Role of nanoparticles for production of smart herbal drug—An overview

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Received 28 August 2012; Accepted 8 January 2013

The development of novel herbal delivery system is of considerable importance to overcome various constraints like poor bioavailability, in vivo stability, aqueous insolubility, intestinal absorption and unspecific site of action. In last one decade many novel carriers such as liposome, nanoparticles, phyto-complex have been reported for successful modified delivery of various herbal drugs like paclitaxel, curcumin, quercetin, Ginkgo biloba L., etc. The objective of this review article is to summarize role of nanoparticles for production of smart herbal drugs. Fifteen herbal plant/plant parts/product have been reviewed along with information regarding botanical identity, active ingredient, mechanism of pharmacological activities, drawbacks related with traditional dose, method of their nano-particle production, mode of action of nano-carriers and their efficacy.

Keywords: Herbal Drugs, Nano-particles, Drug delivery systems, Nano-Carriers.

IPC code: Int. cl. (2011.01)− A61K 36/00

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 limited amount of administered dose reaches the target site, while the majority of the drug get distributed throughout the rest of the body in accordance with its physico-chemical and biochemical properties such as low solubility, reduced absorption, rapid metabolism, instability in highly acidic pH conditions and excretion.² Further it’s axiomatic that the smallest capillaries in the body are 5-6 mm in diameter. Thus the therapeutically active agent being distributed in to blood stream must be significantly smaller than 5 mm, without forming aggregates, to ensure that the particles do not form anabolism.³ Novel drug delivery system (NDDS) for herbal medicines includes targeted drug delivery, reduced dose, increased solubility, enhanced absorption, reduced elimination and metabolism of the drug.⁴

NDDS are advantageous in delivering herbal drug at predetermined rate and exhibits site specific action. In novel drug delivery technology, control of drug distribution is achieved by incorporating the drug in carrier system or in changing the structure of drug at molecular level.⁵ Various novel drug delivery system such as liposome, ethosomes, nanoparticle, proniosomes, floating drug delivery system, micro-emulsions have been reported for the delivery of herbal drugs.¹ ⁶⁻⁸ Nano-particulate drug carriers, includes class of particles with a diam. of 10-1000 nm, are drug-loaded particles prepared by taking natural polymer or synthetic chemicals as the carrier. Compared to micrometer size carriers, nanocarriers provide more surface area and have the potential to increase solubility, enhance bioavailability, improve controlled release and enable precision targeting of the entrapped compounds to a greater extent. As a consequence of improved stability and targeting, the amount of material required to exert a specific effect when encapsulated or incorporated to nanocarriers is much less than the amount required when encapsulated. This is particularly useful when dealing with expensive phytomolecules. A timely and targeted...
release improves the effectiveness of phytomolecules, broadens their application range and ensures optimal dosage, thereby improving cost-effectiveness of the product9,10. As a delivery system nanonization are efficient for both hydrophilic and hydrophobic herbal drugs11 and they can be formulated for the lymphatic, brain, arterial walls, lung, liver and spleen system3.

In present paper role of the nano-particles for production of smart herbal drugs, incorporating botanical, medicinal uses of specific drug, factors affecting their efficiency, nano-formulation of such drug and their potential advantages have been discussed.

