

CONCEPT OF NOVEL DRUG DELIVERY SYSTEM (NDDS) AND FUTURE APPROACHES

Abstract

It is possible to greatly improve the performance of an existing therapeutic molecule by transforming it from its traditional form into a unique delivery method. This can lead to considerable gains in patient compliance, safety, and efficacy. It is possible for an existing drug molecule to be given a new lease on life in the shape of a Novel Drug Delivery System. An correctly designed Novel Drug Delivery System can be a significant step forward in the process of problem-solving when it comes to issues with the release of the drug at a particular site and at a certain pace. Pharmaceutical companies are working on the creation of innovative drug delivery systems because there is a growing demand for medications to be administered to patients in a manner that is both effective and causes fewer adverse effects. This page covers the fundamentals of novel drug delivery systems as well as the various subcategories of such systems.

Keywords: It is possible for an existing drug molecule to be given a new lease on life in the shape of a Novel Drug Delivery System.

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I. INTRODUCTION

A pharmaceutical molecule's performance in terms of patient compliance, safety, and efficacy can be greatly enhanced by switching from a standard form to a unique delivery mode. It is possible to transform an existing medication molecule into a brand-new drug delivery mechanism. Modern drug delivery technologies, which are the consequence of recent developments in our understanding of the pharmacokinetic and pharmacodynamic behavior of medications, may help us construct an optimal drug delivery system more logically¹. Therapeutic medication concentrations are kept constant for a longer length of time using Novel Drug Delivery Systems (NDDS). In order to decrease drug loss and degradation, eliminate unpleasant side effects, raise medicine bioavailability, and increase the percentage of the drug accumulating in the proper zone, a number of medication delivery and drug targeting systems are now being developed². Before, administering medications in a regulated and targeted manner was merely a pipe dream or, at most, a promise. Pharmaceutical professionals and other experts have undertaken considerable and rigorous research in this area of drug development during the past 15 years. Cells, cell ghosts, lipoproteins, liposomes, micelles, soluble polymers, insoluble or biodegradable natural and synthetic polymers, and soluble polymers can all be used as drug delivery systems. The carriers may respond to stimuli (such as changes in temperature or pH), be targeted (for instance, by conjugating them with specific antibodies against certain distinguishing features of the area of interest), or even slowly disintegrate. The capacity to steer a drug-loaded system to a specific location is known as targeting. There are primarily two methods for selecting the areas where the drug distribution is intended:

- Passive targeting
- Active targeting

Chemotherapeutic drugs concentrate primarily in solid tumours due to the increased vascular permeability of cancerous tissues compared to healthy tissue. Here, passive aiming is shown. Surface functionalization of drug carriers with ligands that are uniquely recognised by receptors on the surface of the cells of interest is a technique that may enable active targeting. This might allow for more accurate targeting of the area of interest given that ligand-receptor interactions can be very selective.

Any drug delivery system is one that includes the following components:

- The drug formulation;
- A medical device or dosage form/technology to administer the drug internally;
- And a mechanism for the drug's release.

The medication needs to be made into the appropriate form for traditional drug delivery methods, such as a liquid for intravenous injection or a crushed tablet for oral consumption. These dose formulations have been found to have serious downsides, such as higher dosage requirements, lower efficiency, toxicity, and unfavourable side effects. New

drug delivery systems have been developed or are being developed to solve the shortcomings of the conventional drug delivery systems in order to meet the expectations of the healthcare business. The controlled drug release and targeted drug delivery categories include these devices.

These new systems have therapeutic benefits such as;

- Improved patient compliance,
- Increased medication effectiveness and site-specific delivery,
- Decreased toxicity and side effects,
- Increased convenience,
- Effective treatments for diseases that were previously incurable and potential applications for prevention³.

II. NOVEL DRUG DELIVERY SYSTEMS

Different drug delivery systems have been created, and some are still under development, with the goals of reducing medicine loss, preventing unwanted side effects, enhancing drug bioavailability, and encouraging and enabling the accumulation of the drug in the necessary bio-zone (site). It has been shown that a range of new carriers are useful for the controlled and long-term delivery of drugs. The language used in the various main categories of new drug delivery systems must be carefully examined.

