication via micro-particulate system is advantageous because microspheres can be ingested or injected, and they can be tailored for desired release profiles and used for site-specific delivery of drugs and in some cases can even provide organtargeted release.
- Drug can be easily released from the formulation.

- It can protect the specific function of drugs, and can release the drugs into an outer phase for a long period.

Ethosome

Ethosomes are phospholipids-based elastic nano-vesicles having high content of ethanol (20%-45%). Ethanol is known as an efficient permeation enhancer and has been reported to be added in the vesicular system to prepare the elastic nano-vesicles. Ethosomes were developed as novel lipid carriers composed of ethanol, phospholipids and water and to improve the delivery of various drugs to the skin. It enables drugs to reach the deep skin layers and/ or systemic circulation. Due to high content of ethanol, the lipid membrane is packed less tightly in comparison with conventional vesicles, but it has equivalent stability [43]. For the delivery of diverse group of proteins and peptides molecules, ethosomes are preferable. Drug is administered by ethosomes in the form of gel, cream for patient comfort. Ethosomal herbal formulations are shown in Table 6.

Table 6: Herbal ethosomal formulations

Active ingredients	Biological activity	Application of ethosomal formulations	References
Sophora Alopecuroides	Anti-endotoxic, anti-cancer and anti-inflammatory	Ethosome enhances delivery of drugs through the stratum corneum barrier into the deep layer of the skin	[45]
Matrine	Antibacterial, anti-inflammatory, anti-rheumatism and anti-tumour anti-inflammatory effect	Increase the per cutaneous permeation	[46]

Advantages of ethosomal drug delivery

- Ethosomes enhance transdermal permeation of drug through skin.
- Ethosomes are a platform for the delivery of large amounts of diverse groups of drugs.
- The ethosomal drug is administered in semisolid form, resulting in improved patient compliance [43.44].

Solid lipid nanoparticles

It is a technique developed in the 1990s. It is a colloidal carrier used especially for the delivery of lipophilic compounds. It is prepared by different methods — the homogenization and the warm micro-emulsion. The average mean size of solid lipid nanoparticles ranges from 50 nm to 1000 nm. Solid lipid nanoparticles are composed of lipid matrix, which becomes solid at room temperature and also at the body temperature [47]. The main features of solid lipid nanoparticles (SLNs) with regard to parenteral application are the excellent physical stability, protection of incorporated labile drugs from degradation. To cross bloodbrain barrier, it should be made for selection of lipids and surfactants. The SLNs are prepared by different methods such as homogenization and the warm micro-emulsion high-speed stirring ultrasonication and solvent-diffusion method. Lipids show compatibility with lipophilic drugs and increase the entrapment efficiency and drug-loading into the SLN [48]. A variety of SLN herbal formulations are shown in Table 7.

Table 7: SLN herbal formulations

Active ingredients	Biological activity	Applications of SLN herbal formulations	Reference
Curcumin	Anti-tumour, antioxidant and anti-inflammatory	activities Increase in stability	[49]
Curcuminoids	Anti-malarial activity	Increase in activity	

Advantages of SLN herbal formulation

- It provides controlled release and site-specific drug targeting.
- Large-scale production can be done.
- In this formulation, both lipophilic and hydrophilic drugs can be loaded.
- Another advantage is that it is made of lipid matrix (physiological lipids), which decreases danger of chronic and acute toxicity.

CONCLUSION

Herbal medicine is globally accepted as a alternative system of therapy in the pharmaceuticals . But the drug delivery system for herbal drugs is quite traditional and out of date. An extensive research is going on in the

area of novel drug delivery and targeting for plant actives and extracts. However, research in this area is still at the exploratory stage. A number of plant constituents like flavonoids, tannins, terpenoids etc. showed enhanced therapeutic effect at similar or less dose when incorporated into novel drug delivery vesicles as compared to conventional plant extracts. Hence, there is a great potential in development of novel drug delivery system for valuable herbal drugs as it provides efficient and economical drug delivery. Also, the trend of incorporating NDDS for herbal drugs has also been adopted at industrial scale.

