



## “A Review On “Cdds” For Anthelmintic Drug”

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### Abstract:-

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 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.

**Key-Word:-** Controlled drug delivery systems, inert, biocompatible, mechanically strong, comfortable for the patient, easy to fabricate and sterilize.

### Introduction

Controlled drug delivery is one which delivers the drug at a predetermined rate, for locally or systemically, for a specified period of time. Continuous oral delivery of drugs at predictable and reproducible kinetics for predetermined period throughout the course of GIT. Controlled release drug delivery employs drug-encapsulating devices from which therapeutic agents may be released at controlled rates for long periods of time, ranging from days to months. Such systems offer numerous advantages over traditional methods of drug delivery, including tailoring of drug release rates, protection of fragile drugs and increased patient comfort and compliance. ( Harish Gopinath,2012)

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the higher cost of controlled-release systems compared with 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. (Harish Gopinath, 2012)

## CONTROL RELEASE DOSAGE FORM

The United States Pharmacopoeia (USP) defines the modified-release (MR) dosage form as “the one 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 such as solutions, ointments, or promptly dissolving dosage forms”. One class of MR dosage form is an extended-release (ER) dosage form and is defined as the one that allows at least a 2-fold reduction in dosing frequency or significant increase in patient compliance or therapeutic performance when compared with that presented as a conventional dosage form (a solution or a prompt drug-releasing dosage form). The terms “controlled release (CR)”, “prolonged release”, “sustained or slow release (SR)” and “long-acting (LA)” have been used synonymously with “extended release”. (Harish Gopinath, 2012).

Nearly all of the currently marketed monolithic oral ER dosage forms fall into one of the following two technologies:

1. Hydrophilic, hydrophobic or inert matrix systems: These consist of a rate controlling polymer matrix through which the drug is dissolved or dispersed.
2. Reservoir (coated) systems where drug- containing core is enclosed within a polymer coating. Depending on the polymer used, two types of reservoir systems are considered.
  - a) Simple diffusion/erosion systems where a drug-containing core is enclosed within hydrophilic and/or water-insoluble polymer coatings. Drug release is achieved by diffusion of the drug through the coating or after the erosion of the polymer coating.
  - b) Osmotic systems where the drug core is contained within a semi-permeable polymer membrane with a mechanical/laser drilled hole for drug delivery. Drug release is achieved by osmotic pressure generated within the tablet core.

## Advantages and Limitations of Control Release Dosage Forms

### Clinical Advantages

- Reduction in frequency of drug administration
- Improved patient compliance
- Reduction in drug level fluctuation in blood
- Reduction in total drug usage when compared with conventional therapy
- Reduction in drug accumulation with chronic therapy
- Reduction in drug toxicity (local/systemic)
- Improvement in bioavailability of some drugs because of spatial control
- Economical to the health care providers and the patient
- Stabilization of medical condition (because of more uniform drug levels)

### Commercial / Industrial Advantages

- Illustration of innovative/technological leadership
- Product life-cycle extension
- Product differentiation
- Market expansion
- Patent extension
- Encapsulation Dissolution control
- Seed or granule coated
- Micro encapsulation
- Matrix Dissolution control
- Diffusion controlled release
- Reservoir type devices
- Matrix type devices
- Diffusion and Dissolution controlled systems
- Ion exchange resins
- Osmotically controlled release (Rajesh Tiwari,2015)

### MULTIPAL DOSGE FORM

Oral administration of medicines has an advantage for patient's compliance. Most of the solid dosage forms administered orally are tablets. Tablets have many advantages over other dosage forms, such as ease of transportation, application and production, high patient compliance, accurate dosing, control of drug release and stability. However, the desired release profile, therapeutic effect or ease of use in pediatrics or geriatrics, difficulty in swallowing may not be achieved by conventional tablets. Drug delivery system ensure reaching the effect area of the administered drug and sufficient concentration of the drug at the site of action. Conventional tablets may not be sufficient for treatment due to fluctuation in the blood

concentration of the drug. Repeated doses may lead to toxic concentrations. Single unit or multi-unit dosage forms with different release profiles have been developed in order to provide effective treatment by reducing fluctuation in the concentration. In single unit systems, the release of the drug is changed using matrix or membrane systems. In multi-unit systems such as pellets and mini tablets, the dose is divided into subunits and spread to the entire gastrointestinal tract. Mini tablets are systems designed to resolve the disadvantages of conventional solid dosage forms. This new approach is promising to overcome therapeutic obstacles such as swallowing difficulty, multiple dosing, as well as the development of dosage forms that allow successful treatment by combining different delivery systems. (Ranjith K,2015)

### Multiple Unit Dosage Forms

The purpose of drug delivery systems is delivering the drug to a particular site and providing the desired drug concentration for effective treatment at that site. Conventional dosage forms cause fluctuations in the blood concentration of the drug, and the drug may lead to toxic concentrations in blood or may be inefficient. The main purposes of designing sustained or controlled drug delivery systems are reducing the frequency of dosing and increasing its efficiency by localizing the area of action of the drug to a specific region. (Ranjith K,2015)

Oral controlled release drug delivery systems are divided into two classes:

- Single unit dosage forms, such as tablets, capsules,
- Multi-unit dosage forms, granules, pellets or mini tablets.

