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Review Article

A Review on Novel Drug Delivery System: A Recent Trend

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ABSTRACT

Plants are nature's remedies and have been used by human beings on earth since ancient times for food and medicine. Today there are global movements towards finding of herbal medicaments in plants to bring them in market via a suitable drug delivery system for mankind. The basic thought behind it is treatment of each disease is hidden in nature. However, delivery of herbal drugs also requires modification with the purpose to achieve sustain release, to increase patient compliance etc. previously herbal drugs could not attract scientists towards the modifications of novel drug delivery systems due to processing, standardizing, extracting and identification difficulties. But now days with the advancement in the technology, novel drug delivery systems (NDDS) open the door towards the development of herbal novel drug delivery system. With use of advance techniques protection from toxicity, enhancement in stability, improved bioavailability of herbal formulations, protection from physical and chemical degradation can be achieve. Novel drug delivery technologies have gained the importance to achieve modified delivery of herbal drugs their by increasing the therapeutic value as well as reducing toxicity. The present reviews gives information regarding various novel techniques used for improving safety and efficacy of phytomedicines and application of novel formulation. The main goal for developing such delivery systems is to minimize drug degradation and loss, to prevent harmful side effects and to increase bioavailability. Targeting is the ability to direct the drug loaded system to the site of interest. Among drug carrier one can name soluble polymers, microparticles made of insoluble (or) biodegradable natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes and micelles. Two major mechanisms can be distinguished for addressing the desired sites for drug release, (a) Passive and (b) Active targeting. Controlled drug carrier systems such as micellar solutions, vesicles and liquid crystal dispersions, as well as nanoparticle dispersions consisting of small particles of 10 – 400 nm show great promise as drug delivery systems. Hydrogels are three dimensional, hydrophilic, polymer networks capable of imbibing large amounts of water or biological fluids.

Keywords: New drug delivery system, Phytosome, Nanoparticles, Microsphere, Transdermal Drug Delivery System Carriers, Colloidal drug carriers

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INTRODUCTION

Herbal formulation means a dosage form consisting of one or more herbs or processed herbs in specified quantities to provide specific nutritional, cosmetic benefits, and/or other benefits. Herbal preparations are obtained by subjecting whole plant, fragmented or cut plants, plants parts to treatments such as distillation, extraction, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates ¹. Herbal drug itself is complex structure of many active constituents; as all of them provide synergistic action and enhance the therapeutic value ². Herbal drugs have lesser side effects ^{3,4}.

Novel drug delivery systems can include those based on physical mechanisms and those based on biochemical mechanisms. Physical mechanisms also referred as controlled drug delivery systems include osmosis, diffusion, erosion, dissolution and electro transport. Biochemical mechanisms include monoclonal antibodies, gene therapy, and vector systems, polymer drug adducts and liposomes. Targeting is the ability to direct the drug-loaded system to the site of interest. Two major mechanisms can be distinguished for addressing the desired sites for drug release: (i) Passive and (ii) Active targeting.

Therapeutic benefits of some new drug delivery systems include optimization of duration of action of drug, decreasing dosage frequency, controlling the site of release and maintaining constant drug Levels ^{5,6,7}

ADVANTAGES OF NOVEL DRUG DELIVERY SYSTEM

1. Protection from physical and chemical degradation.
2. Sustained delivery.
3. Improved tissue macrophages distribution.
4. Enhancement of stability.
5. Enhancement of pharmacological activity.
6. Protection from toxicity.
7. Increased bioavailability.
8. Enhancement of solubility⁸.

RECENT DEVELOPMENTS IN NOVEL DRUG DELIVERY SYSTEM OF HERBALS

1. Phytosome
2. Liposome
3. Nanoparticles
4. Emulsions
5. Microsphere
6. Ethosome
7. Solid lipid nanoparticle
8. Niosomes
9. Proniosomes
10. Transdermal Drug Delivery System
11. Dendrimers
12. Liquid Crystals
13. Hydrogels⁹

PHYTOSOMES

Phytosomes are lipid compatible molecular complex which are composed of "phyto" which means plant and "some" meaning cell-like¹⁰. Complexing the polyphenolic phytoconstituents in the molar ratio with phosphatidyl choline results in a new herbal drug delivery system, known as "Phytosome". 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 extracts¹¹.

