Novel drug delivery systems: An effective platform for improved therapy

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Abstract
Recent advances in drug pharmacokinetic and pharmacodynamic behavior now allow for a more logical approach to the creation of an ideal drug delivery system. It is already apparent that multidisciplinary efforts will mostly be responsible for future success in drug delivery research. Any therapeutic agent that can be made safer and more effective while using an enhanced drug delivery method represents a step forward in the treatment of human diseases as well as significant marketing potential for pharmaceutical companies. The best drug delivery systems send a predetermined dose of medication to the intended site at the right time and place, depending on the etiology and physiological requirements of the body. Traditional pharmaceutical dosage forms are unable to regulate how quickly a medicine is delivered to the target site. Because higher doses frequently result in serious side effects during treatment, novel drug delivery systems (NDDS) are carriers that keep the drug concentration in the therapeutic range for longer periods of time and also, in addition, may deliver the content to the targeted site if so desired and as needed. As a result, the distribution of drugs in non-target tissue and body fluids necessitates therapeutic doses that could greatly exceed the amount required in target cells.

Keywords: Novel drug delivery system, Therapeutic dose, Pharmacokinetic, pharmacodynamic

Introduction
To achieve the desired therapeutic outcome, a pharmaceutical molecule is delivered to its target site using a variety of tactics, formulations, production methods, storage systems, and technologies. Technologies that carry medications to or through the body are referred as drug delivery. One of these technologies is the delivery method, such as an oral tablet or an injection for a vaccination [1]. There have been considerable developments, and even more advancements are anticipated in the years to come, in the utilization of principles relating to drug formulation, mode of administration, site-specific targeting, metabolism, and toxicity. Drug delivery tries to alter a drug's pharmacokinetics and specificity through the use of various excipients, drug carriers, and medical devices [2].
To deliver a medicine to a particular area of the body, various formulations, strategies, technologies, and systems are employed. The dosage and route of administration of a medicine are perfectly interwoven with the idea of drug delivery[3].The technology requires a thorough understanding of the physiological obstacles to effective drug delivery, such as the movement of drugs through cells and tissues and the transport of drugs through the circulatory system and metabolism. The proper administration of medications is dependent on a number of factors, and the study of the drug delivery system is multidisciplinary [4].

Different types of drug delivery systems
1. Oral dispersible drug delivery system
2. Gastroretentive drug delivery system

3. Mucoadhesive drug delivery system
4. Nano suspension drug delivery system
5. Aquasome drug delivery system
6. Phytosomes drug delivery system
7. Buccal drug delivery system
8. Lipid based system drug delivery system
9. Emulgel
10. Nanogel

Oral dispersible drug delivery system

The most frequent and recommended method of administering medications, whether they are in solid or liquid dosage forms, is oral administration. Solid dose forms are preferred because they are simple to administer, precise in their amount, allow for self-medication, reduce pain, and most importantly to ensure patient compliance. The two most frequently used solid dose forms are tablets and capsules. But many people have trouble swallowing hard gelatin capsules and tablets. Dysphasia is the medical term for this swallowing issue [5]. All patient demographics have been observed to experience this issue, including geriatric and pediatric patients in particular. Therefore, these traditional dosage forms have a high incidence of noncompliance and ineffective therapy with regard to swallowing, especially for children, the elderly, and anyone with mental retardation. Orally disintegrating pills are also known as mouth-dissolving tablets, rapid-dissolving tablets, fast-dissolving tablets, and orally disintegrating tablets. Orodispersible tablets are a term that has recently been used by the European Pharmacopoeia. The various methods of preparation of oro dispersible tablets are molding method, Compaction method, Spray-drying method, Freeze-drying method.

Gastroretentive drug delivery system

Gastro retentive dose forms deliver the medication to the target site of action in a regulated manner. The bioavailability of medications that are metabolised in the upper gastrointestinal tract is improved by these systems. The goal of gastro retentive medication delivery is to target site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects by extending gastric residence duration. Drugs with gastroretentive dose forms have much longer gastric retention times (GRT) because they can stay in the gastric region for extended periods of time [6]. Systems for regulated drug delivery that are gastro-retentive are effective ways to increase the bioavailability of many medications. The idea of GRDDS is to extend the gastric retention period. By utilizing the cutting-edge GRDDS approach, medications that need regulated delivery and increased bioavailability can be created. GRDDS can be divided into two categories: floating systems and non-floating systems. According to the method of floating, floating systems are further divided into effervescent systems and non-effervescent systems, while non-floating systems are divided into four separate classes according to the mechanism utilised for gastro retention [7].

