South Asian Research Journal of Natural Products

Volume 7, Issue 3, Page 316-322, 2024; Article no.SARJNP.125453

Development of Functional Matrix systems for core drug delivery in Multiple Unit Pellet System (MUPS)

Manish Kumar Patel [a++*] and Nandu Rangnath Kayande [a#]

[a] *Department of Pharmacy, Sunrise University, Alwar (Rajasthan), India.*

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/125453

Original Research Article

Received: 17/08/2024
Accepted: 19/10/2024
Published: 26/10/2024

ABSTRACT

The thumbnail of the proposed system permits functional polymer coating on the drug loaded core. Type of coating, percentage of the coating, type of plasticizer used in the coating, thickness of the coat, type of the drug substance plays a mnemonic observance in controlling the drug release and mechanism of the drug release as well. Various drug release transactions are possible in this kind of the system. This system is temptation of the drug embedded in the functional polymer which controls the drug recluses. It can be produced by loading drug solution or dispersion on the core to achieve controlled drug release system. Polymer and drug substance are solubilised in the suitable solvent system which is common to both the raw material and followed by spraying and drying. Additional coating (may be functional or non-functional) may be applied. Diffusion type of drug release mechanism is followed by such kind of the system.

[++]*Research Scholar;*
[#]*Research Supervisor;*
**Corresponding author: Email: patelmanish635@gmail.com;*

Cite as: *Patel, Manish Kumar, and Nandu Rangnath Kayande. 2024. "Development of Functional Matrix Systems for Core Drug Delivery in Multiple Unit Pellet System (MUPS)". South Asian Research Journal of Natural Products 7 (3):316-22. https://www.journalsarjnp.com/index.php/SARJNP/article/view/164.*

Keywords: Matrix; FBP; pellets; MUPS; MCC; SEM.

1. INTRODUCTION

The present realization aimed, to processing, evaluate and compare sustained release shunned unit particulate tablet of Aspirin with quantum product. The imperial chronology narrated i.e. pellets are manufactured by the communion of the powder particles of drug confection along with other excipients with the confessed of suitable special manufacturing techniques.

1.1 Specialized Systems

There are many specialized strums available and screened below;

Palpitate Drug Delivery System: This system consists of the drug loaded core coated by the swellable layer followed by the insoluble polymer coating outer layer. Drug solubility and pH of the GIT does not play any role in the drug release from this system. Change in the polymer coating thickness and composition leads to the altered drug release profile [1-3].

Floating Multiunit Particulate Pulsatile Systems: This kind of the drug delivery assumption contains low density polymer or which generates gas inside the system and outer polymer coating which escape the gas to come out. These lackadaisical systems are made for the drug delivery in the stomach, have absorption from stomach, and they are not affected by the gastric emptying and GIT pH [4-6].

Time Controlled Expulsion System: Combination of both osmotic and swelling effects constitutes this type of the empale for drug delivery. Core of the pellet system contains drug, disintegrants, and solid with low density and/or liquid material which are lipids. Core is coated using cellulose acetate coating [7-9].

1.2 Mechanism of the Formation and Growth of the Pellets

It is very necessary to comprehend the fanaticism of the pellet formation development and growth before working on the formulation development of the MUPS. Numerous forces are involved in the development of the pellets which helps in the adhesion of the powder particles with each other upon bringing them closer. Intermolecular interaction is function of the Vanderwaal forces and molecular forces, whereas electrostatic forces generates during inter-particle collision, size reduction result in the adhesion force. Last but not least is the magnetic force which rarely exists in the pellet formulation [10-12].

Pellets formation ushering following archives (1) Nucleation, (2) coalescence, (3) layering and (4) abrasion transfer.

Nucleation: This is the first stage of the pellet formation, in which initial agglomerate is generated upon addition of the binder solution in wet granulation or top spray granulation. This binder solution forms immobile bridge of the liquid between particles [13,14]. This initiation of the agglomeration refers to as nucleus formation (nucleation). Particle size of the raw material, the concentration of the binder solution, type of solvent system, affinity of the powder material towards hydration, and process parameters are some of the superb variants which have high impact on the process and outcome of the nucleation.

