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Review on Controlled Drug Delivery System

Yash Rajendra Kawalkar, Rajlaxmi S Deolekar, Siddhesh Eknath Ingle, Pritesh Rajendra Bele
New Montfort Institute of Pharmacy, Ashti, Wardha, Maharashtra, India
yash.kawalkar22@gmail.com

Abstract: *Oral drug delivery is the most convenient option as the oral route provides maximum active surface area among all drug delivery system for administration of various drugs. The attractiveness of these dosage forms is due to awareness to toxicity and ineffectiveness to drugs when administered by oral conventional method in the form of tablets and capsules. An appropriately designed controlled release drug delivery system can be a major advance towards solving problems concerning the targeting of a drug to a specific organ or tissue and controlling the rate of drug delivery to the target site. Oral Sustained release (SR) / Controlled release (CR) products provide an advantage over conventional dosage forms by optimizing bio-pharmaceutics, pharmacokinetic and pharmacodynamics properties of drugs in such a way that it reduces dosing frequency to an extent that once daily dose is sufficient for therapeutic management through uniform plasma concentration providing maximum utility of drug with reduction in local and systemic side effects and cure or control condition in shortest possible time by smallest quantity of drug to assure greater patient compliance. The present article contains brief review on various formulation approaches for controlled release drug delivery system. Keywords: Controlled drug delivery system, Drug release mechanism, Modified Release, Sustained Release.*

Keywords: CDDS, SUSTAINED RELEASE, DRUG.

I. INTRODUCTION

Conventional drug delivery systems (DDS) have a very limited command of their distribution of the drugs and nearly no command of successful target concentration. This form of dosage will result in ever changing plasma concentrations which are unpredictable.[1] Oral drugs absorbed quickly in the food pipe and quickly lost from the blood are normally film-coated or prolonged microencapsulated to the period of distribution and the action of drugs. Most of these types, however, have some physiological shortcomings such as transit periods for gastrointestinal (GI), partial releases of drugs from devices, or the prolonged duration of prescription residence in small intestine upper location contributing to low bioprotein-dosage forms of the long-term release[2] Simple pills and injections are recognized for a long time to be not the best method of medicinal use. To develop methods of drug management, attempts have been increased to design efficient DDS, with cooperation between polymer physicists, pharmacologists, engineers, chemists, and medical researchers, and important advances have been made in managed delivery since research began several decades ago.[3] The intrinsic features of formulation design, GI physiology, pharmacodynamic ,and, pharmacokinetics are essential to achieve a uniform distribution via oral administration, irregular mode of delivery, and design of dosage forms[4]

One of medical research, chemistry, the sciences of materials, manufacturing, and the pharmaceutical industry, as well as other associated bio-science, is the field of controlled drug delivery. DDS continuity in achieving a better living quality and human health is the reason for recent increasing interest and efforts by researchers in this area. Its scope also includes various areas from medicine, agriculture, and biotechnology[5]

Dosage forms provide a wide variety of delayed action formulations which have a pre-determined rate and pre-determined sustained release of its active ingredients. For this method, the primary goal is to include an extended length of action to ensure better compliance with patient conditions[6]

Controlled drug delivery systems can include the maintenance of drug levels within a desired range, the need for fewer administrations, optimal use of the drug in question, and increased patient compliance. While these advantages can be significant, the potential disadvantages cannot be ignored like the possible toxicity or non-biocompatibility of the materials used, undesirable by-products of degradation, any surgery required to implant or remove the system, the chance of patient discomfort from the delivery device, and the higher cost of controlled-release systems compared with

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traditional pharmaceutical formulations. The ideal drug delivery system should be inert, biocompatible, mechanically strong, comfortable for the patient, capable of achieving high drug loading, safe from accidental release, simple to administer and remove, and easy to fabricate and sterilize. The goal of many of the original controlled-release systems was to achieve a delivery profile that would yield a high blood level of the drug over a long period of time. With traditional drug delivery systems, the drug level in the blood follows the in which the level rises after each administration of the drug and then decreases until the next administration. The key point with traditional drug administration is that the blood level of the agent should remain between a maximum value, which may represent a toxic level, and a minimum value, below which the drug is no longer effective.[7]

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Advantages of Controlled Drug Delivery[9]

- Maintenance of drug levels within a desired range.
- Delivery of "difficult" drugs: slow release of water- soluble drugs, fast release of low solubility drugs
- Less dosing and increased patient compliance.
- release systems was to achieve a delivery profile that would yield a high blood level of the drug over a long period of time. With traditional drug delivery systems, the
- Eliminate over or under dosing
- Prevention of side effects
- Reduction in Health care cost
- Improved efficiency in treatment:
- Reduction in adverse side effects and improvement in tolerability

II. PRINCIPLES OF CONTROLLED DRUG DELIVERY

A perspective drug delivery systems can be defined as mechanisms to introduce therapeutic agents into the body. Chewing leaves and roots of medical plants and inhalation of soot from the burning of medical substances are examples of drug delivery from the earliest times. However, these primitive approaches of delivering drugs lacked a very basic need in drug delivery; that is, consistency and formity (a required drug dose). This led to the development of different drug delivery methods in the later part of the eighteenth and early nineteenth century. Those methods included pills, syrups, capsules, tablets, elixirs, solutions, extracts, emulsions, suspension, cachets, troches, lozenges, nebulizers, and many other traditional delivery mechanisms. Many of these delivery mechanisms use the drugs derived from plant extracts he modern era of medicine development started with the discovery of vaccines in 1885 and techniques for purification of drugs from plant sources in the late nineteenth century, followed by the introduction of penicillin after its discovery in 1929, and a subsequent era of prolific drug discovery. The development and production of many pharmaceuticals involves the genetic modification of microorganisms to transform them into drug-producing factories. Examples are recombinant deoxyribonucleic acid (DNA), human insulin, interferon [for the treatment of acquired immunodeficiency syndrome (AIDS) related Kaposi's sarcoma, Hairy cell leukemia, Hepatitis B and C, etc.], interleukin-2 (Renal cell and other carcinomas), erythropoietin (for the treatment of anemia associated with chronic

