Review Article

A New Path for Drug Delivery by Multiple Unit Pellet System (MUPS)

Harshada Rajendra Bafna[1], Nitin Rajendra Shirsath[2], Vaibhavkumar Arun Jagtap[3]

From, [1]Assistant Professor, Department of Quality Assurances, [2]Assistant Professor, Department of Pharmaceutics, [3]Professor, Department of Pharmaceutics, Gangamai College of Pharmacy, Nagaon, Dhule, MH, India

ABSTRACT

Innovative delivery system that are helpful in enhancing therapeutic objectives and reducing adverse effects are the focus of pharmaceutical research. The advantages of tablets and pellet-filled capsules are combined into a single dose form by MUPS, one of the more complex and inventive technologies. Continuous drug distribution into the bloodstream is made possible by the breakdown of these pills in the stomach and intestine. The current article examines the potential benefits, desirable pellet characteristics, different pelletization methods, MUPS-influencing factors, drug release mechanisms, and pharmaceutical applications, as well as the challenges associated with compaction and the crucial elements that must be considered for MUPS production to be successful.

Key words: MUPS; Innovative delivery system; Multiple Unit Pellet System; Benefits; Process variables

The acronym for Multiple-Unit Pellet System is MUPS. Nonetheless, the term is commonly used to describe MUPS that have been compressed into tablets from the standpoint of research and the pharmaceutical industry [1]. The name "Pellet" has historically been used to refer to a wide variety of well-produced, geometrically defined agglomerates made from various starting materials under infinite processing circumstances [2]. Pellets are typically between 0.5 and 1.5 mm in size, though they can be made in a wide range of diameters [3]. Pharmaceutical businesses mainly produce pellets for use in oral controlled-release dosage forms that can deliver medications in site-specific, gastroresistant, or sustained-release manners. The usage of pellets in dosage form design and development has increased as a result of the growing advancements in pharmaceutical delivery technology [4].

Actually, due to its many advantages, a tablet is the solid dosage form that is most commonly used for oral administration. Similar therapeutic benefits can be obtained via controlled release capsules, a kind of solid oral formulation that frequently includes a range of coated pellets. Around the world, a small number of people and businesses are conducting research on the difficult subject of MUPS compaction. Microparticles, which can be made of natural or synthetic polymers, are tiny, freely-moving particles that range in diameter from 1 to 1000 µm. The advances in genetics and biotechnology have led to the development of many powerful and specialized drugs. Because of a number of problems, including the restricted solubility, poor stability, and narrow therapeutic index of many new medications, safer drug delivery is necessary [5–6].

Access this article online

Quick Response Code

Received – 09th May 2024
Initial Review – 01st October 2024
Accepted – 31st December 2024

The cores of these pellets, granules, sugar seeds, mini-tablets, powders, and crystals made of ion exchange resin particles include pharmaceuticals. It is more typical to load multiparticulates into capsule shells rather than compressing them into tablets. Because MUPS have better dispersion, transportation, and surface area, as well as better bioavailability and lower inter-subject variance, they are employed more often than unit dose forms [7-8]. MUPS improve medication safety because, if a multi-unit dosage form's film covering is destroyed, the drug contained in that small subunit will be released, altering the release behavior of that particular subunit, which makes up a tiny percentage of the entire dose.

The entire medicine will be discharged into the stomach if the enteric coating on a single unit or monolithic is destroyed, resulting in irritation or ulceration, dosage dumping, or the loss of the full dose. There may be more consequences if one unit fails than several units. The pharmaceutical industry as a whole started investing money in pellet technology research and, whenever possible, buying state-of-the-art equipment suitable for pellet production after the advantages of pellets over single units became clear. Pellets can be made using a variety of production processes, depending on the use and the producer's preferences [9]. The methods used for pelletization and granulation are almost the same. The most often used methods include extrusion, spheronization, solution or suspension stacking, and powder layering.

Correspondence to: Harshada Rajendra Bafna. Department of Quality Assurances, Gangamai College of Pharmacy, Nagaon, Dhule, MH, India.