REFERENCES

1. Biju SS, Talegaonkar S, Mishra PR, Khar RK. Vesicular system: an overview. Indian J Pharm Sci. 2006; 68(2): 141-153.
2. Atmakuri LR, Dathi S. Current trends in herbal medicines. J Pharm Res. 2010; 3(1):109-113.
3. Uhumwangho MU, Okor RS. Current trends in the production and biomedical applications of liposomes: a review. J Biomed Sci. 2005; 4: 9-21.
4. Yadav D, Suri S, Choudhary AA, Sikender M, Hemant, Beg NM, et al. Novel approach: Herbal remedies and natural products in pharmaceutical science as nano drug delivery systems. Int J Pharm Tech. 2011;3:3092-116.
5. Kuntal M, Mukherjee K, Ahamed H. Enhanced therapeutic benefit of Quercitin- phospholipid complex in carbon tetrachloride induced acute liver injury in rats: A comparative study. Iran J Pharmacol Ther. 2005;4:84-90.
6. Yue PF, Yuan HL, Li XY, Yang M, Zhu WF. Process optimization, characterization and evaluation in vivo of oxymatrine-phospholipid complex. Int J Pharm. 2010;387:139-46.
7. Naik SR, Panda VS. Hepatoprotective effect of Ginkgoselect Phytosome in rifampicin induced liver injury in rats: evidence of antioxidant activity. Fitoterapia. 2008;79:439-45.
8. Sikarwar MS, Sharma S, Jain AK, Parial SD. Preparation, characterization and evaluation of Marsupsin-phospholipid complex. AAPS PharmSciTech. 2008;9:129-37.
9. Pathan R, Bhandari U. Preparation and characterization of embelin-phospholipid complex as effective drug delivery tool. J Incl Phenom Macrocycl Chem. 2010.
10. Semalty A, Semalty M, Singh D. Supramolecular phospholipid polyphenolics interection: The phytosome strategy to improve the bioavailabilty of phytochemicals J Incl Phenom Macrocycl Chem. 2010;67:253-60.
11. Kidd P, Head K. A review of the bioavailability and clinical efficacy of milk thistle phytosome: a silybin-phosphatidylcholine complex (Siliphos). Altern Med Rev. 2005;10:193-203.
12. JuQun XI, Guo R. Studies on molecular interection between puerarin and pc liposome. Chinese Sci Bull. 2007;52:2612-7.
13. Ajazuddin, Saraf S. Applications of novel drug delivery system for herbal formulations. Fitoterapia. 2010;81:680-9.
14. Chen C. Inhibiting the vascular smooth muscle cells proliferation By EPC and DPPC liposome encapsulated magnalol. J Chin Inst Chem Eng. 2008;39:407-411.
15. Chen J, Chen Z, Wang W. Ammonium sulphate gradient loading of brucine into liposome: effect of phospholipid composition on entrapment efficiency and physicochemical properties in vitro. Drug Dev Ind Pharm. 2010;36:245-253.
16. Ghosh D, Ghosh S, Sarkar S, Ghosh A, Das N, Das Saha K, et al. Quercetin in vesicular delivery systems: evaluation in combating arsenic-induced acute liver toxicity associated gene expression in rat model. Chem Biol Interact. 2010;186:61-71.
17. Hazra B, Kumar B, Biswas S, Pandey BN, Mishra KP. Enhancement of the tumour inhibitory activity, in vivo, of diospyrin, a plantderived quinonoid, through liposomal encapsulation. Toxicol Lett. 2005;157:109-17
18. Gortzi O, Lalas S, Chinou L. Re-evaluation of bioactivity and antioxidant activity of myrtuscommunis extract before and after encapsulation in liposome. Eur Food Res Technol. 2008;226:583-90
19. Fadda AM, Sinico C, Lai F, Logu AD. Liposomal incorporation of artimisia arborescenceL. Essential oil and in vitro antiviral activity. Eur J Pharma Biopharma. 2005;59:161-8.
20. Rong G, JuQun X. Studies on molecular interection between puerarin and PC liposomes. Chinese Sci Bull. 2007;52:2612-7
21. Vyas SP, Khar RK. Targeted and controlled drug delivery novel carrier systems. Edn -IInd, CBS publishers and distributors, N. Delhi: 2002. p. 15-6, 346-8.
22. Prabhu N, Gowari K, Raj D. Synthesis of silver phyto nanoparticles and their antibacterial activity. Digest.J.Nano. Biostructure.2010;5:185-189
23. Chang CH, Huang WY, Lai CH, Hsu YM, Yao YH, Chen TY, et al. Development of novel nanoparticles shelled with heparin for berberine delivery to treat Helicobacter pylori. Acta Biomater. 2011;7:593-603.
24. Kumari A, Yadav SK, Pakade YB, Kumar V, Singh B, Chaudhary A, et al. Nanoencapsulation and characterization of Albizia chinensis isolated antioxidant quercitrin on PLA nanoparticles. Colloids Surf B Biointerfaces. 2011;82:224-32
25. Wang F, Zhou L, Gu F. Characterization of anticancer hypocrellin A encapsulated with silica nanoparticles. J Therm Anal Calorim. 2010;102:69-74

