CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.7125070

Available online at: http://www.iajps.com *Review Article*

COMPREHENSIVE REVIEW ON COATED PELLETS

Aditya Vinayak Dubewar, Prof.V.J.Masirkar
Department – Industrial Pharmacy
Sudhakarrao Naik Institute of Pharmacy,Pusad

Article Received: August 2022 **Accepted:** August 2022 **Published: September** 2022

Abstract:
Multiple unit-controlled release dosage forms offer various advantages over their single unit counterparts. Most of these advantages are associated with the uniform distribution of multiparticulates throughout the gastrointestinal tract. Though coated pellets can be filled into hard gelatin capsules, tablet formulation is the preferred one because of various advantages associated with it. However, compression of coated pellets is a challenging task necessitating the optimization of various formulation and process variables. The key formulation variables include composition, porosity, size, shape and density of the pellets; type and amount of polymer coating; nature, size and amount of tableting excipients. The pellet core should be strong with some degree of plasticity. It should be highly porous, small, with an irregular shape. The critical density to achieve prolonged release was reported to lie between 2.4 and 2.8 g/cm^3. Acrylic polymer films are more flexible and more suitable for the coating of pellets to be compressed into tablets. Thicker coatings offer better resistance to frictional forces. Solvent based coatings are more flexible and have a higher degree of mechanical
stability than the aqueous based ones. The tableting excipients should have cushioning property. They should not be significantly different in size and density from those of the pellet cores in order to avoid segregation. Addition of 30%-60% of tableting excipients is necessary to avoid any damage to the polymer coat and to retain its functional property.

Corresponding author:
Aditya Vinayak Dubewar ,
Department – Industrial Pharmacy
Sudhakarrao Naik Institute of Pharmacy,Pusad

QR code

Please cite this article in Aditya Vinayak Dubewar et al, Comprehensive Review On Coated Pellets., Indo Am. J. P. Sci, 2022; 09(9).

INTRODUCTION:

Multiparticulate oral drug delivery systems have acquired a center stage in the arena of pharmaceutical research and development; thus provide greater opportunities in extending the first step of future pharmaceutical development [1].

Multiparticulate drug delivery systems include pellets, granules, micro particles (like microspheres, microcapsules, and nano particles), mini tablets, mini depots, multiparticulate pulsatile drug delivery systems [4].

Pelletized dosage forms date back to the 1950s, when the first product was introduced to the market. In 1949, research scientists of SmithKline & French developed tiny drug pellets that are filled into capsules. Since then, these dosage forms have gained considerable popularity because of their distinct advantages such as enhancement of drug dissolution; ease of coating with desirable release characteristics like sustained, controlled, delayed, site-specific or pulsatile delivery of drug from coated pellets; uniform packing; ease of capsule filling because of better flow properties due to its spherical shape; even distribution in the GI tract and less GI irritation [2,3].

In the present study, fluid bed coating (FBC) process was employed for the preparation of diltiazem HCl pellets. Fluidized bed processor is an equipment that can perform multiple functions like coating, drying, granulation, and pelletizing. It is applied for specific manipulation of the particle surface characteristics.[5-7]

Furthermore, the importance of inert pellet cores is shown by the fact that starter pellet cores made of various excipients are likewise available commercially to the pharmaceutical industry. Thanks to a sophisticated combination of manufacturing and modern analytical techniques (like image analysis), excipient manufacturers now offer even personalized, tailor-made, reproducible particle size distributions (PSD) to formulate and produce drug- loaded pharmaceutical pellets.

Diltiazem HCl is a calcium channel blocker which is widely used in the treatment of variant angina, hypertension, and supraventricular tachyarrhythmias.It is freely soluble in distilled water, chloroform, and methanol. Diltiazem HCl is rapidly absorbed (90%) after oral administration, but availability is only 30%-40% in systemic circulation and bioavailability varies between individuals. It has an elimination half-life of 3-5 h and is slightly prolonged after multiple dosing.[8] Based on the above physical, chemical, biopharmaceutical properties and clinical relevance, diltiazem HCl was selected as the drug candidate for developing controlled release pellet formulations.

