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Formulation of Sustained Release Pellets by Extrusion Spheronization Technique – A Review

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ABSTRACT: Multiple-unit dosage forms, are thought to offer numerous therapeutic benefits like uniform distribution throughout the gastrointestinal tract, increasing drug absorption and decreasing peak plasma fluctuations as compared to single unit dosage forms. Sustained release dosage forms minimize side effects, decrease administration frequency, maintain plasma concentrations within therapeutic ranges, and provide a consistent concentration of absorption site. Pellets are free flowing spherical dosage forms that have better flow characteristics, a less friable dosage form, and a narrow particle size distribution. The process of extrusion-spheronization is the most commonly used technique for producing pellets. This article gives an outline on the different excipients used in the sustained release pellet formulation that are prepared using extrusion spheronization method.

KEYWORDS: Multiple unit dosage form, sustained release,Pellets,extrusion spheronization Method

I. INTRODUCTION

Recently, there has been an increase in the use of multiple unit dosage forms, like pellets and granules. When compared to single-unit dosage forms, these multiple-unit dosage forms, are thought to offer numerous therapeutic benefits. They can distribute uniformly throughout the gastrointestinal tract (GI tract), increasing drug absorption and decreasing peak plasma fluctuations, lowering the chance of local GI tract irritation and dose dumping, lowering dosage frequency and raising patient compliance, enhancing the active ingredient's safety and effectiveness [1]. A large number of multi-particulate drug delivery systems are oral dosage forms made up of several small, distinct units, each of which possesses a few desired properties. The drug dosage in these systems is split among several subunits, each of which usually consists of thousands of spherical particles with a diameter of 0.05 to 2.00 mm. The active ingredient is therefore present in pharmaceutical formulations as a number of tiny, independent subunits in multi-particulate dosage forms[2].

Sustained release dosage forms aim to enhance the pharmaceutical activity of the medication by achieving greater duration of action and better selectivity.In order to increase patient convenience, sustained release formulations can be used to lower the dosage frequency [3]. Drug delivery systems with sustained release minimize side effects, decrease administration frequency, maintain plasma concentrations within therapeutic ranges, and provide a consistent concentration at the absorption site [4]. The goal of sustained release drug delivery systems is to continuously release medication over an extended period of time in order to achieve a prolonged therapeutic effect. Several factors are necessary for the development of a successful sustained release formulation, including: from the identification of possible therapeutic candidates to the process variable optimization during the preparation [5].As a dosage form, pellets have been gaining more and more attention recently. Therapeutic benefits of using pellets as a drug delivery system include decreased gastrointestinal tract irritation and a decreased chance of adverse effects from dose dumping [6].

Pellets has been used to characterize a range of geometrically defined, systematically produced agglomerates that were obtained from various starting materials under various processing conditions. Their typical size falls between 0.5 and 1.5 mm, and they are primarily meant to be taken orally. In addition to their technological benefits, pellets as a drug delivery system have better flow characteristics, a less friable dosage form, a narrow particle size distribution, ease of coating, and uniform packing.Some desired benefits of pellets include their ability to design and develop flexible dosage forms, reduce variability in drug dissolution and plasma profiles, and uniform packing

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characteristics, improve drug safety and efficacy, and allow the drug to freely spread throughout the GI tract [7].Pelletized delivery system (PDS) uses pellets or beads made by layering powders or solutions on nonpareil seeds or by using techniques like marumerization, spheronization, and pelletization.The process of extrusion-spheronization is the most commonly used technique for producing pellets [8]. Extrusion/spheronization is a cost-effective technique for creating pellets with high drug loading and strength. When processing pellets using the extrusion-spheronization technique, a number of formulation and processing parameters must be determined and managed [9].The ability to incorporate higher levels of active components without producing excessively larger particles is one advantage of extrusion-spheronization over other techniques. Another is the ease with which two or more active agents can be combined in any ratio within the same unit, and the ability to modify the physical characteristics of the active ingredients and excipients to produce particles with high bulk density, low hygroscopicity, high sphericity, dust-free, narrow particle size distribution, and smoother surface [10].

