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A REVIEW ON NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT

Although the search for a novel drug delivery system (NDDS) has been ongoing for a while, it has gained steam in recent decades. Compared to the traditional dosage form, NDDS offers a number of benefits, including improved therapeutic results. Since NDDS is one method of introducing new items into the controlled market, it is also preferred in the new patent regime. Over the past few decades, a variety of NDDS have been developed, including: Aquasome, Dendrimers, Multiple Emulsions, Microemulsions, Liposomes, Niosomes, Pharmacosomes, Osmotically Modulated Drug Delivery Systems, Transdermal Therapeutic Systems (TTS), Self-Regulating Drug Delivery System, Brain Targeted Delivery System, and Nanoparticles.

While another study indicated that U.S. sales of advanced drug delivery systems were over $54.2 billion in 2004 and would reach $153.5 billion by 2011, a recent analysis shows that the global market for NDDS was 37.9 billion in 2000 and would grow to 75 billion by 2005. Similar trends are being seen in India, where certain pharmaceutical companies have changed their research priorities to create NDDS. Both the public and commercial sectors in India are conducting extensive research, and the Indian market offers a variety of these items.

Keywords: Novel Drug Delivery System, Vehicles, Phytosome.

1. INTRODUCTION

Novel Drug Delivery System (NDDS)

A **novel drug delivery system** is a modern approach that uses new technologies and innovative methods to deliver medicines safely and effectively to produce the desired effect. It is a **formulation or device** that delivers a drug to a **specific part of the body** at a **controlled rate**.

Novel substances are **new compounds** that were not previously known to drug experts, including some **illicit drugs** and **counterfeit medicines**. NDDS plays a very important role in **increasing therapeutic efficiency**, **reducing toxicity**, **improving patient compliance**, and even enabling **new medical treatments**.

The main **routes** of NDDS include:

- Oral
- Parenteral (injection)
- Sublingual
- Topical
- Transdermal
- Nasal
- Ocular
- Rectal
- Vaginal

However, drug delivery is **not limited** to these routes; several other innovative routes are also being explored.

2. AIM AND OBJECTIVES

AIM:

A review of **Novel Drug Delivery Systems (NDDS)** — exploring recent advancements and their applications.

OBJECTIVES:

1. To provide a detailed overview of **traditional drug delivery systems**.
2. To focus on **nanotechnology-based advancements** in drug delivery.
3. To study how innovations improve **drug stability, solubility, and bioavailability**.
4. To explore NDDS applications in areas like **cancer, brain disorders, and infections**.

5. To highlight the role of **biodegradable and sustained-release systems**.
6. To examine how NDDS improves **patient convenience and treatment compliance**.

Need for NDDS

Traditional dosage forms have several problems such as:

- High doses with low bioavailability
- Instability
- First-pass metabolism
- Irregular plasma drug levels
- Rapid drug release

NDDS helps to **overcome these limitations** by improving drug performance, patient compliance, product stability, and shelf life.

Due to their improved properties and better safety, **nanoparticles** have gained much attention. They are widely used in many applications and have unique **pharmacokinetic and pharmacodynamic** properties.

Nanoparticles are very small particles, **10–100 nanometers in diameter**, that can carry both **small and large molecules** to the target tissue. Drugs may be **dissolved, encapsulated, or adsorbed** within these nanoparticles.

They can improve **drug stability**, **enzyme resistance**, and **drug solubility** in the bloodstream. While designing nanoparticles, factors such as **release pattern**, **size**, and **surface properties** must be carefully controlled to ensure targeted action and optimal dosing.

The first nanoparticles were made from **non-biodegradable polymers** such as polyacrylamide, polymethyl methacrylate, and polystyrene. Later, **biodegradable polymeric nanoparticles** were developed, which could carry drugs or proteins either **within their matrix** or **on their surface**.

Depending on how they are prepared, nanoparticles can be:

- **Nanospheres** – where the drug is evenly dispersed throughout the matrix.
- **Nanocapsules** – where the drug is enclosed within a cavity surrounded by a polymeric membrane.

In recent years, nanoparticles have also been used as **DNA carriers in gene therapy**, especially those made with **hydrophilic polymers** like polyethylene glycol (PEG), which help prolong circulation time and deliver DNA or proteins to specific organs.

