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Potential of Novel Drug Delivery Systems for Herbal Drugs

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ABSTRACT

Recently the use of herbal medicines has been increased all over the world due to their miraculous therapeutic effects and fewer adverse effects as compared to the modern medicines. However, delivery of herbal drugs also requires modifications with the purpose to achieve sustained release, to increase patient compliance etc. Previously herbal drugs could not attract scientists towards the development of novel drug delivery systems due to processing, standardising, extracting and identification difficulties. But now days with the advancement in the technology, novel drug delivery systems opens the door towards the development of herbal drug delivery systems. Novel drug delivery technologies have gained the importance to achieve modified delivery of herbal drugs thereby increasing the therapeutic value as well as reducing toxicity. For last one decade many novel carriers such as liposomes, nanoparticles, phytosomes and implants have been reported for successful modified delivery of various herbal drugs e.g. curcumin, quercetin, silybin, ginkgo etc. The objective of this review article is to summarize various novel drug delivery technologies which have been developed for delivery of herbal drugs, to achieve better therapeutic response.

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Key words: Phytosome, polymeric micelles, ethosomes, curcumin, nanoparticles, novel carriers.

INTRODUCTION

In the past few decades, considerable attention has been focussed on the development of novel drug delivery systems for herbal drugs. Novel herbal drug carriers cure particular disease by targeting exactly the affected zone inside a patient's body and transporting the drug to that area. Novel drug delivery system is advantageous in delivering the herbal drug at predetermined rate and delivery of drug at the site of action which minimizes the toxic effects with the increase in 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 presystemic 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 phytosomal carriers have been studied for effective delivery of herbal extracts of ginseng, ginkgo biloba etc. Direct binding of phosphatidylcholine to herbal extract components led to better absorption characteristics as compared to conventional delivery of herbal extracts. Other vesicular assemblies like microspheres, nanoemulsions, polymeric nanoparticles etc. have been proved beneficial to carry herbal components. The present review article was aimed to provide an overview of different types of drug delivery systems incorporating active ingredients and potential advantages of such systems.

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LIPOSOMES:

Liposomes are biodegradeable, colloidal and spherical vesicles (0.05-5.0 μm in diameter) composed of a bilayer membrane entrapping an aqueous core. Liposome membranes can be composed of naturally-derived

phospholipids with mixed lipid chains and a variation of head groups or of pure synthetic lipids with defined acyl chains and head groups. The phospholipids align themselves side-by-side with their lipophilic heads orienting themselves towards each other. Drugs with widely varying lipophilicities can be encapsulated in the liposomes, either in the phospholipids bilayer, in the entrapped aqueous volume or at bilayer interface. Liposomes usually formed from phospholipids have been used to change the pharmacokinetic profile of not only drugs, but herbs, enzymes etc. Liposomal based drug delivery is advantageous specifically in enhancing the therapeutic index of anti-cancer agents, either by increasing the drug concentration in the tumour cells and by decreasing the exposure to normal cells. Various targeting strategies can be exploited using liposomal drug delivery. A variety of herbal liposomal formulations have been reported for herbal drugs where liposome are able to enhance product performance by solubility enhancement, improving bioavailability, targeting at site of action and prolonged release of drug (Table 1).

Essential oil from rhizomes of *Atractylodes Macrocephala Koidz* has been entrapped into liposomes by using rapid expansion of supercritical solutions (RESS) technique. The rhizome contains the essential oil and their oxide derivatives which are useful for the treatment of various digestive diseases and tumours. Incorporation of oil into liposomes improved the solubility thereby enhancing the bioavailability of the essential oil obtained from *Atractylodes Macrocephala Koidz* with reduction in side effects. Similarily, the antimicrobial activity of essential oil obtained from *O. Dictamnus* has been found to be increased after encapsulation into liposomes[5]. Extracts of *Tripterygium wilfordi* has been incorporated into liposomes by thin film dispersion method, which led to increased stability at suitable temperature and reduced side effects[6]. Quercetin liposomes have been prepared for oral and intranasal delivery by using mixture of egg phosphotidylcholine, quercetin and dispersion in polyethylene glycol. Both of the liposomal formulations showed the increase in anxiolytic and cognitive effects. Reduction in dose as well as increase in the bioavailability was observed with the intranasal liposomes as compared to oral administration. Hence, these proved to be potential systems for delivery of quercetin to the central nervous system[7]. Hybrid liposomes of the silymarin extract were reported for buccal administration using cholesterol and stearyl amine for the treatment of liver disease. The interaction between the silymarin and phosopholipids led to increased permeation thereby increased bioavailability. An increase in mucoadhesion of these liposomal formulations led to the increase in hepatoprotective activity[8].