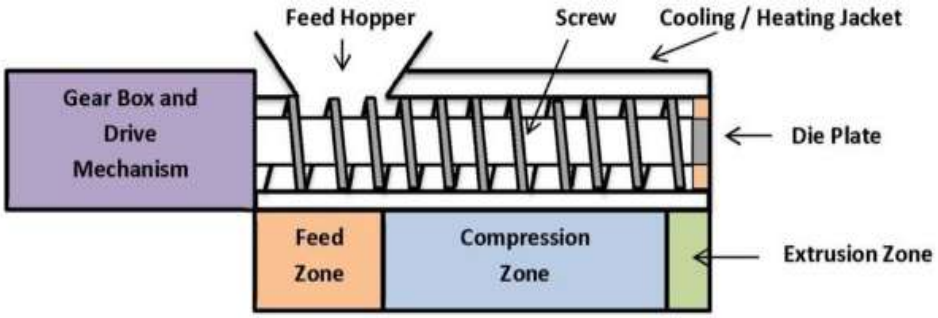

Fig 1 Different parts of Extruder

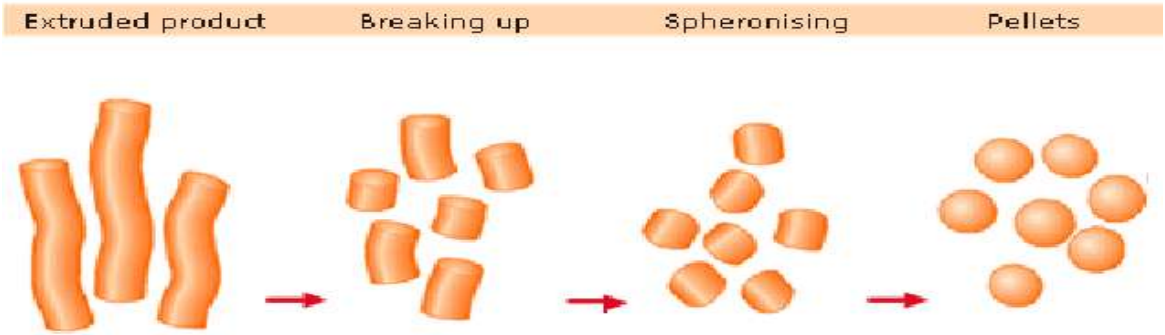

Fig 2Stagesin Formation of Pellets

Reducing dosage frequency, increasing drug effectiveness through localization at the intended site of action, lowering dosage, and ensuring consistent and even drug delivery are the primary considerations in the design of these sustained release dosage forms. Since these formulations are well known for providing continuous drug release over a long period of time, hydrophilic polymer matrices are frequently used when creating sustained dosage forms.Sustained release systems can be used to shield the drug from deterioration in an acidic environment, such as the stomach's low pH. When this happens, the medication shouldn't be released until it has reached the small intestine. Polymers are required as an essential control measure for release and as a film-forming agent in order to fulfil this mission [11].

II. MATERIALS AND METHODS

Materials Used for sustained release pellets

- Filler: Microcrystalline Cellulose, Starch, sucrose
- Binder: Sucrose, Starch, HPMC, PVP

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- Lubricant: Glycerine, PEG, Magnesium stearate
- Separating agent: Talc, silicon dioxide
- Disintegrants: Alginate, cross carmellose sodium.
- pH adjuster: Citrate, Phosphate
- Surfactant: SLS, Polysorbate
- Spheronization enhancer:MCC, Sodium CMC
- Glidant: Talc, starch, Magnesium stearate
- Release modifier: Ethyl cellulose, Shellac

Pellets are made up of a variety of formulation aids, such as disintegrant, which promotes the disruption of pellets (such as talc), binders, which bind powders and maintain pellet integrity (such as hydroxyl propyl methylcellulose, polyvinylpyrrolidone), filler/diluent, which adds bulk (such as dibasic calcium phosphate, lactose, microcrystalline cellulose, starch, and sucrose), lubricant, which lowers the coefficient of friction between individual particles or between the particles and the surfaces of the processing equipment, lubricant, which reduces the coefficient of friction between individual particles or between the particles and the surfaces of the equipment (such as magnesium stearate), separator, which encourages the separation of pellets into distinct units during a pelletization process (such as talc), disintegrant, which promotes the disruption of pellets (such as croscarmellose sodium, sodium starch glycolate), and spheronization enhancer, which facilitates the production of spherical pellets (microcrystalline cellulose**)[10]**.