The controlled release pellets of diltiazem HCl with ethyl cellulose and hydroxylpropyl methylcellulose phthalate (HPMCP) by employing fluid bed coating technique. Ethyl cellulose 7 cps, a high-viscosity grade polymer, was used for regulating the drug release from the pellet formulations. HPMCP, an enteric coating polymer, was used in the present study to regulate the drug releaseat varied GI pH conditions. An attempt was made to optimize the composition of these two polymers to achievethe controlled release of drugs from the pellets. Pellets offer a great flexibility in pharmaceutical solid dosage form design and development. They are better than other dosageforms in terms of ease of coating, sustained, controlled, or site-specific delivery of the drug from coated pellets, uniform packing, even distribution in the GI tract, and less GI irritation.[9] HPMC E5 was used as a film former in the present investigation. Croscarmellose sodium was used asthe disintegrant to create channels in the coating for drug release. Povidone was used as the binder to achieve uniformdrug layering in the present study.[10,11]

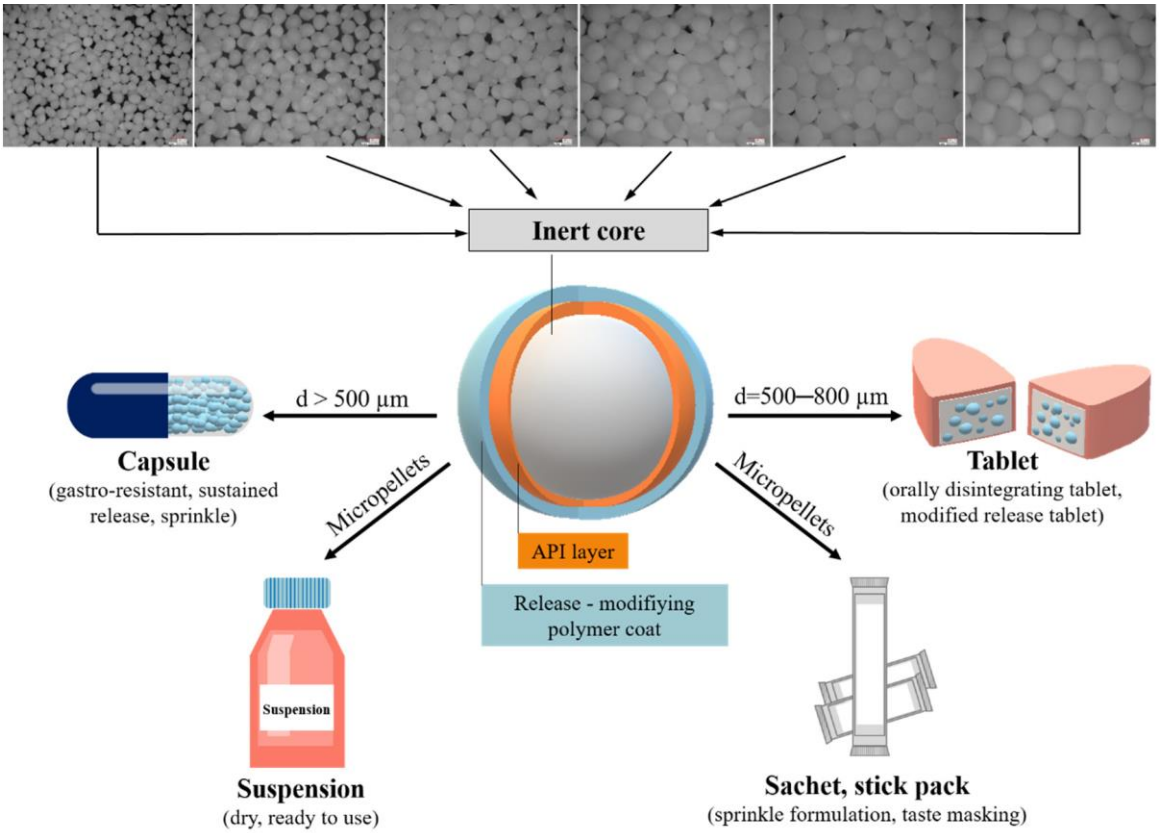
ADVANTAGES:

