



Review Article

“Novel Drug Delivery Systems in Contemporary Medicine: Strategies for Targeted and Controlled Drug Delivery”

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ABSTRACT

Conventional drug delivery systems often suffer from limitations such as poor bioavailability, drug instability, rapid drug release, and fluctuating plasma drug concentrations, which can compromise therapeutic efficacy and patient compliance. Novel Drug Delivery Systems (NDDS) have emerged as advanced pharmaceutical approaches designed to overcome these challenges by enabling targeted, controlled, and sustained drug delivery. This review highlights the development, significance, and applications of NDDS in modern therapeutics. Various carrier-based systems, including liposomes, nanoparticles, microspheres, and niosomes, are discussed alongside advanced transdermal delivery techniques such as sonophoresis, osmotic pump systems, and microencapsulation. The key characteristics, advantages, limitations, and factors influencing the performance of NDDS are critically examined. Particular emphasis is placed on polymeric nanoparticles and liposomal systems, focusing on their structural design, fabrication techniques, and potential for site-specific drug targeting and controlled release. Recent advances in biotechnology and pharmaceutical engineering have further enhanced the efficiency and clinical applicability of NDDS, offering improved therapeutic outcomes, reduced dosing frequency, and enhanced patient adherence. Overall, NDDS represent a transformative strategy in drug delivery, contributing significantly to the optimization of drug therapy and the advancement of personalized medicine.

Introduction

The purpose of novel drug delivery systems is to administer medications continuously over a long length of time in the bloodstream at predictable and repeatable kinetics. New Drug Delivery System (NDDS) carriers come in a wide variety of grade levels. Overdose, Andrews, instability, initial effects, variations in plasma concentration, and fast release are among the issues with conventional formulations. Basic: Product shelf life, patient compliance, protection, and efficacy. NDDS will deal with these problems. With the advent of Novel Drug Delivery Systems (NDDS), which promise a new era of accuracy and effectiveness in therapeutic treatments, the drug delivery landscape is experiencing a dramatic journey. This thorough analysis aims to disentangle the complex web of NDDS by exploring the most recent discoveries, developments, and their potential to completely transform how we use and deliver medications. Conventional medication administration techniques have historically encountered difficulties with poor patient adherence, off-target effects, and insufficient bioavailability. In the world of modern medicine, new techniques known as novel drug delivery systems are presented in cases where certain medications have slow progress in severe diseases. This method involves combining the medicine with a carrier or altering the drug's molecular structure to ensure controlled drug distribution. These will regulate the drug's pharmacokinetics, pharmacodynamics, toxicity, immunogenicity, and efficacy. A novel medicine delivery method that was once merely a dream is now a reality. It has been usual practice to develop new medications with safe and effective therapies, but this has been very expensive, time-consuming, and labor-

intensive. Subsequently, it was discovered that the drug's distribution inside the biological system has a significant impact on the system's efficacy and safety because the drug acts appropriately at target areas. Nowadays, people are paying more attention to nanoparticles as they become more aware of their advantages for the environment and how they affect human health and environmental sustainability. Numerous methods are used in a wide range of applications to create nanoparticles.

The sizes of nanoparticles range from 10 to 100 nm. A number of factors, including release pattern, size, and surface characteristics that define the particular surface in the production of nanoparticles, must be taken into consideration. It is also important to comprehend the consequences of employing the appropriate medication on quality and cost. For instance, proteins or medications may be included in polymeric nanoparticles. These bioactive materials may be chemically or physically present on the surface, or they may be preserved in the polymer matrix in solid or solution form. Drugs for premade nanoparticles can be employed in the nanoparticle preparation process. These bioactive compounds can be chemically or physically bonded to the particle surface, or they can be trapped as solid solutions or particles in the polymer matrix. While the nanoparticles are being manufactured, the medicine or drugs can be added. Both biodegradable and non-biodegradable polymers can be used to create drug-carrying nanoparticles. This thorough analysis explores the fascinating realm of NDDS, revealing its mysteries and demonstrating its revolutionary potential. The different nano drug carriers are displayed in the list below¹.

