International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 **ijppr.humanjournals.com** ISSN: 2349-7203

Preparation and Evaluation of Salicylic Acid Spherules

Aparna.C*, Abhinay varma, V. Lavanya, S. Harshini, Y. Shravya, P. Brahmam

Sri Venkateshwara College of Pharmacy, Madhapur, Hitech city, Hyderabad, 500081, Telangana, India.

Received: 2025-4-01 Revised: 2025-4-12 Accepted: 2025-4-20

ABSTRACT:

"Spherules are small, rounded or spherical pellets that are used as a multi-particulate carrier for drug delivery." Spherules were prepared to improve flow properties and to control the release characteristics of the drug. Salicylic acid was used as a model drug in this study. Spherules were prepared by "Bed coating during sliding" (BCDS) of granules. These spherules were further coated with polymers to show the versatility of the process. Spherules are uniform in size and regular in shape when compared to granules. Flow properties and *invitro* dissolution studies were conducted for both spherules and granules. Angle of repose of spherules was found to be 21.3° which is better than that of granules which have an angle of repose of 30.6°. Granules released 65% of drug in 5 hours when compared to spherules whose drug release was found to be 98% in 3hours which indicates improvement in the drug release. Hence it is proved that spherules have better flow properties and improve the release characteristics of the drug. Thus, this is a robust and versatile platform for developing novel drug delivery systems (NDDS).

Keywords: Spherules, Granules, Spheronization, BCDS

I. INTRODUCTION

Granulation may be defined as a size enlargement process that converts fine or coarse particles into physically stronger and larger agglomerates having good flow properties, better composition characteristics, and uniformity. The particles produced by granulation are called granules. Granules increase the uniformity of the API in the project, increasing the density of the blend so that it occupies less volume. Spherules are small, rounded or spherical pellets that are used as a multi-particulate carrier for drug delivery. Granulation is not possible for materials that are sensitive to heat or moisture because the granulation technique exposes the drug to water and high temperatures that degrade the sensitive materials. Due to low porosity, granules are poorly water soluble. Spheronization is the most widely used method of manufacturing spherules, which produces spherules with high drug loading capacity and better flow properties than granules and pellets. Spherules were made by wet granulation followed by bed coating during sliding (BCDS). Salicylic acid was chosen as a model drug.

Advantages of spherules

● It improves the flow property of material [9].

● Coating of granules can help in achieving the controlled release of drugs [10].

● It eliminates the process of the tablet coating which helps in better release of the drug.

● Coating of granules into spherules 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 dependent 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.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

Limitations of spherules

- It is very difficult to achieve the uniform coating of the granules.
- It is difficult to achieve the smooth coating on the surface of each granule.
- It is possible that the coating may break during the compression process [11].
- Some coating solutions may cause problems with the drug.
- Moisture entrapment may take place during the granule coating process [12].
- Coating layer may break or crack during the drying [13].

Applications of Spherules

- Helps in the process of microencapsulation for achieving sustained release dosage forms [14].
- Spherules can be used in anticancer therapy and gene therapy, which is useful in the treatment of genetic disorders.
- Spherules increase the bioavailability and stability of the drug.

II. MATERIALS AND METHODOLOGY

Salicylic acid, ethyl cellulose, starch, magnesium stearate, talcum powder and acetone were purchased from SD Fine-Chem Limited, Mumbai. HPMC K100M was a gift sample from Colorcon, Mumbai.

The objective of the study was to prove that spherules are superior to granules. Hence, we have taken the granules and spherules formulation directly from the literature. Granules were prepared by taking accurately weighed quantities of active pharmaceutical ingredient (API) and all the other excipients, as mentioned in Table 1. They were passed through sieve number 22 in order to remove foreign material and to get uniform particle size. Salicylic acid was taken along with HPMC and starch and enough granulating agent (water) was added slowly to prepare a wet mass. Granules were prepared by the wet granulation technique and sieved using sieve number 20 to get uniform sized granules. Granules were then dried in a hot air oven for 15 min at 120°C. Further magnesium stearate was added to the dried granules for lubrication [3].