- Pellets offer more sophisticated drug-delivery systems as they provide greater advantages over other single unit drug- delivery systems.
- **Process Advantages:** As subunits various kinds of particles with defined less-porous surface, spherical shape, low surface area to volume ratio are suitable for flexible and uniform drug - polymer coating.
- **Formulation Advantages:** Pellets offer greater flexibility in the design and development of active ingredient into oral dosage forms like tablets, capsules and suspensions with significant therapeutic advantages over single units
- **Therapeutic Advantages:** When administered orally, pellets pass the pylorus even in theclosed state and disperse freely throughout the gastro-intestinal tract and maximize the drug absorption. [11]

DISADVANTAGE:

- In accordance with single units, the volume per dose is high because of its high bulk density.
- **Mechanism of Pellet Formation and Growth:** The mechanism of pellet formation and growth is necessary to review by a

formulator for the development of formulation in a more skillful perspective and set the trends for future developments in the area of pellets.



MATERIALS AND METHODS:

Materials

Preparation of povidone solution

Isopropyl alcohol, PVP K-30 (polyvinyl pyrrolidone), and Tween 80 were taken into stainless steel propeller-type stirrer mixer and mixed for 10 min. The solution was filteredthrough nylon cloth into SS tank.

Drug Loading

Sugar pellets were charged into fluidization basket. The drug and croscarmellose powder blends were also charged into the fluidized basket and povidone solution was atomized onto the materials while the air was allowed to circulate into the basket at an air flow rate of 2000-4500 cfm to keep the materials under fluidized state. The process of fluidization was continued for 10 min. The drug-loaded pellets from the FBC were spread into the trays uniformlyand dried at 60°C temperature for about 3 h. After drying, the pellets were sifted by using vibro sifter to remove the fines and to separate the uniform-sized pellets.

Preparation of HPMC E5 Solution

HPMC E5 and water were taken into the stainless-steel tank and mixed for 10 min with propeller-type stirrer. Thesolution was filtered through nylon cloth into SS tank.

Sub-Coating

The drug-loaded pellets were charged into fluidization basket. HPMC E5 polymer solution was atomized onto the materials while the air was allowed to circulate into the basket at an air flow rate of 2000-4500 cfm tokeep the materials under fluidized state. The process of fluidization was continued for 10 min. Coating of thepellets was done under specified conditions like inlet temperature of 40°C and outlet temperature of 35°C, withan air pressure 2.5 kg/cm^2. Damper was adjusted such thatpellets should not hit the upper screen. Flow rate rpm wasadjusted to 18-22 rpm. The drug-loaded pellets from the FBC were spread onto the trays uniformly and dried at 60°C temperature for about 3 h. After drying, the pellets were sifted by using vibro sifter to remove fines and the uniform-sized pellets were collected.

Preparation of HPMCP Solution:

HPMCP, cetyl alcohol, acetone, and isopropyl alcohol weretaken into the tank and mixed for 10 min at 1300 rpm byusing propeller-type stirrer and filtered through nylon clothinto SS tank.

Polymer Loading

The HPMC-coated pellets were charged into fluidization basket. Polymer solution was atomized onto the materialswhile the air was allowed to circulate into the basket at anair flow rate of 2000-4500 cfm to keep the materials underfluidized state. The process of fluidization was continued for 10 min. Pellets were coated under specified conditions likeinlet temperature of 40°C and outlet temperature of 35°C,with an air pressure of 2.5 kg/cm^2. Damper was adjusted such that pellets should not hit the upper screen. Flow rate rpm was adjusted to 24-28 rpm. The drug-loaded pellets from the FBC were spread onto the trays uniformly and dried at 60°C temperature for about 3 h. After drying, thepellets were sifted by using vibro sifter to remove fines and the uniform-sized pellets were collected.

