



Novel Drug Delivery Systems: An Overview

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Abstract

The performance of an existing medicinal molecule in terms of patient compliance, safety, and efficacy can be greatly enhanced by evolving it from a traditional form to a unique delivery mechanism. An old medication molecule can be given new life as a Novel Drug Delivery System. The limitations of the conventional drug delivery methods are addressed by the innovative drug delivery system, which is a novel method of drug administration. A significant improvement in the ability to release a drug at a specified spot and rate is possible with a novel drug delivery system that is properly developed. Pharmaceutical companies are working to create novel drug delivery systems in order to give medications to patients effectively and with fewer side effects. The fundamentals of novel drug delivery systems, as well as their various varieties, are covered in this article. The scientific requirements to be incorporated in novel drug delivery systems, such as nanoparticles, microemulsions, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles, and so on, can be met by modern phytopharmaceuticals research, though, by determining pharmacokinetics, mechanism of action, site of action, required precise dose, etc.

Keywords: Novel drug delivery system, Conventional drug delivery, Pharmaceutical companies, Pharmacokinetics.

Introduction

The way a medicine is administered can significantly affect how effective it is. Concentrations above or below this range may be hazardous or fail to yield any therapeutic benefit for some medications, which have an optimal concentration range within which maximum benefit is obtained¹. The very gradual improvement in the effectiveness of treating serious diseases, on the other hand, has indicated an increasing need for a multidisciplinary approach to the delivery of medicines to targets in tissues.

This led to the development of fresh concepts for managing the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition and effectiveness of medications. These innovative approaches-often referred to as drug delivery systems (DDS)-combine polymer science, pharmaceuticals, bioconjugate chemistry and molecular biology. Various drug delivery and drug targeting systems are now being developed to reduce drug degradation and loss, to prevent negative side effects, to boost medication bioavailability, and to raise the percentage of the drug accumulating in the necessary zone¹. Previously simply a pipe dream or at most a potential, controlled and novel drug delivery is now a reality. Pharmaceutical and other experts have conducted considerable and rigorous study in this area of drug development during the past 15 years. Soluble polymers, microparticles comprised of insoluble or biodegradable, natural and synthetic polymers, cells, cell ghosts, lipoproteins, liposomes, and micelles are examples of drug carriers. The carriers can be engineered to slowly degrade, react to stimuli

(such changes in temperature or pH), and even be targeted (e.g., by conjugating them with specific antibodies against certain characteristic components of the area of interest). The capacity to steer a drug-loaded system to a specific location is known as targeting. To address the intended areas for drug release, two main processes can be identified:

- (i) Passive and;
- (ii) Active targeting¹

The preferential accumulation of chemotherapeutic drugs in solid tumors as a result of the increased vascular permeability of tumor tissues in comparison to healthy tissue is an example of passive targeting. Surface functionalization of drug carriers with ligands that are specifically recognized by receptors on the surface of the cells of interest is a method that might enable active targeting. This might enable more exact targeting of the location of interest because ligand-receptor interactions can be quite selective.

Any drug delivery system may be defined as a system comprising of:

- a) Drug formulation
- b) Medical device or dosage form/technology to carry the drug inside the body
- c) Mechanism for the release

The formulation of the medicine into an appropriate form, such as a crushed tablet for oral administration or a solution for intravenous administration, is a traditional drug delivery

method. It has been discovered that these dose forms have significant drawbacks, including greater dosage requirements, decreased effectiveness, toxicity, and negative side effects. To fulfill the demands of the healthcare industry, new drug delivery systems have been developed or are being developed to get around the drawbacks of the traditional drug delivery systems. These systems fall under the categories of targeted medication delivery systems and controlled drug release systems.

The therapeutic benefits of these new systems include:

- Increased medication effectiveness and site-specific delivery
- Reduced toxicity and side effects
- Enhanced convenience
- Effective therapies for diseases that were once incurable
- Potential applications for prevention
- Better adherence from the patient.

Drug delivery methods don't have a standardized definition that is widely accepted. It is presumable that it is based on the two fundamental factors of Route of entry (A) and Dosage form (B). Any component of (A X B Cartesian)'s product is considered a drug delivery mechanism. Such a definition suggests that this group contains a sizable number of individuals.