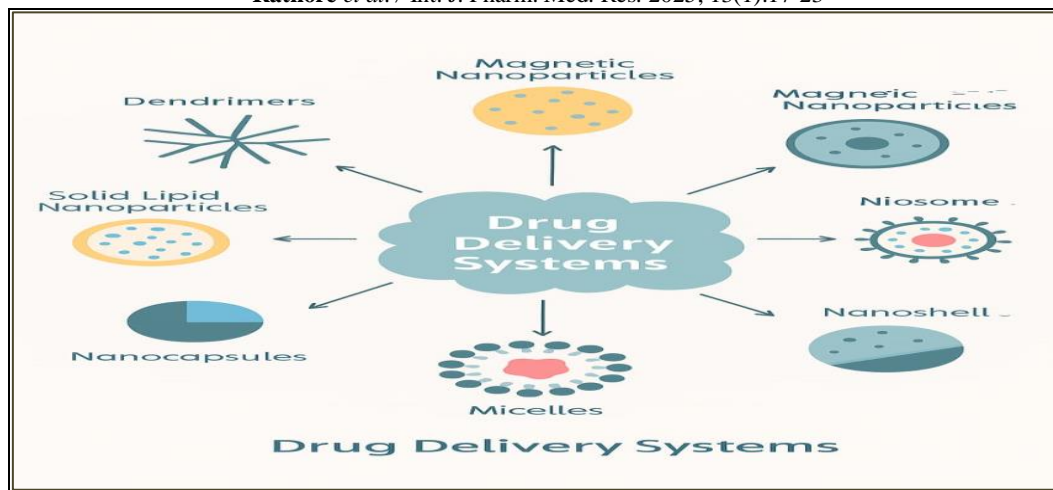


Fig.:1 Classification Of Drug Delivery System

1.1 Definition :

Novel Drug Delivery Systems (NDDS) are innovative approaches and technologies designed to enhance the safety, therapeutic efficacy, and patient compliance of pharmaceuticals. These technologies improve medication bioavailability, target certain body locations, and allow regulated release¹.

1.2 Features of Novel Drug Delivery System

- ❖ Provide controlled delivery of drug
- ❖ Cost-effective.
- ❖ Increase the bioavailability
- ❖ Easy to administer, safe and reliable.

1.3 Factors affecting NDDS

- 1) NDDS also vary on Route of drug administration .
- 2) Chronic therapy
- 3) The disease level
- 4) Physicochemical property of drug molecules are of the main factor of drug efficiency.
- 5) Site of action

1.4 Advantages of novel drug delivery system

- 1) It provide sustained delivery.
- 2) NDDS improved tissue macrophages distribution.
- 3) Drugs are protection from physical and chemical degradation.
- 4) Enhancement of pharmacological activity.
- 5) Enhancement of drug stability.

1.5 Disadvantages of novel drug delivery system

1. Requires highly sophisticated technology for the formulation of NDDS drugs.
2. requires skilled man power for manufacturing, storage and administration.
3. Dose dumping can occur.
4. The immune reactions can be occurred against intravenous administered carrier systems.

5. Difficult to maintain stability of dosage forms.

6. Drug loading can be slow.

1.6 Carrier based Drug Delivery System:

- A) Liposomes
- B) Nanoparticles
- C) Microspheres
- D) Niosomes

1.7 Transdermal Drug Delivery Systems:

- A) Sonophoresis
- B) Osmotic pump
- C) Microencapsulation

2. Carrier based Drug Delivery System:

2.1 Liposomes- Liposomes are a type of vesicle made up of one, several, or many phospholipid bilayers. Polar medicinal molecules can be encapsulated due to the polar nature of the liposomal core. Depending on their affinity for the phospholipids, amphiphilic and lipophilic compounds are solubilized within the phospholipid bilayer. Niosomes are produced when nonionic surfactants, rather than phospholipids, participate in the bilayer building process. Channel proteins function as a size-selective filter that only permits the passive passage of tiny solutes such as ions, nutrients, and antibiotics within the hydrophobic domain of vesicle membranes without losing their activity. As a result, medications enclosed in a nanocage functionalized with channel proteins are successfully shielded from proteolytic enzymes' early destruction. However, the concentration differential between the inside and outside of the nanocage allows the drug molecule to diffuse via the channel. These "smart" liposomes show potential for uses like treating infections or inflammatory illnesses that call for exact temporal and spatial control of medication release. Despite its benefits, problems including high production costs and possible instability during storage are also being investigated[1-3]

