World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

Check for updates

Integrating multiple-unit pellet system and gastro-retentive drug delivery systems: A new era in oral drug delivery

Shivangi Patidar *, Gaurav Goyanar, Nirmal Dongre and Raghvendra Dubey

Institutes of Pharmaceutical Science, Sage University, Indore, MP-452020, India.

World Journal of Biology Pharmacy and Health Sciences, 2024, 20(02), 514–524

Publication history: Received on 03 October 2024; revised on 15 November 2024; accepted on 17 November 2024

Article DOI: https://doi.org/10.30574/wjbphs.2024.20.2.0898

Abstract

Delivery Systems (GRDDS) are advanced pharmaceutical formulations designed to extend the residence time of drugs in the gastrointestinal (GI) tract, thereby enhancing the bioavailability of medications, particularly those with narrow absorption windows or significant first-pass metabolism. By improving drug solubility and absorption, GRDDS offers a strategic approach to optimizing therapeutic outcomes. Meanwhile, Multiple-Unit Pellet Systems (MUPS) utilize a multiparticulate design consisting of small, spherical pellets that enhance the pharmacokinetic and pharmacodynamic profiles of drugs, providing several advantages over traditional single-unit dosage forms. The integration of MUPS with GRDDS presents a novel formulation strategy aimed at harnessing the strengths of both systems. This combination not only aims to improve drug absorption but also to optimize therapeutic efficacy and enhance patient compliance. By leveraging the benefits of extended gastric retention and uniform drug distribution, this synergistic approach holds significant promise for advancing drug delivery technologies and improving clinical outcomes.

Keywords: GRDDS; MUPS; Bioavailability; Targeted Delivery**;** Mucoadhesive.

1 Introduction

1.1 Gastroretentive Drug Delivery System (GRDDS)

This System is a specialized pharmaceutical formulation that aims to prolong the time that a dosage form stays in the gastrointestinal (GI) tract, especially in the stomach area. Due to the need for GRDDS to in an area for a longer period, the bioavailability of the drugs improves especially those with narrow absorption windows or those which are subject to high first pass effects.

Key Features:

- Extended Residence Time:: It is the designed purpose of how long the product will sit in the stomach that GRDDS are built to accommodate.
- Improved Bioavailability: Presence of these products within the stomach for longer periods allows the solubility and absorption of drugs not well absorbed over the intestines to be improved.
- Controlled Release: A number of dosed GRDDS may probably also be designed to impart controlled or extended release of the drug thus minimizing the fluctuations of plasma drug levels.
- Targeted Delivery: GRDDS may be enhanced to be retentive in particular zones of the GI Tract so as to produce more desirable effects for certain drugs.

* Corresponding author: Shivangi Patidar.

Approaches:

Gastroretentive Drug Delivery Systems are used to increase the dwell time of dosage forms in the GI tract with the aim of increasing their bioavailability and their therapeutic effects. The following approaches can be used to enhance the gastroretention, each of which has limitations

2 Floating Drug Delivery Systems (FDDS)

The following doses can be described as a new form of delivery system that is designed to be in close contact with the stomach. Such ability makes it possible for the dosage to remain at the surface of the gastric fluids thus increasing the time the drugs reside in the stomach and are absorbed, hence benefiting the drugs that have narrow therapeutic window and specific absorption loci.

2.1 Mechanism of Action

Due to their low density, these systems help prevent the buoyancy of the gastric fluids for longer retention inside the stomach.

2.2 Types of FDDS

2.2.1 Effervescent Floating Systems:

These systems have effervescent agents such as Sodium bicarbonate and instant coffee, Tolcapone, or Propofol that react with the gastric acid to form carbon dioxide gas which then forms bubbles that forces the formulation to buoy.

2.2.2 Non-Effervescent Floating Systems:

Employ low density materials that are added to the matrix polysaccharides (microcrystalline cellulose, polystyrene) in order to increase the porosity.