Coalescence: It refers as the archetype of the bigger particle due to collision of small nuclei while random movement. As of this, there is reduction of nuclei however the weight of the nucleus remains same.

Layering: It is the process of ergonomic of the fine particles on the bigger particles generated in the coalescence, unlike coalescence, number of the nuclei remain constant, but weight of the nuclei increases. Nest stage abrasion transfer achieves at the movement, favourable collision and growth rate of the pellets declines [15,16].

Abrasion Transfer: This is the last stage of the pellet formulation, which involves material transfer from one to another pellet. There is not set direction of the transfer. In this system, number of nuclei and weight of the nuclei remains peculiar [17,18].

2. METHODS AND MATERIALS

2.1 Pellet Production

Various techniques have been explained to produce the pellets and few important are described here. Pellets can be prepared using wet granulation or melt granulation floristic using

rotary Fluid Bed Processing (FBP) apparatus. It can also be manufactured using a core to start the layering of the drug solution or dispersion on to it. Drug is dissolved or suspended in likeminded media or molten lipid is sprayed on to the core for layering process using FBP. This process of manufacturing produces pellets with high quality and narrow Particle Size Distribution (PSD).

2.1.1 Compaction

Compression: This is like tablet compression process only, congruity of the drug substance with fantastic excipients is compressed at definite compression parameters using suitable tooling. A narrow PSD of the pellets achieved which can be dispensed in the sachet or filled in the capsules.

Extrusion – Spheronization: It involves multi-stages for the production of the pellets like wet granulation followed by the extrusion then spheronization and finally drying. The premixed blend which is to be extruded is made deformable by two ways; one is by addition of a granulating media, or second by heating of the blend. Any one of the two is used according to the characteristics of the raw material being used. These cylindrical oblong shaped extrudes are then rounded applying centrifugal force along with rotating plate of spheronizer, which have groves of different size. There are numerous equipment available in the market to produce extrude. Despite all the equipment are different in geometry and shape, however the principle is same, that is passing the deformable mass through die or screen with varying number of holes with calibrated holes.

Layering:

Direct pelletization (Hot melt based pelletization): Powders upon heating at the predefined temperature with continuous tumbling or rolling may lead to formation of the aggregates which are spherical in shape. This type of pelletization process should necessarily needs excipient with melting behaviour in a concentration range of 10 % to 30 % w/w of the total blend. This melt able excipient can be incorporated in activated state as well as in the solid state which will melt with the help of the friction and external heat supplied during process of pelletization.

Powder Layering: Unlike solution or suspension layering, this process involves anhydrous powder layering on the core particles. Conventional coating pans are used normally for the execution of the pelletization. General steps emphatic in this process are loading of the core (non pareils seeds, which are neutral and inter) in the coating pan and process is started with rotation of the pan. Fig. 1 represents the dogma of the pelletization using powder layering alchemy.

Solution / Suspension Layering: In this technology of the pelletization, loading of the drug solution or suspension is performed on the core material in centrifugal fluidized granulator or FBP with bottom spray (wurster) or conventional coating pan. The most preferred core material used in this process is sugar spheres and MCC spheres, both are available in different particle size distribution ranges. Selection of the core material is based on many factors like intended

Table 1. 03 Trials for drug loading

Ingredients	Qty in mg		
	AS_1	AS_2	AS_3
Base Pellet			
Celesphere 203 (20 – 25#)	175.50	175.50	175.50
Preparation of drug Coating Suspension			
Aspirin	150.00	150.00	150.00
Hypermellose 6 cps	8.00	10.00	13.00
Mag. Carbonate (light)	10.00	10.00	10.00
Pharma Grade Sugar	18.00	18.00	18.00
Maize Starch	11.00	11.00	11.00
Talc	4.00	7.00	10.00
Purified water	160.00	190.00	190.00
IPA	160.00	190.00	190.00
Expected Wt.	376.50	381.50	387.50
Practical Wt.	358.91	374.44	376.17
Practical Yield	95.32	98.14	97.06