Coating for the pellets are done in-order to modify the release rate of the drug. The coatings Eudragit L30D-55 and Eudragit NE30D were used to create drug-loaded pellets with a sustained release [11]. Eudragit S100 was dissolved in quantity sufficient acetone and was used for the sustained release enteric coating[12].

Extrusion Spheronization Method

The procedure is to make extrudes from the powder material first, and then use a spheronizer to turn the extrudes into beads. Any type of powder drug, Ayurvedic, food ingredient, could be used as the powder material [13].

The powders with drug, fillers, lubricants are added then appropriate quantity of binder was added slowly during constant mixing. The wet mass was extruded at room temperature, through a die size of mainly 0.8 mm diameter and 4 mm in length by 20 rpm equipped with an axial screen extruder, the extrudate was collected in a container before it was spheronized. On a spheronizerwith 40 cm in diameter equipped with a grooved plate, for 2 and 10 min at 2000 rpm. The pellets were dried at 40±2°C for 24 h[14].

Fig 3Formation of Pellets using spheronizer

The dough mass can be extruded also through mini screw extruder with 1 mm pore size at speed of 25 rpm. The extrudates collected and were spheronized in spheronizer at 800 rpm for 20 min [14].

The type of extruder used and the speed and time of the method varies according to the excipients used.

In brief, the processof extrusion spheronization can be explained as

- Preparation of the wet mass (Granulation).
- Shaping the wet mass into cylinders (Extrusion).
- Breaking up the extrudate and rounding of the particles into spheres (Spheronization)

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- Drying of the pellets

Granulation is the process of preparing the material's plastic mass. The commonly used granulators includes planetary mixer, high-shear or sigma blade mixers. Extrusion is a process that creates extrudates by applying pressure to a prepared plastic mass until it flows out of an orifice. The length of the extrudate can change depending on the physical properties of the materials to be extruded, the extrusion process. Screw extruder is the common type of extruder used. Spheronization is the process by which extruded, cylindrically shaped particles break into uniform lengths and progressively take on spherical shapes; plastic deformation is responsible for this shaping. The pellets are dried as the process's last step. The pellets can be dried in an oven, on a fluidized bed, or at room temperature or elevated temperature [10].

Evaluation of the Pellets

The preformulation studies are performed for investigation of the physical and chemical properties of the drug substances and the excipients. This includes the parameters like organoleptic properties, solubility, bulk density, moisture content, angle of repose, and tapped density [15].

To verify whether there is an interaction between the drug and the excipients, drug-excipient studies were conducted by using FTIR. A KBr pellet method is commonly used. The physical mixtures and pure drug were formed into discs, and the FTIR was used to assess the compatibility of the mixtures. To determine the chemical interaction between API and excipients, the spectrum of the pure drug was compared with a physical mixture of the drug and excipients. To investigate and find any incompatibilities, the spectra of the excipients and the pure drug are compared [16].

The drug and excipients and the prepared pellets can be analysed for its micrometric properties, like bulk density, tapped density that are done mainly using 50ml graduated measuring cylinder. The volume of powder and the pellets are measured and then the cylinder is tapped mechanically for 100 times. The compressibility index and Haussner's ratio can be computed from the values. The angle of repose can be determined using funnel method.

Another important evaluation parameter for the prepared pellets is in-vitro release studies. This is usually done using Apparatus type II (Basket Type)[16].

III. CONCLUSION

From the above discussion, one can say that the sustained release formulation helps in the dose effectiveness and patient compliance. The formulation of pellets by extrusion spheronization is one of the simplest method for the preparation of sustained release pellets. This method is a multi-step batch process that helps in creating pellets with high loading and strength. Improvement in the instrumental system gives a potential chance to achieve different goals that may be economical and technical.

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