2.2.3 Floating Microspheres:

Consists of certain particles of a few microns in diameter which are free floating in the stomach cavity and can be used for sustained drug release.

2.2.4 Floating Bilayer Tablets:

Owing to the presence of a rapid release and sustained release layer in a single dose, the bilayer tablets offer patients' convenience along with an optimal release profile while being kept afloat.

3 Mucoadhesive Drug Delivery Systems

MDDS, or Mucoadhesive Drug Delivery Systems, are formulations that are suggested to adhere to the mucosal surfaces of the body like those found in the gastrointestinal tract, the nasal cavity, the vaginal cavity, and the oral cavity. This adherence of drugs allows for more efficient drug contact with an absorption site for maximum therapeutic efficacy and bioavailability.

3.1 Mechanism of Action

Mucoadhesive drug delivery systems (MDDS) polymer particles/ materials work on the principle of bonding to the mucus layer of the surfaces. Such polymers could create either physical or chemical interactions with the glycoprotein of mucus (mucin) which allows the drug release system to stay in place at the mucosal surface for a longer time.

3.2 Types of Mucoadhesive Drug Delivery Systems

3.2.1 Mucoadhesive Hydrogels:

These are gel formulations with a high water content able to expand when moisture is present in a mucosal area and which releases drugs on that site over time.

Mucoadhesive Tablets

These are tablets with mucoadhesive components that dissolve in the mucous and deliver the drug contained in the tablets. These are prepared compositions for oral administration.

Mucoadhesive Films/Patches:

These helps in drug delivery at localized areas as they are in the form of indirect/rectified patches for the initial stage. This leads to developing films/ patches that attach to mucosal surfaces for targeting oral or buccal cavity regions.

Mucoadhesive Micro- or Nanoparticles:

These are minute particles that stick to mucosal surfaces and are capable of controlled drug release over extended durations, thereby enhancing drug absorption.

4 Swelling and expanding system

These delivery systems are unique compositions that are designed to swell upon immersion in any biological fluid for instance, the fluids present in the stomach or intestine. Relevant studies suggest that these systems are capable of controlling the release of drug or other active substances through their swelling 'behavior' thus ensuring a controlled release profile thereby optimizing the bioavailability.

4.1 Mechanism of Action

Swelling and its expansion is a mechanism that is brought about by the continuous interactions between the formulation and the neighboring aqueous phase, whereby water is imbibed and the volume eventually rises. This may cause:

- Increased Surface Area: The expansion is effective in enlarging the surface area that is available for drug release.
- Controlled Drug Release: The use of different polymers of various swelling index reduces the rate at which the drug is released.

4.2 Types of Swelling and Expanding Systems

4.2.1 Hydrophilic Matrices:

These systems are made up of hydrophilic polymers which have the ability to take in water and swell. When the polymer swells, the expansion of the polymer matrix helps in the gradual release of the drug.

4.2.2 Floating Swellable Systems:

These systems combine swelling and buoyancy, which allows them to stay above the gastric fluid increasing retention times, thus allowing controlled drug release.

4.2.3 Hydrogels:

These are cross linked networks which have an appreciable swelling degree due to their high water absorption capacity. They are used for drug release that can be activated by different environmental triggers (stimulus) such as, temperature or pH changes.

4.2.4 Gastroretentive Systems:

This includes a number of formulations which have the aim of swelling when food is present in the stomach to prolong the gastric residence time and hence improve drug absorption.

5 Bioadhesive Systems

These systems are formulations that are made to adhere on biological tissues so that the absorption site is available for longer periods. Such systems employ bioadhesive polymers that will bind to the mucosal surfaces of the body in different areas like gastrointestinal tract, nasal cavity, oral cavity, etc

5.1 Mechanism of Action

Bioadhesive systems operate in a few different ways:

- Adhesion to Mucosal Tissues: Bioadhesive polymers have either physical or chemical bonds (which amongst other substances can include mucin, which is the principal component of mucus) allowing formulations to attach to mucosal surfaces.
- Prolonged Residence Time: These systems providing targeted therapy by increasing the residence time of the drug at the absorption site due to its adherence to the tissue
- Controlled Drug Release: This enhanced bioavailability can take place because the formulation is designed to release the drug slowly over an extended period.