1. Composition

- Diethyl ether or ether/methanol mixture

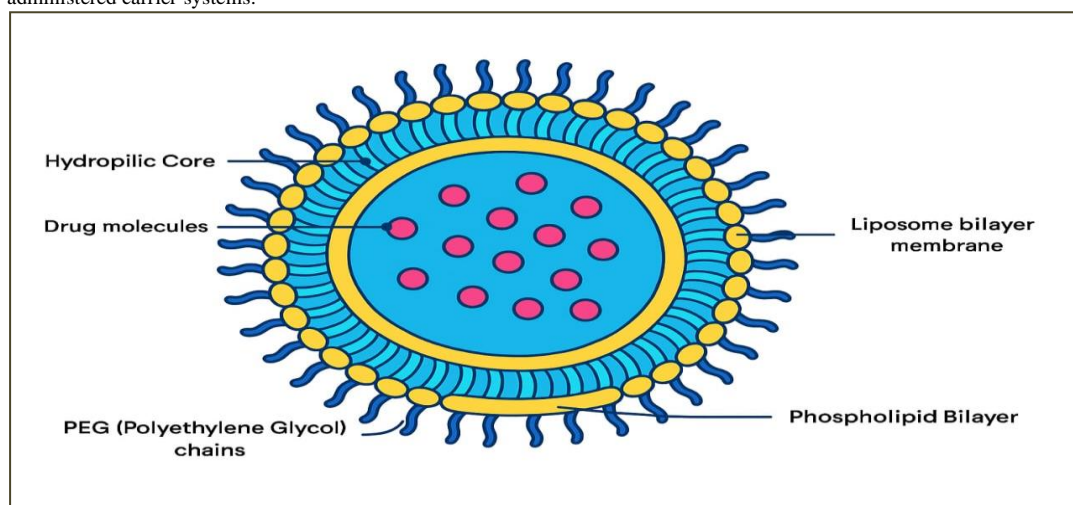


Fig. 2: structure of liposome

2. Method of Preparation

There are several ways to formulate liposomes. The final features of liposomes are significantly influenced by the phospholipid type and the

manufacturing procedure. The processes used to create liposomes can be divided into:

A. The Bangham method of thin-film hydration: In this method, all lipids and the hydrophobic drug are dissolved in a suitable organic solvent using a round-bottom flask. The organic solvent then progressively evaporated at decreasing pressure, creating a thin film layer. The generated thin film is then hydrated at a temperature higher than the transition temperature (T_m) of the employed lipid using an aqueous buffer solution. The hydration solution may contain a hydrophilic substance or medications to be introduced into the aqueous core of the liposomes. The rate of hydration affects how well drugs are

encapsulated. The encapsulation efficiency increases with a slower rate of hydration. Using bath or probe sonicators or extrusion through polycarbonate membranes with specific pore sizes are the two ways to control liposome resizing, lamellarity types, and particle distributions. The extrusion method produces more stable liposomes with greater encapsulation effectiveness than sonication. Sonication can hydrolyze or break down encapsulated drugs and/or lipids in addition to creating SUVs liposomes. Liposome solutions may become contaminated with metal due to probe sonication (FIG.:3).

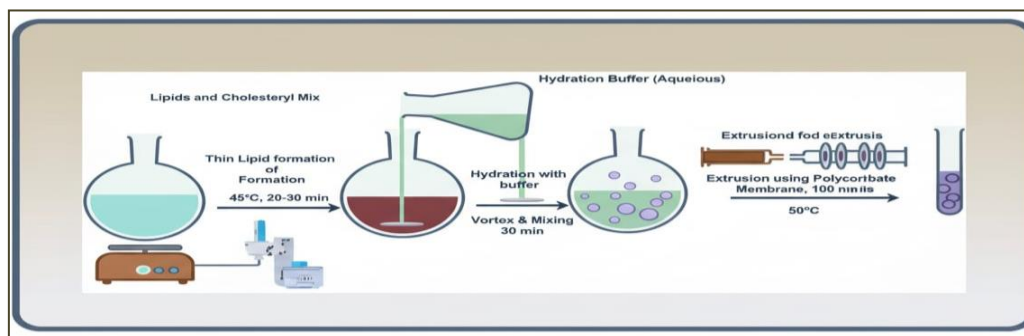


FIG.:3 Thin-Film Method

B. Reverse phase evaporation technique: The reverse phase evaporation approach is based on inverted micelles or water-in-oil emulsions, where the aqueous phase contains the pharmaceuticals of interest and the organic phase is composed of lipids to create liposomal bilayers. We put this lipid mixture in a flask and let the solvents evaporate to create lipid films. The organic phase, which is mostly composed of isopropyl and/or diethyl ether, is then used to dissolve the lipid films once more. The inclusion of the water phase creates a two-

phase system, and the subsequent sonication results in a homogeneous dispersion. The mixture turned into a thick gel as the organic solvent slowly evaporated, forming an aqueous suspension with liposomes. One benefit of the reverse phase evaporation method over the thin-film hydration method is higher internal aqueous loading. Techniques like centrifugation and dialysis can be employed to eliminate the residual organic solvent, even if some may still be present and be able to interact with the lipids or the medications[4-6](Fig. 4)