Preparation of EC Solution

Ethyl cellulose, diethyl phthalate, talc, Isopropyl Alcohol (IPA) and acetone were taken into the SS tank. They weremixed in a homogenizer for 15 min and filtered through nylon cloth into SS tank.

Polymer Loading

The HPMCP-coated pellets were charged into fluidization basket. EC polymer solution was atomized onto the materialswhile the air was allowed to circulate into the basket to keep the materials under fluidized state. The process of fluidization was continued for 10 min. The fluid bed coatingprocess variables were given in the Table 1.

Finally the coated pellets were dried at ambient conditionsfor 2 h and sifted through vibro sifter to collect uniform-sized pellets.

Table 1: Fluid bed coating process variables

Process controls	Specifications
Batch size	500 G
Inlet air temperature	40°C
Outlet air temperature	35°C
Product temperature	35°C
Chamber humidity	60% RH
Air flow	2000-4500 cfm
Nozzle aperture	1.2 mm
No. of spray guns	1
Spray direction	Bottom spray
Spray pressure	2.5 kg/cm^2
Spray time	10 min
Secondary drying	60°C

The composition of various diltiazem hydrochloride-controlled release pellets is given in Table 2.

Table 2: Composition of various diltiazem HCl pellets prepared by fluid bed coating

Ingredients for 10 g	FDL 1	FDL2	FD L3	FD L4	FD L5	FD L6	FD L7	FD L8	FD L9	FDL 10	FDL 11
Diltiazem HCl	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728	5.728
Povidone	0.376	0.376	0.376	0.376	0.376	0.376	0.276	0.276	0.276	0.276	0.276
Ethyl cellulose	0.010	0.012	0.014	0.016	0.018	0.020	0.020	0.020	0.020	0.020	0.020
HPMC E_5	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240	0.240
HPMC phthalate	0.020	0.020	0.020	0.020	0.020	0.020	0.010	0.012	0.014	0.016	0.018
Cetyl alcohol	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015	0.015
Diethyl phthalate	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016
Acetone	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308	2.308
IPA	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543	5.543
Talc	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037	0.037
Croscarmellose sodium	0.055	0.055	0.055	0.055	0.055	0.055	0.056	0.056	0.056	0.056	0.056
Sugar spheres	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518	3.518
Purified water	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847	1.847
Tween-80	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027	0.027

Evaluation of Physical ParametersPercentage Yield

All the batches of controlled-release diltiazem pellets prepared by fluid bed coating were evaluated for percentage yield of the pellets. The actual percentage yields of pelletswere calculated by using the following formula. The % yields of various batches of pellets are given in Table 3.

$$\text{Percentage yield of pellets} = \frac{\text{Practical yield of pellets}}{\text{Theoretical yield of pellets}} \times 100$$

Particle Size Determination

The average particle size of the pellet formulations of diltiazem hydrochloride was analyzed by simple sieve analysis method. The particle size of various batches of pellets is given in Table 3.

Friability

The friability of the core pellets of diltiazem hydrochloride [12] was determined as % weight loss after 100 revolutions of10 g of pellets in a friabilator. The friability values of variouspellets formulations are given in Table 3.

Drug Content

One gram of diltiazem hydrochloride pellets from each batch was taken at random and crushed to a fine powder.The powdered material was transferred into a 100 mlvolumetric flask and 70 ml of distilled water was added to it.It was shaken occasionally for about 30 min and the volume was made up to 100 ml by adding distilled water. About 10 ml of the solution from the volumetric flask was taken and centrifuged. The solution from the centrifuge tube was collected and again filtered by using Millipore filter. Thenthe filtrate was subsequently diluted and the absorbance was measured at 238 nm for diltiazem hydrochloride. This test

***In Vitro* Dissolution Studies**

One hundred and twenty milligram equivalent weight of diltiazem hydrochloride containing pellets was

collected and weighed at random from each batch of pellet formulation and dissolution studies were performed in a calibrated 8-station dissolution test apparatus (Disso 2000) equipped with paddles (USP apparatus II method),[13] employing 900 ml of distilled water as the medium. The paddles were operated at 100 rpm and the temperature was maintained at 37 □ 1°C throughout the experiment. Five milliliter of the samples was withdrawn at regular intervals up to 24 h and replaced with an equal volume of fresh dissolution medium to maintain a constant volume of the dissolution medium throughout the experiment. Samples withdrawn at various time intervals were suitably diluted with the same dissolution medium and the amount of drug released was estimated by ELICO double-beam spectrophotometer at 238 nm. The dissolution studies on each formulation were conducted three times. Necessary corrections were made for the loss of drug due to each sampling.

