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A review on multi particulate drug delivery system

M Vaishnavi [1], Dr. B Haarika [2], R Prashanthi [3], Dr. M Swetha [4*]

[1] Student, Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University, Telangana, India

[2] Professor &HOD Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University, Telangana, India

[3] Assistant Professor Department of Quality Assurance, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University, Telangana, India

[4] Associate Professor, Department of Pharmaceutics, Sarojini Naidu Vanita Pharmacy Maha Vidyalaya, Affiliated to Osmania University, Telangana, India

* Corresponding Author: **Dr. M Swetha**

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Abstract

The strategies, formulations, production processes, storage arrangements, and technologies used in the delivery of drugs to their intended therapeutic location are referred to as drug delivery systems. By attaching the medication to a carrier particle—a microsphere, nanoparticle, etc.—that regulates the drug's release and absorption properties, this technique offers an excellent method for drug delivery. This particulate medication delivery technique relies heavily on microspheres and micro particles because of their small size and effective carrying capacity. When compared to traditional dose forms, these administration methods offer a number of benefits, such as increased patient compliance, decreased toxicity, and enhanced efficacy and convenience. These days, multiparticulate drug delivery technologies are particularly useful for creating delayed-release or controlled-release oral formulations with little risk of dose dumping, adaptability in blending to provide various release schedules, and a brief and repeatable stomach residence period. The carrier utilized to generate the multi particles and the percentage of drug within them is two of the many parameters that affect the release of drug from micro particles. Furthermore, multiparticulate drug delivery methods offer a wealth of possibilities for creating novel oral formulations with controlled and delayed release, expanding the frontiers of pharmaceutical development.

Keywords: Drug delivery system, multiparticulate drug delivery system, delayed release, dose dumping

1. Introduction

Early in the 1950s, the idea of a multiple unit dosage form was first proposed. Oral dose forms referring to multiple small minute units, each demonstrating a range of properties is known as multi-particulate drug delivery methods. The dosage of the medicinal compounds in these systems is divided across a large number of subunits, each of which is made up of thousands of spherical particles with a diameter of 0.05–2.00 mm [1]. These components are packed into sachets and crushed or encapsulated into tablets to provide the entire dose [2]. Pellets, granules, micro particles (microspheres, microcapsules, and micro beads), mini tablets, mini depots, and multiparticulate pulsatile drug delivery systems are examples of multiparticulate drug delivery systems [3] Multi particulates can be prepared in a variety of ways, varied techniques yield multi particulates with unique characteristics and need for varied processing conditions. Pelletization, granulation, spray drying, and spray congealing are a few techniques. It is possible for drug particles to be stacked around or trapped inside multi particulates. To obtain the required drug-release profile, these multi particulates are then molded in a variety of ways [4].

The development of multiparticulate dosage forms has gained a lot of attention recently due to their potential advantages over single unit systems, including enhanced bioavailability, a lower risk of systemic toxicity, a lower risk of local irritation, and predictable gastric emptying.