Email: harshadabafna@gmail.com

2. MUPS benefits Over Pellet-Filled Capsules Or Conventional Modified-Release Tablets

They can be divided into the proper dosage strengths without changing the composition or the procedure. Pellets containing the active drug in liquid, capsule, or dissolving tablet form offer significant therapeutic advantages over single unit dose forms. For instance, the extrusion-spheronization process was used to create pantoprazole pellets for the treatment of peptic ulcers [10].

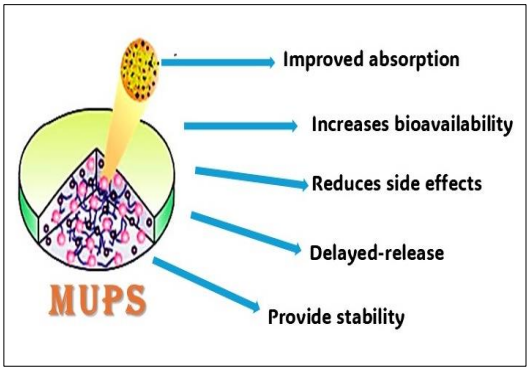

Figure 1. Benefits of MUPS

2.1 Pharmacokinetic advantages

Micro pellets in MUPS travel from the stomach into the small intestine swiftly yet consistently due to their small size, which lowers the possibility of localized discomfort, enhances uniform absorption of medications, and boosts bioavailability. For instance. For both juvenile and geriatric patients, Prevacid SoluTab is a mouth-dissolving MUPS with a pleasant taste. When using delayed-release formulations, rapid enteric coating is encouraged by the consistent evacuation of micro pellets from the stomach into the small intestine, drug release and degradation, resulting in an early peak time and peak plasma concentration (t-max and C-max). There is less potential for dose dumping, more constant drug release, and inter-subject variance when controlled-release formulations are used [11–12].

2.2 Pharmacodynamic advantages

Pellets dissolve medications in the gastrointestinal tract more rapidly and consistently due to their small size and greater surface area, which promotes constant, regulated pharmacological action and uniform drug absorption. Compared to a traditional pellet-filled capsule, the MUPS dosage form has a significantly greater number of pellets, which helps to further reduce intra- and inter-subject variability in medication absorption and clinical response. Furthermore, there is less chance of partial medication release and dose dumping (in the stomach) [13].

2.3 Patient friendly dosage form

A mouth-disintegrating medication with a pleasant flavor, Prevacid SoluTab is appropriate for older people and children who have difficulty in swallowing pills or capsules. The orodispersibl MUPS can be taken without water to encourage swallowing and salivation, particularly when traveling. Lower volume or smaller tablets are more patient-compliant than capsules, and they can be divided into the appropriate dosage strengths without requiring formulation changes. Additionally, they can be employed to produce distinct release properties in separate or identical locations of the gastrointestinal system.

2.4 Processing advantages

Because of their roughly spherical shape and ease of conversion into tablets, MUPS have better flow characteristics than typical granules used for tabletting. Furthermore, these formulations require less lubrication during the tablet-making process, which lowers the cost of MUPS relative to tablets. MUPS offers all the advantages of tablets over capsules, including improved inert matrix physicochemical and microbiological stability. speed of processing using the existing tableting infrastructure in comparison to capsules. Lower processing costs since the product is more resistant to manipulation and processing is completed more quickly. Compression causes fewer dust problems than with conventional tablets [14–15].

2.5 Investigation, Dissection and Assessment

Pellets offer a high degree of flexibility in designing and developing oral dosage forms such as suspension, sachet, tablet, and capsules [16]. MUPS offer the chance to examine the change in size, shape, and density of pellets after compaction by retrieving the pellets from highly lubricated compacts or disintegration tubes.

3. Mechanism of Drug Release from MUPS

The following are possible mechanisms for drug release from MUPS:

3.1 Diffusion: On contact with aqueous fluids in the gastrointestinal tract (GIT), water diffuses into the interior of the particle. Drug dissolution occurs and the drug solutions diffuse across the release coat to the exterior [17].

3.2 Erosion: Certain coatings have the ability to progressively dissolve over time, releasing the medication that is inside the particle [18].

3.3 Osmosis: When the proper conditions are met, allowing water to enter can cause an osmotic pressure to build up inside the particle [19].