Carrier based drug delivery system

- A) Liposomes
- B) Nanoparticles
- C) Microspheres
- D) Monoclonal antibodies
- E) Niosomes
- F) Resealed erythrocytes as drug carriers

Transdermal drug delivery systems

- A) Sonophoresis
- ♣ Supramolecular delivery systems
- ♣ Variable release delivery systems
- B) Osmotic pump
- C) Microencapsulation

Drug delivery carriers

Micellar solutions, vesicle and liquid crystal dispersions, as well as nanoparticle dispersions made up of tiny particles with a diameter of 10–400 nm, all hold considerable potential as colloidal drug carrier systems. The objective when creating these formulations is to produce systems with ideal drug loading and release characteristics, a long shelf life, and low toxicity². The medicine that has been integrated affects the system's microstructure and may even change it as a result of molecular interactions, particularly if the drug has amphiphilic and/or mesogenic features.

Pharmaceutical carriers

For drug delivery applications, micelles created by the self-assembly of amphiphilic block copolymers (5-50 nm) in aqueous solutions are of great interest. Drugs can be delivered at concentrations that are greater than their intrinsic water solubility by becoming physically trapped in the center of

block copolymer micelles. Additionally, the hydrophilic building pieces have the ability to make hydrogen bonds with their watery environment and create a solid shell around the micellar core. As a result, the hydrophobic core's contents are effectively shielded against hydrolysis and enzymatic deterioration. Additionally, the corona might inhibit the reticuloendothelial system from recognizing the micelles, leading to their preliminary removal from the bloodstream. Amphiphilic block copolymers' ability to easily adjust their chemical composition, total molecular weight, and block length ratios, which enables control over the size and shape of the micelles, is a final characteristic that makes them appealing for drug delivery applications. The stability of the associated micelles can be improved as a result of functionalizing block copolymers with cross linkable groups. Block copolymer micelles can be substituted with certain ligands to activate a wider variety of sites with considerably higher selectivity³.

Liposomes

Vesicles called liposomes might have a lot, a little, or only one phospholipid bilayer inside of them. Polar medicinal molecules can be encapsulated due to the liposomal core's polar nature. According to their affinity for phospholipids, amphiphilic and lipophilic compounds are solubilized within the phospholipid bilayer. Niosomes are produced when nonionic surfactants participate in the bilayer synthesis rather than phospholipids. In the hydrophobic region of vesicle membranes, channel proteins can be inserted without losing their functionality, operating as a size-selective filter that only permits passive diffusion of tiny solutes like ions, nutrients, and antibiotics. As a result, pharmaceuticals that are enclosed in nanocages functionalized with channel proteins are efficiently shielded from proteolytic enzymes' premature breakdown. The drug molecule, however, is able to diffuse through the channel, driven by the concentration difference between the interior and the exterior of the nanocage⁴⁻⁸.

Dendrimers

Dendrimers are symmetrical macromolecules with nanometer-sized, highly branching, monodisperse structures. A central core, branching units, and terminal functional groupings make them up. The environment of the nanocavities and, subsequently, their solubilizing capabilities are determined by the core together with the internal units, whilst the solubility and chemical behavior of these polymers are determined by the exterior groups. Attaching targeting ligands to the dendrimers' exterior surfaces influences the efficiency of targeting, and functionalizing the dendrimers with polyethylene glycol chains increases their stability and protects them from the Mononuclear Phagocyte System. The characteristics of both the liquid and solid states are combined in liquid crystals. They are capable of taking on various geometries and can incorporate aqueous medicinal solutions in alternative polar and non-polar layers (i.e., a lamellar phase)^{9,10}.

Nanoparticles

Nanoparticles are in the solid form and can be either amorphous or crystalline, with sizes ranging from 10 to 200 nm for nanospheres and nanocapsules. They have the capacity to adsorb and/or encapsulate a medication, shielding it from enzymatic and chemical deterioration. Given their uses in the controlled release of drugs, the ability to target specific organs or tissues, the ability to carry DNA in gene therapy, and the ability to deliver proteins, peptides, and genes orally, biodegradable polymeric nanoparticles have received a lot of attention recently as potential drug delivery devices¹¹.

Grouping of nanomaterials:

A) Nanowires- Glowing silica nano wire is wrapped around a single strand of human hair. It looks delicate. It is about five times smaller than virus applications for nano wires include the early sensing of breast and ovarian malignancies.