Advantages of phytosome

1. Phytosome increases the absorption of active constituents, so its dose size required is small.
2. There is appreciable drug entrapment and improvement in the solubility of bile to herbal constituents, and it can target the liver.
3. In Phytosome, chemical bonds are formed between phosphatidylcholine molecules, so it shows good stability¹².
4. Phytosome improves the percutaneous absorption of herbal phytoconstituents¹³

LIPOSOMES

Tiny pouches made of lipids, or fat molecules surrounding a water core widely used for clinical cancer treatment. Several different kinds of liposomes are widely employed against infectious diseases and can deliver certain vaccines. During

cancer treatment they encapsulate drugs, shielding healthy cells from their toxicity, and prevent their concentration in vulnerable tissues such as those of patient kidneys and liver. Liposomes can also reduce or eliminate certain common side effects of cancer treatment such as nausea and hair loss.

They are form of vesicles that consist either of many, few or just one phospholipid bilayers. The polar character of liposomal core enables polar drug molecules to be encapsulated. Amphiphilic and lipophilic molecules are solubilized within phospholipid bilayer according to their affinity towards phospholipids.¹⁴

Advantages of liposomes

1. The high biocompatibility.
2. The easiness of preparation.
3. The chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds.

The simple modulation of their pharmacokinetic properties by changing the chemical composition of the bilayer components¹⁵.

Use of Liposomes

Another major and important advancement in the novel drug delivery systems is the use of liposomes for carrying the drugs to the site of action. Liposomes in both modified and unmodified forms are able to change the course of pharmacokinetic parameters of the drugs. These are widely used in delivering the cytotoxic agents to the tumour tissue and preventing side effects like myelosuppression. These are also used in targeting through receptor-mediated endocytosis. Modified liposomes also have huge applications in targeting various drugs to the organs like heart, liver, kidney, lungs and bones¹⁶

NANOPARTICLES

Nanoparticles (including nanospheres and nanocapsules of size 10-200 nm) are in the solid state and are either amorphous or crystalline. They are able to adsorb and/or encapsulate a drug, thus protecting it against chemical and enzymatic degradation. In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices in view of their applications in the controlled release of drugs, in targeting particular organs / tissues, as carriers of DNA in gene therapy, and in their ability to deliver proteins, peptides and genes through the peroral route^{17,18}

Advantages of herbal nanoparticle delivery system

1. Nanoparticulate system delivers the herbal formulation directly to the site of action.
2. Increased efficacy and therapeutic index.
3. Increased stability via encapsulation.
4. Improved pharmacokinetic effect.
5. Producing with various sizes, compound surface properties¹⁹.

EMULSIONS

Emulsion is a biphasic system in which one phase is intimately disperses in the other phase in the form of minute droplets in ranging in diameter from 0.1µm 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 microemulsion is also called nanoemulsion, and the sub-micro-emulsion is called liquid emulsion²⁰. Microemulsion is

a clear, thermodynamically stable, frequently in combination with a co-surfactant ²¹.

Advantages of emulsion-based formulations

1. It can release the drug for a long time because it is packed in the inner phase and makes direct.
2. Contact with the body and other tissues.
3. As a result of the lipophilic drugs being made into o/w/o emulsion, the droplets of oil are phagocytosed by macrophages and increase its concentration in liver, spleen and kidney.
4. 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.
5. The new type, viz., Elemenum emulsion, is used as an anti-cancer drug and causes no harm to the heart and liver ²².

MICROSPHERES

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, gelatin microspheres, polypropylene dextran microspheres, 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 ²³.

ETHOSOMES

Ethosomes are developed by mixture of phospholipids and high concentration of ethanol. This carrier can penetrate through the skin deeply lead to improve drug delivery into deeper layer of skin and in blood circulation. These formulations are useful for topical delivery of alkaloids in form of gel and cream for patients comfort. They show increase in their permeability through the skin by fluidizing the lipid domain of the skin. Unstable nature and poor skin penetration are limits for Ethosomes topical delivery. The Ethosomes was developed and examined for their ability the topical absorption of Tetrandine through dermal delivery, and the relation of formulations to the pharmacological activity of Tetrandine loaded in the formulation was also accessed. Result of the drug levels in rat plasma showed that when Tetrandine loaded Ethosomes were topically administered in rats the drug level was low to be detected in rat plasma. In conclusion, Ethosomes were demonstrated to be promising carrier for improving topical delivery of Tetrandine via skin ²⁴.