5.2 Types of Bioadhesive Drug Delivery Systems

5.2.1 Bioadhesive Tablets:

These bioadhesive tablets are solid dosage forms that consist of bioadhesive polymers and is designed to easily dissolve and release the medication whilst remaining attached to the mucosal surface.

5.2.2 Bioadhesive Gels and Hydrogels:

These gel formulations expand when moisture is added and stick onto the desired areas

5.2.3 Bioadhesive Films/Patches:

While allowing for the sustained action release of the drug, these patches or thin films are intended to attach to mucosal regions.

5.2.4 Bioadhesive Microspheres and Nanoparticles:

These are considered to be small particles known to adhere to the mucosal tissue and deliver drugs in a specified time manner which facilitates absorption.

6 Magnetic Drug Delivery Systems

As a new approach to drug targeting these formulations use the therapeutic effect of magnetic fields to concentrate and guide therapeutic agents to specific parts of the body. When combined with therapies such as monoclonal antibodies, magnetic systems allow drug release directly at the disease site and thus enhance therapy.

6.1 Mechanism of Action

This is act through several major ways:

- Magnetic Targeting: These are nanoparticles which have been loaded with drugs. When the drugs are administered to a patient, guidance through an external magnetic field directs the drugs towards a particular site (such as tumor cells) ensuring a particular drug concentration is maintained within that area.
- Controlled Drug Release: The application can also push out the drug embedded within the magnetic particles which would ensure that delivery occurs in a controlled manner.
- Enhanced Uptake: The localized increased concentration of magnetic particles can enhance the amount of drug taken up by cells at the target region hence improving the bioavailability and the therapeutic outcomes.

6.2 Types

6.2.1 *Magnetic Nanoparticles:*

These are made up of materials such as iron oxide and other biological systems. These functionalized with targeting ligands or drug.

6.2.2 *Magnetic microspheres:*

These spheres are larger than nanoparticles and so can be used to load more drugs in them. They are recommended for targeted therapy, more so, for cancer treatment.

6.2.3 Magnetically responsive hydrogels:

Drug responsive hydrogels which can swell in the presence of a magnet would allow for a controlled method of releasing the drug.

6.2.4 Magnetic liposomes:

These are liposomes that are loaded with drugs and magnetic particles and therefore can provide drug delivery and sustained release capabilities.

7 Biodegradable and Expandable Systems

Biodegradable and Expandable delivery systems are state of the art pharmaceutical formulations that help to deliver controlled release drug which also has an ability to get degraded in the body over a period of time. Biodegradable delivery systems are supplemented with an expansion feature to these delivery systems such that once these systems come into contact with body fluids, they expand in size greatly resulting in an improved drug release kinetics and therefore faster therapeutic effects.

7.1 Mechanism of Action

Biodegradation: The systems that are designed to have controlled drug release and degradation in the body tissues are commonly referred to as biodegradable systems. These types of systems release the encapsulated drugs in a controlled manner and they degrade over time as a result of enzymes or hydrolysis reactions occurring in the tissue.

Expansion: When the pump systems come in contact with body fluids, these systems expand and increase in their volume. This increase in volume will enable these systems to enable prolonged contact with the site of absorption which in turn leads to improved drug bioavailability.

7.2 Types of Biodegradable and Expandable Systems

7.2.1 Biodegradable Hydrogels:

The crosslinked polymer networks absorb water and swell considerably. These hydrogels deliver drugs by diffusion and via the biodegradation of polymers.

7.2.2 Expandable Microparticles:

Microparticles that have already been administered that can increase in size, providing a slow release owing to progressive degradation.