Paclitaxel
Paclitaxel (PTX, 5β, 20-epoxy-l, 2 α, 4, 7β,10β,13α-hexahydroxytax-1-I-en-9-one, 4,10-diacetate 2-benzoate 13-ester) is a major anticancer drug isolated from the bark of Taxus brevifolia Nutt. (Taxaceae) has anti-neoplastic activity particularly against various types of solid tumours. PTX is approved in many countries for its use as second line treatment of ovarian and breast cancers11. PTX has a unique mechanism of action; it disrupts the dynamic equilibrium within the microtubule system and blocks cells in the late G2 phases and M phase of cell cycle, thereby inhibit cell replication. However, the high lattice energy of paclitaxel results in very limited aqueous solubility (approximately 0.7–30 μg/ml11,12) contributing to only two commercialized dosage forms of injectable paclitaxel [Taxol® and Abraxane®]. Taxol® is 50:50 (v/v) mixture of Cremophor EL (polyethoxylated castor oil) and dehydrated alcohol. Serious side effects, such as hypersensitivity reactions13. In clinical therapy, high doses of anti-histamines and glucocorticoids are co-administered to overcome these adverse effects, but this strategy has raised the possibility of additional pharmacokinetic and pharmacodynamic issues with paclitaxel. To eliminate Cremophor EL from the paclitaxel formulation, many alternative Cremophor EL-free formulations of paclitaxel have been investigated. Abraxane® is one of those Cremophor EL-free paclitaxel formulations and was approved by the FDA in 2005. Despite its improved clinical profile, Abraxane® has not replaced Taxol in cancer chemotherapy, mostly due to its high cost14. Therefore, alternative and cost-effective parenteral formulations of paclitaxel are still needed15.

Incorporation of PTX into nanoparticles enhanced its anti-tumoral activity compared to Taxol®16. In mice, PTX-loaded nanoparticles showed noticeable anti-tumor efficacy and enhanced survival rates, compared to Taxol®. Moreover, nanoparticles can escape from the vasculature through leaky endothelial tissue that surround the tumour and then accumulate in certain solid tumours by the so-called Enhanced Permeation and Retention (EPR) effect17. Nanoparticles were also prepared by interfacial deposition method (nano precipitation)18 and by sequential simplex optimization method15. Paclitaxel nano-particles are stable at 4°C over 3 months thus enhance drug stability, support sustained drug release and improve bioavailability.

Curcumin
Curcumin or diferuloylmethane is a yellow polyphenol extracted from the rhizome of turmeric (Curcuma longa, L.) (Zingiberaceae). It has potent anti-cancer properties as demonstrated in plethora of human cancer cell line and animal carcinogenesis models. Despite considerable promise of being an efficacious and safe compound for cancer therapy and chemoprevention; curcumin has not been embraced by the cancer community as a "panacea for all ills". The vital reason for this reticence is the reduced bioavailability of orally administered curcumin, such that therapeutic effects are essentially limited to the tubular lower GI tract (i.e., colorectum)19, 20. Nanoparticle-based drug delivery approaches have potential for rendering hydrophobic properties of curcumin, thus circumventing the pitfalls of poor solubility. Nanoparticles of curcumin (nano-curcumin) have been prepared by a process based on a wet-milling technique. Unlike curcumin, nano-curcumin is freely dispersible in water in the absence of any surfactants. A principal cellular target of nano-curcumin in cancer cells is activated nuclear factor kappa B (NFκB), with many of the pleiotropic effects of curcumin being ascribed to inhibition of this seminal transcription factor21. NanoCurc™, a recently described polymeric nano-particle formulation of curcumin, has been used to inhibit malignant brain tumor growth through modulation of cell proliferation, survival and stem cell phenotype22, 23.

Quercetin
Quercetin, 3, 3′, 4′, 5′-7-pentahydroxy flavonoid excreted from air dried plant part of Spohora japonica L. (Fabaceae) mainly from bark and leaf. The antioxidant activity of quercetin is higher than well-known antioxidant molecules like ascorbyl, trolox24. It
is abundantly found in varying concentrations in berries between 53 -153 mg/kg of dry weight of plant material. This molecule is an important constituent of wine and its concentration varies from 1 to 33 μM. The antioxidant properties are attributed to number and position of free hydroxyl groups in quercetin molecule. The flavonoid glycosides are rapidly hydrolyzed in small intestine or by bacterial activity in colon to generate quercetin aglycones, which is further, metabolized into glucuronidated or sulfated form of quercetin. This molecule is retained in large intestine for approximately 6h after oral administration. However, it is chemically unstable, especially in aqueous alkaline medium, which possibly involves loss of hydroxyl ions on the C-ring of quercetin. Apart from the antioxidant activity, this molecule also shows anticancer and antiviral activities. In spite of this wide spectrum of pharmacological properties, the use of quercetin in pharmaceutical field is limited due to its low aqueous solubility and instability in physiological medium. These properties of quercetin result in poor bioavailability, poor permeability, instability and extensive fast pass metabolism before reaching the systemic circulation. To improve the aqueous solubility and stability, quercetin-loaded nano-particles with gelation of chitosan with tripolyphosphate anions, poly-D, L-lactide (PLA) nano-particles by solvent evaporation method and by using bovine serum albumin have been prepared.