The dissolution profiles of all the pellet formulations of diltiazem hydrochloride were compared with the marketed extended-release pellet formulation of diltiazem hydrochloride by using a model-independent approach of similarity factor *f*2, with all time points included in the *in vitro* dissolution studies.[14,15] The equation for calculating similarity factor is:

$$f2 = 50 \log\left\{\left[1 + \frac{1}{n}\sum_{J=1}^{N}(Rt - Tt)^2\right]^{-0.5}(100)\right\}$$

where "*n*" is the number of dissolution time and R_t and T_t are the reference (theoretical) and test dissolution values a time "*t*," respectively.
Dissolution profile was considered satisfactory if *f*1 value was below 15 (nearing zero) and *f*2 value was more than 50. Two dissolution profiles were considered similar when the *f*2 value was 50–100.

Characterization of Pellets
The selected formulations were subjected to Differential Scanning Calorimetry (DSC) studies to identify any possible interaction between drug and polymers during the coating process. The surface characteristics of the pellets were determined by Scanning Electron Microscopy (SEM) analysis.

Accelerated Stability Studies
The formulations which showed good *in vitro* performance (FDL10 and FDL11) were subjected to stability studies under accelerated temperature and relative humidity (RH) conditions (40°C and 75% RH) for 3 months. Test samples withdrawn after 3 months were subjected to various tests, including visual inspection for any appreciable change on the pellet surface, assay, and dissolution.

Method of Preparation:
There are various techniques to prepare pellets, which are grouped by specific criteria. From fluid-bed granulation to spray drying, the success of the pellets will depend on the complicated relationship between the formulation, the equipment and the development and manufacturing process. Currently, the most common and highly discussed technique for creating pellets is extrusion-spheronisation. This technique is a multi-stage process consisting of seven steps that produce pellets from wet granules, converting a pharmaceutical formulation into a spherical product:[7]

- **Dry mixing:** the first stage is to achieve a homogenous powder dispersion.
- **Wet massing:** the second stage creates a wet granulation to produce a plastic mass for extrusion.
- **Extrusion:** the third phase produces rod-shaped particles with a uniform diameter and shape from the wet mass (extrudate).
- **Spheronisation:** the fourth stage involves adding the extrudate to a rotating friction plate; it is then broken into smaller cylinders with a length equal to their diameter, which becomes rounded by the frictional force.
- **Drying:** enough time must be allowed during the fifth stage for the desired moisture level to be achieved.
- **Screening:** the sixth stage, which is optional, is screening the pellets to achieve a targeted mean size.
- **Coating:** the final stage, which is optional, is adding a supplementary coating for functional or cosmetic reasons.[7]

Using the latest technology, the whole process can be performed in a single closed system. Extrusion-spheronisation has been found to be effective for otherwise poorly soluble active pharmaceutical ingredients (APIs). It is renowned for being a streamlined and efficient pathway to development that offers high throughput and low wastage.

Along with producing pellets of uniform size, the pellets created have a low friability, meaning they are unlikely to chip, crumble or break under compression

both during and after the production process.[9]

Recent Advances in Pelletization Technique:[13]

1.Hot-melt Extrusion and Spheronization: It is a solvent free technique finds a great advantage for drugs that show sign of instability due to residual water during processing and storage. Consequently no additional film coating is needed to attain controlled release and hence release is favored by; (a) diffusion mechanism for formulations with water-insoluble polymers such as ethylcellulose or carnauba waxes;and (b) both by diffusion and erosion with water-soluble polymers such as hydroxypropyl cellulose. This technique is employed for the production of pellets, specific rate release dosage forms like tablets, capsules, transdermal implants etc. A hot melt extrusion line consists of a feed hopper, extruder with 3 distinct sections in the heating barrel and spheronizer. Extrusion is carried out in a rotating screw extruder preferably single screw extruder due to relatively low cost, credibility and ruggedness.