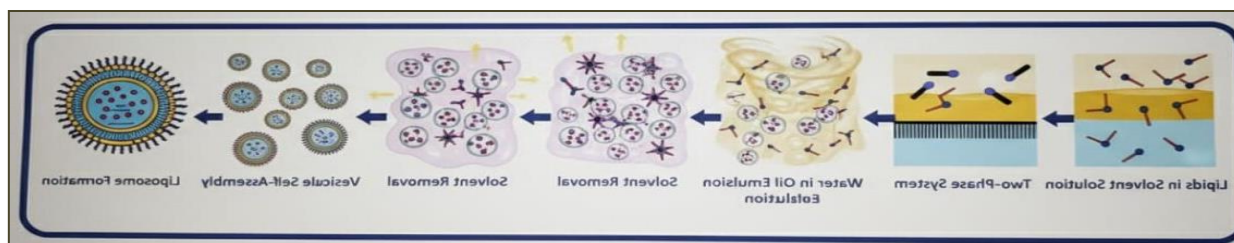


Fig.:4 Flow Chart Of Reverse Phase Evaporation Method.

Table No. 1:Description of different types of liposomes and their benefits

| Type | Description | Benefits Applications |
|--|---|---|
| Conventional Liposomes Composed of naturally occurring phospholipid Offer basic drug encapsulating and delivery functionalities | Drug delivery for variety of disease, and disorders. | Enhanced drug solubility, bioavailability, controlled delivery potential. |
| Cationic Liposomes Possess positively charged surface, interacting with negatively charged cell membrane. | Gene therapy, DNA delivery, non-viral vector delivery. | Efficient gene transfection, enhanced cellular uptake,potential for targeted delivery. |
| Steath Liposomes Modified with polyethylene glycol (PEG) chains, reducing immune system recognition and prolonging circulation in the bloodstream. | Cancer therapy, drug delivery to specific tissues. | Reduced clearance by reticuloendothelial system, longer circulation time improved tumor targeting. |
| Stimuli-Responsive Liposomes Engineered to release their cargo in response to specific stimuli like PH changes, temperature or enzyme | Targeted drug delivery to diseased tissue controlled release based on biological cues | Enhanced therapeutic efficacy reduced side effects, imopproved drug targeting potential. |
| Multifunctional Liposome Combined with targeting ligands , imaging agent or other functionalities for enhancing targeting and monitoring. | Targeted therapy for specific disease diagnosis and treatment integration. | Increased drug delivery efficacy, real-time tracking of drug delivery, personalized medicine potential. |

Nanoparticles

The solid state of nanoparticles, which include nanospheres and nanocapsules with sizes ranging from 10 to 200 nm, can be either amorphous or crystalline. They can encapsulate or adsorb a medication, shielding it from enzymatic and chemical deterioration. While nanospheres are matrix systems where the drug is physically and evenly distributed, nanocapsules are vesicular systems where the medication is contained within a cavity surrounded by a special polymer membrane. Both biodegradable and non-biodegradable polymers can be used to create drug-carrying nanoparticles. Biodegradable polymeric nanoparticles have garnered a lot of interest as possible drug delivery vehicles in recent years due to their potential for controlled drug release, targeting specific organs or tissues,

serving as DNA carriers in gene therapy, and delivering proteins, peptides, and genes orally. Biodegradable polymeric nanoparticles have garnered a lot of interest recently as possible drug delivery vehicles due to their potential for controlled drug release, targeting specific organs or tissues, serving as DNA carriers in gene therapy, and delivering proteins, peptides, and genes orally.

