# "Formulation and evaluation Coated Spherules"

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**Abstract: The spherules in addition provides an opportunity to modify its surface properties by polymer film coating. It improves the functional properties such as appearance, drug release and integrity of particles during processing of spherules. Also the spherules have low surface area to volume ratio so less amount of coating solution is required. Granules and pellets shape is not necessarily spherical in nature. Coated spherules can also be an option for coating instead of coating the tablet. Instead of the tablet coated spherules help in reducing the disintegration time of the tablet. It can also help in the reducing the manufacturing cost of the final tablet as coating, spheronization & drying can be occur at the same time which also help in reducing the time of manufacturing**

**Keywords: Propranolol , Lactose ,Mcc ,Pvp .**

**Introduction:**

InManufacturing of coated spherules produces spherules having high drug loading capacity and better flow properties as compared to normal granules and pellets. This is because in granules and pellets the shape is not necessarily spherical in nature. The spherules in addition provides an opportunity to modify its surface properties by polymer film coating. Surface coatings improve the functional properties such as appearance, drug release and integrity of particles during processing of spherules. As compared to granules, spherules have low surface area to volume ratio so less amount of coating solution is required.[1]

Spheronization is generally done with fluidized bed drying (FBD), where the droplets are dried in air under circulation produce spherules with irregular shape and surface roughness due to rapid drying. Thus, alternative methods are required that can be adopted in small and large process to produce uniform spherules. Low cost production of spherules can be achieved by wet granulation followed by "bed coating during sliding (BCDS)" as these processes can be engineered to regular pharmaceutical unit operations and scaled up. Granulation can be done by sieving followed by sizing. The spheronization by BCDS can lead to uniform sized particles as polishing of coated starch particles to granules are happening during sliding, that can lead to conversion of granules to spherules. The spherules can be surface modified by polymer film coating.

**ADVANTAGES:**

➢ To improve the flow property of material.
➢ Coating of granules can help in achieving the controlled release of drug.
➢ It eliminates the process of the tablet coating which helps in better release of the drug.
➢ Coating of granules can help in manufacturing the multiple drug tablet as the coated granules cannot interact with each other.
➢ Enteric coating of the granules can help to achieve the target drug delivery.
➢ Coating of granules with the pH dependant soluble polymer can help in releasing the drug at a specific site in the body.
➢ Coating of granules also helps in protection, masking the taste and odour of the drug.
➢ Some drug which causes the GI irritation can also be coated with polymer to decrease the GI irritation.[3]

**DISADVANTAGES** :

➢ It is very difficult to achieve the uniform coating of the granules.
➢ It is difficult to achieve the smooth coating on the surface of the each granule.
➢ It is possible that the coating may get break during the compression process.
➢ Some coating solution my cause problem with the drug.
➢ Moisture entrapment may take place during the granule coating process. Coating layer may get break or crack during the drying.

**Method of Preparation**:

There are various techniques to prepare spherules or 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-spheronization. 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).
• Spheronization: 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.[6]

**Structure of Propranolol, Lactose , MCC ,PVP:-**

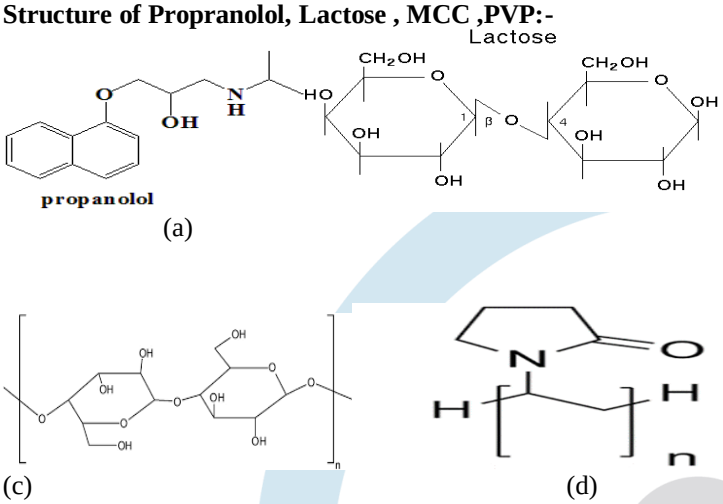


**Figure 1: Structure of (a) Propranolol, (b) Lactose , (c) MCC ,(d) PVP**

**2. PREPARATION:**

Beaker method

Wet granules (10gm) was accurately weighed and taken into 250ml beaker and rotated in clockwise direction at 45° angle. While rotating ethanol: water (50:50 v/v) mixture were sprayed to granule bed for maintaining the wetness. Small amount of starch powder was added while rotating, to improve the flow properties and 6-7 drops of starch solution (prepared by adding 3 drops of 5% starch paste in 7ml distilled water) are also added or sprayed to this rotating granule bed for improving the binding of small fines of starch powder to get the spherules. The prepared spherules were then sieved (sieve no 22 and 44) to get uniform sized spherules. Coating solution were prepared by dissolving polymer (500 mg), dye (100 mg), and talc (400 mg) dissolved in acetone (25 ml). Coating solution were sprayed to the spherule bed with constant rotation. After coating the spherules were spread on petridish and kept at 60 C in hot air oven for 20 min to prepare dried polymer coated spherules.