A) Nanocantilever- This tiny carbon cantilever's honeycomb mesh serves as the fly's eye's surface. Beams with a single end anchored are known as cantilevers. They serve as sensors in the nano realm, perfect for identifying the presence of incredibly small compounds in biological fluid.

B) Nanoshells- Gold-coated hollow silica spheres make up nanoshells. In order for the shells to target certain cells, such as cancer cells, scientists can attach antibodies to the surfaces of the shells. One day, polymers holding drugs will also be incorporated into nanoshells.

C) Quantum dots- Quantum dots, which are tiny semiconductor particles, can act as markers for specific types of cells or substances in the body. They are able to achieve this because the type of cadmium employed in their cores affects the wavelengths of radiation that they release. Cadmium telluride is used for the far infrared and near infrared, cadmium sulphide for the ultraviolet to blue, and cadmium selenide for the majority of the visible spectrum.

D) Nano pores- Applications for cancer research and treatment involve nanopores. They are holes that have been engineered into particles that are so small that DNA molecules can flow through them one strand at a time, enabling extremely accurate and effective DNA sequencing. Drug producers can control the pace of drug diffusion in the body by incorporating nanopores into the surface of pill capsules that are just a little bit larger than the molecules of the medication.

E) Gold nanoparticles- The transmission electron microscopy image of these nanoparticles reveals that they have a solid core. In order to create super sensitive detection methods for DNA and protein markers connected to various types of cancer, including breast and prostate cancer, researchers at North Western University are employing gold particles.

F) Nanotubes - Carbon atoms are arranged in hollow cylinders called nanotubes. Additionally, they can be filled with liquid and sealed to create test tubes or prospective drug delivery systems.

Carbon nanotubes

It is possible to modify carbon nanotubes so they circulate easily inside the body. Both covalent and non-covalent bonds are capable of carrying out these alterations. Changes can lengthen or shorten the duration that blood circulates through the body. When carbon nanotubes are altered to be soluble in aqueous bodily fluids, their toxicity is minimal. They easily access the cells. Larger than normal cells and showing leaking, cancer cells are found in tumors. Large molecules that move slowly can enter cancer cells and build up there. Animal investigations have shown that carbon nanotubes carrying active substances are capable of doing this. Researchers have also using carbon tubes to deliver prodrugs, or precursors to active pharmaceutical ingredients. as in: Cisplatin¹²⁻¹⁶.

Microspheres

Microspheres are naturally biodegradable powders made of proteins or synthetic polymers that flow freely and preferably have a particle size of less than 200 m. Polymers are the materials utilized to create Microspheres.

They are classified into two types

1. Synthetic Polymers

2. Natural polymers

Synthetic polymers are divided into two types.

a. Non-biodegradable polymers

♣ Poly methyl methacrylate (PMMA)

♣ Glycidyl methacrylate

♣ Epoxy polymers

b. Biodegradable polymers

♣ Lactides, Glycolides & their co polymers

♣ Poly alkyl cyano acrylates

♣ Poly anhydrides

Synthetic polymers

A possible medication carrier for parenteral as well as other ophthalmic, oral preparations is poly alkyl cyano acrylates. A good carrier for narcotic antagonist, anti-cancer drugs including cisplatin, cyclo phosphamide, and doxorubicin is poly lactic acid. Co-polymers of poly lactic acid and poly glycolic acid have been used in the formulation of sustained release formulations for antimalarial medications as well as for many other medications. It has been explored to increase the precorneal residence duration for ocular administration using poly anhydride microspheres (40 m). Timolol maleate is packaged in poly adipic anhydride for ocular administration. Functional microspheres are those made of poly acrolein. Since the surficial free CHO groups over the poly acrolein can react with the NH₂ group of the protein to create Schiff's base, they do not need any activation steps. When delivered parenterally, non-biodegradable drug carriers have the potential to cause long-term carrier toxicity because they stay in the body after the drug has been fully released. Parenteral applications are better suited for biodegradable carriers that break down in the body to non-toxic breakdown products since they do not raise the issue of carrier toxicity.

Natural polymers

Natural polymers obtained from different sources like proteins, carbohydrates and chemically modified carbohydrates.

Proteins: Albumin, Gelatin, and Collagen

Carbohydrates: Agarose, Carrageenan, Chitosan, Starch
Chemically modified carbohydrates: Polydextran, Poly starch.