7.2.3 Biodegradable Stents:

Implants that can expand once implanted in the body and therefore are widely used for vascular purposes. They are impregnated with drugs which are released as the stent resorbs.

7.2.4 Expandable Tablets:

They are solid dose forms that can increase in volume as a result of water contact, hence allowing increased duration of action before elimination from the gastrointestinal system.

8 Controlled Release Systems

Controlled release systems are drug delivery formulations designed to release a therapeutic agent or drug for a fixed period of time at a predetermined rate. The purpose of these systems is to provide a continuous effective level of drug concentration in the required region in the blood and also to return less secretion level changes that can cause side effects or cut drug efficacy.

8.1 Mechanism of Action

Controlled release systems are classified depending on how the formulation is designed. Some of the processes are:

- Diffusion: The drug is released from the surface of the porous polymer drug delivery system into the disease-site. The polymer architecture and the drug solubility influence the drug release.

- Erosion: In this mechanism, the matrix encasing the drug gets eroded over a period allowing the drug to be released as the matrix material is broken down. This may include surface erosion, bulk erosion, or both.
- Swelling: Certain systems, on the other hand, upon interaction with the environment expand due to fluid absorption allowing for controlled drug release as more surfaces of the drug are exposed because the matrix is swollen.
- Osmotic Pressure: Osmotically designed systems have an internal environment which allows the drug to be expelled from the reservoir through a small opening at a constant rate.

8.2 Types of Controlled Release Systems

8.2.1 Matrix Systems

In this system drug which is to be delivered is first added in a polymeric matrix. The drug is released as a result of diffusion or erosion.

8.2.2 Reservoir Systems

Housed within a reservoir, the drug is encircled by a membrane that controls the rate. This design ensures a more accurate control of the drug's release when it's required.

8.2.3 Microencapsulation

Drugs that are protected by minute polymer shells can be released depend on shell material properties.

8.2.4 Implantable Systems

Something that is surgically implanted within the body that releases drugs over a long time period. Mainly aimed for chronic diseases.

8.2.5 Transdermal Systems

Transdermal patches are known to deliver medication into the body via skin at a controlled rate, thereby providing systemic effects without the need for injections.

8.3 Advantages of GRDDS

GRDDS provide many advantages, especially for drugs that require more time to be released slowly and have better absorption along the GI tract. These are the main advantages:

- Prolonged Gastric Retention: GRDDS makes it possible to extend the pharmaceutical retention in the stomach leading to increased absorption and increased therapeutic effectiveness of the drug.
- Enhanced Bioavailability: The increased gastric emptying time of GRDDS increases the residence time of the drug in the GIT. This enables the absorption of more poorly soluble drugs due to enhanced bioavailability.
- Controlled Release of Drugs: These systems achieve such a sustained effect that the plasma concentration does not fluctuate in the formulation and so drug delivery does not need to be as frequent.
- Minimized Variability in Drug Absorption: GRDDS can alleviate the variability due to different physiological responses in gastric retention time and intestinal times and variability in drug absorption consequently.
- Reduced Side Effects: GRDDS can be able to lessen negative effects caused by higher concentrations of drugs in in the plasmic due to a surge of a medication concentration.
- Targeted Drug Delivery: Available GRDDS can be employed to confine drug release to the stomach and upper GIT hence they can be used to manage peptic ulcers or extend drug release to the esophagus to manage gastroesophageal reflux disease.
- Improved Patient Compliance: Sustained medication release attributes lead to lower the number of doses required making GRDDS more damnable.
- Potential for Multiple Drug Delivery: These systems can be developed to allow co-administration of more than one drug, thus allowing combination therapies in a single dosage form.
- Ease of Administration: GRDDS normally are in the forms of ordinary dosage forms such as tablets and capsules hence patients feel comfortable using them.
- Reduced Risk of Dose Dumping: GRDDS are capable of minimizing dose dumping that occurs when large amounts of drug is released at once by making way for controlled release mechanisms.