Definition

Nanoparticles are **solid particles**, either **amorphous or crystalline**, with sizes ranging from **10–1000 nm** (usually 10–200 nm). They can act as carriers where the drug is **dissolved, trapped, encapsulated, or attached** to their surface.

Drug Delivery System (DDS)

A **drug delivery system** is a **formulation or device** that helps introduce a drug into the body and improves its **efficacy and safety** by controlling the **rate, timing, and site** of drug release.

It involves:

1. Administration of the drug,
2. Release of the active ingredients, and
3. Transport of the drug to the site of action through biological membranes.

Types of Drug Delivery Systems

1. Conventional / Traditional Drug Delivery Systems

These are the older, commonly used methods. They are simple, safe, and familiar but have limitations like poor control over drug release.

Examples include:

- Oral
- Injectable
- Topical
- Inhalation
- Rectal and Vaginal
- Transdermal

- Sublingual and Buccal
- Controlled-release formulations

2. Novel Drug Delivery Systems

These are advanced methods that improve how drugs are delivered, enhance therapeutic action, and reduce side effects.

Examples include:

- Nanocapsules, Nanoshells
- Nanocrystals, Dendrimers
- Microsponge, Nanosponge
- Solid Lipid Nanoparticles
- Micelles, Hydrogels
- Transfersomes, Phytosomes, Cubosomes
- Nanosuspensions and Nanoemulsions
- Liposomes, Ethosomes, Niosomes

Drug Delivery Carriers

Drug carriers include systems like **micelles, vesicles, liquid crystals, and nanoparticles** (10–400 nm in size). These carriers improve the drug's performance and help it reach the desired site more effectively.

Drugs incorporated into these carriers can interact with their structure, affecting how they behave. **Amphiphilic block copolymers** are especially useful because their **size and shape** can be adjusted for specific drug delivery purposes. Adding **cross-linkable groups** helps make them more stable and allows **better control of drug release**.

By attaching **specific ligands**, these systems can target drugs more precisely to the desired site of action.

Need for Novel Drug Delivery Systems

About **95% of experimental drugs** today have poor pharmacokinetic or biopharmaceutical properties. NDDS is needed to:

- Deliver drugs directly to the target site
- Reduce harm to healthy tissues
- Improve therapeutic effects and safety

Reasons include:

1. **Pharmaceutical:** Poor solubility and inconsistent dosing
2. **Biotechnology:** Low absorption and instability in the body
3. **Pharmacodynamics:** Short half-life and wide drug distribution
4. **Clinical:** Poor therapeutic index

Advantages of NDDS

1. More user-friendly medication
2. Better treatment outcomes
3. Fewer side effects
4. Reduced healthcare costs
5. Control over how long a drug acts
6. Less frequent dosing
7. Site-specific drug release
8. Constant drug levels in the body
9. Fewer emergency treatments
10. Direct delivery to the central nervous system
11. Better tissue penetration
12. Improved solubility of drugs

Disadvantages of Novel Drug Delivery Systems (NDDS)

1. May cause **local side effects** at the site of administration.

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2. **Designing and developing** NDDS is complex and time-consuming.
3. Requires **high research and development costs**.
4. **Regulatory approval** is more difficult because detailed safety and efficacy testing is needed.
5. Some **new materials** used in NDDS may raise **biocompatibility and long-term safety** concerns.
6. **Advanced technologies** may not be easily available in **developing or resource-limited regions**.
7. Some systems use **non-biodegradable materials**, which can pose **environmental challenges**.
8. **Disposal** of these devices or carriers can contribute to **environmental pollution**.

Types of Novel Drug Delivery Systems

1. Phytosomes
2. Liposomes
3. Nanoparticles
4. Emulsions
5. Microspheres
6. Ethosomes
7. Solid Lipid Nanoparticles
8. Niosomes
9. Proniosomes
10. Transdermal Drug Delivery Systems
11. Dendrimers
12. Transferosomes

(Figure 2: Types of Novel Drug Delivery Systems)

1. Phytosomes

Most herbal medicines contain **bioactive compounds** like **flavonoids**, which are poorly absorbed when taken orally. To improve absorption, these **water-soluble plant molecules** (mainly polyphenols) are made **lipid-compatible**, forming **phytosomes**.