**Formula for Spherules**:-

| Sr.no | Ingredients | Quantity tekan |
|---|---|---|
| **1** | Propranolol | 40mg |
| **2** | Lactose | 60mg |
| **3** | MCC | 58.2mg |
| **4** | PVP | 6mg |

**Table no. 1 –formula for spherules**

**Formula for coating spherules:-**

| Ingredients | F1 | F2 | F3 | F4 |
|---|---|---|---|---|
| **Eudragit L-100** | 5gm | 2.5gm | - | - |
| **Ethyl Cellulose** | - | - | 2.5gm | 5gm |
| **Polyethylene glycol (PEG)** | 2.0gm | 2.0gm | 2.0gm | 2.0gm |
| **Acetone** | 50ml | 50ml | 50ml | 50ml |
| **Titranium dioxide** | 0.1%w/v | 0.1%w/v | 0.1%w/v | 0.1%w/v |

**Table no. 2 – Formula for coating spherules**

**3. Results and discussion**

**Preformulation test** :

| Sr.no | Concentation of drug ug/ml | Absorbance |
|---|---|---|
| 1 | 0 | 0.0899 |
| 2 | 2 | 0.107 |
| 3 | 4 | 0.1123 |
| 4 | 6 | 0.1254 |

| | | |
|---|---|---|
| 5 | 8 | 0.1564 |
| 6 | 10 | 0.1765 |

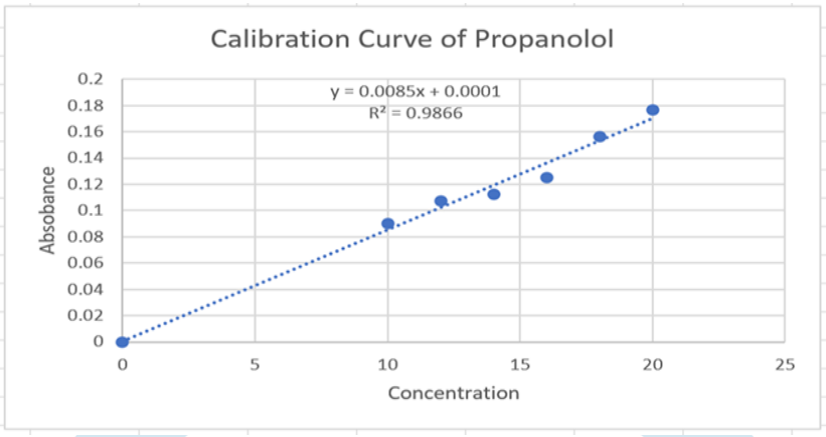


**Fig -Standard calibration curve of Propranolol**

**Physcical evaluavtion results**

| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
|---|---|---|---|---|---|---|---|---|
| **Angle of repose** | **41.49** | **40.56** | **40.98** | **31.61** | **35.55** | **33.89** | **33.18** | **32.78** |
| **Bulk density** | **0.896** | **0.812** | **0.789** | **0.896** | **0.872** | **0.796** | **0.825** | **0.765** |
| **Tapped density** | **0.617** | **0.658** | **0.681** | **0.785** | **0.685** | **0.674** | **0.653** | **0.678** |
| **Particle size** | **0.79mm** | **0.80mm** | **0.85mm** | **0.91mm** | **0.74mm** | **0.77mm** | **0.81mm** | **0.87mm** |
| **% drug content** | **92.20** | **92.57** | **92.89** | **94.89** | **93.78** | **93.90** | **91.65** | **90.89** |

**Table no.3- Physical evalution result**

**Dissolution Result:**

The ultimate aim of this present work was to develop sustained release drug delivery system of propranolol.

Dissolution of the coated Spherules

| | Cumulative percent drug release | Cumulative percent drug release | Cumulative percent drug release |
|---|---|---|---|
| | F1 | F2 | F3 |
| 0 | 0 | 0 | 0 |
| 1hrs | 25.12 | 23.34 | 25.54 |
| 2hrs | 40.02 | 40.20 | 40.35 |
| 3hrs | 58.75 | 58.67 | 59.89 |
| 4hrs | 62.41 | 62.34 | 64.56 |
| 5hrs | 70.03 | 70.13 | 71.43 |
| 6hrs | 73.45 | 73.58 | 74.76 |
| 7hrs | 80.39 | 81.49 | 82.58 |
| 8hrs | 85.40 | 85.76 | 86.56 |
| 9hrs | 87.35 | 87.45 | 88.30 |
| 10hrs | 89.01 | 89.25 | 89.67 |
| 11hrs | 90.37 | 90.50 | 91.01 |
| 12hrs | 92.56 | 92.39 | 91.67 |