4. Factors Influencing Design of MUPS

Formulation variables: composition, porosity, polymer coating size and amount, nature, and tableting excipient size and amount are the main formulation variables.

4.1 Core Pellet: Pellets are a unique type of granulates that have a smooth surface, low porosity, extremely regular round shape, and a typical size range of 0.2-2 mm. Homogeneous and

inhomogeneous pellets can be distinguished based on the medication distribution within them.

***4.1.1 Type and composition*:** Enteric coated pellets and a minimum of one tablet excipient make up the multiple unit compositions.

***4.1.2 Pellet size*:** The size of the pellets has an impact on both the drug release from the compacted pellets and the compaction properties.

***4.1.3 Pellet shape*:** The most crucial feature is the pellets' sphericity, which can be ascertained using a variety of techniques.

***4.1.4 Pellet porosity*:** This is another important component that influences the compaction pattern and, in turn, the integrity of the polymer coat during compression.

4.1.5 Pellet density: Pellet density is very significant, particularly if a prolonged gastric stay is desired. Density has little to no significance when it comes to modifying the stomach residence time of medicinal dose forms (both multiple and single units).

4.1.6 Elasticity: Pellet composition has a direct bearing on elasticity. The center of the pellet should be robust and somewhat flexible.

***4.2 Coverage*:** Coating of polymers: When it comes to maintaining the integrity of the polymer film during compression, the coating's quantity matters. Generally speaking, a thicker coating is more resistant to damage than a thinner one.

4.3 Cushioning excipients: Tablet formulations include excipients with protecting (cushioning) qualities to preserve the integrity of coated pellets. The MUPS produced hard tablets with low friability and predictable drug release profiles when 60–70% cushioning grains were added [20].

5. Types of MUPS

There are two types of MUPS that can exist:

MUPS made of coated pellets.

MUPS made up of pellets of matrix material.

While the latter kind of MUPS is less popular than the former, it does have certain advantages over compaction of polymer-coated pellets.

5.1 MUPS made of coated pellets

The ability of sustained-release multiparticulates to release the medication as planned even after compaction is a challenge. Polymer-coated pellets were compressed either alone or in conjunction with other excipients to create tablets.

5.2 MUPS made up of pellets of matrix material

Pellets that are naturally made of excipients that remain inside the pellet structure's matrix and slow down the release of the medication are referred to as matrix pellets [21].

6. Preparations of MUPS

MUPS preparation entails the following actions

6.1 Preparation of pellets: Pelletization is the process of combining excipients and active medicinal substances into spherical beads known as pellets [22-23]. There are numerous methods available for making pellets. Some of the traditional coating methods used for pellatization include the following:

6.1.1 Layering

The layering method involves covering nuclei—which may be inert starting seeds or crystals of the same material—with successive layers of pharmacological entities in the form of liquid, dry powder, or crystals [24]. They include solution/suspension layering and powder layering. Example: Omeprazole magnesium is suspended in a micronized state and subsequently deposited on 0.250–0.355 mm diameter sugar microspheres. To segregate the omeprazole from the subsequent enteric coating, these pellets are subcoated. Pellets are compressed into tablets, film-coated, and mixed with tabletting excipients after a final protective over-coating.

6.1.2 Extrusion and Spherization

Extrusion spherization was created as a pelletization technique in the early 1960s. Multiparticulates for applications involving controlled drug release were its primary use. For oral solid dosage forms with controlled release and few or no excipients, it is particularly beneficial to make dense granules with a high drug loading. Extrusion spheronization is a complicated process that uses wet mass extrusion and spheronization to create evenly sized spherical particles called spheroids, pellets, beads, or matrix pellets, depending on the materials and technique used. The primary advantage over alternative methods of creating drug-loaded spheres or pellets is the ability to incorporate large amounts of active components without creating unacceptable large particles (i.e., few excipients are required). Despite the wide range of potential applications, improved processing and controlled medication release are most commonly mentioned [25]. The following are the processing steps for pelletization and extrusion:

6.1.2.1 Dry mixing

All of the ingredients are dry combined to create a consistent powder dispersion using a twin shell blender, plane tray mixer, high speed mixer, and trumbler mixer. This kind of formulation frequently uses lactose monohydrate (LM), microcrystalline cellulose, and glyceryl monostearate (GMS).