Liposomes of *Artemisia arborescens L.* essential oil (exhibiting antiviral activity) has been prepared by sonication technique using hydrogenated and non hydrogenated soy phosphotidylcholine. Increase in the stability and antiherpetic activity was observed when liposomes were made using hydrogenated soy phosphotidylcholine[9]. Liposomes have also been used for the topical application of the capsaicin where increase in the skin permeation as well as prolongation of the duration of action was observed with the liposomal formulation[10]. Inclusion of taxanes (antitumor activity) into the liposomes led to decreased tissue related toxicities of the drug with the increase in the efficacy of drug[11].

MICROSPHERES:

Microspheres are spherical particles consisting of size ideally 1-300 μm. Each particle is matrix of the drug dispersed in the polymer and drug is released as a first order process. The polymers used for the fabrication of the microspheres are biodegradable or non biodegradeable. Various polymers have been used for fabrication of these microparticulate carriers such as Albumin, Gelatin, Modified Starch, Polypropylene, Dextran, Polylactic acid and Polylactide- co-glycolide etc. The drug release is controlled by the dissolution and degradation of the matrix. The release is effected by the size,

Table 1: Liposomal herbal formulations and their applications

Name of Bioactive Component/ Plant	Application	Reference
Essential oil from *Atractylodes macrocephala Koidz*	Increase in solubility and bioavailability	5
Essential oil of *O. dictamnus*	Increase in activity	5
Extracts of *Tripterygium wilfordi*	Reduction in side effects	6
Quercetin	Increase in bioavailability and reduction in side effects	7
Silymarin extract	Increase in hepatoprotective activity	8
Essential oil of *Artemisia arborescens L.*	Increase in stability	9
Capsaicin	Increase in permeation as prolongation of action	10
Taxanes	Decrease in toxicity	11

type of matrix and polymer concentration etc[12]. These microparticulate systems are also advantageous as they can be ingested or injected and tailored for desired release profiles. Various methods such as evaporation technique, ionic cross-linking technique have been reported for preparation of mucoadhesive, buoyant microspheres[13-14]. These microparticulate systems are advantageous as they can be ingested or injected, produce sustained release action and site specific delivery. A number of plant ingredients have been microencapsulated for various applications (Table 2). Gastroretentive floating microspheres of silymarin have been reported for sustained delivery of the drug. Prolonged release of drug (12 hours) was achieved in simulated gastric fluid and resulted in increased drug bioavailability as well as patient compliance[15]. Microencapsulation of *Zedoary* turmeric oil into microspheres via emulsion-solvent diffusion has used been used for bioavailability enhancement and sustained release application[16]. Microspheres of turmeric oleoresin were prepared after emulsification by using spray drying technique. The stable emulsion product protected the resin from degradation from light, oxygen, heat and alkaline conditions and showed increased therapeutic effect[17]. Encapsulation of the herbal extracts of *Piper sarmentosumn* was done by absorption with calcium alginate beads and it was found that there is no effect of method of encapsulation on the encapsulation efficiency so the process can be used at industrial scale for the encapsulation of the herbal extracts[18]. Site specific delivery of rutin from its microspheres (rutin-alginate-chitosan) was observed via targeting to cardiovascular and cerebrovascular regions[19]. Oxidised cellulose microspheres containing Camptothecin were prepared by using spray drying process, Oxidised cellulose microspheres have been successfully used to enhance solubility and cytotoxicity of Camptothecin[20].

NANOPARTICLES:

Nanoparticles are the submicron size particles having size range 10 to 1000 nm.The main advantages of the nanoparticles is their stability and long term storage. The particle size and surface characteristics of nanoparticles can be easily modified for controlled and targeted drug delivery[21]. Nanosizing led to increased solubility of components, reduction in the dose via improved absorption of active ingredient. Nanoparticles are efficient delivery systems for the delivery of both hydrophilic and hydrophobic drugs[22]. Some examples of nanoparticulate drug delivery system incorporating herbal ingredients are depicted in Table 3. Controlled and sustained delivery of the paclitaxel nanoparticles is observed with reduction in toxic effects[23]. Curcumin obtained from the rhizomes of turmeric (*Curcuma longa*) has the anticancer activity but it is limited due to its poor aqueous solubility which led to the poor bioavailability. Nanoparticles containing Curcumin was prepared by using