Gelatin microspheres are an effective means of transporting substances that can alter biological responses, such as interferon, to phagocytes. Starch is a type of carbohydrate. It is mostly composed of the glucopyranose unit, which upon hydrolysis produces D-glucose. It has a lot of free OH groups because it is a poly saccharide. Numerous active chemicals can be integrated into and made active on the surface of microspheres using these free OH groups. A deacylated form of chitin is chitosan. Due to its charge, the effect of chitosan has been taken into consideration. At neutral and alkaline pH levels, it is insoluble, although it combines with other salts to produce salts. Chitosan's amino groups protonate during breakdown, resulting in a positively charged polymer¹⁷⁻¹⁹.

Resealed erythrocytes as drug carriers

The most numerous cells in the human body, erythrocytes, may be used as a drug delivery vehicle. Erythrocytes can be loaded with a number of chemically and physiologically active

chemicals utilizing a variety of chemical and physical techniques, and they are biocompatible, biodegradable, have very long circulation half lifetimes, and all of these characteristics.

erythro = red and

cytes = cell

Erythrocyte is red cell. Erythrocyte is biconcave discs, anucleate Filled with hemoglobin (Hb), a protein that functions in gas transport. It contains the plasma protein spectrin. Healthy adult male=4.5millions/ μ ml

Healthy adult female=4.8million/ μ ml

Immature RBC are called "RETICULOCYTES²⁰."

Erythrocytes

Properties of resealed erythrocyte of novel drug delivery carriers:

- 1) A regulated release of the medicine is required at the target spot.
- 2) It must be the proper size and form and be able to flow through capillaries. And Drug leakage should be kept to a minimum.
- 3) It should have a low harmful effect and be biocompatible.
- 4) It should be able to transport a variety of medications.
- 5) It must have distinct physicochemical characteristics that enable identification of the intended target size.
- 6) After the medicine has been released at the chosen site, the degradation product of the carrier system should be biocompatible. The two should be physically and chemically compatible.
- 7) The carrier system must to be noticeably stable when being stored.

Advantage:

- 1) They are biodegradable by nature because they are a natural component of the body.
- 2) Chemical drug modification is not necessary for the trapping of drugs.
- 3) Drug entrapment does not necessitate chemical alteration of the target material.
- 4) They can be directed towards diseased tissue or organs and have non-immunogenic activity.
- 5) They extend the drug's systemic action.
- 6) It is simple to isolate erythrocytes, and more medication can be contained in a smaller volume of cells.
- 7) They are able to focus the medication on the reticuloendothelial system.
- 8) They make it easier for eukaryotic cells to incorporate protein and nucleic acid by infusing the cells with RBC.

Disadvantage:-

- 1) They have a limited potential as carrier to nonphagocyte target tissue.
- 2) Possibility of clumping of cells and dose dumping may be there²¹.

Drug loaded erythrocytes

One of the expanding and potential systems for the delivery of medications and enzymes is this one. Erythrocytes can be

filled with a range of biologically active chemicals and are biocompatible, biodegradable, have a long circulation half-life, and all of these characteristics. By obtaining blood samples from the target organism and separating the erythrocytes from the plasma, carrier erythrocytes are prepared. The term "resealed erythrocytes" refers to the carriers produced when cells are ruptured and drugs are trapped inside of them utilizing a variety of physical and chemical techniques. When administered again, the drug targets the reticulo-endothelial system through the sluggish circulation of the drug-loaded erythrocytes²²⁻²⁵.

Niosomes

The non-ionic surfactant Span-60, which forms vesicles in niosomes, is often stabilized by the addition of cholesterol and a little amount of an anionic surfactant like dicetyl phosphate. Both niosomes and liposomes have an equivalent ability to transport drugs and do so more effectively than free drugs do. Niosomes are preferred to liposomes because they have higher chemical stability and are more cost-effective. Niosomes that generate surfactants are biocompatible, nonimmunogenic, and degradable. Drugs with higher bioavailability than free drugs, such as nimesulide, flurbiprofen, piroxicam, ketoconazole, and bleomycin, are more effective when they are incorporated into niosomes²⁶.

Transdermal drug delivery system

Transdermal medication delivery is the application of self-contained, discrete dosage forms to intact skin in order to administer drugs to the bloodstream at a controlled rate. An essential component of new drug delivery systems, the transdermal drug delivery system (TDDS) has become well-established^{27,28}. The transdermal route is an intriguing choice for delivery because it is practical and secure.