2.Freeze Pelletization: It is an advanced and a most simple technique for theproduction of spherical pellets by introducing droplets of immiscible molten solid carrier/matrix containing additives like disintegrants, diluents, surfactants and release modifiers with or without drug that is introduced into an inert liquid column. These droplets move either to the top or bottom of the column depending on their density with respect to liquid in the column [30].

- **Cryopelletization:** It is a technique by which freeze dried or lyophilized pellets are formed by solidifying the droplets of aqueous or organic solutions, suspensions or emulsions using liquid nitrogen. The equipment has a perforated plate below which a liquid nitrogen reservoir with a varying speed conveyor belt is present with transport baffle dipped in it. Pellets are frozen by the residence time provided by the conveyor belt due to its varying speed. The frozen pellets are transported into a -60^{O}C storage container and dried in a freeze dryer [31, 32]. The factors that influence the size and shape of droplets are equipment design, process variables, solid content and viscosity of the droplets. The distance between the perforated plate and the reservoir is arranged in such a way that it allows the drops to become spherical before it comes in contact with liquid nitrogen.

CONCLUSIONS:

The multi-unit dosage form pellets that were formulated by fluid bed coating process showed controlled release of drug for a prolonged period of time. Based on the results, the pellets prepared by FBC process were found to be ideal for the preparation of diltiazem hydrochloride controlled-release formulations. Today various starter pellets are commercially available. The cores have several particle size fractions in a narrow size range prepared for the pharmaceutical industryas ready-to-use excipients for drug layering techniques. The manuscript presents the most often used inert cores in the pharmaceutical industry, along with the process of drug layering. The main properties of inert pellets, which may be decisive in the development of a multiparticulate formulation, where the active ingredient surrounds the surface of an inertpellet core, have been described in detail. Numerous commercially available formulations have also been presented. This reflects the use of the starter pellet as an excipient in a wide variety of active ingredients and dosage forms. It is important to note that no so-called universal standard exists among the various inert pellet cores that could be applied to all active ingredients or film coatings. For each drug technology development, the typeand size fraction of the starter pellets must be selected according to the particular active ingredient, dosage strength, and dosage form. For the right decision, it is essential to haveas much knowledge as possible about inert pellet cores.

REFERENCES:

1. Ghebre-Selassie, I. Pellets: A General Overview. In *Pharmaceutical Pelletization Technology*; Ghebre-Selassie, I., Ed.; Drugs and the Pharmaceutical Sciences; Marcel Dekker Inc.: New York, NY, USA, 1989; Volume 37, pp. 1–13.
2. Kállai, N.; Antal, I. Importance and pharmaceutical technological considerations of neutral pellets. *Acta Pharm. Hung.* **2006**, *76*, 208–212. [PubMed]
3. Bruschi, M.L. Modification of Drug Release. In *Strategies to Modify the Drug Release from Pharmaceutical System*; Bruschi, M.L., Ed.; Woodhead Publishing: Sawston, UK, 2015; pp. 15–28.
4. Yun, Y.H.; Lee, B.K.; Park, K. Controlled Drug Delivery: Historical perspective for the next generation. *J. Control. Release* **2015**, *219*, 2–7. [CrossRef] [PubMed]
5. *GlaxoSmithKline DX: L58 Prescribing Information—Dexedrine® Spansule® Sustained-*