These particles can pass past the fenestration of the small blood vessels' epithelial tissue and enter deeply into the tissues. They don't need to form platelet aggregates to enter the systemic circulation. Because of their smaller particle size, they have a large surface area, which facilitates quicker drug release. Engineered carriers allow for the modulation and control of drug delivery rate and particle integrity, which can be triggered by changes in the pH of the surrounding environment, chemical stimuli through the application of a fast oscillating magnetic field, or an external heat source. Drug delivery systems make substantial use of nanoparticles. They can offer regulated release, encapsulate medications, and shield them from deterioration. The selective accumulation of nanoparticles in tumor tissues is made possible by the increased permeability and retention (EPR) effect. Because of their special qualities and prospective uses in a variety of industries, nanoparticles are still the subject of substantial research[11,12]

1. Composition

Depending on their intended function, nanoparticles can be made of a variety of materials. Gold, silver, silica, polymers, and lipids are examples of common materials. Every material has unique qualities that can be customized for specific uses⁸.

2. Types of Nanoparticles

The four main categories of nanoparticles (NPs) are as follows (Fig. 05):

- **Metallic Nanoparticles:** Often utilized in treatments and diagnostics, these particles are made of metals like gold and silver.
- **Polymeric nanoparticles:** Made of biocompatible polymers, they can be used for imaging and medication delivery.
- **Lipid Nanoparticles:** Solid lipid nanoparticles and liposomes are utilized in gene therapy and drug delivery.
- **Ceramic nanoparticles:** These are inorganic materials used in biomaterials, electronics, and catalysis.

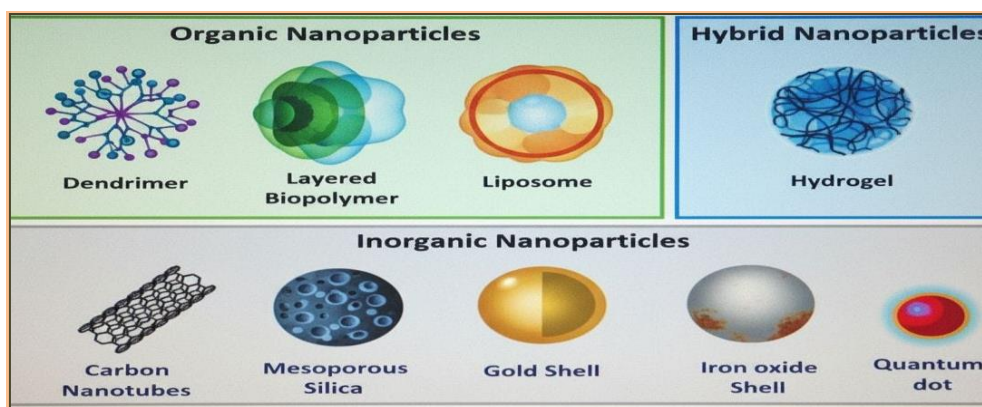


Fig.05: The schematic classification of Nanoparticles

3. Method of Preparation

The two main categories of nanoparticle manufacturing methods are polymerization of monomers and dispersion of premade polymers. The following are some methods for spreading premade polymers:

- Salting out/emulsion diffusion method.
- Spontaneous emulsification method.
- Nonaqueous phase separation method.
- Solvent evaporation method[8-10]

2.3 Microspheres

One drug delivery method that has been extensively studied in cancer chemotherapy is microspheres. They are essentially solid porous particles (diameters ranging from 1 to 100 μm) that can both target their drug load by physically capturing it in blood vessels (chemoembolization) and sustain the therapeutic agent's effect through controlled-release polymeric materials, such as proteins, polysaccharides, polyesters, and lipids, using a variety of methods (emulsification, thermal stabilization, and phase inversion technology).

1. Composition

Microspheres consist of an active drug uniformly dispersed or encapsulated within a polymeric matrix, which controls their stability and drug-release behavior. The polymers may be natural (such as gelatin, chitosan, or alginate) or synthetic (such as PLGA, PLA, or ethyl cellulose). Additional components like cross-linking agents, stabilizers or surfactants, and plasticizers are included to enhance particle stability, uniformity, and controlled drug release[11-12].