- The advantages of administering medications through the skin to produce systemic effects include: Avoiding first pass metabolism
- Preventing gastro intestinal compatibility issues
- Predictable action with a long duration
- Enhancing pharmacological and physiological responsiveness
- Therapy can be stopped at any time with ease.
- Increased patient compliance as a result of the removal of multiple dosing
- The profile Possess the capacity for self-management
- To improve therapeutic efficacy

Sonophoresis

A technique called sonophoresis uses ultrasonic radiation to dramatically accelerate the absorption of topical substances (transdermal delivery) into the epidermis, dermis, and skin appendages. Low molecular weight medications and macromolecules can be quickly and conveniently delivered into the skin using sonophoresis. It is a localized, non-invasive, convenient technique. Sonophoresis is thought to improve medication delivery mechanically by altering the skin tissue in a mixture of heat, chemical, and mechanical ways. For sonophoresis, ultrasound has been employed at a range of frequencies between 20 kHz and 16 MHz, with intensities up to 3W/cm². Percutaneous absorption is known to be affected by ultrasound parameters including treatment duration, intensity, and frequency, with the latter being the most significant. Because ultrasound waves produce micro-vibrations in the skin's epidermis and boost the overall kinetic energy of the molecules making up topical medicines,

sonophoresis occurs. The cavitation, micro-streaming, and heating caused by the ultrasound most likely improve drug delivery. By successfully treating digital polyarthritis with hydrocortisone ointment plus ultrasound in 1954, Fellingner and Schmid first described ultrasound-mediated transdermal delivery of essential chemicals. In hospitals, sonophoresis is frequently utilized to administer medications through the skin. By combining the medications with a coupling agent (gel, cream, or ointment), pharmacists are able to deliver ultrasonic energy from the ultrasound transducer to the skin. Thus, applying ultrasound to the skin makes it more permeable (a process known as sonophoresis) and makes it possible to transfer numerous chemicals both into and through the skin. Physical therapy also uses sonophoresis. Interstitial fluid samples can be extracted for analysis using reverse ultrasound technology. Sonophoresis is therefore being researched as a method of pulling substances like glucose out of the skin in addition to its impact on delivering compounds into the skin²⁹⁻³³.

Mucoadhesive drug delivery systems

The situation in which two materials, at least one of which is biological in nature, are kept together for a long time by interfacial forces is known as bioadhesion. In the field of pharmaceutical sciences, the phenomenon is known as mucoadhesion when the sticky connection is to mucus or a mucous membrane. Mucoadhesive polymers have the potential to considerably extend the residence time of sustained release delivery systems on mucosal membranes. This potential has been demonstrated in drug delivery systems for the eyes, nose, mouth, and vagina. Additionally, there has always been a lot of interest in the development of oral mucoadhesive delivery systems because those that can adhere to certain gastrointestinal (GI) segments would have a number of benefits³⁴⁻³⁸.

Supramolecular drug delivery systems

An intermolecular non-covalent binding contact holds two or more molecular units together and organizes them into a supramolecular system. In addition to serving as models for understanding natural supramolecular self-assembly and molecular recognition, supramolecular structures involving macrocyclic compounds have also generated a great deal of interest as starting points for the development of novel nanomaterials for use in electronics, biomedicine, and pharmaceutical applications³⁵.

Osmotically controlled drug delivery systems

These systems use osmotic pressure as their driving force in order to deliver the medicine in a regulated manner. The most intriguing and well-liked method of drug delivery among all the available technologies is osmotic. Osmotic systems have been the subject of extensive research, and various patents have also been made public. Alza was a leader in the development of osmotic drug delivery systems, and it currently holds the majority of the patents examined as well as various products based on the osmotic principle. These methods can be employed for parenteral as well as oral administration. Gastro-intestinal therapeutic methods include oral osmotic systems. Implantable pumps are used for parenteral osmotic medication delivery. Osmotic pumps come in a variety of shapes and sizes, according to reports in the literature but in general they can be divided in oral and implantable systems³⁹⁻⁴³.

