Formulation and Development of Nimesulide Micro-Encapsulation by Fluidized Bed Processor

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ABSTRACT

A formulation is crucial in ensuring its viability in the current market. Such formulation development is giving rise to new technologies for the creation of products through creative methods; one significant and effective method that is currently being utilized extensively in the pharmaceutical industry is fluid bed technology. This article addresses the many procedures of a fluidized bed processor (FBP) and the underlying idea. FBP has many uses, including drying, pelletizing, granulation powder, or particle coating (micro-encapsulation), and discussing the benefits and drawbacks of the process. Three concepts are involved in the fluid bed process: tangential, bottom, and top sprays. The primary goal is to formulate Nimesulide drug capsules with pre-formulation studies and validation studies included. The polymers used for microencapsulation of Nimesulide are Eudragit RS100 and hydroxypropyl methylcellulose K30 (HPMC K30) followed by 2^2 factorial designs to get better Quality products. FBP provides pharmaceutical products in low time with excellent therapeutic effects. Another secondary goal is to thoroughly examine and comprehend the mechanism of the micro-encapsulation process by air suspension technique.

Keywords: *Fluid bed Technology, Nimesulide, HPMCK30, EudragitRS100, validation studies, pre-formulation studies, Microencapsulation.*

1. INTRODUCTION

Pharmaceuticals employ a fluid bed processor for the granulation, coating, drying, and pelletizing of granule particles. The Fluid Bed Equipment (FBE) approach is designed to decrease manufacturing costs, shorten processing times, and enhance product quality. The newest technique, known as fluid bed processing, makes it possible to granulate, coat, and dry a product in a way that ensures consistent drying and coating. These approaches can use tangential, top, or bottom spraying as their underlying concept. These guidelines rely on where the spray cannon is located within the apparatus. Nimesulide drug formulation by microencapsulation with polymers HPMC K30, Eudragit RS100 method performed into Fluidized bed processor and the drug is used as an analgesic, Anti-inflammatory, and cyclooxygenase inhibitor with 98.5 % to 101.5 % dried substance. Appearance of nimesulide is a yellowish crystalline powder. Freely soluble in acetone, slightly soluble in anhydrous ethanol, and practically insoluble in water [1].

PRINCIPLE OF FLUIDIZATION

A fluidized bed is a bed of solid patches through which hot air is passed at high pressure through the air distribution plate/ bottom of the vessel in the FBP as shown in Figure 1. The fluidization principle states that when a gas is transferred through a snoot at a haste lesser than the settling haste of patches or solids, the patches tend to suspend in the air and continue in the sluice of upward gas. When the patches reach the top of the outfit, they tend to gravitational pull and therefore fall, and this process of suspending continues [2].

Figure -1: Fluidized Bed Processor

CHEMISTRY OF NIMESULIDE

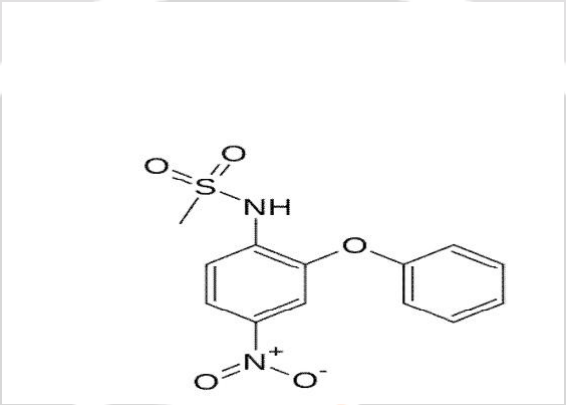


Figure -2: Structure of Nimesulide

Chemical formula = $C_{13}H_{12}N_2O_5S$

Molecular weight =308.31 g/mol

Melting point 143 Celsius

APPLICATIONS OF FLUID BED PROCESSING

Drying: Solids can be dried particularly well with fluid bed drying. The liquid is removed from every flyspeck's entire face during the fluidization process. Excellent heat exchange and the perfect drying time are the benefits [3].

Granulation/ Agglomeration: Agglomeration in the fluid bed is a contemporary fashion for producing granulates from grease paint-disusing liquid islands. The liquid that's scattered may be another binder, organic detergent, or water. The wet grains are moreover cooled or dried. Because of this, the agglomerates are exceptionally answerable in water, loose, and have a low bulk viscosity. Granulation is constantly used for pharmaceutical products [3].