2. Method of preparation

The various methods of preparations are:

A. Emulsion Solvent Evaporation Technique

Using this technique, the drug is dissolved in a polymer that has previously been dissolved in chloroform. The resulting solution is then added to an aqueous phase that contains 0.2 percent sodium PVP as an emulsifying agent. The medication and polymer were separated into fine droplets after being agitated at 500 rpm. These droplets were then collected by filtration, rinsed with demineralized water, and allowed to dry for a full day at room temperature. Solvent evaporation produced the solidified microspheres[13,14]

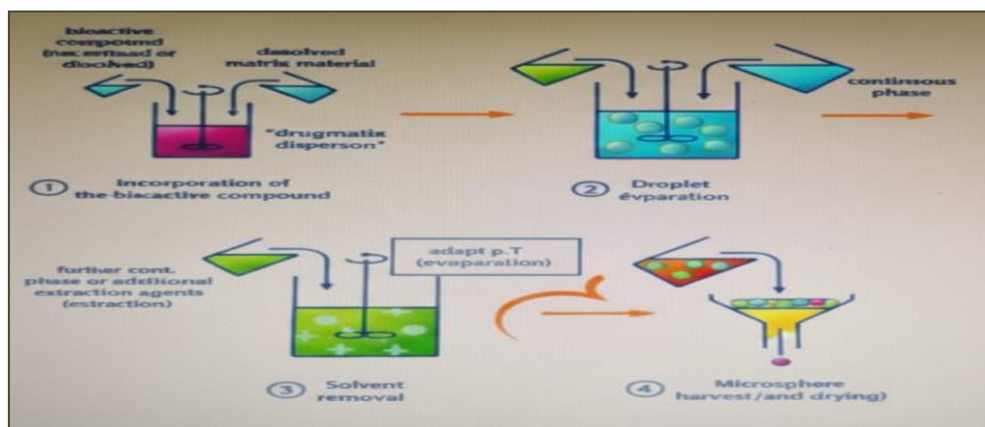


Fig.6: Microspheres by Solvent Evaporation Technique.

2.4 Niosomes

Niosomes are a unique vesicular drug delivery method that can be utilized to administer medications in a sustained, targeted, and regulated way. Liposomes were the first vesicular drug delivery technology; however, they have several disadvantages, such as toxicity, low cost, and stability issues at different pH levels. The disadvantages of liposomes have led to a rise in research interest in niosomes. Niosomes can be either unilamellar or multilamellar. In addition to nonionic surfactants, they might also comprise charged molecules and cholesterol or its derivatives. Because they are made of non-ionic surfactants, niosomes are non-toxic, hence the name [12,13]

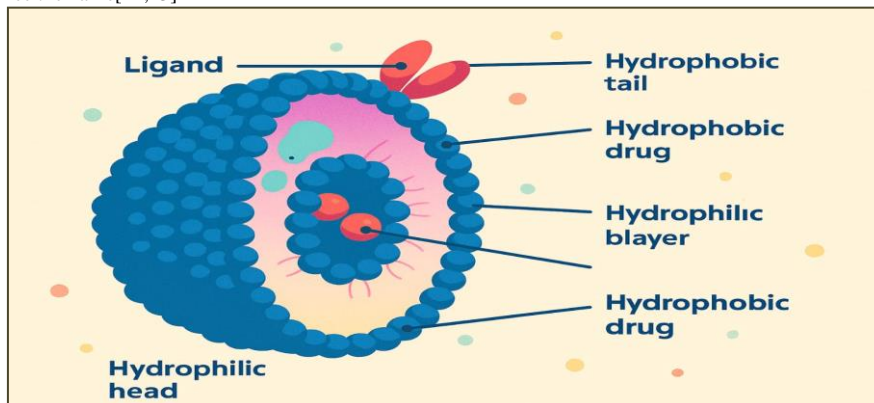


Fig.7: Structure Of Niosome

1. Composition

Niosomes are vesicular drug delivery systems composed primarily of **non-ionic surfactants** that self-assemble into bilayer structures in an aqueous environment. Commonly used surfactants include **Spans, Tweens, and Brij compounds**. **Cholesterol** is added to the formulation to provide membrane rigidity and improve stability and permeability control. In some formulations, a **charge-inducing agent** such as dicetyl phosphate or stearylamine is included to prevent vesicle aggregation and enhance stability. The aqueous core of niosomes can encapsulate hydrophilic drugs, while lipophilic drugs are incorporated within the bilayer, making niosomes versatile carriers for drug delivery [14,15]

2. Method of preparation

A. Ether Injection Method: A 14-gauge needle is used to inject the surfactant into warm water that is kept at 60°C after it has been dissolved in diethyl ether. Next, ether is evaporated to create niosomes with a single layer.