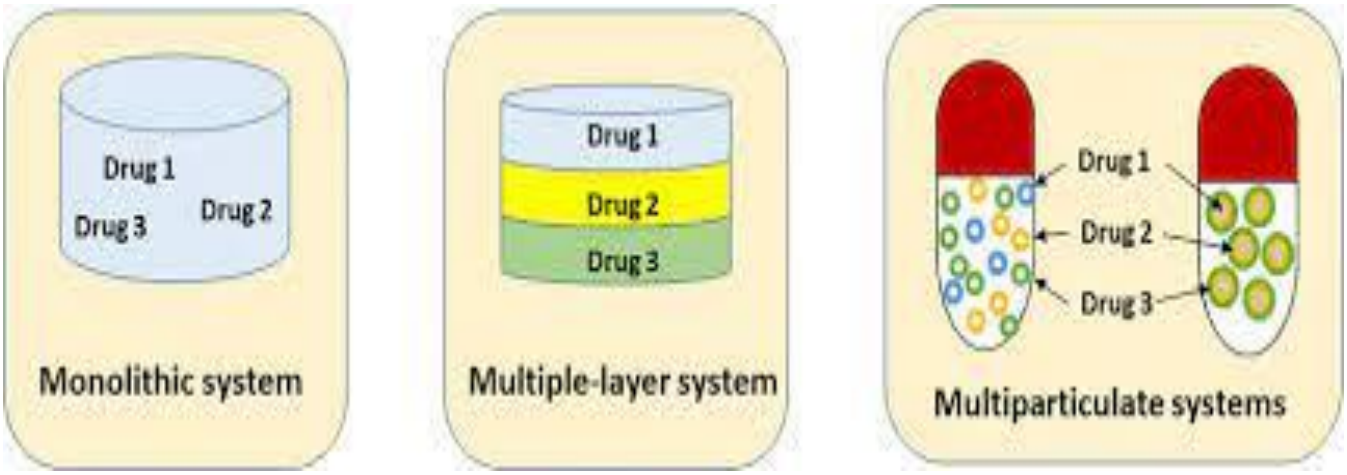

Fig 1: Different types of Multi particulate Drug Delivery system

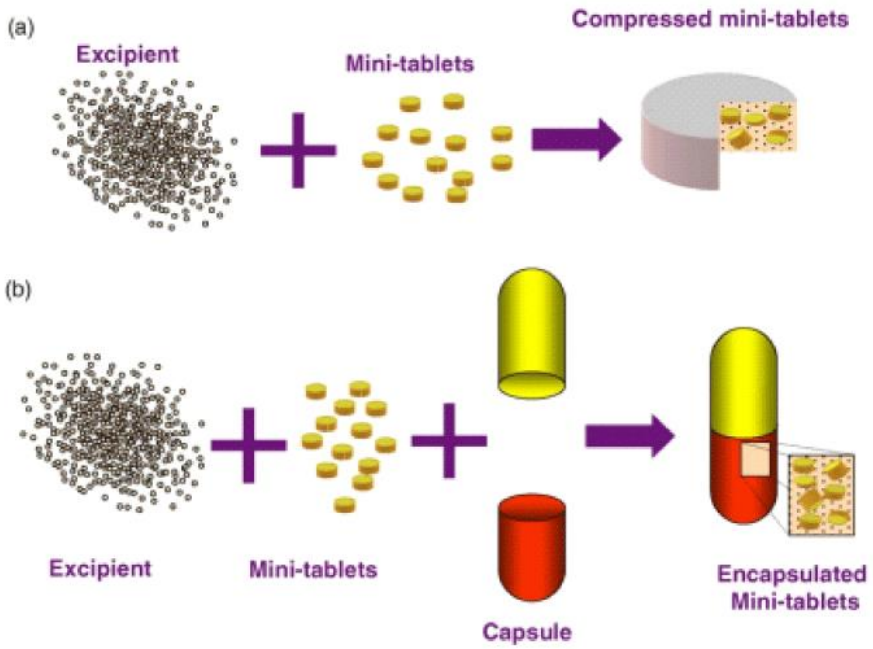

Fig 2: Loading of Mini Tablet

Advantages of Multi particulate Drug Delivery system

- Enhanced absorption capacity.
- Extension of patent protection
- Adaptable
- Lower chance of irritation locally
- No chance of dosage dumping.
- Expected reproducibility and brief duration of stomach occupancy.
- Combining pellets with various compositions or release patterns is simple.
- Boost equilibrium.
- Boost patient compliance and comfort.
- Less variation both within and between subjects [5].

Mechanism of Multiparticulate drug delivery systems:

The following are possible mechanisms by which drug release from multiparticulate may occur:

1. Diffusion

Water diffuses into the particle's interior upon coming into touch with the fluids in the gastrointestinal tract (GIT), causing drug breakdown and the drug solutions to diffuse across the release coat to the outside.

2. Erosion

Coatings are made to slowly dissolve over time, releasing the medication that is inside the particle.

3. Osmosis

The particle's inside begins to build up osmotic pressure Via coating,the medication is driven from the particle and into the outside.

Reasons for designing multi-part medication delivery systems

Drugs are designed and delivered as multiparticulate systems

for a variety of reasons, such as

- The individual subunit particles quickly flow through the g.i.t. after disintegrating. Even with the pylorus closed, these subunits can constantly exit the stomach if their diameter is less than 2 mm. Lower intra- and inter-individual variability in plasma levels and bioavailability are the outcome of this.
- To aid in disintegration in the stomach. Displays more consistent pharmacokinetic behavior than standard (monolithic) formulations.
- Using multiparticulate dose forms may also boost drug safety. 6

Administration of Multiparticulates

Multiparticulates can be taken orally or intravenously. However, historically, patients have favored the oral mode of administration. The dose forms for these multiparticulates can be taken orally as tablets or capsules. The majority of multiparticulate systems on the market come in capsule form. The coating may come off or the release rate may change if they are compacted into tablets. Elan Drug Technologies introduced SODAS®, IPDAS®, and PRODAS®, three multiparticulate drug delivery systems technologies in United States.

SODAS®, or spheroidal oral drug absorption system:

Depending on the needs of the medicine, this technology can be used to achieve a variety of drug release profiles, such as delayed release, pulsatile release, instantaneous release followed by sustained release profiles. It is possible to coat individual beads with certain controlled release polymers and then load them inside hard gelatin capsules.

(IPDAS®), or Intestinal protective drug absorption system

Their purpose was to lessen the gastrointestinal discomfort brought on by irritating medications such as Naproxen. This technology allows pellets made by various methods, such as extrusion-spheronization, solution or suspension layering on to non-pareil seeds, to be compacted into a tablet dosage form. Because of its multiparticulate nature, this system dissolves and moves through the gastrointestinal tract in a controlled way when given to the body, regardless of the feeding condition, hence preventing discomfort. Different polymers and concentrations can be used to achieve desired release profiles. This technology was used in the formulation and marketing of naproxen. Another benefit of the medication is that it only needs to be taken once a day instead of twice a day to once a day and hence reducing the troughs in plasma concentration.

PRODAS®, a programmable oral medication absorption system

It provides the advantages of dose forms in the form of tablets and capsules. Hard gelatin capsules are filled with tiny tablets. Higher dosages of medication can be delivered into the GI system and several areas can be targeted. It is possible to insert various sized micro tablets into the capsule [7].