Advantages of ethosomal drug delivery

1. Ethosomes enhance transdermal permeation of drug through skin.
2. Ethosomes are a platform for the delivery of large amounts of diverse groups of drugs.

3. Ethosomal drug is administered in semisolid form resulting in improvement in patient's compliance ²⁵.

SOLID LIPID NANOPARTICLES

(SLNs) are a new pharmaceutical delivery system or pharmaceutical formulation.

The conventional approaches such as use of permeation enhancers, surface modification, prodrug synthesis, complex formation and colloidal lipid carrier based strategies have been developed for the delivery of drugs to intestinal lymphatics. In addition, polymeric nanoparticles, self-emulsifying delivery systems, liposomes, microemulsions, micellar solutions and recently solid lipid nanoparticles (SLN) have been exploited as probable possibilities as carriers for oral intestinal lymphatic delivery.²⁵

A solid lipid nanoparticle is typically spherical with an average diameter between 10 and 1000 nanometers. Solid lipid nanoparticles possess a solid lipid core matrix that can solubilize lipophilic molecules. The lipid core is stabilized by surfactants (emulsifiers). The term lipid is used here in a broader sense and includes triglycerides (e.g. tristearin), diglycerides (e.g. glycerol behenate), monoglycerides (e.g. glycerol monostearate), fatty acids (e.g. stearic acid), steroids (e.g. cholesterol), and waxes (e.g. cetyl palmitate). All classes of emulsifiers (with respect to charge and molecular weight) have been used to stabilize the lipid dispersion. It has been found that the combination of emulsifiers might prevent particle agglomeration more efficiently.^{26,27}

NIOSOMES

Niosomes are multilamellar vesicles formed from non-ionic surfactants of the alkyl or dialkylpolyglycerol ether class and cholesterol. Earlier studies, in association with L'Oreal have shown that, in general, niosomes have properties as potential drug carriers similar to liposomes. Niosomes are different from liposomes in that they offer certain advantages over liposomes ²⁸.

PRONIOSOMES

Proniosomes gel system is step forward to niosome, which can be utilized for various applications in delivery of actives at desired site. Proniosomal gels are the formulations, which on in situ hydration with water from the skin are converted into niosomes ²⁹.

DENDRIMERS

Dendrimers are precisely defined, synthetic nanoparticles that are approximately 5–10 nm in diameter. They are made up of layers of polymer surrounding a control core. The dendrimers surface contains many different sites to which drugs may be attached and also attachment sites for materials such as PEG which can be used to modify the way of dendrimer which interacts with body. PEG can be attached to dendrimer to 'disguise' it and prevent the body's defense mechanism for detecting it, thereby slowing the process of break down. This fascinating particle holds significant promise for cancer treatment. Its many branches allow other molecules to easily attach to its surface. Researchers have fashioned dendrimers into sophisticated anticancer machines carrying five chemical tools – a molecule designed to bind to cancer cells, a second that fluoresces upon locating genetic mutations, a third to assist in imaging tumor shape using x-rays, a fourth carrying drugs released on demand, and a fifth that would send a signal when cancerous cells are finally dead. The creators of these dendrimers had

successful tests with cancer cells in culture and plan to try them in living animals soon^{30,31}

LIQUID CRYSTALS

Liquid Crystals combine the properties of both liquid and solid states. They can be made to from different geometries, with alternative polar and non-polar layers (i.e., a lamellar phase) where aqueous drug solutions can be included³².

HYDROGELS

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids. They are used to regulate drug release in reservoir-based, controlled release systems or as carriers in swellable and swelling-controlled release devices³³.