6.1.2.2 Wet massing

Wet mass extrusion spheronization, sometimes referred to as cold-mass extrusion spheronization, became the method of

choice for producing dense, spherical pellets with uniform size and shape. Wet massing the powder dispersion produces an appropriate plastic mass for extrusion. Wet mixing requires the addition of a binding liquid, such as glycerol or water [26].

6.1.2.3 Extrusion

The third step in the process is this. The method of extrusion involves pushing a substance through a pre-made hole or aperture until the wet substance forms consistently sized rod-shaped particles. Since it is believed to be a dependable and repeatable process that may yield high-quality spheroids with a limited size range and plenty of mechanical strength, extrusion-spheronization is the most widely utilized technology. Additional methods for creating pellets include spray congealing, rotary processing, high/low shear granulation, suspension/solution layering, and powder layering [27].

6.1.2.4 Spheronization

The fourth stage of the process, called spheronization, aims to round off the rods produced by extrusion into spherical particles. The process of spheronization, which turns rods into spheres, occurs in several stages. Only when the mass is really dry will the rods change to the same degree as dumbbells, and the spheres won't deform. The extrudate rounds into spheres due to frictional forces from particle-particle and particle-equipment collisions. Cross-linked polyvinylpyrrolidone or crospovidone has been successfully used to aid in spheronization to produce pellets [28].

6.1.2.5 Drying

To reach the appropriate moisture content, a drying phase is needed. The pellets can be dried in a fluidized bed dryer, tray drier, or oven at room temperature or at a higher temperature. Drying was completed when the exit air reached 50ºC (around 30 minutes).

6.1.2.6 Screening

In order to attain the intended size distribution, screening may be required; sieves are employed for this purpose.

6.2 Selection of Excipients

Because differing tablet disintegration rates result in varying tabletting excipients, there was a little variation in medication release [29]. The group of binders, fillers, dissolves, lubricants, slip agents, and mixtures there of is used to choose excipients.

6.3 Compression of MUPS

Coated pellet compression is a difficult procedure that requires modifying formulation and process parameters. After compression, it ought should flex and bounce back without endangering the coating. The coated pellets' flat surface is visible in SEM photos. The fact that the pellets separated from the cushioning material at 3 KN [30] indicates that they were adequately protected during tableting. There were no obvious cracks or indentations on the pellet's surface as an appropriate tableting excipient to guard against compression-induced damage to coated pellets containing a medication that dissolves easily in water.

7. Troubles in Developing MUPS Tablets

In order to prevent particle attrition, fragmentation, densification, and deformation, the following aspects should be taken into account when designing and manufacturing MUPS:

1. The coated pellets' resilience in preserving the medication release profile following compression.

2. Harmonious mass of pellets and excipients used in tableting are compatible.

3. The tablets' mechanical strength for subsequent processing, including film or functional testing.

4. Packing and coating.

8. Solutions to Overcome Challenges in MUPS

8.1 Granulation: Good flow and a limited distribution of particle sizes in the tableting mixture inhibit the de-mixing of pellets and extra-granular material. If the coated particles are large in size, size adaptation (controlled by granulation) could be taken into consideration.

8.2 Pellet shape: For a good, even distribution, the pellets' shape should be spherical or almost spherical. Increased spherical form deviation is not the result of typical release from defects and fractures during compression.

8.3 Pellet size: To endure compression pressure, the coated pellets' maximum size is limited to 2 mm. Because they separate with tabletting excipients and expose the transmitted force from the upper punch to the lower punch directly, large-sized pellets cause the coating to burst. Influences the final tablet's content consistency as a result.

8.4 Pellet Density: Compared to pellets with a density of more than 2 g/cm3, those with a density of roughly 1.5 g/cm3 exhibit faster stomach emptying. Pellets that have a diameter of less than 2 mm and a density of less than 2 g/cm3 can pass past the pyloric sphincter in both fed and fasted states, similar to how liquids pass through the stomach.