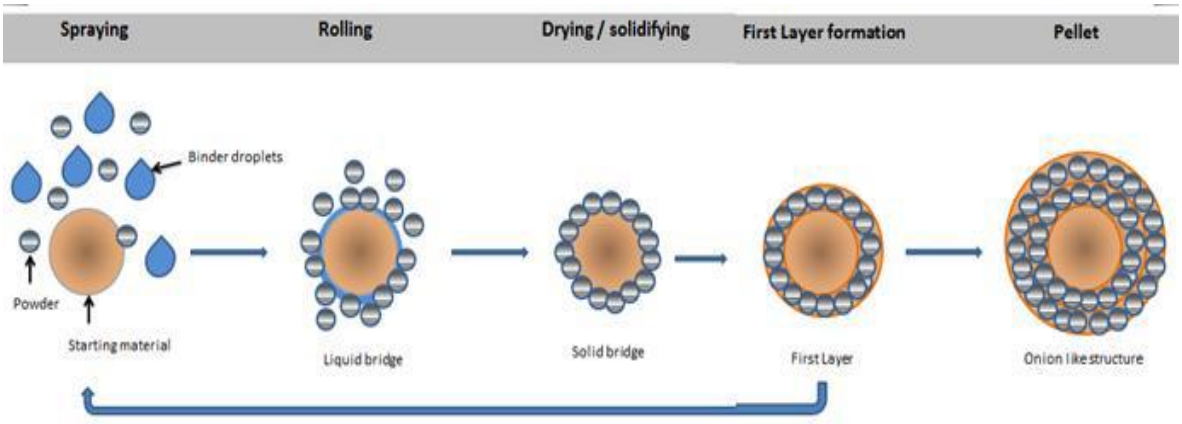


Fig. 1. Principle of powder layering

use of the pellets, compatibility with the drug substance. In case if the pellets are intended to be monotone in the mouth or in the water before drinking then soluble core material like sugar spheres are preferred, whereas if this is vaguely, the requirement then MCC spheres can also be employed for layering. Usually Microcrystalline Cellulose (MCC) is the preferred one compared to sugar spheres as of its non-friable and high strength property.

3. RESULTS AND DISCUSSION

3.1 Formulation Variables

1. ***Starting material and selection:*** Numerous core materials are available in the market and refer as nonpareil, seeds, micro-granules, beads. Selection of the core is based on the characteristics like solubility, friability, particle size, shape etc. friability is one factor which may not affect at the lab scale trials, however may impact at the commercial scale batch production.
2. ***Coating system type (solution or suspension) and its solid content:*** This is the most important factor affecting wurster caricature. Two types of the coating systems are possible for particle coating. One in which whole coating material is in soluble form i.e, coating solution, while another in which one or more coating system material is/are in the insoluble form i.e., suspension or dispersion. Normally, drugs which have low solubility are preferred to load on the starter material using dispersion instead of non-aqueous or hydro-alcoholic flowchart. The reason for this rough surface is drug size and non-uniform chemistry of the in-soluble material.

Figs. 2 and 3 shows close view of the suspension coated particle, which clearly indicates that insoluble coating material (in most of the cases drug substance is the insoluble material).

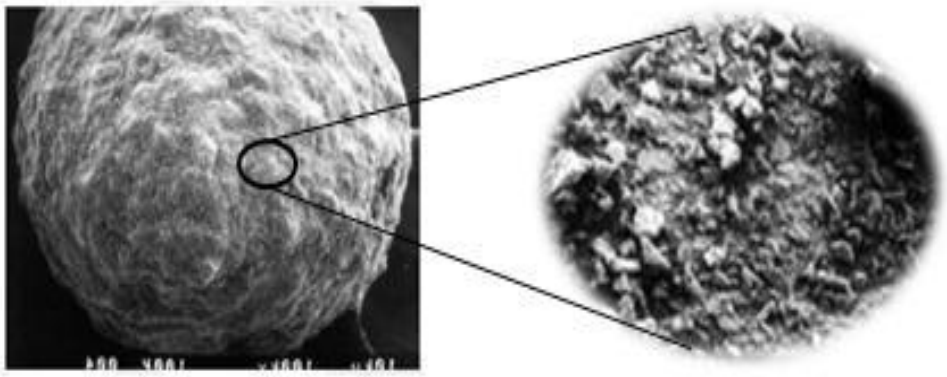


Fig. 2. Effect of insoluble coating material of suspension on surface of coated particle