Drug formulations in multiparticulate crystalline form

A crystalline drug, a glyceride with at least one alkylate group of at least 16 carbon atoms, and a poloxamer make up a multiparticulate for controlled drug release. At least 70% of the drug in the multiparticulate is crystalline. The glyceride/polymer mixture contains embedded crystalline drug particles that make up the multiparticulate. The poloxamer 16 exists as a distinct phase from the glyceride 141 and is largely evenly distributed throughout the glyceride.

The multiparticulate drug delivery system's design

The goal of creating multiparticulate dosage forms is to create a dependable formulation with all the benefits of a single unit formulation without the risk of changing the drug release profile or the behavior of the formulation as a result of variation in units.Several multiparticulate delivery methods, such as pellets, granules, microparticles, nanoparticles, and beads, have been tested. These systems can readily transit through the GI tract due to their reduced particle size when compared to single unit dose forms. Additionally, multiparticulate systems are said to guarantee more consistent medication absorption and be distributed more uniformly throughout the g.i.t. The transit time of food has a smaller impact on the transport of multiparticulate systems than single-unit formulations because the units are freely distributed throughout the g.i.t. The formulation of multiparticulate systems are: 8

A. Reservoir system with rupturable polymeric coating

The reservoir devices in these multiparticulate systems have a layer of rupturable polymeric coating on them. These systems have numerous layers. While some layers are made of rate-controlling polymers, others contain medicinal substances. By applying osmotic or swelling chemicals to each individual unit, the rupturing action is produced. This method can be used to achieve a variety of release patterns, such as the continuous release of active medicinal components for absorption throughout the gastrointestinal tract. Time: The medication will release gradually over a period of 1 to 12 hours, with a lag time of 4 to 10 hours. This can be either a burst or sustained release profile. The polymer barrier's thickness and composition, as well as the coating itself, determine how long the drug will release after the lag-time. The multiparticulate method offers the best release characteristics for individual medications or for medications combined.

B. Reservoir systems with soluble or eroding polymer coatings

Another family of reservoir-type multiparticulate pulsatile systems is based on soluble/erodible polymer coatings. In these systems, the medication is released in a burst from the reservoir core after a certain amount of time, during which the barrier dissolves or erodes Journal of Applied Pharmaceutical Science 01 (05); 2011: 59–63. For these kinds of systems, the coating layer's thickness generally controls the amount of time that passes before the medicine is released. These systems work on the fundamental tenet that pH-sensitive polymers complement each. This sensitivity has been used to inhibit release in the stomach, allowing complete release in the intestine, in addition to significantly increasing solubility at the same place in the g.i.t. But since dissolving is the release mechanism from these systems, a larger ratio of drug solubility to dosage amount is necessary for quick drug release following the lag period [8].

Table 1: Marketed Products

Product	Company	Drug	Release
Losec MUPS	AstraZeneca	Omeprazole magnesium	Delayed release multiple unit pellet system in tablet
Nexium	AstraZeneca	Esomeprazole magnesium	Enteric delayed release pellets in capsule
Toprol XL	AstraZeneca	Metaprolol succinate	Controlled release pellets in capsule
Avinza	King	Morphine sulfate	QD/IR+SR layered beads in capsule
SoluTab	Takeda	Lansoprazole	Delayed release enteric coated microgranules in tablet
Prevacid	Takeda	Lansoprazole	Delayed release enteric coated granules in capsule
Coreg CR	GSK	Carvedilol phosphate	QD/IR+SR polymer coated beads in capsule
InnoPran XL	GSK	Propranolol Hcl	QD / Delayed release SR coated beads in capsule
Spansule	GSK	d-amphetamine sulfate	QD/IR+SR coated beads in capsule
Focalin XR	Novartis	Dexmethylphenidate	QD / Bi-modal pulsatile release IR+Enteric delayed release beads in capsule
Adderall XL	Shire	Mixed salts of a single entity amphetamine	QD /double pulse drug layered and SR polymer coated beads
Carbatrol	Shire	Carbamazepine	BID / IR+SR+Enteric beads in capsule
Equetro ER	Validus	Carbamazepine	BID / IR+SR+Enteric beads in capsule
Metadate CD	UCD, Inc.	Methylphenidate	QD /30%IR + 70% SR coated beads
Pentasa	Shire	Mesalamine	Controlled release beads in capsule
Luvox CR	Jazz	Fluvoxamine maleate	QD / polymer coated beads in capsule
Amrix	Cephalon	Cyclobenzaprine Hcl	QD/ polymer coated beads in capsule

Conclusion

The market for medication delivery systems has come a long way, and it is predicted to grow even faster in the future. New developments in drug delivery technology allow for the integration of drug molecules into innovative delivery systems, which has numerous therapeutic and commercial advantages. Multiparticulate drug delivery systems offer several advantages, including improved adaptability and flexibility of microparticulate dosage forms, giving doctors and product developers powerful new tools to optimize therapy. Consequently, it is not surprising that these systems are growing in popularity.

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