Microencapsulation

The method of microencapsulation involves surrounding or coating tiny droplets or particles of liquid or solid substance with a continuous film made of polymeric materials. First, the

gelatin coacervation process was used to prepare gelatin spheres for the microencapsulation technique, which was developed by Bungen burg de Jon and Kan in 1931. The controlled drug delivery system has been utilized to lessen the drawbacks of traditional therapy and to increase a specific medicine's therapeutic effectiveness. The active substance must be delivered to the target tissue at the ideal rate in order to have the greatest therapeutic efficacy, while also producing the least amount of toxicity and side effects possible. The microencapsulation technique aids in the transformation of liquids into solids, alteration of colloidal and surface properties, protection of the environment, and regulation of the release characteristics of various coated materials. In contrast to microencapsulation, which uses tiny coated particles to create a wide range of dosage forms, macropackaging techniques can achieve some of these features. Innovative drug delivery methods were developed with the goal of optimizing bioavailability by changing the drug's blood concentration's bioavailability. Medicine therapy can be enhanced with sustained and controlled release products, which is a common objective over non sustained and controlled release with the same drug. Microencapsulated products (micro particles) are the small entities that have an active agent know as the core material surrounded by a shell known as the coating material or embedded into a matrix structure. Most Microparticle shells are of organic polymers, but waxes and lipids are also used. Generally the size of the microencapsulated products (microparticles) is considered as larger than 1 micrometer and up to 1000 micrometers in diameter. Commercially available microparticles contained 10- 90% w/w core. A number of core materials can be encapsulated like that live cells, adhesives, flavors, agrochemicals, enzymes, pharmaceuticals. The microencapsulation technology helps to regulate the release characteristics of various coated materials as well as the conversion of liquids into solids, adjustment of colloidal and surface properties, and environmental protection. Techniques for macropackaging can accomplish some of these properties, as opposed to microencapsulation, which employs microscopic coated particles to produce a variety of dose forms. Innovative drug delivery techniques have been created with the intention of improving bioavailability by altering the drug's bioavailability at different blood concentrations. A shared goal over non sustained and controlled release with the same drug is to improve medicine therapy with sustained and controlled release products. The more recent finding in pharmaceutical research is that the rate at which a drug is released from the dosage form can be used to alter how quickly it is absorbed. The sustained action, sustained release, prolonged action, delayed action, and timed release medications are all included in the controlled released dose forms. This has been accomplished by creating novel pharmacological entities, finding new polymeric materials useful for extending the duration of drug release, improving patient safety, and increasing therapeutic efficacy⁴⁴.

Novel drug delivery system: in herbal formulations

The creation of innovative drug delivery systems (NDDS) for herbal medicines has received a lot of interest during the last few decades. Idealistically, the innovative carriers should meet two requirements. The medicine should first be delivered over the course of treatment at a rate determined by the body's needs. Second, it should direct the herbal drug's active ingredient to the place of action. None of these can be satisfied by conventional dosage forms, including prolonged-release dosage forms. Bioactive and plant extracts have been used to create a number of innovative herbal formulations, including

liposomes, phytosomes, nanoemulsions, microspheres, transferosomes, and ethosomes⁴⁵⁻⁵².