- Pharmacological action is delivered at a predetermined rate and at therapeutically effective blood levels by sustained or controlled drug delivery systems.
- The pre-determine rate of drug delivery controls the molecular diffusion of drug molecules in systemic circulation, which affects the release of drug molecules to induce drug action. Medicine is delivered using localized drug delivery systems, which regulate the rate of medication release close to the target.
- Targeted drug delivery employs carriers for passive or active diffusion, one base or self-programmed ways, as well as various methodologies to deliver pharmaceuticals. This technique is typically applied in conjunction with appropriate sensory tools that can identify their receptor at the desired place⁴.

Table 1: Classification of Rate-Regulated Mechanisms in Sustained or Controlled Release Systems.

Type of System	Rate control Mechanism
Diffusion – Controlled	
Reservoir systems (Ocusert)	Through-membrane diffusion
Monolithic systems (Transdermal drug)	Through-membrane diffusion
Delivery system- Nitro -dur)	Delivery system- Nitro -dur)
Water Penetration Controlled	
Osmotic systems (Oros, Alzet osmotic pump)	Osmotic water transport through a semi-permeable membrane
Swelling system(hydrogel)	Water seepage through glassy polymer
Chemically - Controlled	

Pendent systems	combination of pendent group diffusion from bulk polymer and hydrolysis
Ion – exchange resins	Drugs that are acidic or basic exchange ions with resins

III. RECENT DEVELOPMENTS IN NOVEL DRUG DELIVERY SYSTEM

- Phytosome
- Liposome
- Nanoparticles
- Emulsions
- Microsphere
- Solid lipid nanoparticle
- Niosomes
- Transdermal Drug Delivery System⁵

- 1. Phytosomes:** A lipid-compatible molecular complex is referred to as a "phytosome" where "phyto" denotes a plant and "some" denotes a cell-like structure⁶. A new herbal medication delivery method called a "Phytosome" is created by mixing phosphatidyl choline with polyphenolic phytoconstituents in the proper molar ratio. Phytosomes are more efficient herbal products than traditional herbal extracts because they are more easily absorbed and used to produce stronger effects. The pharmacokinetic and therapeutic properties of phytosomes are superior to those of conventional herbal extracts⁷.

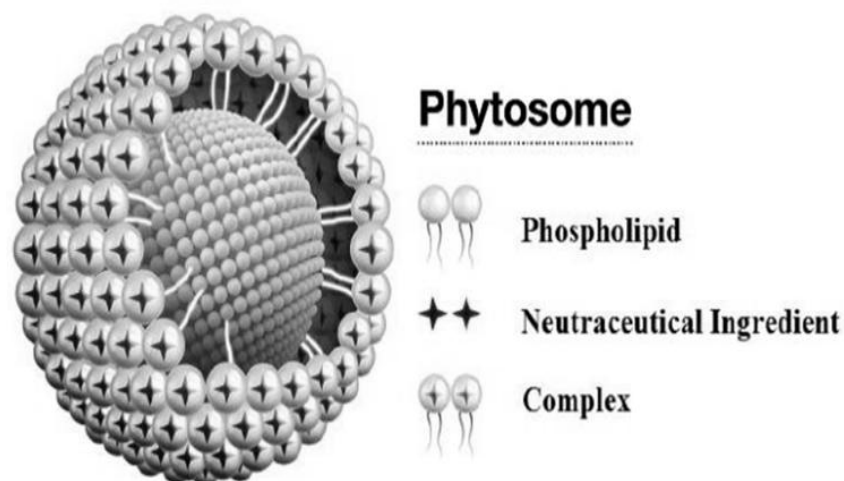


Figure 1: Shows Phytosomes

- **Advantages of Phytosome**
 - A modest amount is needed since phytosome increases the absorption of the active ingredients.
 - The liver can be targeted, and there is a considerable increase in the solubility of herbal compounds in bile as well as drug entrapment.