Table 2: Microsphere herbal formulation and their applications

Name of Bioactive component/ Plant	Application	Reference
Silymarin	Sustained release	15
Zedoary turmeric oil	Increase in bioavailability as well sustained release occurs	16
Extract of *Piper sarmentosumn*	Used for industrial scale	18
Rutin	Specific delivery to cardiovascular and cerebrovascular region	19
Campothecin	Significant decrease in dose	20

Table 3: Nanoparticle containing herbal drugs and their applications

Name of Bioactive component/ Plant	Application	Reference
Paclitaxel	Reduction in side effects	23
Curcumin	Increase in solubility	24
Cuscuta chinensis	Increase in solubility	25
Triptolide	Increase in solubility	26
Zedoary turmeric oil	Increased stability and drug loading	27
Quercetin	Increased drug release and antioxidant effect.	28
Taxol	Sustained release	29
Silybinin	Increase in circulation time	30
Paclitaxel and Doxorubicin	Inhibition of resistance	31

the mixture of crosslinked and random copolymers of N-isopropylacrylamide (NIPAAM) with N-vinyl-2-pyrrolidone (VP) and polyethylene glycol monoacrylate (PEG-A). *In vitro* release studies revealed 40% curcumin release in 24 hours in phosphate buffer at physiological pH and no tissue related toxicity was observed even at 20-fold void range of nanoparticles. The dispersion of nanocurcumin in aqueous media proved them as potential carrier for the treatment of the cancer as compared to free drug[24]. *Cuscuta chinensis* is a Chinese drug containing flavonoids and lignins as active ingredients, used for nourishment of liver and kidney. Poor aqueous solubility of active ingredients led to the poor absorption upon oral administration. *C. chinensis* nanoparticles were prepared by using nanosuspension method and compared with *C. chinensis* ethanolic extract for hepatoprotective and antioxidant effects upon oral administration. An oral dose of *C.chinensis* nanoparticles at 25 and 50 mg/kg showed almost similar hepatoprotective activity as that of ethanolic extract of *C. chinensis* at 125 and 250 mg/kg, fivefold reduction in dose was observed with *C.Chinensis* nanoparticles[25]. Triptolide is known for the anti-inflammatory, immunosuppressive, anti-fertility and anti-neoplastic activities. The aqueous solubility of the drug is very poor and it shows some of the undesirable toxic effects. Nanoparticles and microemulsions containing triptolide were prepared and evaluated for anti-inflammatory activity. The solid lipid nanoparticle formulation showed more anti-inflammatory activity than the microemulsion when evaluated in the rat paw oedema model[26]. Nanocapsules of *Zedoary* turmeric oil was found to produce increased hepatoprotective and anticancer effect as they showed improved stability and increased drug loading[27]. Quercetin nanoparticles were prepared by precipitation technique. Increased antioxidant activity was achieved via improved released characteristics of the drug (74 times higher drug release)[28]. Taxol loaded nanoparticles were produced by emulsion solvent evaporation method and enhanced bioavailability and sustained release of drug was observed with nanoparticles[29]. Solid lipid nanoparticles of silibinin were prepared by using hand shaking method. The solid lipid nanoparticles show the hepatoprotective effects as well as increase in the bioavailability due to increase in the circulation time and solubility of the silybinin[30]. Inclusion of paclitaxel and doxorubicin to nanoparticles by using brij 78 surfactant led to the inhibition of p-gp mediated drug resistance and hence increase in the anticancer activity of the drugs[31].

PHYTOSOMES:

Most of the biologically active components of herbal drugs are water soluble e.g. flavonoids, terpenoids etc. However, these are poorly absorbed due to their large molecular size range (limited/no passive diffusion) or due to poor permeability through the lipid membranes resulting in poor bioavailability. Some herbal components in extracts get destroyed in gastric environment, led to low bioavailability thereby limiting the clinical utility of these plant extracts. Complexation with some clinically useful nutrients such as phospholipids substantially improves the bioavailability of these active components. So these water soluble components could be converted into the lipid compatible complexes by using the phospholipids from soy, mainly phosphotidylcholine. These are called as Phytosomes and can easily cross the lipid membranes[32]. Phytosomes led to enhanced solubility of the poorly lipid soluble drugs and increase in the bioavailability was reported due to increased absorption in the GIT[33]. A number of methods have been reported for preparation of the Phytosomes[34-35]. In phytosomes, the complexation of phospholipids and water soluble active plant components involve chemical bond formation and therefore more stable. Whereas in liposomes no chemical bond is formed; phosphatidylcholine molecules simply surrounds the water soluble components. Phospholipids are also employed as natural digestive aids and carriers for water soluble and lipid soluble nutrients[36-38]. Due to improved absorption characteristics, phytosomes are more bioavailable than conventional herbal extracts. A number of phytosomal formulations have been reported for the delivery of poorly lipid soluble drugs like extracts of *Ginkgo biloba*, grape seed, hawthorn, milk thistle, green tea and ginseng[34, 39-41] as shown in Table 4.