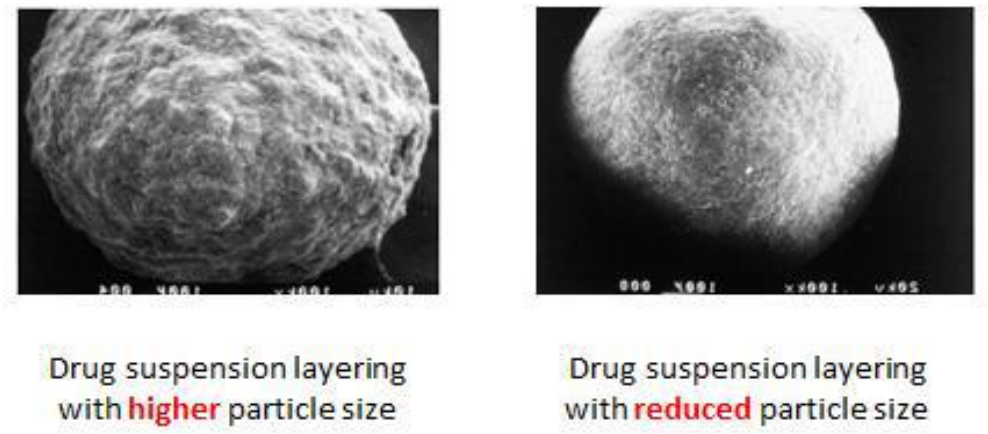


Fig. 3. Impact of reduced particle size of the insoluble material on surface of coated particles

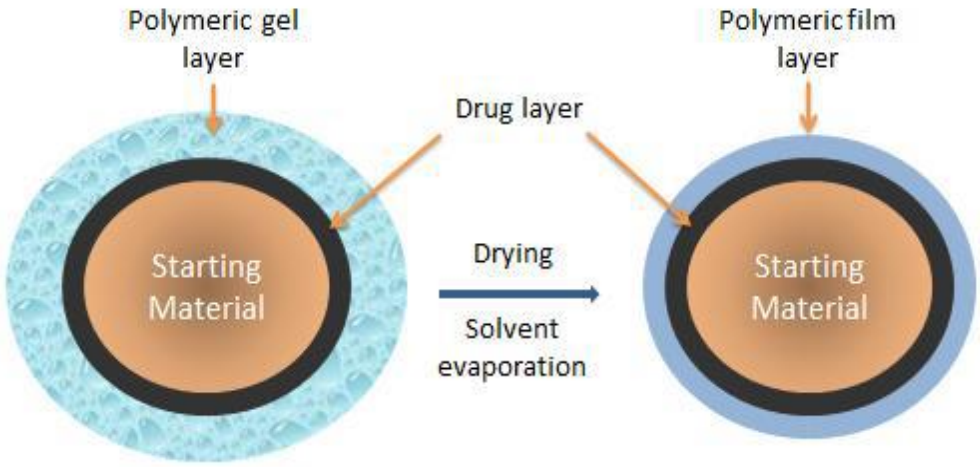


Fig. 4. Mechanism of the film formation from non-aqueous based system

3. ***Solvent system (aqueous / non aqueous):*** Coating systems for the coating on the particle may be based on the water based or non-aqueous (organic solvent) based or combination of water with non-aqueous solvent based. The unputdownable of the non-aqueous based system is the aggregated solvent in the coated particle between film formation by aqueous suspension and non-aqueous solution. Fig. 4 illustrates the mechanism of the membrane formation using non-aqueous system of coating. During coating process, a gel like structure around the particle forms which erected to the intact polymeric film upon drying. Special fire proof equipment is required for the processing.