- Because they form chemical bonds, phosphatidylcholine molecules in phytosomes are stable⁸.
- The percutaneous absorption of herbal phytoconstituents is increased by phytosome⁹

- **Method for Preparation for Phytosomes**¹⁰

- Phospholipids
- Dissolved in an organic solvent that also contains the drug or extract.
- Drug/extract solution of phospholipids in organic solvent Drying
- Development of thin films
- Hydration
- Phytosomal suspension formation.

2. **Liposomes:** Early in the 1960s, Bingham and his colleagues developed liposomes, which went on to become the most thoroughly researched drug delivery method. They were initially employed to research the behaviour of in vitro-simulated biomembranes, but they have since emerged as potent therapeutic tools, particularly for drug delivery and drug targeting⁴.

Lipid or fat molecule-filled tiny pouches with a water core are frequently employed in clinical cancer treatment. Liposomes come in a variety of forms and are frequently used to administer vaccinations and fight infectious diseases. They encapsulate cancer therapy medications in addition to protecting healthy cells from their toxicity and preventing their concentration in delicate organs like the kidneys and liver of cancer patients. Additionally, liposomes can lessen or even completely eradicate a number of typical side effects of cancer treatment, including nausea and hair loss.

They are vesicles made up of one, a few, or several phospholipid bilayers. Polar medicinal chemicals can be encapsulated thanks to the liposomal core's polar nature. Amphiphilic and lipophilic chemicals are soluble in phospholipid bilayers due to their attraction for phospholipids¹¹

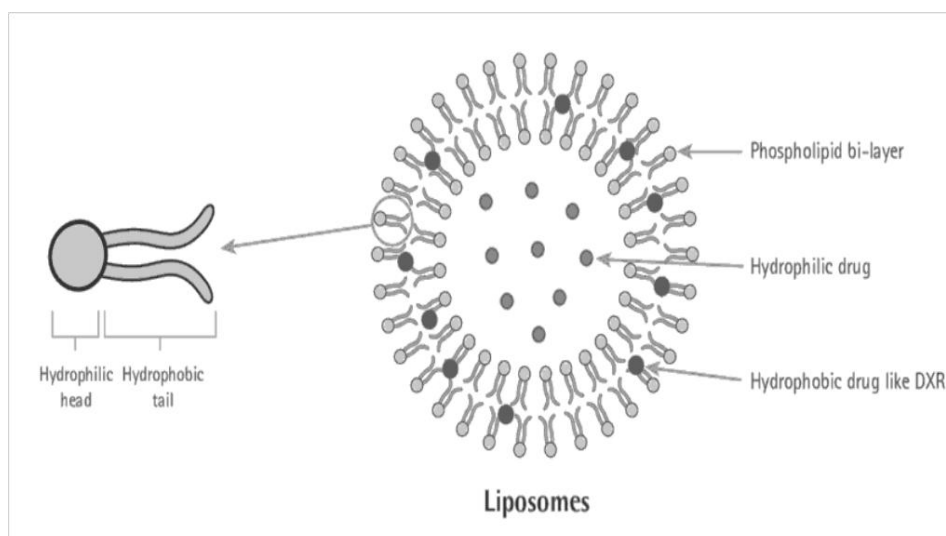


Figure 2: Liposome

- **Liposome Classification based on Structural Features¹²**
 - Multilamellar large vesicles (MLV)
 - Oligolamellar vesicles (OLV)
 - Unilamellar vesicles
 - Small unilamellar vesicles, or SUV
 - Unilamellar vesicles of the MUV size
 - Large unilamellar vesicles, or LUV
 - Giant unilamellar vesicles, or GUV
 - Multivesicular vesicles (MVV)

- **Liposome Classification based on Method of Liposome Preparation¹²**
 - REV - A reverse phase evaporation process that produces a single or oligolamellar vesicle.
 - Multilamellar vesicles generated using the reverse phase evaporation method (MLV/REV).
 - Stable plurilamellar vesicles or SPLV.
 - FAT-MLV Thawed from frozen MLV
 - VET - Vesicles made during the extrusion process.
 - Fusion-prepared FUV-vesicles
 - French press-prepared FPV -Vesicles
 - Dehydration and rehydration vesicles,

- **Advantages of Liposomes**
 - The extensive biocompatibility.
 - The setup's ease of use.
 - The ability to load hydrophilic, amphiphilic, and lipophilic substances due to chemical flexibility.
 - The pharmacokinetic characteristics of the bilayer components can be easily modified by merely changing their chemical makeup¹³.