The nano-encapsulation of quercetin into PLA nanoparticles significantly improves the therapeutic efficacy and bioavailability of this molecule. The in vitro release studies showed that 40–45% quercetin was released within 0–0.5 h showing rapid burst release. This was normally attributed to the fraction of quercetin which was adsorbed close to the surface of the nanoparticles.

**Ginkgo biloba L.**

The leaf extract of *Ginkgo biloba* L. (Ginkgoaceae) has been widely marketed for its brain cell activation properties. However, the existing powder of *G. biloba* extract as such has not shown any remarkable effect for brain cell activation because the granule size and insufficient absorption of active ingredient into the body and plant cell wall is not destroyed. Further it is evident that *G. biloba* contains ginkgolic acid which is a kind of hydrophobic, salicylic acid derivative causing allergy or polyphenolic compound (proanthocyanidin) with water solubility and browning reaction. They must be removed when *G. biloba* extract is used in drugs, food or in cosmetic materials.

*G. biloba* nanoparticles were developed by the combination of dry (gas-phase grinding techniques) and wet processes (liquid-phase grinding techniques). It was demonstrated that extract of *G. biloba* containing nanoparticles increase acetylcholine releasing activity from cerebral cortical synapses and the improvement of stimulation response of hippocampal pyramidal cell. Thus, the nanosized *G. biloba* extract is expected to activate the brain cell and work on the treatment of Alzheimer’s dementia (like loss of memory, thinking, language, judgment, and behavior).

**Breviscapine**

Breviscapine (BVP) is a well-known bioactive flavonoid ingredient (4’, 5,6-tri-hydroxyflavone-7-glucuronide) extracted from whole plant of perennial herb *Erigeron breviscapus* Vant. (Asteraceae) which has therapeutic effect on lung and vascular diseases. Recent pharmacological studies have shown its therapeutic effect on lung and vascular diseases. Breviscapine was useful in inhibiting pulmonary fibrosis, and could reduce the damage due to the oxygen-derived free radicals in bleomycin. *Scutellarin* (4’, 5, 6-tetrahydroxyflavone-7-O-glucuronide), the major active component of breviscapine, prevents vascular endothelial dysfunction in diabetic rats and was capable of inhibiting the proliferation of high glucose and hypoxia-stimulated proliferation of human retinal endothelial cells (HREC), which was possibly related to its ability to suppress the vascular endothelial growth factor (VEGF) expression. *Scutellarin* also inhibited platelet aggregation induced by arachidonic acid (AA), adenosine diphosphate (ADP), and platelet activating factor (PAF).

It is well-known that the cerebrovascular and cardiovascular diseases are chronic, and always need a drug possessing preferable bioavailability and long half-life. However, BVP has very short half-life and poor bioavailability for oral administration. *Scutellarin* has poor solubility in water and can dissolve in ether, chloroform, ethanol, acetic acid and acetone. It is only stable in acidic conditions and rather unstable in alkaline solutions.