Phytosomes have **better bioavailability** than simple herbal extracts because they can easily **pass through lipid-rich cell membranes** and reach the target site. The **phospholipids** used to make them are mainly **phosphatidylcholine** from soy.

Originally developed for **cosmetic uses**, phytosomes are now being explored for **drug delivery** in areas such as **heart disease, inflammation, liver protection, and cancer treatment**. They show improved **pharmacokinetics** and **therapeutic performance** compared to regular herbal extracts.

The word **"Phyto"** means **plant**, and **"some"** means **cell-like structure**. Phytosomes protect the active herbal ingredients from **digestive enzymes and bacterial degradation**, improve **absorption**, and enhance **bioavailability**.

(Figure 3: Liposome vs. Phytosome)

Benefits of Phytosomes

1. Better absorption in the gastrointestinal tract.
2. Improved bioavailability and therapeutic effects.
3. Smaller doses required for the same effect.
4. More stability and longer shelf life.
5. High lipid solubility improves skin penetration (used in cosmetics).
6. Provides additional liver protection due to phosphatidylcholine.
7. Better clinical outcomes compared to traditional herbal extracts.

Method of Preparation

1. Dissolve **phospholipids** and **herbal extract** in an organic solvent.
2. Evaporate the solvent to form a **thin film**.
3. **Hydrate** the film to create a **phytosomal suspension**.

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2. Liposomes

Liposomes are **tiny spherical vesicles** made of one or more **phospholipid bilayers** that surround an **aqueous (water-based) core**. The word "liposome" comes from the Greek words *"lipos"* (fat) and *"soma"* (body).

They are **biodegradable**, **biocompatible**, and can carry both **water-loving (hydrophilic)** and **fat-loving (lipophilic)** drugs. Liposomes can vary in size from **0.05–5.0 µm** and form **spontaneously** when phospholipids are hydrated in water.

Liposomes can **target specific tissues**, such as **tumor cells**, by increasing drug concentration in diseased areas and reducing exposure in normal tissues. This is achieved through the **enhanced permeability and retention (EPR) effect**.

Advantages

1. High **biocompatibility** and **low toxicity**.
2. Easy to prepare and modify.
3. Can carry many types of drugs (hydrophilic, lipophilic, or amphiphilic).
4. Adjustable **pharmacokinetic properties** by changing lipid composition.

Classification Based on Structure

- MLV – Multilamellar Vesicles
- OLV – Oligolamellar Vesicles
- UV – Unilamellar Vesicles
- SUV – Small Unilamellar Vesicles
- MUV – Medium Unilamellar Vesicles
- LUV – Large Unilamellar Vesicles
- GUV – Giant Unilamellar Vesicles
- MVV – Multivesicular Vesicles

Classification Based on Preparation Method

- REV – Reverse Phase Evaporation Vesicles
- SPLV – Stable Plurilamellar Vesicles
- FAT-MLV – Frozen and Thawed Multilamellar Vesicles
- VET – Vesicles Prepared by Extrusion
- FPV – Vesicles Prepared by French Press
- DRV – Dehydration–Rehydration Vesicles

(Figure 4: Structure of Liposomes)

3. Nanoparticles

Nanoparticles are **submicron-sized particles** (10–1000 nm) that can carry both **hydrophilic and hydrophobic drugs**. They are designed to control **particle size, surface properties, and drug release** to ensure that the medicine reaches the target site at the **right dose and speed**.

Biodegradable polymeric nanoparticles are especially useful because they can safely degrade in the body after drug delivery.

There are two main types:

- **Nanospheres** – where the drug is evenly dispersed throughout the particle.
- **Nanocapsules** – where the drug is enclosed inside a polymer shell.

Nanoparticles improve **drug solubility**, **absorption**, and **bioavailability** while reducing required doses and side effects.

Drug Loading Methods

1. **Surface-bound** – Drug molecules are attached to the nanoparticle surface.
2. **Core-bound** – Drug molecules are trapped inside the nanoparticle matrix.

The interaction between the drug and nanoparticle depends on the **chemical nature** of both materials.