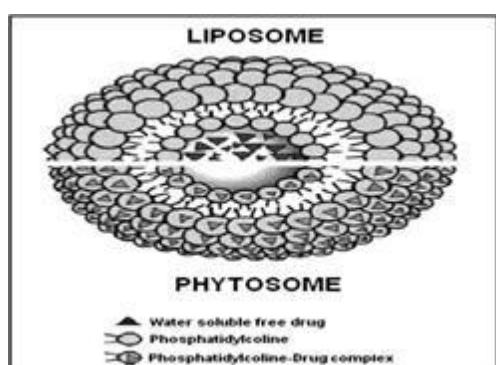


Figure 1: Structure of Liposome & Phytosome

FUTURE PROSPECTS AND OPPORTUNITIES IN INDIA

India is one of the most strategic regions for the pharmaceutical market. Therefore many multinational giants have been keen to invest and grow preferentially in this sector. Developments in the new and advanced techniques in the field of NDDS will create huge demand for variety of excipients usage and development. India is well known for its quick adaptability to new excipients and associated technologies. So market for excipients in India will grow on two aspects; one is in the form of exporting new organic excipients and the second one in the form of employing new excipients in various advanced delivery technologies. Majority of the pharmaceutical companies in the country have been applying and receiving new patents in the field of the Novel drug delivery systems. This eventually, in the near future derives huge demand for the products and services offered by pharmaceutical and allied businesses. Nanotechnology offers various modern applications in novel drug delivery systems that potentially improve the diagnosis, treatment and help monitoring of post-administration transformation of drug composition within the body systems. Another important milestone to be mentioned here is Computer aided Drug Design, which offers a lot of scope for the development of this kind of novel and advanced systems. Computer aided Drug Design helps in designing and developing the drugs and delivery systems consuming less time and resources with more accuracy and quality compared to traditional methods^{34,35}.

MOLECULAR IMPRINTING TECHNOLOGY

The molecular imprinting technology has an enormous potential for creating satisfactory drug dosage forms.

Molecular imprinting involves forming a pre-polymerization complex between the template molecule and functional monomers or functional oligomers (or polymers) with specific chemical structures designed to interact with the template either by covalent, non-covalent chemistry (self-assembly) or both. Once the pre-polymerization complex is formed, the polymerization reaction occurs in the presence of a cross-linking monomer and an appropriate solvent, which controls the overall polymer morphology and macroporous structure. Once the template is removed, the product is a heteropolymer matrix with specific recognition elements for the template molecule. Examples of MIP-based drug delivery systems involve: (i) rate-programmed drug delivery, where drug diffusion from the system has to follow a specific rate profile, (ii) activation-modulated drug delivery, where the release is activated by some physical, chemical or biochemical processes and (iii) feedback-regulated drug delivery, where the rate of drug release is regulated by the concentration of a triggering agent, such as a biochemical Substance, the concentration of which is dependent on the drug concentration in the body. Despite the already developed interesting applications of MIPs, the incorporation of the molecular imprinting approach for the development of DDS is just at its incipient stage. Nevertheless, it can be foreseen that, in the next few years, significant progress will occur in this field, taking advantage of the improvements of this technology in other areas. Among the evolution lines that should contribute more to enhance the applicability of imprinting for drug delivery, the application of predictive tools for a rational design of imprinted systems and the development of molecular imprinting in water may be highlighted³⁶

ADMINISTRATION ROUTES

The choice of a delivery route is driven by patient acceptability, the properties of the drug (such as its solubility), access to a disease location, or effectiveness in dealing with the specific disease. The most important drug delivery route is the peroral route. An increasing number of drugs are protein and peptide based. They offer the greatest potential for more effective therapeutics, but they do not easily cross mucosal surfaces and biological membranes; they are easily denatured or degraded, prone to rapid clearance in the liver and other body tissues and require precise dosing. At present, protein drugs are usually administered by injection, but this route is less pleasant and also poses problems of oscillating blood drug concentrations. So, despite the barriers to successful drug delivery that exist in the gastrointestinal tract (i.e., acid-induced hydrolysis in the stomach, enzymatic degradation throughout the gastrointestinal tract by several proteolytic enzymes, bacterial fermentation in the colon), the peroral route is still the most intensively investigated as it offers advantages of convenience and cheapness of administration, and potential manufacturing cost savings.