The spherules were prepared according to the formula given in Table 2. Granules were taken in a beaker and rotated in a clockwise direction at a 45° angle. While rotating, an ethanol-water (50:50 v/v) mixture was sprayed to the granule bed for maintaining the wetness. A small amount of starch powder was added while rotating to improve the flow property, and 6-7 drops of starch solution (prepared by adding 3 drops of 5% starch paste in 7 ml distilled water) was also added or sprayed to this rotating granule bed for improving the binding of small, fine starch powder to get the spherules. The prepared spherules were then sieved using sieve number 20 to get uniformly sized spherules. The coating solution was prepared by dissolving polymer, sunset yellow, and talc was dissolved in acetone. Coating solutions was sprayed to the spherule bed with constant rotation. After coating, the spherules were spread on a petri dish and kept at 60°C in a hot air oven for 20 min to dry the polymer-coated spherules.

Figure 1: Granules

Figure 2: Spherules

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

Table 1: Formulation table of Granules

IINGREDIENTS	QUANTITY TAKEN (gm)	USES
Salicylic acid	5	API
HPMC	1	Binder
Starch	1.4	Diluent
Magnesium stearate	0.5	Lubricant
Water	q.s	Granulating agent

Table 2: Formulation table of Spherules

INGREDIENTS	QUANTITY TAKEN (gm)	USES
Granules	5	Active ingredient
Ethyl cellulose	0.25	Polymer
Sunset Yellow	2 drops	Colouring agent
Talc	0.2	Adhesive agent
Acetone	12.5 ml	Solvent

Angle of repose:

It is the maximum angle between the surface of the pile of powder and the horizontal plane. The angle of repose of granules and spherules was determined by the funnel method. The accurately weighed granules and spherules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the pile. They were allowed to flow through the funnel freely onto the surface. The diameter of the pile was measured and the angle of repose was calculated using the following equation.

$$\tan \theta = h/r$$

Where 'h' is the height of the pile and 'r' is the radius of the pile.

Particle packing parameters:

Bulk density is mainly used to find out the uniformity of powder particles. Spherules or granules (2 gm) were taken in a 10 ml measuring cylinder to find out the bulk density and tapped density. Bulk density was determined by noting down the volume occupied by spherules and granules after tapping manually 2 times on the flat surface. Tapped density was determined by measuring the tapped volume occupied by spherules after 100 tapings on a flat tabletop. Bulk and tapped density were calculated from bulk and tapped volume by the following formula.

Bulk density = weight taken/bulk volume

Tapped density = weight taken/tapped volume

The compressibility index, or Carr's index, is the measure of the tendency of spherules to consolidate, based on interparticle interactions. Car's index is also known as percentage compressibility and it is determined by the formula:

Carr's index = [Tapped density – Bulk density/ Tapped density] 100

Hausner's Ratio is the ratio of tapped and bulk density. Low values indicate the good flow property of spherules.

Hausner's ratio = Tapped density/Bulk density

Table 3: Relationship between Angle of repose, Carr's index and Hausner's ratio with Flow properties

Angle of Repose	Carr's compressibility index	Hausner'sRatio	Flow Properties
25-30	<10	1.00-1.11	Excellent
31-35	11-15	1.12-1.18	Good
36-40	16-20	1.19-1.25	Fair
41-45	21-25	1.26-1.34	Passable
46-55	26-31	1.35-1.45	Poor
56-65	32-37	1.46-1.59	Very Poor
>66	>38	>1.60	Very Very Poor

Calibration curve of salicylic acid by colorimetry:

Standard graph of salicylic acid was plotted using a colorimeter. The free phenolic hydroxyl group present in salicylic acid reacts with the reagent to form a violet-colored complex, i.e., ferric salicylate, which is proportional to the concentration of salicylic acid.