(Figure 5: Nanoparticle-Based Drug Delivery System)

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4. Emulsions

An **emulsion** is a mixture of two **immiscible liquids** (like oil and water), where one liquid is dispersed in the other in the form of **tiny droplets**. Emulsions generally contain:

- Oil phase
- Water phase
- Surfactant
- Co-surfactant

Emulsions can appear **milky or translucent** depending on droplet size and can be of several types:

- **Ordinary Emulsion (0.1–100 µm)**
- **Microemulsion (10–100 nm)**
- **Submicroemulsion (100–600 nm)**

Microemulsions are also known as **nanoemulsions**.

As a **drug delivery system**, emulsions help target specific organs and provide **sustained drug release**. They also improve the **stability** of drugs, **reduce irritation**, and **enhance penetration** through the skin or mucous membranes.

Herbal drugs like **camptothecin, Brucea javanica oil, coixenolide oil**, and **zedoary oil** have been successfully formulated into emulsions for improved therapeutic effects.

(Figure 6: Types of Emulsion)

5. Microspheres

Microspheres are small, spherical particles ranging in size from **1–50 µm**. They are used to **deliver drugs to specific target sites**, maintain desired drug concentrations, and reduce side effects.

Microencapsulation allows **sustained drug release**, improves **patient compliance**, and reduces **total drug dosage**.

Many plant-derived compounds like **rutin, quercetin, zedoary oil, and tetrandrine** have been made into microspheres.

Specialized types include:

- **Immune microspheres** – coated with antibodies or antigens for targeted immune response.
- **Magnetic microspheres** – guided to target sites using external magnetic fields.

Microspheres are an effective way to **increase drug stability**, **control release**, and **minimize adverse reactions**.

5. ETHOSOMES

Recent advancements in patch technology have led to the development of the **ethosomal patch**, which contains the drug in an **ethosome**.

Ethosomes are mainly made up of **phosphatidylcholine (a lipid), ethanol, and water**. They form **multi-layered vesicles** with a **high drug-carrying capacity**, suitable for both **lipophilic (oil-loving)** and **hydrophilic (water-loving)** drugs.

Ethosomes are **flexible (elastic) vesicles** that can easily pass through the **skin layers** and deliver drugs deep into the skin or even into the **bloodstream**. Compared to normal liposomes, ethosomes show **better drug penetration** through the skin and help in **transdermal and topical drug delivery**.

Ethosomes can efficiently deliver drugs **inside the cells**, including both **hydrophilic and lipophilic drugs**. For example, they increase the skin absorption of **anti-inflammatory herbal drugs** and allow **antibacterial peptides** to reach deep skin cells.

Clinical Studies on Ethosomes

Only a few human studies have been conducted so far:

- **Ethosomal Acyclovir** vs. **Zovirax® cream** (for herpes labialis): Ethosomal acyclovir showed faster healing, quicker crust formation, and reduced pain.
- **Ethosomal Gel with Clindamycin and Salicylic Acid** (for acne): 40 patients used it twice daily for 8 weeks and showed great improvement with fewer pimples and lesions.
- **Ethosomal Prostaglandin E1** (for erectile dysfunction): In 15 patients, 12 showed better penile rigidity and blood flow with no skin irritation.

Figure 8: *Ethosome*

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6. SOLID LIPID NANOPARTICLES (SLNs)

Solid Lipid Nanoparticles (SLNs) are tiny particles (10–1000 nm) made from **solid biodegradable lipids**. They are used to carry both **water-insoluble drugs** and **cosmetic agents** effectively.

SLNs are similar to **liposomes**, but they are **more stable** and made from **safe, natural or synthetic lipids**. They help:

- Protect sensitive drugs from degradation,
- Provide **controlled drug release**,
- Improve **bioavailability**, and
- Reduce **toxicity**.

SLNs can be used for many routes of administration — **oral, dermal (skin), parenteral (injection), ocular, pulmonary, and rectal**.

They are especially good for **lipophilic (fat-soluble)** drugs and show **high biocompatibility** and **low toxicity**.

Figure 9: *Solid Lipid Nanoparticles*

7. NIOSOMES

Niosomes are **microscopic vesicles** made from **non-ionic surfactants** (such as alkyl or dialkyl polyglycerol ethers) and **cholesterol**.