GRDDS benefits include

- Enhanced bioavailability
- It lowers the dose and the frequency of dosing.
- This method reduces drug concentration fluctuations in the blood and aids in drug targeting.
- In GIT, local action is possible as in antacids.
- This system minimises the adverse effects [8].
- It is feasible to establish sustained release.
- It is economical, the safest method of administration, and it works with a variety of medications.

Mucoadhesive Drug Delivery Systems

Drugs can be targeted to a specific area of the body for extended periods of time using mucoadhesive drug delivery systems, which rely on the bioadhesion of certain polymers, which become adhesive upon hydration. Two materials, at least one of which is biological, are held together by interfacial forces in a phenomenon known as bioadhesion. The bonding could occur between an artificial substance and a biological substrate, as in the case of a polymer adhering to a biological membrane. The word "mucoadhesion" refers to the attachment of a polymer to the mucin layer of a mucosal tissue [9]. There are several different ways to provide mucoadhesive medications which includes buccal delivery, oral delivery, vaginal delivery, rectal delivery, nasal delivery and ocular delivery. The theories of mucoadhesion includes adsorption, diffusion, Wetting. Electronic and fracture.

Benefits of oral mucoadhesive drug delivery systems

- Increases bioavailability by extending the dosage form's residence time at the absorption site.
- Great accessibility and quick start-up.
- Quick absorption due to an abundant blood supply and healthy blood flow rates.
- Drugs are guarded against deterioration in the git's acidic environment.
- Increased patient adherence.

Nano suspension drug delivery system

A submicron colloidal dispersion of medicine particles stabilized by surfactants is referred to as a nanosuspension and can be administered orally, topically, or via parenteral or pulmonary routes [10]. The solid particles in nanosuspensions typically have a particle size distribution that is less than one micron, with an average particle size between 200 and 600 nm [11]. Solid lipid nanoparticles are lipidic carriers of pharmaceuticals, whereas nanoparticles are often polymeric colloidal carriers of drugs. With the use of nanosuspension technology, the drug is kept in the necessary crystalline state with smaller particles, which increases the pace at which it dissolves and, as a result, improves bioavailability [12].

Methods of Preparation of nano suspension

- Precipitation Method
- Micro emulsion Template
- Media Milling (Nanocrystals)
- High Pressure Homogenization
- High Pressure Homogenization in aqueous media (Dissocubes)
- High Pressure Homogenization in non-aqueous media (Nanopure)
- Nanojet Technology
- Combination of Precipitation & HPH (Nanoedge)
- Supercritical Fluid Method
- Solvent Evaporation Method

Applications

Drugs that are poorly soluble in aqueous or lipid environments may be made more soluble by using nanosuspensions. By administering the nanosuspension orally or intravenously (IV), for example, the rate of flooding of the active

component rises and the maximum plasma level is reached sooner. This is one of its distinctive advantages over other methods of improving solubility.

- It is helpful for compounds with poor permeability, solubility, or both, which presents a substantial difficulty for the formulators.
- The possibility of intravenous delivery of poorly soluble medications without blocking blood capillaries is made possible by the smaller particle size and can be used for medications that are poorly water soluble.
- The IV mode of delivery allows for rapid breakdown and tissue targeting.
- Nanosuspensions with oral administration offer quick and increased bioavailability.
- Physical stability over the long term brought on by stabilizers.

Aquasome drug delivery systems

Aquasomes are three-layered self-assembled nanoparticulate carrier systems. They are made of a solid phase nano-crystalline core that is coated in an oligomeric film, to which biochemically active molecules are adsorbed with or without modification [13]. As a result, "aquasomes" are carbohydrate-stabilized core nanoparticles, initially created by Nir Kossovsky in 1995. Aquasomes are also known as "Bodies of Water" because of the way that they support and maintain weak biological components like proteins and polypeptides. Three layers make up aquasomes: A solid crystalline core, a carbohydrate coating, and the active ingredient, which is built via non-covalent bonding. Aquasomes are round, 60–300 nm-diameter particles. Tin oxide, nanocrystalline carbon ceramics (diamonds), and brushite (calcium phosphate dihydrate) are the main core materials used to make aquasomes. Drugs that have issues with delivery routes, physical and chemical instability, poor bioavailability, and strong side effects can be delivered via aquasomes.

Properties

- The preservation of bio-active conformation integrity and biochemical stability is achieved by aquasomes in water.
- Aquasomes, whose size and structure stability prevent them from being cleared by the reticuloendothelial system or deteriorating in response to specific environmental stresses.
- Due to their enormous size and active surface area, aquasomes are effectively loaded with large amounts of agents by ionic, non-covalent bonds, van der waals, and entropic forces.