The lipid emulsions (LE, oil-in-water emulsions stabilized by lipid surfactants), used as carrier for breviscapine, might improve the chemical stability of
drug, increase drug loading efficiency, decrease irritation on the surrounding tissue as well as control and modify its pharmacokinetics and tissue distribution. Lipid emulsions as particulate drug-carriers can be produced on large industrial scale and sterilized by autoclaving but avoid drug leakage from carriers like liposomes. Nanocoated breviscapine increases plasma concentration and pharmacological activity of breviscapine hence, enhances blood circulation.

**Triptolide**

Triptolide, a diterpenoid triepoxides isolated from extract of whole plant of *Tripterygium wilfordii* Hook. (Celastraceae), which has been reported to be effective in the treatment of variety of inflammatory and autoimmune diseases, especially rheumatoid arthritis. Ethyl-acetate extract of *T. wilfordii* and its component triptolide inhibit transcription of the iNOS gene and this produces its anti-inflammatory effect. However, its clinical use is restricted due to its scarce water solubility and some toxic effects.

Poly(D,L-lactic/glycolic acid) nanoparticles encapsulating triptolide have been reported to produce anti-inflammatory effect in adjuvant induced arthritis in rats. Nano-coated triptolide also exhibited higher anti-inflammatory and higher aqueous solubility compare to their traditional dose.

**Salvia miltiorrhiza L.**

The dried roots of *S. miltiorrhiza* L. (Lamiaceae), commonly known as Danshen, are widely used as medicines for promoting circulation and improving blood stasis. Danshen is extensively used for treatment of coronary heart, cerebrovascular diseases, and hyperlipidemia. Salvanolic acid B regarded as active components of this plant. Slow pharmacological action is the major drawback of this herbal drug. Nano-coated *S. miltiorrhiza* that exhibited stronger antioxidant bioactivities and also the polar active constituent in nanotechnology samples were released faster than the traditionally powdered samples. Phospholipids complex loaded nanoparticles also enhanced oral bioavailability of salvianolic acid.

**Naringenin**

Naringenin (4′, 5, 7-trihydroxyflavanone, NAR), a natural flavonoid aglycone of naringin, is widely distributed in citrus fruits, tomatoes, cherries, grapefruit and cocoa. It is a well-known antioxidant compound and this property attributed to its structure–activity relationship. The number of hydroxyl substitutions of NAR can donate hydrogen to reactive oxygen species thereby allow acquisition of stable structure, and enable scavenging of these free radicals. NAR has also been extensively investigated for its pharmacological activities, including antitumor, anti-inflammatory, and hepato-protective effects. Despite of its excellent free radical scavenging ability and pharmacological activities, clinical studies exploring different schedules of administration of this drug have been hampered by its extreme water insolubility. The absolute bioavailability of NAR was only achieved 4% in rabbits when administered orally.

Novel naringenin-loaded nano-particles (NARN) delivery system using Eudragit® E and polyvinyl alcohol as a carrier was developed by a simple nano-precipitation technique. Nano-particles delivery system considerably improved the physicochemical profile of naringenin and resulted in enhanced drug release. In addition, NARN presented better hepatoprotective effects than NAR on oral administration through enhancement of its antioxidant and anti-apoptotic activities in the CCl4-induced hepatic-toxicity rat model. The nano-precipitation technique possesses numerous advantages, being relatively straight forward, rapid, and offer reproducible particle size with a narrow distribution. NARN has successfully changed several original physicochemical properties of naringenin, including a reduction in particle size, the amorphous rendering of the crystalline structure, and an enhancement in drug release rate.

**Dodder**

*Cuscuta chinensis* Lam. (Convolvulaceae), a parasitic plant which attacks on many valuable crops and trees. Its seeds are commonly used as herbal medicine and food as a tonic for the liver and the kidney. In clinical setting, *C. chinensis* has been used to improve sexual function, prevent senescence, and regulate the immune system. Its other pharmacological activities include anticancer, anti-inflammatory, anti-ageing and immuno-stimulatory effects. The major chemical constituents are flavonoids and lignans. These compounds may be responsible for its pharmacological activities.