- **Use of Liposomes:** The utilization of liposomes to deliver medications to the site of action is a noteworthy advancement in inventive drug delivery methods. It is possible for modified and unmodified liposomes to change how a medication acts pharmacokinetically. These are widely used to avoid harmful side effects including myelosuppression while delivering cytotoxic medications to cancer tissue. These are also used in receptor-mediated endocytosis for targeting. Modified liposomes have considerable potential for drug delivery to organs like the heart, liver, kidney, lungs, and bones¹⁴.

3. Nanoparticles: Nanoparticles are in the solid state whether they are amorphous or crystalline. Nanospheres and nanocapsules are among them, and their sizes range between 10 and 200 nm. To protect the medication from enzymatic and chemical deterioration, they have the ability to adsorb and/or encapsulate it. Biodegradable polymeric nanoparticles have received considerable attention recently as potential drug delivery systems because of their applications in the controlled release of medications, the targeting of specific organs and tissues, acting as DNA carriers in gene therapy, and being able to deliver proteins, peptides, and genes via the oral route^{15,16}

- **Advantages of Herbal Nanoparticle Delivery System**

- A nanoparticulate delivery system is used to deliver the herbal formulation to the site of action.
- Enhanced therapeutic index and efficacy.
- More stability thanks to encapsulation.
- A more favourable pharmacokinetic result.
- Capable of being produced in a range of sizes and surface characteristics¹⁷.

- **Method of Drug Delivery Using Nanoparticles:** By inhibiting the Reticulo endothelial system, using increased permeability, retention effect, and targeting, nanoparticles administer the medication on-site. Drugs that are carriers of nanoparticles use two types of strategies¹⁵.

- **Surface Bound:** The drug molecules are attached to the surface of the nanoparticles.
- **Core Bound:** Using this method, the drug particles are condensed into the nano pharma matrix and delivered to the target inside the body. By adding or adding to the reaction mixture during polymerization to a solution that comprises previously manufactured nano particles, drugs can be loaded onto nano particles. The key to how nanoparticles interact with pharmaceutical goods may be chemistry, surface adsorption, or any binding or contact. The quantity rely on the polymer's and drug's chemical composition, as well as the conditions for drug loading, the drug's ability to bind other substances, and how the drug interacts with nanoparticles¹⁵.

4. Emulsions: A biphasic system called an emulsion is produced when one phase is intimately distributed in the other phase as tiny droplets with diameters ranging from 0.1 m to 100 m. An emulsion always has an aqueous (water-containing) phase and a non-aqueous (oily liquid-containing) phase. The sub-microemulsion of these is referred to as a liquid emulsion, and the microemulsion is also referred to as a nanoemulsion¹⁸. Typically, a co-surfactant is coupled with a transparent, thermodynamically stable microemulsion¹⁹.

- **Advantages of Emulsion-Based Formulations**

- Because the medication is made directly and packed in the inner phase, the drug can be released gradually.
- Contact with other tissues and the body.

- Lipophilic medications create an o/w/o emulsion, which is phagocytosed by macrophages, increasing the drug's concentration in the liver, spleen, and kidney.
- The herbal formulation in the emulsion improves the drug's ability to permeate skin and mucus while increasing the stability of the hydrolyzed produced material.
- Elemenum emulsion, a new variant, is an anti-cancer drug that has no detrimental effects on the heart or liver²⁰.

5. Microspheres: Natural biodegradable powders with a particle size of less than 200 m are known as microspheres. They are often formed of proteins or synthetic polymers and flow freely. Polymers are the components utilised to create microspheres. They are separated into two groups.

- Synthetic Polymers
- Natural polymers

There are two categories of synthetic polymers.