8.5 Pellet core and Core material: Pellets with a low surface to volume ratio are better because they can result in a smaller area of contact between the particles as they are being consolidated. The pellet core should be somewhat flexible in order to accommodate this, allowing it to deform during compression without damaging the coated film. Microcrystalline cellulose, both in powdered and granulated form, has been the subject of substantial research by numerous scholars. According to their findings, microcrystalline cellulose offers coated particles in both powder and granulated form better protection and displays plastic deformation when compressed. Dicalcium phosphate pellets, for example, should not have a very hard core because this could hinder the flow of the pellets. The surface is subjected

to compression force in this scenario, which deforms it and modifies the release.

8.6 Porosity: Due to its important role in compression, pellet porosity is associated with deformation. Due to their increased porosity, which makes them denser when compression force is applied and forms as deformed coherent units as a result of non-interfering excipients, medium and high porous pellets showed more deformation than low porous pellets. When fewer porous pellets are compacted, the medication releases much more quickly. This occurs as a result of the pellets seeing reduced deformation and densification. The excipients included in the pellets should not alter their medicine release profile. The deformed pellets and extra granular material must pack as tightly as they can.

8.7 Polymer coating and Film flexibility: Polyarchy and cellulose derivatives are examples of polymers that are commonly used to achieve certain release characteristics. Cellulose and its derivatives, including HPMC and HPMCP, form stiff, brittle films that break under compression, in contrast to polyarchy and copolymers of acrylics, which create flexible films that deform readily. Plasticizers that help create flexible films include triacetin, polyethylene glycol, and triethyl citrate. A extremely flexible sheet prevents the coating from separating when compressed and ensures elastic properties. Polymers like Eudragit provide the required degree of elasticity to the film when mixed with triethyl citrate plasticizer.

8.8 Selection of Solvents: Both aqueous and non-aqueous coatings can be applied. Aqueous coating has some drawbacks despite its environmental benefits, such as medication deterioration from trapped moisture; temperature also contributes to this degradation when pellets are dried for extended periods of time to eliminate moisture. However, the sol-to-gel thixotropy of the polymer solution in non-aqueous coatings facilitates coating and causes the solvent to evaporate significantly faster than in aqueous solvents.

8.9 Mechanical resistance: During compression, the elasticity of the film mechanically stabilizes the pellets. By avoiding particle deformation during compression, high mechanical resistance contributes to the preservation of the film's integrity. Larger particle sizes reduce film breakdown by increasing mechanical stability and reducing interparticle interactions.

8.10 Coating thickness: The thickness of the coating layer correlates with the pellets' mechanical resistance during compaction. Below a certain thickness, even very flexible films tend to break, although films with more thickness retain their elastic properties. The thickness of the coating layer is altered by the compaction-induced deformation of the coated pellets, which affects the drug's release profile.

8.11 Extra-granular material and cushioning agents: The stability of films during compression is affected by extra-granular material. Crystalline materials with sharp edges and abrasive surfaces may damage the coating as the compression force increases. As a result, the characteristics of drug release after compaction into tablets are altered. The sort and quantity of coating agent, the selection of additives such plasticizers, the use of cushioning excipients, and the rate of pressure applied must all be closely monitored because the drug release properties of the subunits help to protect the film. The optimum choice is polyethylene glycol, ideally polyethylene glycol 6000, because cushioning materials are naturally waxy. The coated pellets are shielded from compaction pressures by selectively deforming and/or cracking, or by reorganizing themselves inside the tablet structure. Cushioning pellets, which are usually made of excipients, are considered to be softer and more porous than coated medications. The ratio that is believed to be most suitable for reducing coating film damage is 1:3 or 1:4. In medicine, the proportion of drug pellets to cushioning excipients is crucial.

