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Drug Delivery Systems

To acheive marketing approval, a molecule undergoes different development phases and a variety of studies need to be carried out. A new molecule typically involves preclinical testing in animals followed by clinical trials in humans, after which the application is submitted to regulatory agencies for review. In case of new delivery system, since drug molecule is already known, there is no need to carry out full clinical trials.

Types of Drug Delivery Systems

Current drug delivery systems can be categorised as Oral, Pulmonary, Transdermal, Injectables, etc.

A. Oral Drug Delivery Systems

Oral route is one of the most extensively used routes of drug administration because of its obvious advantages of ease of administration, improved patient compliance, and convenience. In immediate release (IR) dosage forms, there is little or no control over release of drug from the dosage form, which most often results in constantly changing, unpredictable, and often sub- or supra- therapeutic plasma concentration. Modified release (MR) dosage form refers to a dosage form for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms. Extended release (ER) and delayed release (DR) dosage forms are two types of MR dosage forms.

ER dosage forms are formulated to make the drug available over an extended period after ingestion. This allows a reduction in dosage frequency compared to the drug presented as a conventional dosage form (e.g., an IR dosage form). These products typically provide numerous benefits, including greater effectiveness in the treatment of chronic conditions, reduced side effects, greater convenience, and higher levels of patient compliance due to a simplified dosing schedule. The term controlled release (CR) and extended release are often used interchangeably. A number of design options are available to control or modulate the drug release from a dosage form. Majority of the oral dosage forms fall in the category of matrix, reservoir, osmotic systems, or ion exchange resins. DR dosage forms release the drug at a time other than immediately following oral administration.

B. Pulmonary Delivery Systems

Pulmonary delivery has been until now primarily used for the treatment of respiratory disease. Recently, the lungs' natural ability to transfer molecules into the blood stream has been utilised for delivering drugs to the systemic circulation. This method is a noninvasive alternative to the painful injections and can lead to rapid onset of action and good bioavailability. Inhalation devices broadly fall into three categories: Pressurised metered-dose inhalers (MDIs), nebulisers, and dry powder inhalers (DPIs). MDIs contain drugs as a solution or a suspension of fine particles in a liquefied propellant held under high pressure. The drug is emitted through an orifice from a metering valve. Nebulizers, on the other hand, do not require propellants and can generate large quantities of small droplets capable of penetrating into the lung. DPI is a device that delivers medication to the lungs in the form of a dry powder and requires some procedure to allow a measured dose of powder to be ready for the patient to take. The drug is typically held either in a capsule for manual loading or a proprietary form from inside the inhaler itself. Once loaded or actuated, the patient puts the mouthpiece of the inhaler into their mouth and takes a deep inhalation, thereby delivering the drug.

C. Transdermal Drug Delivery Systems

Systemic delivery of drugs via transdermal route has generated a considerable interest during the last decade. Transdermal drug delivery systems (TDDS) deliver drugs through the skin into the systemic circulation at a predetermined rate, thereby avoiding metabolism in the gastrointestinal tract and liver. Therefore, the amount of active ingredient required for transdermal delivery can be significantly less than that for oral systems. TDDS provide constant blood levels for one to seven days and increased patient compliance.

D. Injectables

The research efforts in the field of genomics are expected to accelerate the discovery of new therapeutic biomolecules, placing an increased demand on the development of delivery systems for these drugs. This class of drugs are usually characterised by their large size, fragile nature, short biological half-life, and limited ability to cross cell membranes. These properties along with the methods of administration of biopharmaceuticals can limit their clinical applications to certain diseased states that warrant the expense and inconvenience of frequent injection. Several parenteral depot formulations based on biodegradable polymers such as microspheres and implants have become

commercially available to improve the efficacy and prolong activity of several peptide and protein drugs.

Implants can be surgically implanted inside the body from where the drug release takes place at a controlled rate and the duration can be as long as 12 months. Another option is use of biodegradable implants that can be injected using a large gauge needle and they offer the advantage of a single procedure (no need to remove the implant).

Injectable MR dosage forms, typically a matrix is fabricated into an easily injectable form for administration at the desired tissue site (e.g., subcutaneously). The dosage form may be either a solid, gel, or liquid. Solid dosage forms such as biodegradable microspheres consisting of poly(lactic-co-glycolic acid) have been used as an injectable depot delivery system of small-molecule drugs, peptides, and proteins. The injectable gels usually consist of a solvent to dissolve the matrix and/or the therapeutic agent and they form an “implant-like” depot upon injection.

E. Ophthalmic (Ocular) Drug Delivery Systems

Recently, there has been increased attention for ophthalmic drug delivery as these delivery systems require less frequent administration than eye drops, allow continuous drug delivery, and extend the duration of drug action by enhancement of corneal absorption. Ocular delivery systems include viscous solution and hydrogel delivery systems, ocular inserts and contact lenses.

F. Vaginal Drug Delivery

The vagina has been studied as a favorable site for the local and systemic delivery of drugs and this route offers certain advantages, such as avoidance of gut and hepatic first pass metabolism, reduction in gastrointestinal and hepatic side effects, and local targeting of drugs to the reproductive organs. Vaginally administered agents and formulations are mainly being developed to provide “dual prophylaxis” for contraception and protection against microbial infections including AIDS and other sexually transmitted diseases (STDs). Drug delivery technologies that have been used for vaginal drug delivery include the intravaginal ring (IVR) and VagiSite bioadhesive technology.

Future Research and Conclusions

As discussed in this article, drugs can be delivered to a patient through many different delivery systems, including oral, transdermal, injection, pulmonary route, etc. With the sequencing of the human genome, biotechnology companies are rapidly developing a large number of peptide- and protein-based drugs and it is expected that in the next few years, this category will constitute a major portion of the new drugs. These biopharmaceuticals present drug delivery challenges because these are often large molecules that degrade rapidly in the blood stream. Moreover, they have a limited ability to cross cell membranes and generally cannot be delivered orally. The possibility of other routes of administration will be dictated by the drug, disease state, and desired site of action. Some sites are easy to reach such as nasal, buccal, vagina, etc, while others are more challenging to access, simplest example being the brain. Gene therapy is also likely to be one of the most exciting growth sectors as biotech companies become involved in drug delivery.

Nowadays, apart from the research in the technologies mentioned in this article, individualised dosing has emerged as one of the important focus areas. A recent article gives a very good overview of solid and liquid drug dosage forms used in personalized medicine. Solid dosage pen is such a device delivering a swallowable solid monolithical oral dosage form containing individual doses. The device consists of a drug loaded rod (can be manufactured by an extrusion method) that can be fed forward.

Recent advances in the field of micro-fabrication have opened up the possibility of developing a new class of programmable drug delivery systems. One such device is microchip based delivery system. Chip consists of an electrolyte impermeable substrate, which separates the series of reservoir consisting of the component(s) to be released. Based on electrochemical reactions, the membrane disappears and the drug(s) are then diffused or release from the reservoir. Their small size and potential for integration with micro-electronics coupled with ability to store and release drug(s) on demand opens up a whole new world of possibilities in drug delivery.

In conclusion, the market for drug delivery systems has come a long way and will continue to grow at an impressive rate. Today’s drug delivery technologies enable the incorporation of drug molecules into new delivery systems thus, providing numerous therapeutic and commercial advantages. A large number of companies are involved in the development of new drug delivery systems, which is evident by an increased number of products in the market and the number of patents granted in the recent past. Tomorrow’s drugs will definitely be more challenging in terms of the development of delivery systems, and pharmaceutical scientists will have to be ready for a difficult task ahead.

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