Pulmonary delivery is also important and is effected in a variety of ways - via aerosols, metered dose inhaler systems (MDIs), powders (dry powder inhalers, DPIs) and solutions (nebulizers), all of which may contain nanostructures such as liposomes, micelles, nanoparticles and dendrimers. Aerosol products for pulmonary delivery comprise more than 30% of the global drug delivery market. Research into lung delivery is driven by the potential for successful protein and peptide drug delivery, and by the promise of an effective delivery mechanism for gene therapy (for example, in the treatment of cystic fibrosis), as well as the need to replace chlorofluorocarbon propellants in MDIs. Pulmonary drug delivery offers both local targeting for the treatment of respiratory diseases and increasingly appears to be a viable

option for the delivery of drugs systemically. However, the pulmonary delivery of proteins suffers by proteases in the lung, which reduce the overall bioavailability, and by the barrier between capillary blood and alveolar air (air-blood barrier). Transdermal drug delivery avoids problems such as gastrointestinal irritation, metabolism, variations in delivery rates and interference due to the presence of food. It is also suitable for unconscious patients. The technique is generally non-invasive and aesthetically acceptable, and can be used to provide local delivery over several days. Limitations include slow penetration rates, lack of dosage flexibility and / or precision, and a restriction to relatively low dosage drugs³⁷.

CONCLUSION

Novel drug delivery system not only reduces the repeated administration to overcome noncompliance, but also helps to increase the therapeutic value by reducing toxicity and increasing the bioavailability, and so on. Extensive research is going on for herbal drugs to incorporate them in novel drug delivery systems. Application of these novel techniques to natural medicines will lead to enhanced bioavailability, reduced toxicity, sustained release action, protection from GI degradation which cannot be obtained through conventional drug delivery system due to large molecular size, poor solubility, degradation of herbal medicines in Gastrointestinal media.