References

- Reddy PD, Swarnalatha D. Recent advances in novel drug delivery systems. *Int J PharmTech Res.*, 2010; 2(3):2025-2027.
- Muller CC. Physicochemical characterization of colloidal drug delivery systems such as reverse micelles, vesicles, liquid crystals and nanoparticles for topical administration. *Eur J Pharm Biopharm.*, 2004; 58(2):343-356. <https://doi.org/10.1016/j.ejpb.2004.03.028>
- <http://www.azonano.com/oars.asp>
- Sharma A, Sharma US. Liposomes in drug delivery: Progress and limitations. *Int J Pharm.*, 1997; 154(2):123-140. [https://doi.org/10.1016/S0378-5173\(97\)00135-X](https://doi.org/10.1016/S0378-5173(97)00135-X)
- Lau JR, Geho WB, Snedekar GH. Inventors; SDG INC, An Ohio Corporation, Assignee; Targeted Liposomal Drug Delivery System. US Patent 20100209492. 2010 Aug 19.
- Takagi A, Yamashita N, Sonobe T. Inventors; Astellas Pharma INC Tokyo, Assignee; Intracellular Drug Delivery Improving Liposomes. US Patent 20070286898. 2007 Dec 13.
- Lau JR, Geho WB, Snedekar GH. Inventors; Targeted Liposomal Drug Delivery System. US Patent 20070104777. 2007 May 10.
- Zhang Y, Luo B, Iyer L. Inventors; Liposomal Delivery Vehicle for Hydrophobic Drugs. US Patent 20070014845. 2007 Jan 18.
- Yamauchi H, Morita H, Kikuchi H. Inventors; Daiichi pharmaceuticals Co.LTD, Assignee; Liposomes And Liposomal Dispersion. US Patent 20020182248. 2002 Dec 5.
- Verma RK, Garg S, Current status of drug delivery technologies and future directions. *Pharm Tech On-Line.* 2001; 25(2):1-14.
- Torchilin VP. Structure and design of polymeric surfactant-based drug delivery systems. *J Control Release.* 2001; 73:137-72. [https://doi.org/10.1016/S0168-3659\(01\)00299-1](https://doi.org/10.1016/S0168-3659(01)00299-1)
- Turos E, Cormier R, Kyle DE. Inventors; University of South Florida FL, Assignee; Polyacrylate Nanoparticle Drug Delivery. US Patent 20100278920. 2010 Nov 4.
- Sung H, liang H, Tu H. Inventors; Nanoparticle For Protein Drug Delivery. US Patent 20090155374. 2009 June 18.
- Jacobson GB, Zare RN, Markides KE, Shinde RR. Inventors; Encapsulated Nanoparticle For Drug Delivery. US Patent 20080095856. 2008 Apr 24.
- Lobl TJ, Schloss JV, Nagy AI, Pananen JE. Inventors; Neurosystec corporation, Valencia CA, Assignee; Nanoparticle Drug Formulation. US Patent 20080145439. 2008 June 19.
- Singh AN, Mahanti B, Bera K. Novel Drug Delivery System & It's Future: An Overview. *Int J Pharm Engin.*, 2021; 9(2):1070-1088.
- Wu D, Chu CC, Carozza J. Inventors. Injectable Microspheres. US Patent 20110151004. 2011 June 23.
- Sah HK, Inventor; SK Chemicals CO LTD KR. Assignee; Method For Producing Microspheres Loaded with Drugs And Microspheres Loaded With Drugs Produced Thereby. US Patent 20090318569. 2009 Dec 24.
- Shah S. Novel drug delivery carrier: Resealed erythrocytes, *Int J Pharma Biosci.*, 2011; 2(1):394-406.
- Raut D, Sakhare R, Dadge K, Halle PD. Resealed erythrocytes drug delivery: A Review, *Int J Pharm Chem.*, 2013; 2:193-205.
- Gupta A, Mishra AK, Bansal P, Kumar S, Gupta V, Singh R, Kalyan GS. Cell based drug delivery system through resealed erythrocyte-a review. *Int J Pharm Sci Drug Res.*, 2010; 2(1):23-30
- Magnani M, Rossi L, Biagiotti S, Bioanchi M. Inventors; Drug Delivery System. US Patent 20120141540. 2012 June 7.
- Grimald S, Lisi A, Cinti C. Inventors; CNR Conciglio Nazionale Delle Ricerche Roma, Assignee; US Patent 20110262415. 2011 Oct 27.
- Yang VC, Kwon YM, Chung HS, Yang AJ. Inventors; Erythrocyte encapsulated L- asparaginase for enhanced acute Lymphoblastic Leukemia Therapy. US Patent 20100284982. 2010 Nov 11.
- Madhar NVS, Saini A. Niosomes: A novel drug delivery system. *Int J Res Pharm Chem.*, 2011; 1(3):498-511.
- Alcantor N, Williams EC, Toomey R. Inventors; University of South florida, FL, Assignee; Niosome Hydrogel Drug Delivery Systems. US Patent 20100068264. 2010 Mar 18.