Preparation of ferric chloride solution in 1% hydrochloric acid solution:

We have used 1% ferric chloride solution as a coloring agent which was prepared by taking 1 gm of ferric chloride and dissolving it in a 1% hydrochloric acid solution.

Preparation of Stock-A Solution:

100 mg of salicylic acid was weighed accurately and taken in a 100 ml volumetric flask and dissolved in small quantity of methanol. The final volume was made up to 100 ml with distilled water to get the "Stock-A" solution with a concentration of 1mg/ml (1000 µg/ml).

Preparation of Stock-B Solution:

From the Stock-A solution, 1o ml was pipetted out and taken in a 100ml volumetric flask, and the volume was made up to 100 ml using distilled water to get Stock-B solution with the concentration of 100 µg/ml.

Construction of calibration curve of salicylic acid:

From the Stock-B solution, various samples in the range of 1, 2, 3, 4, 5, 6 ml were transferred into a 10 ml volumetric flask each containing 1 ml of 1% ferric chloride solution and the volume was up to 10 ml using distilled water to prepare 10, 20, 30, 40, 50, and 60 µg/ml. These solutions were analysed using colorimeter at 540 nm to measure absorbance and the process was carried out in triplicate. The calibration curve was plotted taking concentration on x axis and absorbance on y axis.

In vitro dissolution study:

Dissolution studies of granules and spherules were performed using USP Type II apparatus. A measured quantity of spherules and granules were taken separately (about 200 mg) and filled into two capsules. Capsules were added into separate baskets that contained 900 ml of distilled water, which was used as a dissolution medium; the temperature was maintained at 37 ± 0.5°C. The speed of the paddle was set at 100 rpm. At regular intervals 5 ml samples were withdrawn, for five hours and the equal amount of dissolution medium was replaced after each interval to maintain sink condition Absorbance of the solutions was measured using a colorimeter at 540 nm. A graph was plotted with time intervals on the X-axis and % cumulative drug release on the Y-axis.

Figure 3

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

III. Results and Discussion

Salicylic acid granules were prepared using the wet granulation technique, Spherules were prepared using these granules by BCDS technique. The objective of this study was to compare spherules and granules.

Flow property:

Flow properties help to determine the proper size of containers, mixing apparatus, and capsules for a given mass of the granules or spherules. The flow properties of granules and spherules are listed in Table 4.

Table 4: Results of the Flow Property evaluation tests

PARAMETER	GRANULES	SPHERULES
Angle of Repose	30.1 ° (Excellent)	21.3 ° (Excellent)
Bulk density	0.40 g/ml	0.51 g/ml
Tapped density	0.48 g/ml	0.57 g/ml
Carr's index	16.6 (Fair)	10.5 (Excellent)
Hausner's ratio	1.2 (Fair)	1.11 (Excellent)

Angle of repose of spherules (21.3 °) was better when compared to granules (30.1°). Carr's compressibility index of spherules (10.5) is lower than that of granules (16.6) and similarly, Hausner's ratio of spherules (1.11) is also less than that of granules (1.2).

This clearly indicates that the flow properties of spherules are better than granules. Based on the above observations, it is clear that the process of spherule formation improves the flow properties of granules, which results in good packing parameters.

Standard Graph:

Standard graph of salicylic acid was plotted by measuring the absorbance of various concentrations. Concentration of salicylic acid was taken on the X-axis, and absorbance was taken on the Y-axis as shown in Figure-4.