9 II Multiple-Unit Pellet Systems (MUPS)

MUPS are a modified pharmaceutical formulation as a form of a multiparticulate system to improve drug delivery. MUPS are developed in the form of small, spherical pellets which can enhance the pharmacokinetic and pharmacodynamic characteristics of the agents thus creating several merits over the conventional mono-conventional dosage forms like tablets and capsules.

9.1 Mechanism of Action

MUPS work by Firstly, MUPS disperse the drug in the form of many small pellets, which can be further…:

- Provide Uniform Drug Distribution: The multiple units ensure that drug release and drug distribution within the gastrointestinal (GI) tract occurs in a more reliable manner.
- Control Release Rates**:** Various units are designed to provide a specified rate of release. This enables immediate, sustained or delayed release.
- Minimze variability: Using multiple pellets instead of a single one can make these two factors, GI transit and pH, less harmful or less important in terms of drug absorption.

9.2 Pellets formation techniques

MUPS are developed by applying the “pelletization” process using a number of technical approaches that provide the desired size of pellets, controlled release and high bioavailability. Following are some of the methods adopted for MUPS pellet preparation:

A. Extrusion-Spheronization

Extrusion-spheronization is a common and popular British trade technique employed in the pharmaceutical industry to develop spherical pellets or granules from powder materials. This particular unit operation is very important for the development of controlled-release formulations, as it enhances uniformity in size and flow properties of finished pellets and increasing drug release.

Process Overview

The extrusion and spheronization process comprises 2 principles steps:

- Extrusion: In manufacturing powdered formulations such as active pharmaceutical ingredients (APIs), and excipients with moisture, kneading is performed so that the wet mixture can be extruded through an extruder. The applied extruder tool will create fluid pressure, which shapes the material to a cylindrical rod and forces it through the die ribs.
- Spheronization: The cut rods are taken into a spheronizer and with a rolling motion, are converted to round pellets. This stage normally accompanies frictional forces and control moisture level to attain the pellet shape and size.

B. Pan coating

Pan coating is a technology that has been widely employed in the pharmaceutical industry as it enables the application of a coating to solid dosage forms like combined pellets and compression coated tablets. In such a technique, the dosage forms are rotated within a coated pan whilst a coating solution is sprayed onto the surface making it possible to have a uniform distribution of coating material

Process Overview

The pan coating process in general can be outlined in specific steps:

- Preparation: The coating solution is usually composed of polymers and plasticizors, colorants and a solvent and it is prepared in such a way that certain properties are caused (ex: film formation ability, adhesion).
- Loading: A coating pan, with tablets or pellets is fed continuously in this particular case, and it is a pan that rotates and gives a uniform coating without bubbles forming.
- Spraying: The liquid is atomised over the rotating dosage forms as the dosage forms change position and the pan is rotated, making it possible for the solution to cover the surfaces of the forms evenly.

- Drying: During spraying, the coating is wet and in a solution form, a solvent is removed in order for the coating to be crust and bind to the material being coated.
- Monitoring: The factors in this case temperature, humidity and coating thickness are controlled during the process in order to achieve a desired quality.

C. Hot Melt Extrusion

The hot melt extrusion (HME) for the pellets is a technique that is utilized for development of such small particles which have rounded edges and are called pellets and consist of active pharmaceutical ingredients embedded in a thermoplastic polymer. This method improves the therapeutic efficacy of poorly soluble drugs and provides controlled-release formulations.

9.2.1 Process Overview

The following steps outline the entire procedure of HME in transforming the active substances into pellets.