B. Micro fluidization technique: In this technique, two fluidized streams interact in microchannels inside the interaction chamber at extremely high speeds. The arrangement of the thin liquid sheet impingement along a single front ensures that the energy supplied to the system stays within the niosome formation area.

a) Hand shaking method: In an RB flask, dissolve the cholesterol and surfactant in the volatile organic solvent. A rotary evaporator is used to

evaporate the organic solvent at room temperature (20°C). The aqueous phase can then be used to rehydrate the dried surfactant film.

b) Sonication method: The surfactant/cholesterol mixture is mixed with a drug solution in buffer. Niosomes are then produced by probe sonicating the mixture for three minutes at 60°C using a sonicator [18].

3. Transdermal Drug Delivery Systems

3.1 Sonophoresis

Sonophoresis, often called phonophoresis, is a non-invasive method that improves the passage of medications or other therapeutic materials through biological barriers, mainly skin, by using low-frequency ultrasonic waves. This technique uses ultrasonic radiation to significantly speed up the absorption of topical drugs (transdermal administration) into the dermis, epidermis, and appendages of the skin. It's a promising method for increasing bioavailability, delivering drugs to certain target areas, and possibly minimizing negative effects. Sonophoresis is a common method used in hospitals to deliver medication through the skin. Pharmacists synthesize the drugs by mixing them with a coupling agent (gel, cream, or ointment) that enables the ultrasound transducer to deliver ultrasonic energy to the skin [19].

1. Mechanisms of action

Although sonophoresis has attracted a lot of attention lately, its mechanisms remain unclear. acknowledged, taking into account the potential for several incidents following ultrasound exposure. These include:

- Cavitation (gas bubble production and oscillation).
- Convective transport is induced.
- Thermal effects (raising the temperature) [17]

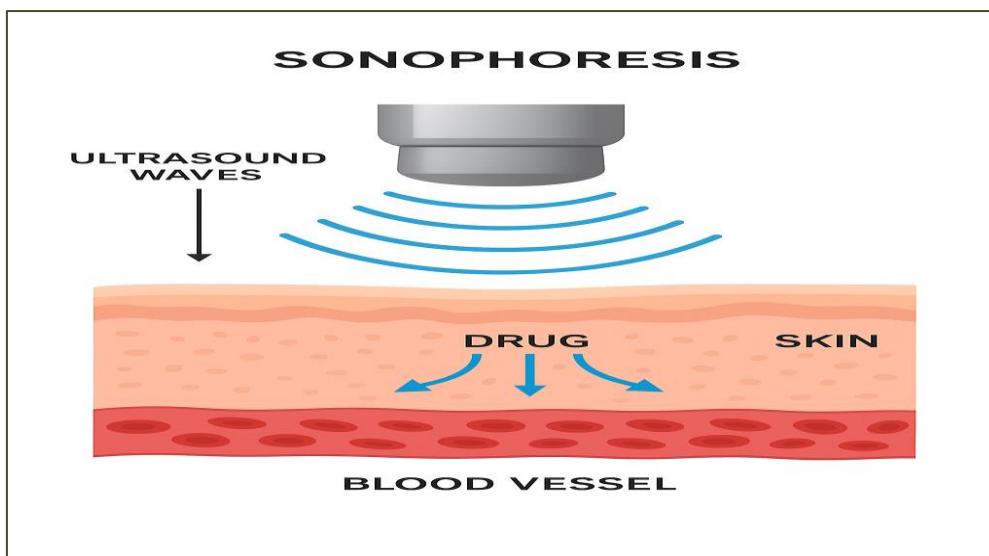


Fig.8: Process Of Sonophoresis

3.2 Osmotic pump

The osmotic pump is a medication delivery method that delivers a regulated and steady rate of drug release over a prolonged period of time by using osmotic pressure. These have one or more drug delivery pores in a semi-permeable membrane covering them, which enables the medication to be administered gradually as a suspension or solution. A compressed tablet covered in a semi-permeable membrane serves as the central component of an oral osmotic system, and delivery orifices are drilled through it using a mechanical drill or a laser beam. These controlled systems, which rely on osmosis and osmotic pressure, are unaffected by many gastrointestinal factors. However, it is important to keep in mind that a number of critical factors, including drug solubility, delivery orifices, osmotic pressure, semi-permeable membrane, and others, influence the design of osmotically controlled drug delivery systems, including membrane thickness, plasticizer type and quantity, and polymer type and nature.