Release Capsules and Tablets; GlaxoSmithKline: Brentford, UK, 2007.
6. Highlights of Prescribing Information: RIOMET ER (Metformin Hydrochloride for Extended-Release Oral Suspension Sun Pharmaceutical Industries Limited). Available online: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212595s0 00lbl.pdf (accessed on 10 January 2022).
7. Venkatesh, G.M.; Stevens, P.J.; Lai, J.-W. Development of orally disintegrating tablets comprising controlled-release multiparticu- late beads. *Drug Dev. Ind. Pharm.* **2012**, *38*, 1428–1440. [CrossRef] [PubMed]
8. Antra MUPS 20 mg|Zusammensetzung|Arzneimitteldatenbank | Aponet.De. Available online: https://www.aponet.de/service/arzneimitteldatenbank/arzneimittel/anwendungsdetails/zusammensetzung/3339612921/Omeprazol (accessed on 11 January 2022).
9. Krämer, J.; Blume, H. Biopharmaceutical Aspects of Multiparticulates. In *Multipaticulate Oral Drug Delivery*; Ghebre-Sellassie, I.,
10. Ed.; CRC Press: Boca Raton, FL, USA, 1994; pp. 307–332.
11. Tang, E.S.K.; Chan, L.W.; Heng, P.W.S. Coating of Multiparticulates for Sustained Release. *Am. J. Drug Deliv.* **2005**, *3*, 17–28. [CrossRef]
12. Podczeck, F., Newton, J.M., 1994. A shape factor to characterize the quality of spheroids. J. Pharm. Pharmacol. 46, 82–85.
13. Podczeck, F., Rahman, S.R., Newton, J.M., 1999. Evaluation of a standardised procedure to assess the shape of pellets using image analysis. Int. J. Pharm. 192, 123
14. Tomer, G., Podczeck, F., Newton, J.M., 2001. Extrusion/ spheronization of a group of chemically similar drug models: I. Extrusion parameters. Int. J. Pharm. 217, 237–248.
15. Marijima, T., McGinity, J. B., pharm. Dev. Technol., 2000, 116,211-221.
16. Woodruff, C. W., Nuselle, N. O., J. Pharm. Sci.,1972,61,787-790.
17. Gandhi, R., Kaul, C.L., Panchagnula, R., Pharm. Sci.Tech.Today, 1999, 2(4),160–81.
18. Otsuka, M., Gao, J., Mastusuda, Y., Drug. Dev. Ind. Pharm., 1994, 20, 2977-2992.
19. Sherrington, P. J., Oliver, R., In; Goldberg, A. S. (ed.), Granulation, Heyden, London, Philadelphia, 1981, pp. 141-152.
20. Holt RI, Cockram C, Flyvbjerg A, Goldstein BJ. Textbook of Diabetes. 4th ed. UK: Wiley-Back Well; 2010.
21. Patel SA, Patel NG, Joshi AB. Multiple unit pellet system (MUPS) based fast disintegrating delayed-release tablets for pantoprazole delivery. Int J Pharm PharmSci 2018;10:138-44.
22. Jain K. Gastro Retentive Drug Delivery: Progress in Controlled and Novel Drug Delivery System. 1st ed. New Delhi: CBS Publisher and Distributer; 2004. p. 82- 90.
23. Asian Edition. The United State Pharmacopeia. New York: Asian Edition; 2000.p. 2059.
24. Grass GM., Robinson JR, Dekker M. In: Banker GS, Rhodes CT, editors. Modern Pharmaceutics. New York: Informa Healthcare USA Inc.; 1996. p. 635.
25. Ali M. Textbook of Pharmacognosy. 2nd ed. New Delhi: CBS Publishers and Distributors; 2012. p. 71-90.
26. Kokate C, Purohit A, Gokhle S. Pharmacognosy. 42nd ed. Pune: Nirali Prakashan;2008.
27. Begum R, Aleemudin M, Gautam T. Effect of natural gums on oral sustained release matrix tablets of chloroxone. Int Res J Pharm 2012;3:426-7.
28. Rao NR, Yadav A. Formultion and evaluation of zero order release glipizide bilayer matrix tablet using natural and synthetic polymers. Int J Curr Pharm Res 2010;2:34-42.
29. Kumar AA. Formulation and evaluation of sustained release valsatran matrixtablets by using natural polymers. Int J Pharm Chem Biol Sci 2012;2:14