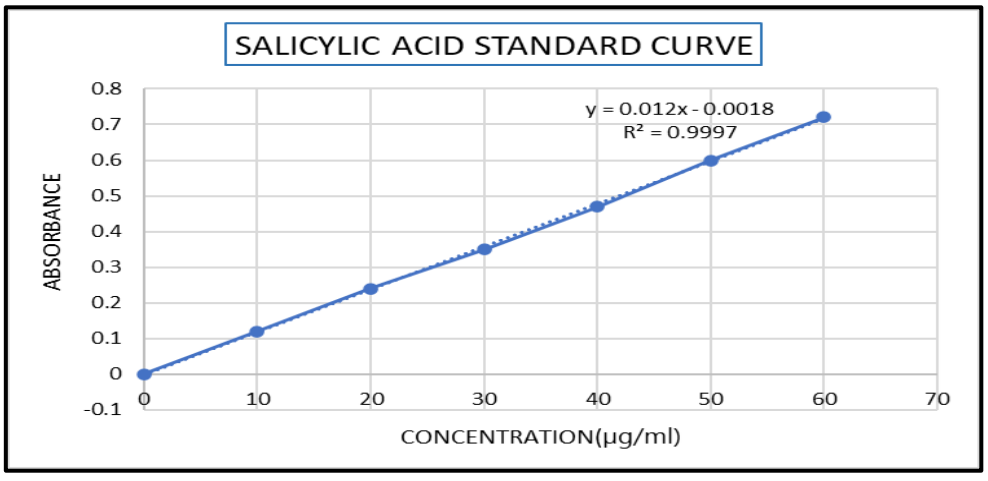

Figure 4: Standard graph of Salicylic acid

The equation of the graph was found to be

$y = 0.012x - 0.0018$, with an R^2 value of 0.9997.

Hence, the graph was found to be linear in the range of 0-60 µg/ml.

In vitro dissolution studies:

Dissolution tests of both granules and spherules were performed, using USP type II apparatus with water as the dissolution medium. Samples were withdrawn at regular intervals and analysed using colorimeter. As seen in table that the total drug release of granules was found to be 65% in a time span of 5 hrs, whereas the spherules had a % CDR of 107% within the same period of time. This explains that the drug release in spherules is better than that of granules as seen in graph 2. Based on our findings, we can say that the spherules have the ability to control the release characteristics of the drug, such as developing extended or sustained release dosage forms.

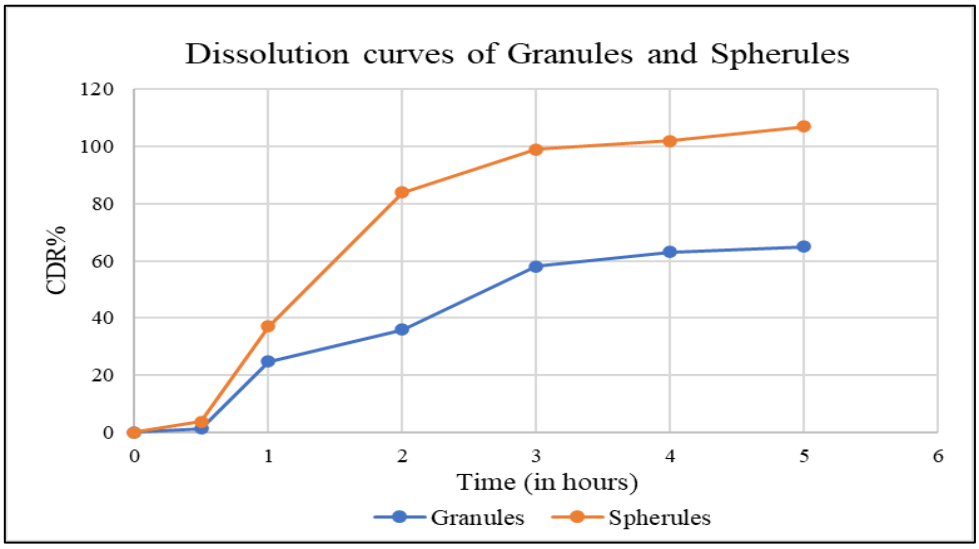

Figure 5: Dissolution Curves of granules and spherules

IV. CONCLUSION:

Polymer-coated spherules were prepared by wet granulation followed by bed coating during the sliding (BCDS) process. The formed polymer-coated spherules have a smooth, uniform shape, and the coating appears uniform, indicating that spherule formation was successful. Prepared spherules were found to possess improved flow properties, which is useful for good packing parameters and increased manufacturing integrity. It was also seen that the drug release is improved in spherules when compared to that of granules., thus making them an alternative for granules in solid dosage form preparation such as tablets and capsules. The coated spherules developed and demonstrated here are a versatile platform for developing different coated spherule-based pharmaceutical formulations using drugs.