Advantages of aquasomes

- Aquasomes maintain the metabolic stability and structural integrity of medication particles.
- Aquasomes have colloidal characteristics.
- The aquasomes suspension has a high likelihood of building up in the muscle and liver and contains biodegradable nanoparticles in the colloidal range.
- Aquasomes offer a medium for preserving the structural integrity and biochemical stability of bioactives due to their water-like features.
- Aquasomes-based vaccines offer a number of benefits as a vaccine delivery mechanism.
- Antigens adsorbed on aquasomal surfaces can cause immunological reactions in both cellular and humeral tissues.

Applications of aquasome

- Epstein-Barr and immune deficiency virus aquasomes employed as vaccines for the delivery of viral antigen must be activated to elicit the proper vaccination treatment antibodies.
- For active targeted intracellular gene therapy.
- Aquasomes were created for the delivery of pharmaceuticals, such as insulin.
- Aquasomes are utilized to distribute enzymes like DNAase and pigments.

Phytosomes drug delivery system

A phytosome is a nanoparticle delivery system designed to transfer polar or nonpolar natural substances. It is made of monolayer or double-layer phospholipids that form vesicles. This system's phospholipid content has the ability to mediate the increase in solubility caused by hydrogen-bonding interactions between water molecules and phosphate groups in a double-layer phytosome carrier, as well as the improvement in permeability of the active compounds caused by phospholipid deformation of cell membranes in conjunction with phytosome carrier [14]. In order to increase the efficiency of natural component compounds, phytosome modification is currently being done. A compound of phospholipids and organic active components is a phytosome. Applying topically or ingesting herbal extracts with phytosome increases absorption. Phytosomes, also known as herbosomes, are phospholipid complexes that are compatible with lipids and include herbal extract linked with phospholipids. It is a vesicular drug delivery system made up of lipid and phytoconstituents. The bioavailability of phytoconstituents is improved by phytosome because it promotes the absorption of phytoconstituents through the GIT. In contrast to liposomes, which have water-soluble contents surrounded by multiple phosphatidyl choline units, phytosomes have phospholipids and phytoconstituents present in a 1:1 or 1:2 ratio. The drug delivery system known as phytosomes has a defined melting point, is easily soluble in non-polar solvents, and is only moderately soluble in lipids.

Advantages

- Better bioavailability and stability of phytoconstituents, as well as both, are desirable. Additionally, they can enhance drug absorption through the skin.
- It enhances lipid-insoluble phytocontituent oral and topical absorption.
- large-scale drug trapping.

Buccal Drug Delivery System

These systems are used to treat both local and systemic problems and are inserted in the mouth between the upper gums and cheek [15, 16]. It is more accessible for the administration and removal of dosage from since it is highly vascular. Additionally, compared to other non-oral routes of drug administration, buccal drug delivery has a high level of patient acceptability. Drug administration via the buccal route may result in extensive first pass metabolism and drug breakdown in the challenging gastrointestinal environment. Passive diffusion into the lipoidal membrane is the predominant method of drug absorption through the buccal mucosa. Following absorption, the drug is moved through the facial vein, which then drains into the jugular vein, passing the liver and sparing it from first pass metabolism. The buccal

route offers one of the probable pathways for ordinary small pharmacological molecules as well as normally big, hydrophilic, and unstable proteins, oligonucleotides, and polysaccharides.

Application of buccal delivery

- The treatment of oral infections, dental caries, mouth ulcers, stomatitis, gingivitis, etc. are examples of local therapies that can be applied to the oral cavity.
- When it comes to the systemic administration of tiny compounds that are subject to first-pass metabolism, the buccal route is of particular interest.
- Simplicity of administration. Therapy can be stopped at any time.
- Allows for long-term localization of the medication to the oral cavity can be given to patients who are unconscious.
- Provides a fantastic route for the systemic administration of medications with high first-pass metabolism, increasing their bioavailability.
- This route can be used to give medications that are unstable in an acidic environment and are degraded by enzymatic processes or the alkaline environment of the colon.
- Rapid systemic absorption; the presence of saliva ensures a comparatively significant volume of water for drug dissolution as opposed to rectal and transdermal routes.For the administration of different hormones, narcotic analgesics, steroids, enzymes, cardiovascular medicines, etc., this route offers an alternative.
- The buccal mucosa has more blood vessels per square centimeter than skin and is more permeable.