In multi-unit dosage forms, the dose is divided into subunits and each unit contains the drug. The total dose is the sum of the drug in the subunits and the dose is dependent on the functionality of the subunits. Multi unit dosage forms are useful when the selected ingredients exhibit additive or synergistic effects or the dose can be reduced according to a single unit dosage form. After administration, the dosage units are spread to the stomach and gastrointestinal tract and the risk of local irritation is reduced as a result of an equal drug release. Multi-unit dosage forms show a more reliable dissolution profile than single units, which means better bioavailability . (Ezgi Ilhan,2017)

The properties of multi-unit and single unit dosage forms are given comparatively at Table 1 .

**Table 1:** Properties of multi unit and single unit dosage forms

Multi Units Dosage Forms	Single Units Dosage Forms
More predictable gastric emptying	Gastric emptying with high variability
Gastric emptying is less dependent on nutritional status	Gastric emptying is highly dependent on nutritional status
Absorption grade does not show intra- and inter-individual variability	Absorption rate and grade show intra- and inter-individual variability
Risks of overdose and local irritation are lower	Risks of overdose and local irritation are higher

### Definition, Properties and Production Equipment

Mini tablets are tablets with diameters  $\leq 3$  mm and have a wide application area. For ease of use, they are usually filled in capsules, or they can be compressed in larger tablets or filled into sachets. Mini tablets are produced with multiple punches using eccentric or rotary tablet press machines. Thanks to easy production techniques, mini tablets can be produced in a certain size and dosage. The variability between series is also low. Apart from productivity, the use of multiple punches in their production increases the amount of dust that can be consumed at a time. Thus, the fill time is shortening. In consequence of the short waiting time, the separation of the powders is prevented.

Advantages of the mini tablets (Ezgi Ilhan, 2017)

- Their production is easy. It is an alternative to pellets and granules due to its reproducible production and dimensional similarity.
- Provides a more uniform release kinetics. Thus, the risk of sudden increase in blood concentration is reduced.
- Formulation development is easy.
- Intra and inter individual variability is low. Because the size is too small, even if the pylor is closed, it can pass to the intestine.
- They can be easily coated thanks to shape and size uniformity.
- The risk of local irritation is reduced because they spread throughout the gastrointestinal tract.
- Drug loading capacity is high.
- Setting the release profile is easy.
- Superiority to pellets:
  - Pellets are usually bead-like structures filled into capsules or compressed in tablets.
  - Pellets are produced by fluid bed granulation or extrusion- spheronization methods, while mini tablets are produced by simple tablet production methods. This saves time and money.
  - The absence of solvent use in production increases the stability.
  - Since the production methods of the mini tablets are easier, the tablets which have uniform size and dosage and do not differ from batch to batch can be produced.
- Superiority to granules:
  - Mini tablets have a smooth surface, stable surface area and high mechanical resistance compared to granules. It can be easily coated and requires less coating material than granules.

## Introduction to anthelmintics

Anthelmintics are drugs that are used to treat infections with parasitic worms. This includes both flat worms, e.g., flukes and tapeworms and round worms, i.e., nematodes. They are of huge importance for human tropical medicine and for veterinary medicine. The World Health Organization estimates that a staggering 2 billion people harbour parasitic worm infections (. Parasitic worms also infect livestock and crops, affecting food production with a resultant economic impact. Also of importance is the infection of domestic pets. Indeed, the companion animal market is a major economic consideration for animal health companies undertaking drug discovery programmes.

Despite the prevalence of parasitic worms, anthelmintic drug discovery is the poor relation of the pharmaceutical industry. The simple reason is that the nations which suffer most from these tropical diseases have little money to invest in drug discovery or therapy. It comes as no surprise therefore that the drugs available for human treatment were first developed as veterinary medicines. There is thus a pitifully small repertoire of chemotherapeutic agents available for treatment . In some respects, this situation has been exacerbated by the remarkable success of ivermectin over the last twenty years, which has decreased motivation for anthelmintic drug discovery programmes . This prompts concern, as anthelmintic resistance has been widely reported in livestock and it may also only be a matter of time before this phenomenon occurs in parasites of humans. (Lindy Holden,2016)

**Table 2. Key drugs registered for the treatment of parasitic worms in humans.**

Schistosomiasis (blood fluke)	Intestinal round worms
Antimonials	Piperazine
Metrifonate	Benzimidazoles
Oxamnaquine	Morantel
Praziquantel	Pyrantel
	Levamisole
Cestodiasis (tape worm)	Avermectins and milbemycins
Niclosamide	Closantel (and halogenated salicylamides)
Benzimidazoles	Emodepside
Praziquantel	
Fascioliasis (liver fluke)	Filariasis (tissue round worms)
Praziquantel	Diethylcarbmazine
Closantel	Suramin
(and halogenated salicylamides)	Ivermectin

Broad spectrum anthelmintics are effective against parasitic flat worms and nematodes. However, the majority of drugs are more limited in their action, e.g., praziquantel, a drug used in the treatment of schistosomiasis and thought to act by disrupting calcium homeostasis), has no activity against nematodes. For the purpose of this review we will focus on drugs used in human and veterinary medicine to treat parasitic nematode infection.

Helminths can be divided into three groups: cestodes, or tapeworms; nematodes, or roundworms; and trematodes, or flukes. The helminths differ from other infectious organisms in that they have a complex body structure. They are multicellular and have partial or complete organ systems (e.g., muscular, nervous, digestive, and reproductive). Several of the drugs used to treat worm infections affect the nervous system of the parasite and result in muscle paralysis. Other drugs affect the uptake of glucose and thus energy stores. All are chemical agents and are generally administered orally, and many are used in both human and veterinary medicine. No anthelmintic, however, is completely effective, completely without toxic effect upon the host, or equally active against all worms.(Lindy Holden,2016)

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