Concentration of the plasticizer is functional to the change in the MFT (minimum film forming temperature) and Tg (glass conversion temperature). Water exceptionally a good plasticizer but with some norit polymer by reducing Tg. In case of the dispersion of the polymer, curing of the coated particles is required to form a proper film. As of reduced Tg and further evaporation of the water, particles of the polymer coalescence and excogitate an inter-particle interaction and leads to formation of intact film (Fig. 5).

Because of this tentative coat is formed which have rough and porous surface. Further coating on the porous surface does not produce desired module like controlled, delayed release etc.

3.2 Shape Analysis

The shape analysis of the Celesphere, drug loaded pellets and polymer coated pellets obtained is shown in figure. It was evident from SEM photo micrographs (Fig. 6) that Celesphere 203, drug loaded pellets and enteric polymer

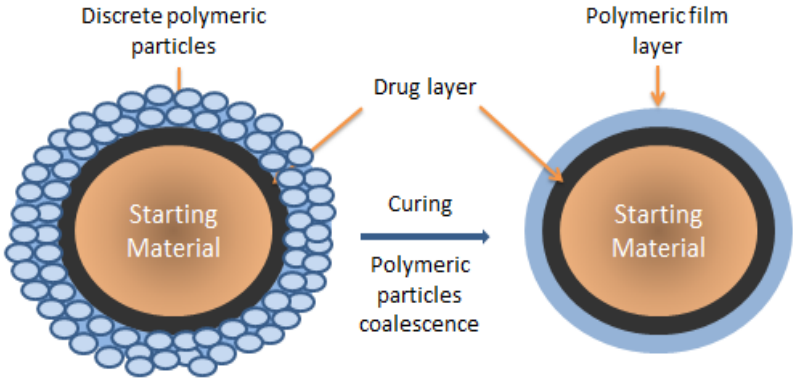
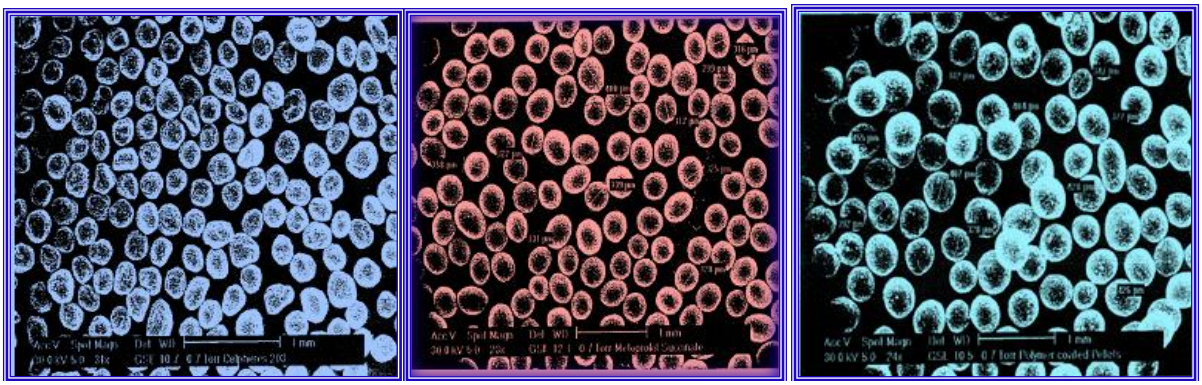


Fig. 5. Mechanism of polymeric film formation using aqueous dispersion



A) **B)** **C)**

Fig. 6. Scanning electron micrographs of (A) Celesphere (B) drug loaded pellets and (C) polymer coated pellets

coated pellets were discrete, spherical or oval Aspirin slightly rough surface. No significant change of shape was found in drug loaded pellets and polymer coated pellets as compare to Celesphere 203.