TRANSFEROSOMES:

Transferosomes are phospholipid vesicles which act as potential carriers for the transdermal delivery of the drug as they overcome the difficulty of penetration through the stratum corneum and can easily penetrate through the intracellular pores of the skin due to their flexibility[42-43] Increased penetration through stratum corneum results from hydration or osmotic force in the skin. Transferosomes are fabricated by using phospholipids (act as vesicle forming material), surfactant (providing flexibility), alcohol (solvent) and buffering agent (as Hydrating medium)[42]. Capsaicin transferosomes were prepared by the high shear dispersion technique and the penetration of the capsaicin transferosomes was found to be more resulting better topical absorption as compared to pure drug[44]. Curcumin is used as potent anti-inflammatory drug, but it shows poor bioavailability when given orally due to less absorption through GI tract. Transferosomes containing the curcumin gel was prepared and an increase in the permeation was observed when compared with the simple gel through the skin, hence they act as potential carriers for the transdermal delivery of the curcumin[45].Transferosomes of the vincristine sulphate were

prepared by using lecithin and sodium deoxycholate in 70/20 ratio. The in vitro tests showed that they can penetrate at zero order rate through the skin[46]. Colchicine transferosomes were prepared by using hand shaking method. The transferosomal preparation of colchicine prevents from the gastrointestinal side effects associated with oral administration of the colchicine and provides the local, sustained and site specific delivery of the colchicines[47].

ETHOSOMES:

Ethosomes are vesicles composed of phospholipids and high concentration of ethanol. High concentration of ethanol in the vesicles led to enhancement in their permeability through the skin by fluidising the lipid domain of the skin. These carriers can penetrate through the skin deeply leading to improved drug delivery into deeper layers of skin and even into blood circulation. These features make them as efficient carriers for topical as well as transdermal route. They can be formulated by hot and cold methods and can be used for both lipophilic as well as hydrophilic drugs. Ethosomes has been reported for transdermal delivery of the hydrophilic and impermeable drugs such as minoxidil, testosterone, bacitracin and cannabidol[48-49]. Ethosomal suspensions of the ammonium glycyrrhizinate (Table 5) was prepared for the dermal administration and used for the treatment of the inflammatory diseases of the skin. The ethosomal suspension showed no toxicity when applied for 24 hours (dermal) and was found to be safe for the use. The increased permeability of the drug via ethosomal preprations led to increase in the bioavailability of the drug as compared to the ethanolic solution of the drug[50]. Ethosomes of the Triptolide were prepared for topical delivery of the triptolide and evaluated in the rat model of erythema. The ethosomal formulation showed an increase in bioavailability due to increase in the accumulation and reduction in erthema more rapidly as compared to the other formulations[51]. Ethosomes of alkaloids of *Sophora alopencerides* were prepared by transmembrane pH gradient technique. The ethosomal formulations led to increase in the permeability through the stratun corenum and are useful for topical delivery of alkaloids[52].

NANOEMULSIONS/ MICROEMULSIONS:

Nanoemulsions and Microemulsions are the emulsions of O/W type having the size range of several microns. They are prepared by using the surfactants which are considered safe for the human use and approved by the FDA. These types of emulsions have higher surface area and hence can easily penetrate through the skin. They are also non toxic and non irritant in nature and can be used in the animals and veterinary purpose[53].Nanoemulsions can be prepared by the high pressure homogenization and microfluidisation technique[54-57]. Nanoemulsions have been reported for the delivery of drugs to cell culture, cancer therapy and as disinfectants[58-59].