They are **similar to liposomes** but are **cheaper**, **more stable**, and **easier to store** because they do not contain phospholipids that easily oxidize.

Niosomes have **both hydrophobic and hydrophilic regions**, allowing them to carry drugs of many solubilities. They help in **reducing side effects**, **slowing drug clearance**, and **prolonging drug release**.

Figure 10: *Niosomes*

Types of Niosomes

Based on **size, layers, and preparation method**:

1. **Multilamellar Vesicles (MLVs):** 0.5–10 µm in diameter
2. **Large Unilamellar Vesicles (LUVs):** 0.1–1 µm in diameter
3. **Small Unilamellar Vesicles (SUVs):** 25–500 nm in diameter

8. PRONIOSOMES

Proniosomes are the **dry or gel form** of niosomes that turn into niosomes **upon contact with water** (for example, when applied to skin).

They are **easy to store**, **stable**, and can form **niosomal dispersions** quickly before use.

Proniosomes are made of **water-soluble carriers coated with surfactants**, and after hydration, they form **drug-loaded niosomes**.

These systems are useful for delivering drugs **at specific sites** in the body.

Figure 11: *Proniosomes*

9. TRANSDERMAL DRUG DELIVERY SYSTEM (TDDS)

The **Transdermal Drug Delivery System (TDDS)** delivers drugs through the **skin** for either **local** or **systemic** effects.

It provides **controlled, continuous drug release**, **avoids first-pass metabolism**, and is **easy to apply**.

TDDS can deliver both **synthetic** and **herbal drugs**. For example:

- **Boswellic acid** (from *Boswellia serrata*) and **curcumin** (from *Curcuma longa*) have been used in transdermal films for long-term drug release.

This method offers **steady drug levels**, **reduced dosing frequency**, and can be **stopped anytime** by removing the patch.

It can also be seen as a **modern version of traditional Ayurvedic herbal poultices**.

10. DENDRIMERS

Dendrimers are **highly branched, tree-like molecules** made synthetically. The term "dendrimer" comes from the Greek word *"dendron"*, meaning "tree."

They have a **central core**, **branches (layers called generations)**, and **outer functional groups**. Their structure allows **precise control over shape and size**, making them suitable for **drug delivery, catalysis, electronics, and gene therapy**.

Dendrimers can carry several drug molecules on their surface or inside their branches, providing **targeted and controlled drug release**.

Figure 12: *Dendrimer Structure*

11. TRANSFERSOMES

Transfersomes are **ultra-flexible (elastic) vesicles** that can squeeze through very small pores in the skin, much smaller than their own size.

They are designed to **enhance drug penetration** through the **stratum corneum** (the outermost skin layer).

They can carry **small molecules, proteins, peptides, and herbal compounds**. Transfersomes were first introduced by **Gregor Cevc in 1991**.

The name comes from *"transferre"* (to carry) and *"soma"* (body).

They are **self-optimizing and stress-responsive**, meaning they can adjust their shape to move through skin layers effectively.

Their flexibility is due to **edge activators** (surfactants) in their lipid bilayer.

Example: **Capsaicin transfersomes** showed better absorption than pure capsaicin.

Transfersomes offer **non-invasive, targeted drug delivery** and can provide **sustained drug release**.

3. CONCLUSION

Novel Drug Delivery System (NDDS) uses advanced techniques and modern dosage forms that are more effective than traditional ones. NDDS ensures the right amount of medicine reaches the right place at the right time. It also helps reduce production costs, improves the use of expensive drugs, and benefits patients by offering better treatment, comfort, and quality of life.

There are two main types of NDDS:

- Targeted Drug Delivery System – delivers drugs directly to the affected area.
- Controlled Drug Delivery System – releases drugs at a controlled rate over time.

NDDS is widely used in fields such as drug targeting, vaccine delivery, gene therapy, and the development of special carriers like liposomes. These innovations make drug treatment more precise, safe, and effective. They maintain steady drug levels in the blood, reduce side effects, and often require smaller doses.

With continued research, NDDS may soon replace many traditional dosage forms, leading to overall improvements in healthcare. Pharmaceutical companies are investing in NDDS research to compete in the global market. Additionally, new fields like Pharmacovigilance help ensure safer medicines, while Pharmacoeconomics focuses on providing affordable healthcare for all.

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