- **Non-Biodegradable Plastics**

- Epoxy polymers
- glycidyl methacrylate
- poly methyl methacrylate

- **Biodegradable Materials**

- Lactides, glycolides, and their associated polymers
- Polyalkyl cyano acrylates
- Poly anhydrides

- **Synthetic Polymers:** Poly alkyl cyanoacrylates have the potential to be employed as a medication delivery method for parenteral and other oral formulations. Narcotic antagonists and anti-cancer drugs including doxorubicin, cyclophosphamide, and cisplatin can be effectively transported by polylactic acid. Co-polymers of poly lactic acid and poly glycolic acid have been used to generate sustained release formulations for antimalarial medications as well as many other treatments. The use of poly anhydride microspheres (40 m) to extend the precorneal residence duration for intraocular injection has been studied. Timolol Maleate is packaged in Poly Adipic Anhydride for ocular injection. the functional polyacrolein microspheres.

There is no need for activation procedures because the NH₂ group of the protein can react with the surface-bound free CHO groups to create Schiff's base. Parenterally administered non-biodegradable drug carriers have the potential to induce long-term carrier toxicity because they continue to exist in the body after the medication has been totally eliminated. Because they do not have to worry about carrier toxicity, parenteral applications are better suited for biodegradable carriers that degrade in the body to non-toxic breakdown products¹

6. Solid Lipid Nanoparticles: The medicine or method of drug delivery known as (SLNs) is new. The use of surface modification, prodrug synthesis, complex formation, permeation enhancers, and colloidal lipid carrier-based techniques are among the

conventional approaches for administering drugs to intestinal lymphatics. Current studies have also concentrated on alternative potential carriers for oral intestinal lymphatic administration, including polymeric nanoparticles, liposomes, microemulsions, micellar solutions, and self-emulsifying delivery systems²¹

A solid lipid nanoparticle's typical shape is spherical, and its diameter ranges from 10 to 1000 nanometers. Lipophilic compounds can be dissolved by the solid lipid core matrix of solid lipid nanoparticles. The emulsifying properties of surfactants aid in lipid core stabilisation. In this context, the term "lipid" can refer to a wide variety of compounds, including triglycerides (such as tristearin), diglycerides (such as glycerolbahenate), mono-glycerides (such as glycerol monostearate), fatty acids (such as stearic acid), steroids (such as cholesterol), and waxes (such as cetylpalmitate). To stabilize the lipid dispersion, various emulsifiers with different charges and molecular weights have been utilised. It has been found that using several emulsifiers can aid to prevent particle agglomeration more successfully^{22,23}

7. **Niosomes:** These lamellar microscopic structures are produced by mixing a cholesterol admixture, a nonionic surfactant, and a charges-inducer. They are then hydrated in watery settings. Pharmaceutical substances with a wide variety of solubilities can be accommodated by the infrastructure of hydrophobic and hydrophilic moiety subunits found in niosomes. Niosomes have been researched for many potential medical applications. The ability to limit drug release of such substances, which has the power to reduce systemic toxicity by encapsulating therapeutic medicines, has significant advantages in clinical application and figure 4's niosome structure²⁴

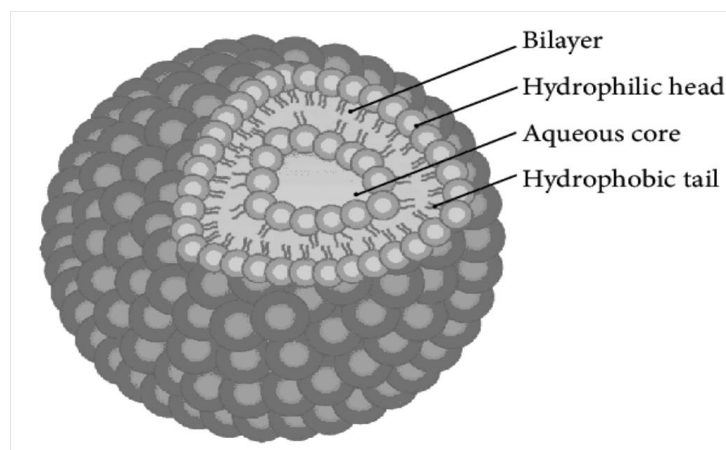


Figure 3: Structure of Niosome

- **Types of Niosomes**

- Niosomes are classified based on number of bilayer, size and method of preparation.
- Multilamellar- 0.5 μ m to 10 μ m in diameter.
- Larger unilamellar- 0.1 μ m to 1 μ m in diameter
- Small unilamellar – 25-500nm in diameter²⁵