REFERENCES

- Cott J. Natural product formulations available in Europe for psychotropic indications. *Psychopharmacol Bull*, 1995;31:745.
- Atram S. Recent development of herbal formulation-a novel drug delivery system. *International Ayurvedic Medical Journal*, 2014; 2(6):952-58.
- Alexis F, Basto P, Levy NE, Radovic MAF, Zhang LF, Pridgen E, et al. HER-2-Targeted Nanoparticle AntibodyBioconjugates for Cancer Therapy. *Chem Med Chem*, 2008; 3:1839- 43.
- Atmakuri LR, Dathi S. Current trends in herbal medicines. *J Pharm Res*, 2010; 3:109-113.
- Niculescu-Duvaz I, Springer CJ. Antibody-directed enzyme prodrug therapy (ADEPT): a review. *Advanced Drug Delivery Reviews* 1997; 26:151-72.
- Manabe T, Okino H, Maeyama R, Mizumoto K, Nagai E, Tanaka M, Matsuda T. Novel strategitherapeutic approaches for prevention of local recurrence of pancreatic cancer after resection: trans tissue, sustained local drug-delivery systems. *Journal of Controlled Release* 2004; 100:317-30.
- Ziaie B, Baldi A, Lei M, Gu Y, Siegel RA. Hard and Soft Micro machining for Biomems. Review of Techniques and Examples of Applications in Microfluidics and Drug Delivery. *Advanced DrugDelivery Reviews* 2004; 56:145-72.
- Muller RH, Runge SA. Solid lipid nanoparticles (SLN) for controlled drug delivery. In: Benita S, editor. *Submicron emulsions in drug targeting and delivery*. Harwood Academic Pub, 1998; 22(7):219-234.
- Jain NK. Controlled and Novel drug delivery, 4th edition, New Delhi: CBS Publishers and Distributors, 2002, 236- 237.
- Amin T, Bhat SV. A Review on Phytosome Technology as a Novel Approach to Improve the Bioavailability of Nutraceuticals. *International Journal of Advancements in Research and Technology*, 2012; 1(3):1-15.
- Hikino H, Kiso Y, Wagner H, Fiebig M. Antihepatotoxic actions of flavonolignans from *Silybummarianum* fruits. *Planta Med*, 1984; 50:248-50.
- Vishvakrama P, Sharma S. Liposomes: An Overview. *Journal of Drug Delivery and Therapeutics*, 2014; 47-55.
- Khar RK, Jain NK. Solid lipid nanoparticle as Novel Nanoparticle system in Targeted and controlled drug delivery. *IJPR*, 102-103.
- Chaturvedi M, Kumar M, Sinhal A, AlimuddinSaifi. Recent development in novel drug delivery systems of herbal drugs. *International journal of Green Pharmacy*, 2011; 5:87-94.
- Kharat A, Pawar P. Novel drug delivery system in herbals. *IJPCBS*, 4, 2014, 910-930.
- <http://www.free-ebooks.net/ebook/Drug-Delivery-Systems-A-Review/html/11#ixzz3XMJX9RBG>
- Soppimath KS, Aminabhavi TM, Kulkarni AR, Rudzinski WE. Biodegradable polymericnanoparticles as drug delivery devices. *Journal of Controlled Release*, 2001; 70:1-20.
- Agnihotri SA, Mallikarjuna NN, Aminabhavi TM. Recent advances on chitosan-based micro andnanoparticles in drug delivery. *Journal of Controlled Release* 2004; 100:5-28.
- Manach C, Scalbert A, Morand C, Remesy C and Jimenez L. Polyphenols: food sources and bioavailability. *Am J ClinNutr*, 2004; 79:727-747.
- Jumaa M and Muller BW. Lipid emulsions as a novel system to reduce the hemolytic activity of lytic agents: Mechanism of protective effect. *Eur J Pharm Sci*, 2009; 9:285-290.
- 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.
- Scarfato P, Avallone E, Iannelli P, Aquino RP. Quercetin microsphere by solvent evaporation: preparation characterization and release behavior. *J Appl Polymer Sci*, 2008; 109:2994-3001.
- Rastogi V, Shukla S, Singh R, Lal N, Yadav P, Microspheres: A Promising Drug Carrier. *Journal of Drug Delivery and Therapeutics*, 2016; 6(3):18-26.
- Jaiswal P, Kesharwani S, Kesharwani R, Patel D, Ethosome: A New Technology Used As Topical & Transdermal Delivery System. *Journal of Drug Delivery and Therapeutics*, 2016; 6(3):7-17.
- Saupe, Anne; Rades, Thomas (2006). "Solid Lipid Nanoparticles". *Nanocarrier Technologies*. p. 41. doi:10.1007/978-1-4020-5041-1_3. ISBN 978-1-4020-5040-4.
- Jenning, V; Thünemann, AF; Gohla, SH. "Characterisation of a novel solid lipid nanoparticle carrier system based on binary mixtures of liquid and solid lipids". *International Journal of Pharmaceutics*. 2000; 199(2):167-77. PMID 10802410.
- Studies on binary lipid matrix based solid lipid nanoparticles of repaglinide: in vitro and in vivo evaluation. Rawat MK, Jain A and Singh S, *Journal of Pharmaceutical Sciences*, 2011; 100(6):2366-2378
- Hunter CA. Vesicular System (Niosomes and Liposomes) for Delivery of Sodium Stibogluconate in Experimental Murine Visceral Leishmaniasis. *J Pharm Pharmacol*, 1988, 161-164.
- Manach C, Scalbert A, Morand C, Remesy C and Jimenez L. Polyphenols: food sources and bioavailability. *Am J ClinNutr*, 2004; 79:727-747.
- Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier J, and Piccerelle, P. *Int.J. Pharm* 2005; 292:1-2, 29-41.
- Yoshio K, Masazumi K, Shuichi A, and Hiroaki N, *J. Control. Release*, 2005; 105(1-2):16-22.
- Prajapati S, Maurya S, Das M, Tilak V, Verma K, & Dhakar R. Dendrimers in Drug Delivery, Diagnosis and Therapy: Basics and Potential Applications. *Journal of Drug Delivery and Therapeutics*, 2016; 6(1):67-92.
- Muller Goymann CC. Physicochemical characterization of colloidal drug delivery systems such as reverse micelles, vesicles, liquid crystals and nanoparticles for topical administration. *Europ J of Pharmaceutics and Biopharmaceutics*, 2004; 58(1):343-356.
- Karaman R. The Future of Prodrugs Designed by Computational Chemistry. *Drug Des*. 2012; 1:1.
- Harshal Ashok Pawar, BhagyashreeDilipBhangale. Phytosome as a Novel Biomedicine: A Microencapsulated Drug Delivery System. *J Bioanal Biomed*. 2015; 7:1.
- Vandermeulen GM, Klok HA. Peptide/Protein Hybrid Material: Enhanced Control of Structureand Improved Performance through Conjugation of Biological and Synthetic Polymers. *Macromolecular Bioscience* 2003; 4:383-98.
- Sood A and Panchagnula R. Peroral Route: An Opportunity for Protein and Peptide Drug Delivery. *Chemical Reviews* 2000; 101:3275-303.