Due to poor water solubility of its major constituents such as flavonoids and lignans, its
absorption upon oral administration could be limited. Nano-particles of this plant have been developed by using nano-precipitation method\(^75\). In this method nanonized ethanolic extract of \(C.\) \(chinensis\) seed produce the nano-coated \(C.\) \(chinensis\) (CN). CN is a water soluble nonionic surface-active co-polymers, possessed solubilizing, emulsifier and suspension stabilizer properties with its two hydrophilic polyoxyethylene chains that are connected by a hydrophobic polyoxypropylene chains\(^76,77\). Compare to ethanolic seed extract, CN exhibits higher hepatoprotective and antioxidant effects at lower dose concentration.

**Silymarins**

Silymarins, a group of naturally occurring penta-cyclic triterpenoid compound extracted from the fruit of milk thistle \(Silybum marianum\) \(L.\) (Asteraceae), exhibits remarkable therapeutic effect in of many liver disorders. Silibinin is the main biological active component, which is largely responsible for its antihapatotoxic activity\(^78\). Silibinin and its derivative, dehydroisilybin, inhibit glucose uptake by directly interacting with GLUT4 in 3T3L1 adipocytes\(^79\). It also could form dimmers region selectively through bond formation and tautomerisation\(^80\). Various clinical and pharmacological effects of silymarin have been reported, such as targeting cancer cell metastasis\(^80\) inducing activation of death receptor and mitochondrial apoptotic pathways in human breast cancer MCF7 cells\(^81\). However, silymarin’s poor solubility in water and oil has resulted in permeation through the intestinal epithelial membrane and low absorption in rats’ gastrointestinal tracts\(^82\).

Silymarin loaded solid lipid nano-particles (SlySLNs) was prepared by cold homogenization technique and characterized by using mean diam., entrapment efficiency and drug loading. Under optimal conditions, the prepared SlySLNs has a mean diam. of 190.9 nm, entrapment efficiency of 95.9\%, and drug loading of 8.6\%.\(^83\) Further SLNs composed of stearic acid and surfactant Brij 78 (polyoxyethylene 20 stearyl ether) can incorporate fairly large amounts of silibinin (up to 7.55\%) as colloidal carriers. Silibinin-loaded nano-particles are dispersed in an amorphous state and can be used for parenteral administration\(^84\).

SLNs of various sizes (150, 500 and 1000 nm) prepared by Compritol 888 ATO as the material and silymarin as a model drug investigated to determine the effects of particle size on their oral absorption. It was observed that the AUC of 150 nm SLNs was 2.08 fold higher than that of 500 nm SLNs and 2.54 fold higher than that of 1000 nm SLNs administered orally to rats \((P<0.05)\). The oral bioavailability of 150 nm SLNs was remarkably higher than the other two sizes. Oral bioavailability of SlySLNs in Beagle dogs confirmed that SLN was a good carrier for improving the oral bioavailability of poorly soluble drugs\(^85\).

**Genistein**

Genistein (5, 7, 4’ triatomic isoflavone) is a primary active component of soybean, scoparius and other leguminous plants. It’s a phytoestogen,\(^86\) antioxidant\(^87\) and also decreases risk of osteoporosis, cardiovascular disease, breast and uterine cancer\(^88,89\).

Due to its poor aqueous solubility and low serum level after administration\(^90\), there is need to develop smart drug delivery system for this important isoflavone\(^91\). Various drug delivery systems including self-nano-emulsified system, super-magnetic system and chitosan microspheres have been used to increase the dissolution and bioavailability of genistein. Genistein encapsulated in Fe\(_3\)O\(_4\)-carboxymethylatted chitosan nanoparticles shows greater water solubility than free genistein\(^92\). Genistein nanoparticles by nano-precipitation method with utilizing Eudragit\(^R\) E have been prepared\(^91\).