26. Jia L, Zhang D, Li Z, Duan C, Wang Y, Feng F, et al. Nanostructured,lipid carriers for parenteral delivery of silybin: Biodistribution and pharmacokinetic studies. Colloids Surf B Biointerfaces. 2010;80:213-8.
27. Leonard K, Ahmmad B, Okamura H, Kurawaki J. In situ green synthesis of biocompatible ginseng capped gold nanoparticles with remarkable stability. Colloids Surf B Biointerfaces. 2011;82:391-6
28. Fu ZY, Zhang JY, Wang WM, Wang H. Microencapsulation of radiax saliva miltiorrhiza nanoparticles by spray drying. Powder Technol. 2008;184:114-21
29. Xu HW, Fang Q, Wang JS, Wang PM. Study on preparation of paclitaxel loaded PEG-PLGA nanoparticles in vitro experiment. China Hospital Pharmacy Journal. 2008;28:11-4.
30. Cui F, Wang Y, Wang J, Feng L, Ning K. Preparation of an entericsoluble solid-state emulsion using oily drugs. Int J Pharma. 2007;338:152-6.
31. Sun HW, Ouyang WQ. The preparation of neem oil microemulsion (Azdirachta Indica) and the comparission of acaricidal time between neemoil microemulsion and other formulation in vitro. J Shanghai Jiao Tong Univy (Agric Sci.) 2007;1:60-5.
32. Sun SW, Yeh PC. Analysis of rhubarb anthraquinones and bianthrones by microemulsion electrokinetic chromatography. J Pharma Biomed Ana. 2005;36:995-1001
33. Ruan J, Liu J, Zhu D, Gong T, Yang F, Hao X, et al. Preparation and evaluation of self-nanoemulsified drug delivery systems (SNEDDSs) of matrine based on drug-phospholipid complex technique. Int J Pharma. 2010;386:282-90.
34. Vicentini FT, Simi TR, Del Ciampo JO, Wolga NO, Pitol DL, Iyomasa MM, et al. Quercetin in w/o microemulsion: In vitro and in vivo skin penetration and efficacy against UVB-induced skin damages evaluated in vivo. Eur J Pharm Biopharm. 2008;69: 948-57
35. Cui F D, Yin Y,Choi M K,Chung S. Docetaxel microemulsion for enhanced bioavailability: Preparation and in vitro and in vivo evalution. J Cont Rel. 2009; 140: 86-94
36. Wong HL, Bendayan R, Rauth AM, Li Y, Wu XY. Chemotherapy with anticancer drugs encapsulated in solid lipid nanoparticles. Adv Drug Deliv Rev. 2007;59:491-504.
37. Muller RH, Wissin SA. Encycbpedia Nanosci Nanotechnol. 2004;10:42-56.
38. Scarfato P, Avallone E, Iannelli P, Aquino RP. Qucertin microsphere by solvent evaporation: preparation characterization and release behaviour J Appl Polymer Sci. 2008;109:2994-3001
39. Cheng-Bai, Di Z, Xia C, Dan J. Preparation and characterization of biodegradedable polylactide microsphere encapsulating Ginsenoside Rg3 Chem Res Chinese Univ 2008;24:588-91
40. Natrajan V, Madhan B, Sehgal P. Formulation and evalution of qucertin polycaprolactone microsphere for the treatment of Rheumatoid arthritis. J Pharm Sophora Alopecuroides Sci.2010;100:195-205
41. Han X, Wang S, Yang L. Study of the preparation of sustained release microsphere containing zedoary turmeric oil by the emulsion solvent diffusion method and evalution of the self emulsification and bioavailability of oil. Colloids Surf B. 2006; 48:35-41
42. Xio L, Zang Y H, Jin X H. Preparation of floating rutin aliginate chitosan microsphere. Chinese Trad Herbal Drugs. 2008;3:209-212
43. Touitou E. Godin B. Ethosome novel vesicular carrier for enhanced delivery: characterization and skin penetration properties. J Cont Rel. 2000;3:403418
44. Zhou Y, Wei Y, Liu H, Zhang G, Wu X. Preparation and in vitro evaluation of ethosomal total alkaloids of Sophora alopecuroides loaded by a transmembrane pH-gradient method. AAPS PharmSciTech 2010;11:1350-8
45. Zhaowu Z, Xiaoli W, Yangde Z, Nianfeng L. Preparation of matrine ethosome, its percutaneous permeation in vitro and anti-inflammatory activity in vivo in rats. J Liposome Res. 2009;19:155-62.
46. Zhaowu Z, Xiaoli W, Yangde Z, Nianfeng L. Preparation of matrine ethosome, its percutaneous permeation in vitro and anti-inflammatory activity in vivo in rats. J Liposome Res. 2009;19:155-62.
47. Pople PV, Singh KK. Development and evaluation of topical formulation containing solid lipid nanoparticles of vitamin A. AAPS Pharm Sci Tech. 2006;7:91.
48. Gande S, et al. Pharmacokinetic applicability of a validated liquid chromatography tandem mass spectroscopy method for orally administered curcumin loaded solid lipid nanoparticles to rats. J Chromatogr B Analyt Technol Biomed Life Sci 2010;878:3427-31
49. Nayak AP, Tiyaboonchai W, Patankar S, Madhusudhan B. Curcuminoids loaded lipid nanoparticles: Novel approach to treat malaria treatment. Amsterdam: Elsevier B.V; 2010.