Lipid Based Drug Delivery System

The term "lipid-based drug delivery systems" (LBDDS) refers to a variety of formulations that include a medication that is suspended or dissolved in a lipid excipient. Esters of fatty acids, or lipids, are hydrophilic groups like glycerol, polyglycerol, or polyalcohol that are connected to lipophilic hydrocarbon chains. The length of the fatty acid chain and the level of unsaturation determine the excipient's melting range, solubilization potential, and miscibility qualities. The Hydrophilic Lipophilic Balance (HLB), a gauge of excipient dispersibility in aquatic conditions, describes the amphiphilicity or dual polar and non-polar nature of lipids [17]. Drug release from lipid-based formulations is primarily governed by four essential principles: solubility, dispersion, digestion, and absorption.

Classification of Lipid-Based Drug Delivery System

- Microemulsions
- Nanoemulsions
- Self-emulsifying Delivery Systems
- Liposomes
- Nanostructured Lipid Carriers
- Transfersomes
- Niosomes

Emulgels

Emulgels are a new type of drug delivery technology that has gained popularity in recent years for the delivery of hydrophobic medicines. This formulation, which combines emulsion and gel, is regarded as a revolutionary kind of drug delivery mechanism. Emulgel is an example of this kind of blend. It is a fusion of an emulsion and a gel [18]. Both an oil-in-water and a water-in-oil type emulsion and gel are used to make emulgel. Drug delivery using the water-in-oil type is utilized for hydrophobic medications and the oil-in-water type is used for lipophilic drugs [19]. The emulgel has several benefits, including being clear, aesthetically beautiful, thixotropic, greaseless, easy to spread and remove, emollient, non-staining, and bio-friendly. It also has a good skin penetration rate and a lengthy shelf life.

Application of emulgel

- A higher level of patient acceptance.
- Offer specialized medicine delivery.
- Simple therapy termination.
- Increased bioavailability allows even modest doses to be effective as compared to other semisolid traditional preparations.
- More stable than transdermal preparations
- A hydrophobic medication can be integrated into an emulgel by using an emulsion as the ultimate delivery vehicle for the gel.
- Simple and inexpensive preparation.
- Drug loading capacity outperforms other cutting-edge methods like niosomes and liposomes [20].

Nanogels

Nanogels are defined as nanoscale particles made of physically or chemically connected polymer networks that inflate when exposed to a suitable solvent. When polynucleotides and poly ethylene glycol (PEG) were initially being delivered via cross-linked bifunctional networks made of polyion and nonionic polymers, the term "nanogel" was first used to describe these networks. It is currently necessary to develop smart nano-systems that can be successful for therapy and the advancement of clinical trials due to the growing field of polymer sciences [21, 22]. Nanoscale cross-linked hydrophilic polymer particles are known as nanogels. They enable for the spontaneous loading of medicines in aqueous conditions since they are soluble in water [23].After the drug molecules are added, the nanogel collapses to form dense nanoparticles. Nanogels have a network that enables molecular integration and a huge surface area that is adjustable. Inorganic molecules like quantum dots, DNA, and RNA have all been incorporated.

Properties of nanogels

Biocompatibility and degradability
Swelling property in aqueous media
Higher drug loading capacity

Application of nanogels

- Cancer treatment entails administering medications with strong therapeutic efficacy and expected low toxicity to adjacent tissues.
- Immune disorders [24].
- Diabetics: It has been created an injectable nano-network that reacts to glucose and releases insulin.
- Nanogel is a promising technology for delivering ODN (godeoxynucleotides) to the brain in cases of neurodegenerative disease
- A nanogel made of protein molecules dissolved in solution has been used to stop bleeding. On the nanoscale, the proteins self-assemble into a biodegradable gel.

Advantages

- Very good biocompatibility.
- Recyclable
- Negative immunological reactions.
- The reticuloendothelial system is kept from invading.
- Cross-linking densities can control the release of medicines.
- Due to its extremely small size, it has good penetration capabilities [25].
- Applied to medications and charged solutes that are both hydrophilic and hydrophobic.
- Strong transportable qualities.

Conclusion

The novel drug delivery Systems (NDDS), which is far superior to conventional dosage forms, combines cutting-edge techniques with newly developed dosage forms. A revolutionary drug delivery system has advantages such as appropriate dosing at the right time and location, economical use of expensive drugs, excipients, and production cost reduction, benefit to patients in the form of better therapy, increased comfort, and an overall higher standard of living. Pharmaceutical science makes use of cutting-edge delivery and targeting strategies for medications.

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