Table 4: Phytosomal Herbal Products

Phytosomes	Source	Use
Silybin Phytosomes	Silybin flavonoids from *Silybium marianum*	Hepatoprotective, antioxidant for liver
Ginkgo Phytosomes	Ginkgo flavoinoids from *Ginkgo biloba*	Protects brain and vascular linings.
Ginseng Phytosomes	Ginsenosides from *Panax ginseng*	Nutraceutical and immunomodulator
Green Tea Phytosomes	Epigallocatechin from *Thea sinensis*	Anti cancer, Nutraceutical
Grape Seed Phytosomes	Procyanidins from *Vitis vinifera*	Nutraceutical, systemic antioxidant, cardio protective.
Olive oil phytosomes	Polyphenols from *Olea europaea* oil	Antioxidant, anti-inflammatory

Table 5: Herbal Transferosomal and ethosomal formulations

Name of Bioactive component/ Plant	Application	Reference
Capsaicin Transferosomes	Increased skin penetration	44
Curcumin Transferosomes	Increased skin penetration	45
Vincristine Transferosomes	Increase in permeability	46
Colchicine Transferosomes	Reduction in GIT side effects	47
Ammonium Glycyrrhizinate ethosomes	Increased drug permeation through dermis.	50
Triptolide	Increase in Bioavailability	51
Sophora alopencerides	Increase in Permeability	52

Curcumin which is used as anti-inflammatory drug have poor solubility when given orally. To increase the oral absorption of the curcumin self microemulsifying drug delivery system was formulated using the surfactant, cosurfactant and ethyl oleate. The increase in the oral absorption of curcumin was observed with the self microemulsifying drug delivery system as compared to the simple emulsion[60]. Self nanoemulsified drug delivery system (SNEDDS) was developed for the delivery of the ubiquinone which is based upon the eutectic properties of the drug. This system led to increase in the solubility thereby enhancing the bioavailability of drug as well as decrease in the precipitation of the drug in the vehicle[61]. Microemulsion and Nanoemulsion formulations for various herbal bioactives have been reported and depicted in Table 6.

POLYMERIC MICELLE FORMULATIONS:

Micelles exhibit easily controllable and good pharmacological properties so they can be used to carry a number of drugs[62-63]. Micelles consists of an inner hydrophobic core capable of solubilizing lipophilic substances and an outer hydrophilic corona which serves as the stabilizing interface between the internal hydrophobic core and external aqueous environment[64]. Polymeric micelles consist of hydrophobic core stabilized by the hydrophilic polymer chains exposed to the aqueous environment. The size of the polymeric micelles ranges from 10-100 nm[65]. Polymeric micelles have been reported for the delivery of the poorly soluble herbal drugs. Artemisinin from *Artemisia annua L.* and Curcumin from the roots of *Curcuma longa L.* are used as antimalarial drugs, but these are poorly soluble drugs. Micelles formulations of these drugs with sodium dodecyl sulphate led to 25 fold increase in solubility of these drugs[66].The polymeric micellar formulation of paclitaxel led to increase in the solubility of the drug. The micellar formulation of paclitaxel has been used for the treatment of LNcap prostate tumours[67].

TRANSDERMAL SYSTEMS*:*

Transdermal drug delivery devices are the polymeric formulations which are applied over the skin and deliver the drug at predetermined rate and for predetermined time. This is the non-invasive route of drug administration; the drug present in the formulation permeates into the systemic circulation by diffusion to stratum corneum and further to the effected organ. There are various types of the transdermal delivery devices which can be formulated by using the polymer matrix, adhesive bandage and permeation enhancers. Transdermal delivery system provides the advantage of the controlled drug delivery, enhanced bioavailability, reduction in side effects and easy application[68]. Transdermal drug delivery systems are potentially used for the sustained delivery of the drugs up to several days or even months. Various vesicular systems are also reported for the transdermal delivery of herbal drugs and to increase the penetration and sustained action e.g. transdermal films containing boswellic acid (*Boswellia serrata*) and curcumin (*Curcuma longa*) were formulated for the treatment of inflammation. The combination was used to produce the synergistic action of the drugs. The increase in the efficacy of the drug was observed with the formulation of transdermal films[69-70].

IMPLANTS*:*

These are the polymeric devices which are used for the controlled and sustained delivery of the drugs. These are directly placed in the body fluids/cavities and are fabricated by using biodegradable polymers. A microsurgery is always required for the insertion of these devices[12]. Implants of the extract of danshen (*Radix Salviae Miltiorrhizae*) were developed using the chitosan and gelatin. This drug is used for healing of muscles and tissues in the abdominal cavities. The sustained action was reported with these implants upto 28 days. The wounds and tissues were observed to be healed best with this type of implantable system and also prevented the patient from frequent dosing[71].