ACKNOWLEDGEMENT

We would like to acknowledge the management of Sri venkateshwara college of pharmacy for providing the resources for the conduct of this study.

V. REFERENCES:

1. Vyshma KV, Hansan M, Krishnapriya Madhu, Kaladhar Kamalasanan, Radhakrishnan R. Formulation of different polymer coated spherules from granules. 2019 Jan 1;11(4).
2. Shingare VS. Formulation and Evaluation of Different Polymer-Coated Spherules from Granules.IJRASET. 2024 May 8;12(5):570–2.
3. Dhas NB, Gosavi MP, Chopade BL, Salve MT. Formulation and evaluation of aspirin tablet. Int J Adv Res Innov Ideas Educ. 2024;10(3):1065-1073.
4. Kotwal R, Mohan R, Kawade R. Formulation and Evaluation of Different Polymer Coated Spherules from Granules. Int J Pharm Sci. 2024;2(12):397-404.
5. Joshi NH, Mahale AM, Bhawde VA, Suroshe RS, Rathod SU. Formulation and Evaluation of Coated Spherules. Int J Res Anal Rev. 2024;2(8):33-45.
6. Preparation And Evaluation Of Aspirin Granules Prepared By Wet Granulation Technique, By Using Different Types Of Binders Sachin Dudhe , P.C. Meshram

7. KV, Hansan M, Madhu K, Kamalasanan K, Radhakrishnan R. Formulation of different polymer coated spherules from granules. J Pharm Sci Res. 2019;11(4):1633-1637.
8. Aarti Vitthal Mogal, Dhawale Tejaswini. Formulation of Different Polymer Coated Spherules from Granules.IJFMR. 2023 Mar 8;5(2).
9. Prajapati, Vipul D, Jani, Girish K, Kapadia, Jinita R. Current knowledge on biodegradable microspheres in drug delivery. Expert Opinion on Drug Delivery. 2015;12(8):1283-1299.
10. O'connor, R. E., Schwartz, J. B.. Spheronization II: Drug Release from Drug-Diluent Mixtures. Drug Development and Industrial Pharmacy. 1985;11(9-10):1837-1857.
11. Miller, Robert A., Leung, Edwin M. K., Oates, Randal J.. The Compression of Spheres Coated with an Aqueous Ethylcellulose Dispersion. Drug Development and Industrial Pharmacy. 1999;25(4):503-511.
12. Schaafsma, Stefan H., Kossen, Nico W. F., Mos, Marinus T., Blauw, Levy, Hoffmann, Alex C.. Effects and control of humidity and particle mixing in fluid-bed granulation. AIChE Journal. 1999;45(6):1202-1210.
13. Schneider, Monica, Maurath, Johannes, Fischer, Steffen B., Weiß, Moritz, Willenbacher, Norbert, Koos, Erin. Suppressing Crack Formation in Particulate Systems by Utilizing Capillary Forces. ACS Applied Materials & Interfaces. 2017;9(12):11095-11105.
14. Gauthier, Pascale, Cardot, Jean-Michel, Beyssac, Erick, Aiache, Jean-Marc. Single process for manufacturing spheres with a lipid base (HCO). Pharmaceutical Development and Technology. 2010;17(3):303-314.

How to cite this article:
Aparna.C et al. Ijppr.Human, 2025; Vol. 31 (4): 177-183.

Conflict of Interest Statement: All authors have nothing else to disclose.