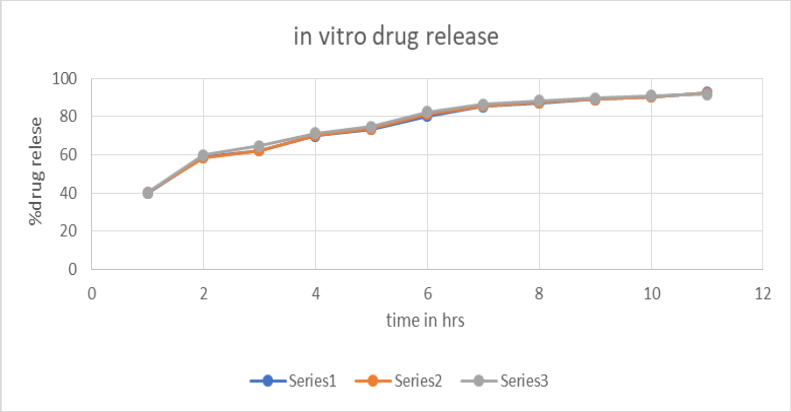


**Table no.4-In vitro dissolution data of F1,F2and F3Formulation**

| | Cumulative % drug Release | Cumulative % drug Release | Cumulative % drug Release |
|---|---|---|---|
| | F4 | F5 | F6 |
| 0hr | 0 | 0 | 0 |
| 1hr | 25.73 | 23.67 | 24.89 |
| 2hr | 29.99 | 30.56 | 33.76 |
| 3hr | 33.89 | 35.67 | 37.89 |
| 4hr | 38.90 | 37.56 | 40.89 |
| 5hr | 40.23 | 43.34 | 44.56 |
| 6hr | 45.54 | 47.59 | 49.89 |
| 7hr | 50.67 | 52.76 | 55.65 |
| 8hr | 58.78 | 57.30 | 59.60 |
| 9hr | 63.89 | 65.74 | 68.45 |
| 10hr | 69.79 | 72.89 | 76.78 |
| 11hr | 80.67 | 79.90 | 91.45 |
| 12hr | 98.45 | 95.34 | 94.56 |

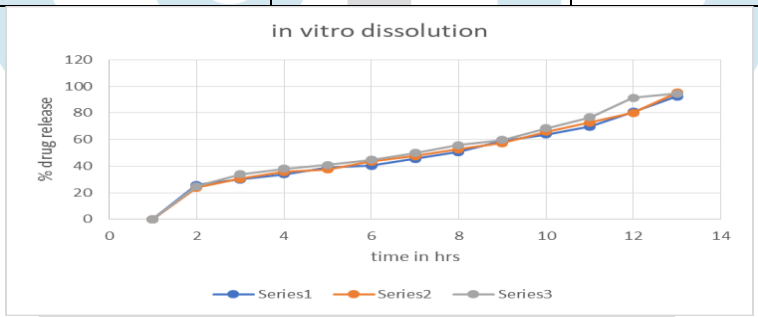


**Table no.5-In vitro dissolution data of F4,F5and F6Formulation**

| | | |
|---|---|---|
| | F7 | F8 |
| 1hrs | 22.94 | 19.12 |
| 2hrs | 29.91 | 25.87 |
| 3hrs | 50.13 | 27.66 |
| 4hrs | 52.67 | 33.98 |
| 5hrs | 55.6 | 38.56 |
| 6hrs | 62.4 | 47.41 |
| 7hrs | 69.57 | 56.96 |
| 8hrs | 71.88 | 68.92 |
| 9hrs | 78.95 | 75.53 |
| 10hrs | 82.61 | 86.66 |
| 11hrs | 89.91 | 97.49 |
| 12hrs | 97.41 | 97.82 |

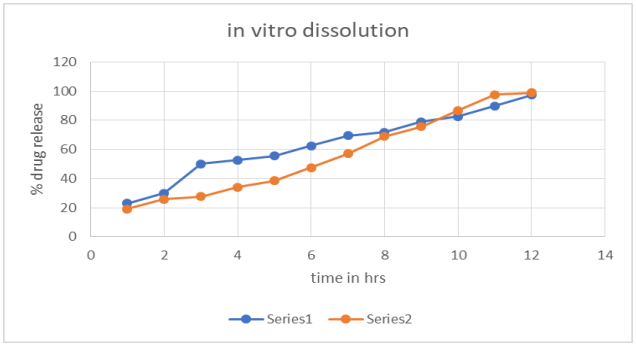


**Table no.6-In vitro dissolution data of F7 and F8 Formulation.**

## 4. Conclusion

The spherules of prepared by using extrusion and spheronization technique were found to be non- sticky, spherical, free flowing with uniform size. Also the coated spherules by fluidized Bed Process were non- sticky, free flowing, uniformly coated with eudragit L-100. All the batches shown satisfactory results. The optimized F2 batch containing coating polymer Eudragit L100 in 6% concentration has shown continuous sustained release of propanalol up to 12hrs . So it can be conclude that the lactose and MCC with extrusion spheronization technique can produce free flowing, uniform size and spherical spherules of Propanolol. Also the sustained release of propanolol could be obtained by coating with Eudragit L- 100 as coating polymer. The fluidized Bed Process was found to be faster and convenient for uniform coating of spherules.

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