- Arunachalam A, Karthikeyan M, Vinay Kumar D. et al., Transdermal drug delivery system: a review. *Curr Pharm Res.*, 2010; 1(1):70-81. <https://doi.org/10.33786/JCPR.2010.v01i01.015>
- Sharma B, Saroha K, Yadav B. Sonophoresis: An advanced tool in transdermal drug delivery system. *Int J Curr Pharm Res.*, 2011; 3(3):89-97.
- Easterbrook TJ, Gosden E, Meyer E. Inventors; Transdermal Drug Delivery device. US Patent 20110190716. 2011 Aug 4.
- Tang J. Inventor; Stabilised Transdermal Drug Delivery System. US Patent 20110182949. 2011 July 28.
- Nisato G, Baret JC. Inventors; Koninklijke Philips Electronics N.V, NC, Assignee; Transdermal Drug Delivery Patch. US Patent 20100222751. 2010 June 10.
- Heiati H, Weimann L. Inventor; Pharmapatch LLC, San Diego CA, Assignee; Multiple Nozzle Transdermal Drug Delivery System. US Patent 20100143448. 2010 Sept 2.
- Vinod KR, Reddy R, Banji D, Reddy V, Sandhya S. Critical review on mucoadhesive drug delivery systems. *Hygeia J Drugs Med.*, 2012; 6(1):7-28.
- Yoon HJ, Jang WD. Polymeric supramolecular systems for drug delivery. *J Mater Chem.*, 2010; 2:211-222. <https://doi.org/10.1039/B910948J>
- Zerbe HG, Paiement N. Inventor; Oral Mucoadhesive Dosage form. US Patent 20110028431. 2011 Feb 3.
- Sambasivam M. Inventor; Convatec Technologies INC, NV, Assignee; Ostomy Devices With Mucoadhesives. US Patent 2010010064. 2010 Apr 22.
- David AE, Zhang R, Park YJ, Yang AJM, Yang VC. Inventors; Mucoadhesive Vesicles For Drug Delivery. US Patent 20090232899. 2009 Sept 17.
- Gupta S, Singh RP, Sharma R, Kalyanwat R, Lokwani P. Osmotic pumps: A Review. *Int J Comprehen Pharm.*, 2011; 6(1):1-8.
- Patel H, Patel U, Kadikar H, Bhimani B, Daslaniya D, Patel G. A review on osmotic drug delivery system. *Int Res J Pharm.*, 2012; 3(4):88-94.
- Nghiem T, Jackson G. Inventors; Biovail Laboratories International S.R.L, Assignee; Multiparticulate Osmotic Delivery System. US Patent 20090004281. 2009 Jan 1.
- Patel HB. Inventor; Reliant pharmaceuticals INC., Assignee; Oral Osmotic Drug Delivery System. US Patent 20080248114. 2008 Oct 9.
- Kidane A, Bhatt PP. Inventors; Osmotic Drug Delivery System. US Patent 20070254032. 2007 Nov 1.
- Kumar A, Sharma P, Banik A. Microencapsulation as novel drug delivery system. *Int Pharm Sci.*, 2011; 1(1):1-7.
- Saraf AS. Applications of novel drug delivery system for herbal formulations. *Fitoterapia.* 2010; 81:680-689. <https://doi.org/10.1016/j.fitote.2010.05.001>
- He ZF, Liu DY, Zeng S, Ye JT. Study on preparation of ampelopsin liposomes. *J Chine Mat Med.*, 2008; 33(1):27-30.
- Rane S, Prabhakar B. Influence of liposome composition on paclitaxel entrapment & pH sensitivity of liposomes. *Indian J Phys Ther Res.*, 2009; 1(3):914-917.
- Godin B, Touitou E. Mechanism of bacitracin permeation enhancement through the skin & cellular membrane from an

- ethosomal carrier. *J Control Release*. 2004; 94(2-3):365-379.
<https://doi.org/10.1016/j.jconrel.2003.10.014>
48. Youfang C, Xianfu L, Hyunjin P, Richard G. Artemisinin nanoparticles. *Nanomed Nanotechnol Biol Med.*, 2009; 5:316-322.
49. Shimada S. Composition comprising nanoparticle Ginkgo biloba extract with the effect of brain function activation. US Patent 8105637; 2012 Jan 31.
50. Bhattacharya S. Phytosomes: Emerging strategy in delivery of herbal drugs & nutraceuticals. *Pharma Times*. 2009; 41(3):9-12.
51. Wu JH, Yen FL, Lin LT, Tsai TR, Lin CC, et al., Preparation, physicochemical characterization & antioxidant effects of quercetin nanoparticle. *Int J Pharm.* 2008; 346:160-168.
<https://doi.org/10.1016/j.ijpharm.2007.06.036>
52. Sampath Kumar KP, Bhowmik D, Chiranjyoti B, Chandira M, Tripathi KK. Innovations in sustained release drug delivery system and its market opportunities. *J Chem Pharm Res.*, 2010; 2(1):349-360