- **Advantages of Niosome**

- Niosomes are compatible, non-toxic, biodegradable, and non-immunogenic.
- Niosomes have the capacity to contain significant amounts of material in relatively small vesicles.
- Niosomes are more effective, happy, and compliant than conventional oily formulas.
- Chemicals that are hydrophilic, lipophilic, and amphiphilic can all be captured by niosomes. (The distinctive composition of medicines).
- Niosome characteristics including kind, flow, and size can be easily observed alterations to production procedures and structural design.
- Oral, parenteral, and administrative methods can all be used to give niosomes. available in a variety of forms, including topical, powders, semisolids, and solutions.
- The niosome is easy to store due to the chemical stability of the structural structure²⁶.

8. Transdermal Drug Delivery System: Applying self-contained, discrete dose forms to intact skin in order to give medications to the bloodstream at a controlled rate is known as transdermal medication delivery. The transdermal drug delivery system (TDDS), a crucial element of contemporary drug delivery systems, is now a part of these systems^{27,28}. Because it is efficient and secure, transdermal delivery is an exciting option.

The benefits of giving medicines topically to achieve systemic effects include:

- Steer clear of first-pass metabolism
- Avoiding problems with gastro intestinal compatibility
- Predictable behaviour that lasts a long time
- Increasing physiological and pharmacological response.
- Therapy can be easily interrupted at any time.
- Improved patient compliance as a result of the removal of multiple dosing
- The summary possess the ability to regulate oneself
- To enhance treatment effectiveness

IV. FUTURE PROSPECTS AND OPPORTUNITIES IN INDIA

India is one of the major markets for the pharmaceutical sector. As a result, several multinational behemoths are prepared to invest and develop in this field. A result of advancements in novel and cutting-edge NDDS methods, there will be a strong need for the utilization of various excipients. The ability of India to quickly absorb novel excipients and related technology is well known. As a result, there will be two avenues for the Indian market for excipients to expand: First, by exporting cutting-edge organic excipients, and second, by incorporating fresh excipients into a range of cutting-edge delivery techniques. The bulk of the country's pharmaceutical companies have been submitting fresh patent requests and getting them approved in the field of inventive medication delivery techniques. This will consequently result in an immediate rise in demand for the goods and services provided by pharmaceutical firms and other related enterprises. Modern nanotechnology has the ability to improve diagnosis, therapy, and help with the monitoring of post-administration medication

composition changes in body systems. This is especially true with new drug delivery methods. The development of computer-aided drug design is an important milestone that merits discussion in this context since it opens up many opportunities for the development of these kinds of innovative, new systems. With computer-aided drug design, it is possible to manufacture drugs and their delivery systems with more accuracy and quality while consuming less time and resources than with traditional methods^{29,30}

V. CONCLUSION

The Novel Drug Delivery Systems provide health practitioners with a wide choice of arsenals to cure illnesses with previously unheard of efficacy, safety, and accuracy. Clinically, the NDDS allows for medication tailoring to the site of action, which minimizes dose-related side effects in addition to smoothing the saw-tooth pattern of drug levels in blood. Herbal medicines are the subject of extensive study to include them in NDDS methods. Due to the large molecular size, poor solubility, and GI degradation of herbal medicines, the application of these novel techniques to natural medicines will result in improved bioavailability, reduced toxicity, sustained release action, and protection from GI degradation, which cannot be obtained through conventional drug delivery system. A major number of the standard dosage forms are anticipated to be replaced by these NDDS in the near future as more and more research efforts are directed in this direction, which is anticipated to improve health care delivery overall.

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