- Formulation Preparation: The ingredients in this case include the active ingredient, thermoplastic polymers and other excipients if required such as plasitcizer or stabilizers. From the results it can be concluded that the polymer is an important factor in determining the release rate and the stability as well.
- Melting and Mixing: The formulation mixture is poured in the extruder h v heat and shear is applied to it. This was due to the fact that the polymers dissolved and the actual active ingredients were uniformly suspended in the molten polymer mixture.
- Extrusion: The uniform melt gets pushed through a die. In the case of pellet manufacture, small sized dies are utilized and the strands of the fused glass are produced.
- Cooling and Pelletization: The strands are cooled after extrusion and they are subsequently fragmented to small pellets. There are various ways in which this can be accomplished such as strand cutting or rotating pelletizers which shear the strands at the exit of the die.
- Post-processing: The pellets may also be dried or coated to gain an additional property such as stability, modify released profile, and improve overall appearance.

D. Spray Drying

Spray drying for Multiple-Unit Pellet Systems (MUPS) is integrating the spray drying technique with the formation of smaller spheroid pellets which are API containing pelleted within a polymer. This helps mostly in improving the formulation of controlled-release medications along with solubilizing agents for poorly soluble formulations.

Process Overview

For MUPS, the spray drying process usually involves the following steps:

- Preparation of Feed Solution: A homogenized feed solution or suspension is prepared which includes the API, the needed excipients (such as polymers, plasticizers and/or stabilizers), and solvents. Polymer type is very important to control the release profile.
- Atomization: The feed solution is atomized through a spray nozzle into fine droplets. This improves the drying rate volumetrically.
- Drying: The atomized droplets are sprayed into a hot air chamber so that the solvent could vaporize in a short time and solid particles are formed. The hot air temperature and the volume of air are both regulated to avoid the thermal degradation of the API.
- Formation of Pellets: When the solvent evaporates, spheres begin to join together in forming the pellet structure. The morphology and size of the pellets can be influenced by the formulation and processing conditions.
- Separation and Collection: Dried pellets are removed from the air stream with cyclone separator or bag filter and are then poised for the next stage.
- Post-processing: Further step may include modification of the pellets by either milling or coating to improve their features or alter the drug release profile.

E. Fluidized Bed Granulation

This method help to manufacture granules or pellets by use of a fluidized bed of particles. This technique is useful in the production of MUPS since such drugs can be biorelease controlled providing improved bioavailability of the used APIs.

Process Overview

The fluidized bed granulation utilized in the manufacture of MUPS can be broken down to the following steps:

- Preparation of the Powder Blend: Taking into account the active component, excipients (such as binders, fillers and disintegrants) as well as other component, these are accurately weighed and mixed homogeneously into powder blend.
- Fluidization: The powdered mixture is first placed in a fluidized bed granulator. Air is injected from below the bed through a screen and suspends the particles in it making it fluidized. This makes it possible for granulation to take place.
- Granulation: The coating granulating solution is sprayed on the fluidized powder. The liquid aids the un-coalesced particles in binding together, forming a larger sized damp granule until the water content evaporates. There is scope for constant modification or control of the parameters for better production of granules with specific and desired dimensions.
- Drying: Over a period, granules are dried utilizing high-temperature air due to which water molecules are removed from the structure of the granule. Similarly, this process also assures that the final properties are attained so that the granules remain stable and flowable.
- Cooling and Collection: All of the processes have amplification of drying the granules being the last one. Granules after being dried are then cooled down and are collected more static if need be so that these sensitive materials require progressive transformations like mesh or coating.

F. Melt Granulation

Melt granulation is a technique used in the pharmaceutical formulation where a binder is melted with the active pharmaceutical ingredient and along with excipients to produce granules. This technique is great for the production of MUPS as they enhance sustained release of drugs with efficient bioavailability.