8.12 Electrostatic charges: During the tablet compression cycle, the pellet surfaces may become electrostatically charged, which could disrupt their flow. Typically, talc is added to address this issue since it functions as a glidant. Comparative dissolving experiments should be carried out while developing multiparticulate tablets in order to find any potential variations in the release rates of the tablets and the uncompressed tabletting mixture. To guarantee consistent medication releases, the disparity between the two dissolution profiles must not surpass 10% [31-33]**.**

9. Process Variables

9.1 Compression force applied: By increasing the force beyond the minimum necessary to create a compact to a specific value which varies depending on the formulation film ruptures and the rate of dissolution are accelerated Compression force modifies the dissolving profile according to the intended formulation type and, to a greater extent, causes damage to the polymeric functional coating. When a delayed release formulation is used, a polymer coat rupture causes the medicine to be released into acidic media, which causes the drug to degrade.

9.2 Compression speed: To maintain homogeneity in the final mixture during tabletting, the tabletting rate is controlled. The pressure used for tabletting is appropriately set. Compression speed is most likely the formulation's ideal value. Excessive speed can lead to incorrect die fill. Punch heads and compression rollers can come into more touch with one another, which will stop capping and laminating [34].

9.3 Compression velocity: To corresponds more to the dwell duration the amount of time the punch head spends in contact with the compression roller during the compression cycle. MUPS have a higher propensity to cap during compression. Increased dwell time inhibits capping and lamination by promoting the creation of strong bonds between the compressed particles.

9.4 Variables related to equipment: With a few modifications, any tablet compression device can be used to prepare MUPS. To create pills and tablets, the Tablet Compression Machine uses granulated powder. A die and specific punches work together to form a cavity. The powder inside this hollow is fused when punches are squeezed with a certain amount of power. To compress powder and make tablets, the rotary tablet press machine consists of many rotating stations. Tablet compression devices basically work on hydraulic pressure. All tablet machines require this pressure. Without being reduced, it passed through the static fluid. It is appropriate to increase pressure since any externally supplied pressure is transmitted in the same direction in all directions through static fluid.

To manufacture a tablet, the granulated powder material must be metered into a cavity made by a die and two punches. Punches must be pressed firmly together to fuse the material together. There are two varieties of tablet presses: single station and multi station respectively. In terms of feature requirements and production output, these machines function differently. They can also manufacture odd-shaped tablets. To lessen weight variations between batches, they usually have a high-pressure system installed. Due to several benefits, single-punch tablets are a great choice for small-scale research and manufacturing. Single-punch presses are also designed to be as silent as feasible. The weight and quantity of tablets in MUPS may vary more as a result of the segregation procedure.

Demixing is usually caused by differences in the sizes, forms, surfaces, and densities of the pellet and additional granular tabletting excipients. When pellets with a limited size distribution are compressed with additives of similar size and shape, mass and content uniformity can be achieved. It is essential to take into account the excipient-to-pellet ratio in addition to the importance of particle and pellet size, shape, and density in order to attain the optimal MUPS. Any tabletting blend must have a minimum of 50% w/w pellet concentration to avoid segregation. For instance, enteric-coated pantoprazole pellets were compressed into orodispersible tablets for usage by elderly and pediatric patients, and pantoprazole (Multiunit Particulate System) pills were made easier to administer [35].

10. Disintegration and Dissolution Behaviour of MUPS

MUPS are anticipated to break down in one of the following ways since they are frequently made with particles that have modified release characteristics:

1. Quick disintegration in the mouth, if the MUPS includes modified-release or taste-masked coated particles that are formulated as a compact in an Oro dispersible base (orally dissolving tablets), such as Prevacid SoluTab.

2. Quick disintegration in the gastrointestinal tract upon swallowing or oral administration (Losec MUPS).

3. Slowly and gradually eroding MUPS in the GIT to release particles coated with polymers, like Toprol XL, gradually. Individual coated multiparticulates that split out as a result of MUPS disintegration exhibit the desired dissolving behavior, which is frequently determined by the coating type or pellet matrix design [36-38].

CONCLUSION

Multi-particulate pellet compositions are known as MUPS (Multiple Unit Pellet Systems). These days, MUPS don't truly reflect an easy choice; rather, they represent a formulation of first choice. The process of compaction of coated pellets into multiunit particles (MUPS) is actually quite intricate, involving structural deformation or even rupture of the subunits. The increased cohesiveness between the pellets may prevent tablet disintegration and/or significantly alter the drug release profile of the subunits. Put differently, pellet compacts must possess a specific crushing strength in order to endure the mechanical shocks that occur throughout the manufacturing, packing, and dispensing processes. This technical project article examines the benefits, necessary preparations, and relevant literature for the manufacturing of MUPS tablets.