MICROPELLETS:

These are the solid particles which fall in the range of 1-1000μm. Controlled release pellets are used for the delivery of drugs to specific sites and for the extended period of time. These are also used for the delivery of the two incompatible

Table 6: Nanoemulsios and Microemulsion formulation of herbal bioactives

Name of the Bioactive component	Target site/ biological activity	Reference
Norcantharidin microemulsion	Liver	76
Puerarin Microemulsion	Cardiovascular and cerebrovascular disease	77
Ligustrazine hydrochloride microemulsion	Intestinal obstruction after abdominal surgery	78
Silybin Nanoemulsion	Liver	79
Berberine Nanoemulsion	Tumor	80
Matrine Nanoemulsion	Anti-bacterial, Anti- inflammatory, anti-virus	81

drugs simultaneously at same or different sites. The main advantage of the pellets is that it prevents dose dumping which occurs with the conventional dosage forms. Pellets are also used for the coating and taste masking of the formulations[72]. Pectin-hydroxypropyl methylcellulose (HPMC) coated curcumin pellets were prepared for delivery of the curcumin in the colon to treat the inflammatory disease. The release rate of the drug was found to be dependent on ratio of the Pectin and HPMC. The drug release from the pellets is induced by the pectinolytic enzymes present in the colon. Therefore, these pellets were used for the delivery of the drug specifically to the colon[73]. Andrographolide (*Andrographis paniculata* wall.) micropellets were prepared by adding sodium alginate into the sodium chloride solution. The micropellets have been found to release the drug away from the upper part of GIT and prevents the GIT irritation problems i.e. vomiting, loss of appetite and nausea[74].

COMPLEXATION*:*

Solubility of the poorly soluble herbal drugs is the major problem in the formulation of appropriate dosage form. An appropriate solubility is must for the achievement of desired therapeutic concentration of the drug in systemic circulation. There are various methods by which solubility of the poorly soluble drugs can be enhanced i.e. solid dispersions, microemulsions, eutectic mixtures and complexation etc. Complexation is the association between the two or more molecules to form a nonbonded entity with a well defined stochiometry. Various complexing agents such as EDTA, cyclodextrins and polymers have been used for the complexation[12]. Curcumin is poorly soluble drug hence its oral use is limited owing to its solubility. The solubility of the Curcumin was increased by the formation of the curcumin soya lecithin complex and evaluated for the hepatoprotective activity. The in vitro permeation study of the complex showed increase in the permeability of the drug leading to greater hepatoprotective activity as compared to the pure curcumin[75].

RECENT PATENTS ON HERBAL CONTROLLED RELEASE FORMULATIONS:

Some of recent patents on controlled release novel herbal formulations are depicted in Table 7. This also illustrates plant actives along with type of dosage form that can be fabricated.

CONCLUSION

Herbal drugs/plant actives possess a lot of therapeutic potential that should be explored via application of novel drug delivery technology. Large molecular size, lipid solubility, degradation in acidic stomach are certain problems which limit the therapeutic activity of these extracts *in vivo* though these possess excellent bioactivity *in vitro*. Application of novel drug delivery systems led to enhanced bioavailability of plant actives by increasing the permeability and solubility as well as reduction in side effects. A number of plant constituents like flavanoids, tannins, terpenoids etc. showed enhanced therapeutic effect at similar or less dose when incorporated into novel drug delivery vehicles as compared to conventional plant extracts. Hence there is great potential in development of novel drug delivery system for valuable herbal drugs as it provides efficient and economical drug delivery and the trends of incorporating NDDS for herbal drugs have also been adopted at industrial scale.

Table 7: Recent patents on novel herbal formulations

US patent No.	Active ingredient	Novel System incorporate	Reference
US 5948414	Opioid analgesic and aloe	Nasal Spray	82
US 6340478 B1	Ginsenosides	Microencapsulated and controlled release formulations	83
Us6890561 B1	Isoflavones	Microencapsulated formulation	84
US6896898 B1	Alkaloids of Aconitum Species	Transdermal delivery system	85
US patent 2005/ 0142232 A1	Oleaginous oil of *Sesamum indicum* and alcoholic extract of Centella asiatica	Brain Tonic	86
US patent 2007/ 0042062 A1	Glycine max containing 7s globulin protein extract, curcumin, *Ginger officinalis*	Herbal Tablet dosage form	87
US patent 2007/ 0077284A1	Opioid analgesic (phenanthrene gp)	Transdermal patch	88
US patent 7569236132	Flavonoids(such as quercetin) and Terpenes (ginkgolide A, B, C and J)	Microgranules	89

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