Process Overview

Generally, the manufacturing process of MUPS using melt granulation involves sequentially carrying out the following steps:

- Preparation of the Powder Blend: A homogeneous mixture is prepared from the API, excipients such as fillers and disintegrants, and a suitable thermoplastic binder. The binder selected is of great importance in resulting granule characteristics.
- Melting the Binder: The binder is heated to the point of its melting. This may be accomplished high-shear granulator or an extruder.
- Granulation: The molten binder is added to the powder mixture. The binder in the process of melting gradually proceeds to surround the particles thus facilitating agglomeration and formation of the granules. Mixing is done until a set granule size and granule distribution is reached.
- Cooling and solidification: The granules are cooled in order to solidify the binder. Solidifying the binder improves stability and integrity of the granules. Cooling of the granules can be achieved in a cooling chamber or other means.
- Sizing and sieving: The granules that have been cooled have to be sized and sieved to achieve the desired or target consistent particle size. Oversized granules may be left out and milled to the desired size.
- Coating: Controlled release is possible by coating the granules with a polymeric cover that alters the release profile.

G. Lyophilization

Lyophilization, commonly referred to as freeze-drying, is a dehydration technique that aims to remove water from sensitive materials by applying vacuum after freezing them. In the case of Multiple-Unit Pellet Systems (MUPS), lyophilization is utilized in such a way that stable dry pellets with active pharmaceutical ingredient (API) are produced without affecting the efficacy and integrity of the pellets.

Process Overview

The procedure for lyophilization for MUPS involves the following activities:

- Preparation of the Formulation: Relevant formulation is done which involves inputting the active Pharmaceutical Ingredient, its excipients (which can be such as stabilizers, bulking agents, and cryoprotectant),

and solvent (made mostly of water). The formulation must be homogeneous in order to enhance the ease of even freezing and even drying of the formulation.

- Freezing: The formulation temperature is lowered instantly below the freezing point so that ice crystals can be easily formed. This is an important step as it affect the qualiy and structure of the final lyophilized product.
- Primary Drying (Sublimation): The temperature is elevated at a vacuum. The ice directly vapours under these conditions, which does not pass through liquid phase, thus removing a major part of the water content owing to the fact that the ice simply sublimates.
- Secondary Drying (Desorption): After the first drying, the temperature is raised quite considerably to allow for total moisture removal This step guarantees that the product's moisture content will be low, a factor needed for the final product's stability.
- Sealing and Packaging: After drying, the rehydrated lyophilized pellets are packed in Packs that are moisture resistant, to avoid rehydration and to protect them from the external environment.

Advantages of MUPS

There are several advantages of MUPS over traditional single-unit oral dosage forms, hence enabling their applications in pharmaceuticals formulations. Some of the benefits are as stated below:

- Enhanced Bioavailability: Enhanced bioavailability of MUPS is thought to support their presence at the target area or their reabsorption through cells. Whereby MUPS provide solubility improvements and help in absorption for poorly soluble drugs.
- Uniform Drug Distribution: The multi particulate nature of MUPS provides a more proportional and even distribution of the drug deposition in the GIT, and thus the differences that are experienced in single unit forms are reduced.
- Controlled Release Profiles: Controlled release profiles suitable for MUPS include both sustained release while instantaneous profiles can also be developed when Engineered MUPS allow for any dose that is needed.
- Reduced Side Effects: Reduced side effects are due to the fact that the drug will not reach the peak plasma levels in a minute. This avoids the toxicity profile thus providing safety for the patient.
- Improved Patient Compliance: MUPS in most cases enable the development of an extended-release dosage form thus patients need not take many doses.
- Flexibility in Formulation: With MUPS, multiple drugs and excipients can be included, thus creating combination therapies and meeting patient-specific formulation requirements.
- Minimized Gastrointestinal Variability: The multiple units lessen the effect of individual differences in GI motility and pH which increases variability in drug absorption.
- Reduced Risk of Dose Dumping: Due to the drug being encapsulated in numerous pellets, the risk for dose dumping, common with single unit dosage forms, is much lower.
- Easier Coating and Modification: The small dimensions of the pellets enable better control of the application of the coating that modulates the drug release rate.
- Potential for Targeted Delivery: MUPS are formulated to improve delivery of the drug to target areas in the GI tract to achieve localised treatment

10 Conclusion

The fusion of MUPS and GRDDS holds significant promise for improving the oral delivery of various drugs, especially those with poor bioavailability or those requiring targeted delivery to the upper GI tract. This represents an innovative and highly effective strategy for optimizing oral drug delivery. By leveraging the strengths of both systems, it is possible to develop formulations that offer controlled, sustained, and targeted release profiles, ultimately improving therapeutic outcomes and enhancing patient satisfaction.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Reference

[1] Singh, B. N., & Kim, K. H. (2000). Floating drug delivery systems: An approach to oral controlled drug delivery via gastric retention. *Journal of Controlled Release*, 63(3), 235-259.