Eudragit\(^R\) E cationic copolymers widely utilize to improve the solubility of poorly water soluble drugs. It has a basic site containing tertiary amine group which are ionized in gastric fluid. Therefore, it easily dissolves in gastric environment. It was found that genistein-loaded nano-particles possessed higher (241.8\%) relative bioavailability compared to genistein alone\(^91\). There were two mechanism to explain this enhance drug dissolution rate (1) both genistein and Eudragit\(^R\) E are hydrophobic substances, which generated strong affinity between them (2) enhancement of drug dissolution could be attributed to the reduction of particle size, the enhanced hydrophilic properties of the drug when encapsulated in Eudragit\(^R\) E polymer and enhanced wettability at the acidic pH provided by the dissolved Eudragit\(^R\) E. Finally, the hydrophilic and hydrophobic portion of poloxamer penetrates into genistein nano-particles during the nano-precipitation process to form a stable nano-particle delivery system.

**Centella asiatica** \((L.)\) Urban.

A small herbaceous creeping plant, \(C.\) \(asiatica\) \((L.)\) Urban. (Apiaceae) is used as a medicinal herb in
Ayurvedic medicine. It possesses anxiolytic activity$^{92}$. It increases pentobarbitone-induced sleeping time and decreases immobility in the forced swim test$^{93}$. It also elicits anti-anxiety effects in the elevated plus maze$^{94}$. Its aqueous extract was reported to have cognitive-enhancing as well as antioxidant effects in rats$^{95}$. Moreover, it is also used for the treatment of leprosy, wounds, cancer, fever, and syphilis, acne and allergy$^{96}$. The most prominent group of biologically active compounds isolated from C. asiatica are the terpenes, e.g. asiaticoside, madecassic acid, madecassoside and asiatic acid. Asiaticoside is the most abundant triterpene glycoside, which is effective in wound$^{97}$. Several derivatives of asiaticoside and asiatic acid were found to show protective effect against beta amyloid-induced neurotoxicity associated with the dementia of Alzheimer’s disease$^{98}$. Dermatological, extract of C. asiatica has been used in scar management and in cosmetic formulation$^{99}$. The antitumor and cytotoxic properties of the crude extract and partially purified fractions of C. asiatica were also reported$^{100}$. Partially purified extract was more effective on tumor cells than the crude extracts$^{101}$. C. asiatica extract (CAE) possesses high potential biological activities; its clinical usage is limited to some extent due to its poor physical stability. CAE shows high hygroscopicity. The powder extract is promptly liquefied within a few minutes when exposed to normal environment. Therefore, the development of nano-particles which the extract is entrapped inside could lead to significant advantage as the extract is protected from external moisture.

Chitosan-alginate nano-particle of CAE has been prepared by using ionic gelation principle$^{101}$. Nano-capsulation of CAE provided physical stability compared to its non nano-particle form.

**Artemisia annua L.**

A single stemmed annual herb, Artemisia annua L. (Asteraceae) is indigenous to Asia and grows to a height of about 2 m. Artemisinin or qinghaosu is the active principle of A. annua$^{102}$. Artemisinin is an endoperoxide containing sesquiterpene lactone. Despite the potent antimalarial action of ART, it suffers from poor pharmacokinetic properties and short half-lives Artemisinin is chemically unstable and poorly soluble in water or oil$^{103}$. Nano-coated artemisinin by self assembly procedure using polyelectrolyte on natural drug crystals have been developed and these nano-capsules dispersed well in aqueous solutions and hydrophilicity of ART crystals were also improved after encapsulation$^{103}$. 