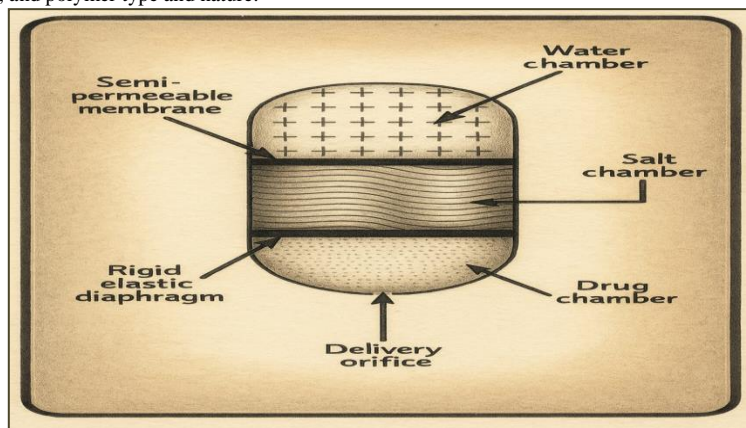


Fig.9: The Rose-Nelson pump

3.3 Microencapsulation

The process of microencapsulation entails covering or encasing small liquid or solid droplets or particles with a continuous polymeric layer. In order to create gelatin spheres for the microencapsulation technology, which was developed by Bungen burg de Jon and Kan in 1931, the gelatin coacervation procedure was first employed. The controlled drug delivery system has been used to improve the therapeutic efficacy of a particular medication and reduce the drawbacks of conventional therapy. To maximize therapeutic efficacy and minimize toxicity and adverse effects, the active ingredient must be administered to the target tissue at the optimal pace. Liquids can be transformed into solids, surface and colloidal properties can be changed, the environment can be protected, and the release characteristics of different coated materials can be controlled with the help of microencapsulation. Micromanaging techniques can accomplish some of these features in contrast to microencapsulation, which uses tiny coated particles to create a wide range of dosage forms[20]

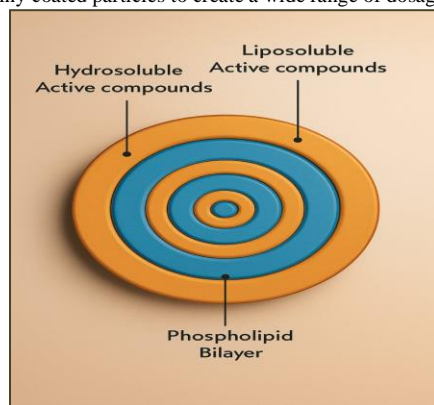


Fig.10: The microencapsulation process

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Mechanism of action: Microencapsulation works by enclosing an active substance within a protective coating or matrix to control its release and improve stability. After administration, the encapsulating material acts as a barrier that protects the drug from environmental degradation and prevents immediate release. Drug release from microcapsules occurs through mechanisms such as diffusion through the coating, dissolution or erosion of the encapsulating material, or rupture of the capsule wall in response to external stimuli like pH, enzymes, temperature, or mechanical stress. This controlled release mechanism allows the drug to be delivered in a sustained, targeted, or site-specific manner, thereby enhancing therapeutic efficacy and reducing side effects[21]

Conclusion

By overcoming the drawbacks of conventional drug delivery techniques, novel drug delivery systems mark a substantial breakthrough in the pharmaceutical industry. By increasing medication stability, targeting effectiveness, controlled release, and bioavailability, NDDS improves therapeutic performance. While transdermal techniques increase the number of non-invasive delivery alternatives, carrier-based systems like liposomes and nanoparticles offer creative ways to transfer and safeguard medications.

1. Mechanism of action:

- The drug solution or suspension is forced through a delivery aperture at a regulated rate by this pressure.
- This layer protects the enclosed material from outside influences and regulates its release.
- The device is made up of a semi-permeable membrane that encloses a compartment that holds the medication and an osmotic agent.
- Osmotic pressure is produced when the system is exposed to bodily fluids because water seeps through the membrane and into the apparatus.
- The active substance is surrounded by a protective coating, usually comprised of polymers, lipids, or proteins[18]

NDDS continues to advance with continued research and technology advancements despite obstacles such as formulation complexity, stability problems, high manufacturing costs, and possible immunological reactions. NDDS is anticipated to further transform drug administration by providing safer, more efficient, and patient-friendly therapy options as cutting-edge materials and engineering processes advance.

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