[2] Patel, V., & Patel, M. (2012). Gastroretentive drug delivery systems: A review. *Journal of Pharmaceutical Sciences and Research*, 4(9), 1997-2005.

[3] Müller, R. H., & Maeder, K. (2005). Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in drug delivery. *Journal of Pharmaceutical Sciences*, 94(12), 2771-2782.

[4] Desai, S. D., & Bolton, S. (1993). Design and evaluation of floating drug delivery systems. *Pharmaceutical Research*, 10(3), 317-323.

[5] Srinivas, S. R., & Sandeep, K. (2009). Recent advances in gastroretentive drug delivery systems: A review. *International Journal of Pharmaceutical Sciences and Nanotechnology*, 2(2), 684-692.

[6] Chawla, G., Gupta, P., & Rathi, S. (2003). Development of gastroretentive drug delivery systems. *Indian Journal of Pharmaceutical Sciences*, 65(5), 499-505.

[7] Nayak, A. K., & Maji, R. (2010). Gastroretentive drug delivery systems: A review of methods and formulations. *Drug Development and Industrial Pharmacy*, 36(5), 587-601.

[8] Bhagat, H., & Nair, S. (2014). Gastroretentive drug delivery systems: Review article. *International Journal of Pharmaceutical Sciences and Research*, 5(1), 45-58.

[9] Bansal, A. K., & Singh, B. N. (2010). Gastroretentive drug delivery systems: A review. *International Journal of Pharmaceutics*, 390(1), 1-11.

[10] Erdönmez, D., & Yüksek, N. (2020). Floating drug delivery systems: A promising strategy to improve drug bioavailability. *Acta Pharmaceutica Sinica B*, 10(3), 563-579.

[11] Gander, B., et al. (2000). "Multiple-unit pellet system: A promising approach for oral drug delivery." *International Journal of Pharmaceutics*, 194(1), 39-54.

[12] Omar, S., et al. (2016). "Pharmaceutical pelletization techniques: A review of the key methods." *European Journal of Pharmaceutics and Biopharmaceutics*, 106, 62-74.

[13] Patel, A. K., et al. (2019). "Recent advancements in the production of multiparticulate drug delivery systems." *Pharmaceutical Development and Technology*, 24(6), 765-775.

[14] Jain, R. K., & Kapoor, S. (2006). "Multiple-unit pellet system (MUPS): An effective drug delivery system for oral administration." *Journal of Pharmaceutical Sciences*, 95(1), 100-110.

[15] Srinivasan, M., et al. (2013). "A review on pelletization: Pharmaceutical applications and techniques." *Pharmaceutica Analytica Acta*, 4(6), 212.

[16] Hernández-Pérez, J. M., et al. (2020). "Lyophilization and Spray Drying Techniques for MUPS: A Comparative Study." *Journal of Controlled Release*, 321, 136-146.

[17] Ryu, J. H., et al. (2017). "Hot Melt Extrusion of Pellets for Drug Delivery: Principles and Applications." *Pharmaceutical Technology*, 41(5), 44-52.

[18] Kim, S. H., & Hwang, Y. S. (2014). "Development of pellet systems for controlled drug release." *Journal of Pharmaceutics*, 8(7), 301-318.

[19] Bodmeier, R., & Paeratakul, O. (2005). "Multiple-unit pellet system (MUPS) tablets: A versatile oral dosage form." *Journal of Pharmaceutical Sciences*, 94(10), 2115-2125.