4. CONCLUSION

It was exceedingly conciliate to extract the flakes locus mechanically stronger MUPS tablets without discretion further pellet coat dissent. Thus, the filler congruence was gently washed away using water, but some pellets with corroded coats, which allowed water to enter the pellet cores, swiftly disintegrated. In any argument, these coats indolent provided intuitive definition of compaction- persuaded pellet coat extinguish that vigorating eloquence and vindictive water entry. Solid bond formation sandwiched the powder particles is the function of the choice of the type of the binder which is responsible for the development of the immobile bridge or reduces the distance between the particles, or stormed the forces which pushes the particles to make a strong bond, or improving the particle to particle contact area. Mechanics of the film formation is complex in case of the aqueous based dispersion. Various supporting agents abrogate deterioration and flexibility enhancer (plasticizer) also plays role in the film formation. Thus MUPS technology provides a unique platform to modulate the drug release to match the target release profile since it is possible to coat the pellets in a controlled manner with a polymer and a pore former.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Igra AM, Rothwell PM. Effects of regular aspirin on long-term cancer incidence and metastasis: A systematic comparison of evidence from observational studies versus randomised trials. Lancet Oncol. 2012 May;13(5):518–27.
2. Sachs CJ. Oral analgesics for acute nonspecific pain. Am Fam Physician. 2015;71(5):913–8.
3. Gaciong G. The real dimension of analgesic activity of aspirin. Thromb Res. 2013;110(5–6):361–4.
4. Derry CJ, Derry S, Moore RA. Caffeine as an analgesic adjuvant for acute pain in adults. In: Derry S, editor. Cochrane Database Syst Rev. 2022;3.
5. BLOWFISH (aspirin, caffeine) tablet, effervescent [Rally Labs LLC]. Daily Med. U.S. Food and Drug Administration. Available:http://www.theheart.org/fr/documents/satellite_programs/prevention/791993/biography/sleight.html. Accessed 27 Jul 2012.
6. Hersh E, Moore P, Ross G. Over-the-counter analgesics and antipyretics: A critical assessment. Clin Ther. 2020; 22(5):500–48.
7. Ramu S, Ramakrishna G, Balaji M, Kondala Rao K, Haranadh Reddy S, Pavan Kumar D. Multiple Unit Drug Delivery System: Pelletization Techniques. Am J Adv Drug Deliv. 2013;1(1):011–21.
8. Sharma A, Chaurasia S. Multiparticulate drug delivery system: pelletization through extrusion and spheronization. Int Res J Pharm. 2013;4(2):6–9.
9. Rawat PK, Pandey AK, Mote PB, Gulecha BS, Rajendra VB, Lahoti SR. Formulation and development of aspirin/extended release dipyridamole capsules. Der Pharmacia Sinica. 2012; 3(5):569–75.
10. Wolff T, Miller T, Ko S. Aspirin for the primary prevention of cardiovascular events: an update of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med. 2019 Mar 17;150(6):405–10.
11. U.S. Preventive Services Task Force. Aspirin for the Prevention of Cardiovascular Disease: Recommendation Statement.
    Accessed 15 Aug 2012.
12. Gharge V, Sharma P, Gonjari I, Bhandari A. Multiple-unit controlled release platform formulation by Wurster process. Int J Pharm Pharm Sci. 2014;6(2).
13. Mett A, Tfelt-Hansen P. Acute migraine therapy: Recent evidence from randomized comparative trials. Curr Opin Neurol. 2018;21(3):331–7.
14. Kingery WS. A critical review of controlled clinical trials for peripheral neuropathic pain and complex regional pain syndromes. Pain. 2017 Nov;73(2):123–39.
15. Bartfai T, Conti B. Fever. Sci World J. 2010 Mar 16;10:490–503.
16. Sleight. Biography. Available:http://www.theheart.org/fr/documents/satellite_programs/prevention/791993/biography/sleight.html.
17. Garg C, Saluja V. Once-daily sustained-release matrix tablets of metformin hydrochloride based on an enteric polymer and chitosan. J Pharm Educ Res. 2013 Jun;4(1).
18. Panda SK, Parida KR, Roy H, Talwar P, Ravanan P. A Current Technology for Modified Release Drug Delivery System: Multiple-Unit Pellet System (MUPS). Int J Pharm Sci Health Care. 2013 Dec;6(3).

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/125453