REFERENCES

1. Majeed SM, Al-Shaheen MK, Al-Zidan RN, *et al*. Multiple Unite Pellet Systems (MUPS) as drug delivery model. Journal of Drug Delivery and Therapeutics. 2020; 10(6):231-5.
2. Kállai-Szabó N, Farkas D, Lengyel M, *et al*. Microparticles and Multi-unit Systems for Advanced Drug Delivery. European Journal of Pharmaceutical Sciences. 2024: 106704.
3. Kayrak-Talay D, Dale S, Wassgren C, *et al*. Quality by design for wet granulation in pharmaceutical processing: assessing models for a priori design and scaling. Powder technology. 2013; 240:7-18.
4. Shankar PS, Ganesh PD, Bhanudas SR. Pelletization: a most significant technology in the pharmaceuticals. World J pharm Res. 2014; 3(6):1972-2003.
5. Bathool A, Vishakante GD, Khan MS, *et al*. Pelletization as a key tool for oral drug delivery: A review. Journal of Pharmacy Research. 2011; 4(10):3282-6.
6. Debotton N, Dahan A. Applications of polymers as pharmaceutical excipients in solid oral dosage forms. Medicinal research reviews. 2017; 37(1):52-97.
7. Maderuelo C, Lanao JM, Zarzuelo A. Enteric coating of oral solid dosage forms as a tool to improve drug bioavailability. European Journal of Pharmaceutical Sciences. 2019; 138:105019.
8. Yadav N, Verma A. Pharmaceutical pellets: a versatile carrier for oral controlled delivery of drugs. Indian J. Pharm. Educ. Res. 2016; 50(3):S146-60.
9. Dey NS, Majumdar S, Rao ME. Multiparticulate drug delivery systems for controlled release. Tropical journal of pharmaceutical research. 2008; 7(3):1067-75.
10. Adepu S, Ramakrishna S. Controlled drug delivery systems: current status and future directions. Molecules. 2021; 26(19):5905.
11. Komati S, Swain S, Rao ME, *et al*. Mucoadhesive multiparticulate drug delivery systems: An extensive review of patents. Advanced pharmaceutical bulletin. 2019; 9(4):521.
12. Shukla D, Chakraborty S, Singh S, *et al*. Lipid-based oral multiparticulate formulations–advantages, technological advances and industrial applications. Expert opinion on drug delivery. 2011; 8(2):207-24.