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renal failure/AIDS/antiretroviral agents, chemotherapy associated anemia in nomnyloid malignancy patient), and tissue plasminogen activator[10]

It is now possible to produce oligonucleotide, peptide, and protein drugs in large quantities, while gene therapies also appear to be clinically feasible. Each of these therapeutic agents, by virtue of size, stability, or the need for targeting, requires a specialized drug delivery system. While the conventional drug delivery forms are simple oral, topical, inhaled, or injections, more sophisticated delivery systems need to take into account pharmacokinetic principles, specific drug characteristics, and variability of response from one person to another and within the same person under different conditions.

The efficacy of many therapeutic agents depends on their action on target macromolecules located either within or on the surface of particular cells types. Many drugs interact with enzymes or other macromolecules that are shared by a large number of cell types, while most often a drug exerts its action on one cell type for the desired therapeutic effect. Certain hormones, for example, interact with receptor mechanisms that are present in only one or a few cell types. An ideal gene delivery system should allow the gene to find its target cell, penetrate the cell membrane, and enter into the nucleus. Further, genes should not be released until they find their target and one has to decide whether to release the genes only once or repeatedly through a predetermined way[11]

Thus, the therapeutic efficacy of a drug can be improved and toxic effects can be reduced by augmenting the amount and persistence of drugs in the vicinity of the target cells, while reducing the drug exposure to the nontarget cells. This basic rationale is behind controlled drug delivery. A controlled drug delivery system requires simultaneous consideration of several factors, such as the drug property, route of administration, nature of delivery vehicle, mechanism of drug release, ability of targeting, and biocompatibility. It is not easy to achieve all these in one system because of extensive independency of these factors. Further, reliability and reproducibility of any drug delivery systems is the most important factor while designing such a system. The emphasis here is on the need for precision of control and to minimize any contribution to intraand intersubject variability associated with the drug delivery system. There are many different approaches for controlled drug delivery applications.[12]

III. OVERVIEW OF THE DEVELOPMENT OF DRUG DELIVERY SYSTEMS

To obtain a given therapeutic response, the suitable amount of the active drug must be absorbed and transported to the site of action at the right time and the rate of input can then be adjusted to produce the concentrations required to maintain the level of the effect for as long as necessary. The distribution of the drug-to-tissues other than the sites of action and organs of elimination is unnecessary, wasteful, and a potential cause of toxicity. The modification of the means of delivering the drug by projecting and preparing new advanced drug delivery devices can improve therapy. Since the 1960s, when silicone rubber was proposed as an implantable carrier for sustained delivery of low molecular weight drugs in animal tissues, various drug delivery systems have been developed. At the beginning of the era of controlled drug delivery systems, a controlled release system utilizes a polymer matrix or pump as a rate-controlling device to deliver the drug in a fixed, predetermined pattern for a desired time period[13]

These systems offered the following advantages compared to other methods of administration:

[1] the possibility to maintain plasma drug levels a therapeutically desirable range, the possibility to eliminate or reduce harmful side effects from systemic administration by local administration from a controlled release system, drug administration may be improved and facilitated in underpriviledged areas where good medical supervision is not available the administration of drugs with a short in vivo half-life may be greatly facilitated, continuous small amounts of drug may be less painful than several large dose, improvement of patient compliance, and the use of drug delivery systems may result in a relatively less expensive product and less waste of the drug. The first generation of controlled delivery systems presented some disadvantages, that is possible toxicity, need for surgery to implant the system, possible pain, and difficulty in shutting off release if necessary. Two types of diffusion-controlled systems have been developed. The reservoir is a core of drug surrounded with a polymer film. The matrix system is a polymeric bulk in which the drug is more or less uniformly distributed.

Since the pioneering work in controlled drug delivery, it was demonstrated that when a pharmaceutical agent is encapsulated within, or attached to, a polymer or lipid, drug safety and efficacy may be greatly improved and new therapies are possible[14]

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The controlled release aspect of sustained drug delivery systems pertain to a reliable and reproducible system whose rate of drug delivery is independent of the environment in which it is placed. This requirement emphasizes the need for precision of control and elimination of undesired contribution associated with the drug delivery system. Modulated Drug Delivery (Nonzero-Order Release Profile). A significant challenge in drug delivery is to create a delivery system that can achieve manipulable nonzero-order release profile. This could be pulsatile or ramp or some other pattern. In some cases it is also required that the release should be immediate. A pulsatile release profile within the therapeutic window Feedback Controlled Drug Delivery. The ideal drug delivery system is the feedback controlled drug delivery system that releases drug in response to a therapeutic marker. This can be classified into two classes: modulated and triggered device. A modulated device involves the ability to monitor the chemical environment and changes drug delivery rate continuously in response to the specific external marker, while in a triggered device no drug release takes place until it is triggered by a marker. These different approaches of drug delivery can have different routes of administration. Some of the most preferred routes are oral, pulmonary inhalation, transdermal, transmucosal, and implantable systems. Implantable Controlled Drug Delivery Devices. Although most controlled drug delivery systems are designed for transdermal, subcutaneous, or intramuscular uses, implantable devices are very attractive for a number of classes of drugs, particularly those that cannot be delivered via the oral route or are irregularly absorbed via the gastrointestinal (GI) tract[15]

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