**Berberine**

Berberine, a naturally occurring isoquinoline alkaloid, is present in the roots, rhizome and stem bark of a number of medicinal plants such as *Berberis vulgaris* L. (Berberidaceae), *Hydrastis canadensis* L. (Ranunculaceae), *Phellodendron amurense* Rupr. (Rutaceae), *Coptis chinensis* Finet & Gagnepain (Ranunculaceae) and *Tinospora cordifolia* Thunb. (Menispermaceae). Berberine has tremendous potential to cure many physiological disorders; hence it has been used in the Ayurvedic, Unani, and Chinese as well as Homoeopathic medicine$^{104}$. Berberine inhibits activator protein 1, a key transcription factor in inflammation and carcinogenesis, in human cell lines$^{105}$ possesses antitumor properties and effectively inhibit cyclooxygenase-2 transcriptional activity in human colon cancer cells$^{106,107}$. Berberine is known to inhibit DNA topo-isomerase II$^{108}$. Moreover, the anti-tumor properties of berberine are now recognized by researchers and clinical oncologists. The effects of berberine on human malignant brain tumor, esophageal cancer and human leukemic and human colon cancer cell lines have been achieved$^{109-111}$. Berberine loaded NPs are successfully prepared using single emulsion, multiple emulsion and ionic gelation methods for sustained drug release.

**Camptothecin**

Camptothecin (CPT) is a cytotoxic quinoline alkaloid isolated from bark and stem of Happy tree (*Camptotheca acuminata* Decne) (Nyssaceae). It has anticancer properties and inhibits DNA enzyme topoisomerase. CPT shows poor aqueous solubility and severe toxicity. To overcome these disadvantages certain analogues of CPT like Topotecan, Lurtotecan, Irrinotecan (CPT-11) and 9-aminocaptothecin (9-AC) were synthesized. These synthetic derivatives have better aqueous solubility, tumor efficiency and lesser toxic effect as compared to camptothecin$^{109,110}$. However, these analogues require larger in quantity to obtain high efficacy and they also exhibits slow pharmacological actions$^{114}$. CPT loaded nanoparticles by using poly (DL-lactic acid) (PLA) and poly (ethylene glycol)-block-poly (propylene glycol)-block-poly (ethylene glycol) (PEG-PPG-PEG)$^{114}$ and by self-assembly method$^{115}$ have been prepared. Compared to traditional drugs
and their derivatives these nanoloaded CPT having high water solubility, high dose retention in body and they also worked at lower concentration.

**Conclusion**

Herbal medicine is the oldest form of health care known to mankind. It is an integral part of the development of modern evaluation. In present review the studied plant/plant parts or their product have been reported or utilized as anticancer, antioxidant, anti-anxiety, anti-malarial, liver and kidney tonic and also for cardiovascular diseases. These medicinal properties attributed by metabolites like savianolic acid B, triptolide, ginkolic acid, isoquinoline alkaloid, silbinin and paclitaxol, etc. However, many herbal drugs possessed poor aqueous solubility, physical instability, low absorption, lower bioavailability and slow pharmacological actions. To overcome these disadvantages, drug delivery systems that contain nanocarriers have been developed. Nano-coating herbal drug were produced by using various methods like homogenization technique, sequentional simplex optimization, solvent evaporation method and wet and dry precipitation technique etc. Because of their small size and high surface area to volume ratio, nanoparticles drug carriers improves pharmacokinetic and bio-distribution of surface modification polymeric nanoparticles. Asparagus racemosus L., etc.

**References**


Enhanced the oral bioavailability of savianolic acid B by physicochemical properties and the hepatoprotective effects of naringenin in orally administered rats with CCl\textsubscript{4} induced acute liver failure, Pharm Res, 2008, 26, 893-902.

Comparison of metabolic pharmacokinetics of naringin and naringenin in orally administered rats with CCl\textsubscript{4} induced acute liver failure, Pharm Res, 2008, 26, 893-902.

Enhanced the oral bioavailability of savianolic acid B by physicochemical properties and the hepatoprotective effects of naringenin in orally administered rats with CCl\textsubscript{4} induced acute liver failure, Pharm Res, 2008, 26, 893-902.


Lucia RD, Pharmacological and toxicological studies on *Centella asiatica*, *Fitoterapia*, 1997, 68, 413-416.