13. Pradhan P, Mahajani SM, Arora A. Production and utilization of fuel pellets from biomass: A review. Fuel Processing Technology. 2018; 181:215-32.
14. Bhat BB, Mehta CH, Suresh A, *et al*. Controlled Release Technologies for Chronotherapy: Current Status and Future Perspectives. Current Pharmaceutical Design. 2023; 29(14):1069-91.
15. Abdul S, Chandewar AV, Jaiswal SB. A flexible technology for modified-release drugs: multiple-unit pellet system (MUPS). Journal of controlled release. 2010; 147(1):2-16.
16. Wilson MW. Manufacturing platforms for patient-centric drug products. Developing Drug Products in an Aging Society: From Concept to Prescribing. 2016:447-83.
17. Sosnik A, Seremeta KP, Imperiale JC, *et al*. Novel formulation and drug delivery strategies for the treatment of pediatric poverty-related diseases. Expert Opinion on Drug Delivery. 2012; 9(3):303-23.
18. Pai KG, Dhirajlal BP. Multiple Unit Particle System (MUPS): Novel technology for preparation of Extended Release (ER) tablets. Research Journal of Pharmacy and Technology. 2013; 6(8):856-64.
19. Hamman H, Hamman J, Steenekamp J. Multiple-unit pellet systems (MUPS): production and applications as advanced drug delivery systems. Drug Delivery Letters. 2017; 7(3):201-10.
20. Shah SJ, Shah PB, Patel MS, *et al*. A review on extended-release drug delivery system and multiparticulate system. World J. Pharm. Res. 2015; 4(8):724-47.
21. Mansoori S, Dev A, Gupta S. An overview of pelletization techniques used in multiparticulate drug delivery system. World J Pharm Res. 2017; 6(8):720-41.
22. Rahman MA, Ahuja A, Baboota S, *et al*. Recent advances in pelletization technique for oral drug delivery: a review. Current drug delivery. 2009; 6(1):122-9.
23. Hapgood KP, Smith RM. Wet granulation and mixing. Pharmaceutical Blending and Mixing. 2015:153-82.
24. Srivastava S, Mishra G. Fluid bed technology: overview and parameters for process selection. International Journal of Pharmaceutical Sciences and Drug Research. 2010; 2(4):236-46.
25. Mehta KA, Rekhi GS, Parikh DM. Extrusion–spheronization for granulation. Handbook of Pharmaceutical Granulation Technology. New York: Marcel Dekker. 2005.
26. Reddy CP, Gopinath C. Evaluation of compression process variables for multiunit particulate system (MUPS) tablet by QbD approach. Journal of Drug Delivery and Therapeutics. 2018; 8(1):48-56.
27. Simmons DM, Gierer DS. A material sparing test to predict punch sticking during formulation development. Drug development and industrial pharmacy. 2012; 38(9):1054-60.
28. Pan X, Chen M, Han K, *et al*. Novel compaction techniques with pellet-containing granules. European journal of pharmaceutics and biopharmaceutics. 2010; 75(3):436-42.
29. Sangwai M, Sardar S, Vavia P. Nanoemulsified orlistat-embedded multi-unit pellet system (MUPS) with improved dissolution and pancreatic lipase inhibition. Pharmaceutical Development and Technology. 2014; 19(1):31-41.
30. Panda SK, Parida KR, Roy H, *et al*. A current technology for modified release drug delivery system: Multiple-Unit Pellet System (MUPS). J. Pharm. Sci. and Health Care. 2013; 3(6):51-63.
31. Stuiver M, Soma K, Koundouri P, *et al*. The governance of multi-use platforms at sea for energy production and aquaculture: challenges for policy makers in European Seas. Sustainability. 2016; 8(4):333.
32. Boyapati I, Awasthi R, Kulkarni G. Formulation, characterization, and in vitro release studies of modified release multiple unit particulate system (MUPS) of venlafaxine hydrochloride. Journal of research in pharmacy (online). 2022; 26(1):75-87.
33. Van der Merwe CJ, Steyn JD, Hamman JH, *et al*. Effect of functional excipients on the dissolution and membrane permeation of furosemide formulated into multiple-unit pellet system (MUPS) tablets. Pharmaceutical Development and Technology. 2022; 27(5):572-87.
34. Osei-Yeboah F, Lan Y, Sun CC. A top coating strategy with highly bonding polymers to enable direct tableting of multiple unit pellet system (MUPS). Powder Technology. 2017; 305:591-6.
35. Ozarde YS, Sarvi S, Polshettiwar SA, *et al*. Multiple-Unit-Pellet System (MUPS): A Novel Approach for Drug Delivery. Drug Invention Today. 2012; 4(12).
36. Cal K, Mikolaszek B, Hess T, *et al*. The use of Calcium Phosphate-based starter pellets for the preparation of Sprinkle IR MUPS formulation of Rosuvastatin Calcium. Pharmaceuticals. 2023; 16(2):242.
37. Patel S, Patel N, Misra M, *et al*. Controlled-release domperidone pellets compressed into fast disintegrating tablets forming a multiple-unit pellet system (MUPS). Journal of Drug Delivery Science and Technology. 2018; 45:220-9.
38. Shinde MB, Shinde GV, Patel RS, *et al*. Computational predictability of polyethylene glycol encapsulated modified release multiple unit pellets formulation of metoprolol succinate using different multivariate models. Materials Technology. 2022; 37(12):2090-105.

How to cite this article: Bafna HR, Shirsath NR, Jagtap VA. A New Path for Drug Delivery by Multiple Unit Pellet System (MUPS). Indian J Pharm Drug Studies. 2024; Online First.

Funding: None; *Conflicts of Interest: None Stated*