Powder Coating / Particle Coating: By applying defensive flicks, ultramodern film coating widely modifies the product's characteristics. During coating, it's pivotal to apply the coating material extremely slightly. The coating must offer a perfect seal free from rips or mechanical damage. Film coating is an extremely protean process that requires a high position of specialized skill [4].

Pelletizing: The powder combined and bedewed before pearling. It's possible to add a detergent or binding agent contemporaneously. Agglomerates are created by centrifugal stir and spheroid into homogeneous, thick bullets [4].

TYPES OF FBS TECHNIQUES

Top spray process: Top spray is used for granulation, coating, and drying. The spray snoot is located above the expansion chamber. The coating liquid is scattered down onto a bed of fluidized patches as shown in Figure 23[3].

Bottom spray process: The bottom-spray (Wurster) fluid-bed system is veritably popular in the pharmaceutical assiduity for coating to modify or control medicine release. The hot air is passed through the fluidized bed; particulate material is lifted in the air sluice, and the result/ suspense is scattered on the fluidized bed for granulation and coating as shown in Figure 3[3,4].

Tangential spray: The snoot is introduced at the side of a product vessel/ expansion chamber. During processing, three mechanical forces beget flyspeck movement, mixing, and granulation. First, the spinning of the fragment generates a centrifugal force. Second, a lifting force is generated by the hot air passing through the malleable fragment gap. Third, the gravitational force causes material to fall onto the fragment. These forces give good mixing, performing in grains, drying, and coating with good content uniformity as shown in Figure 3[4].

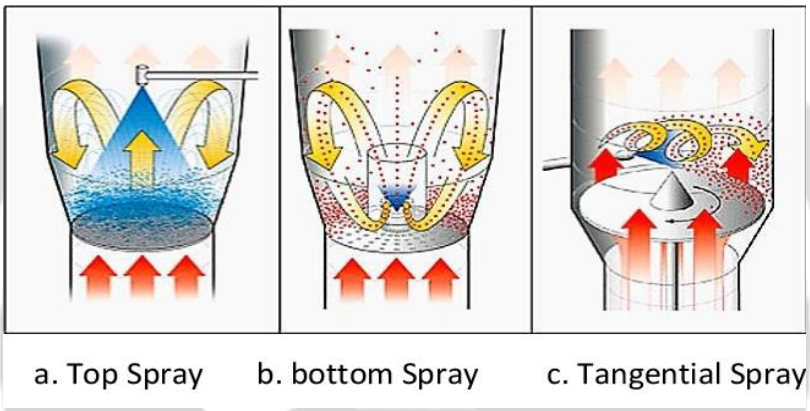


Figure- 3: FBS Techniques

2. NIMESULIDE PRE-FORMULATION STUDIES

It is the first step in the rational development of dosage forms of drug substances. Investigation of the physical and chemical characteristics of a pharmacological ingredient both by itself and when coupled with excipients is referred to as pre-formulation testing. It provides the details required to describe the makeup of the drug substance and establish a framework for its administration when combined with pharmaceutical excipients [5].

SOLUBILITY: the drug solubility was studied in different solvents it is a major parameter that determines the compatibility of the drug with a suitable solvent, from this, we find it freely soluble in acetone, slightly soluble in anhydrous ethanol, and practically insoluble in water.

MELTING POINT: Nimesulide shows a melting point of 138 -143 Celsius compared to the standard 143 Celsius from the monograph.

Potential Of Hydrogen (PH): Nimesulide PH was found to be PH 7 by using a PH meter.
Ultraviolet (UV) spectroscopy.

INSTRUMENTATION

(A) A UV spectrophotometer was used which is manufactured by Equiptronics and available in the analysis lab in college Figure 4.
Method: the stock solution was prepared with 10 mg nimesulide diluted with 100 ml acetone, from the above-prepared stock solution different concentrations of 5,10,15,20,25 parts per million (ppm) were taken by using a

pipette and then diluted to 10 ml using acetone as a solvent. scanned under a U. V spectrophotometer from a range of 200-400 nm Table no.1. The readings of different concentrations give absorbance at 259 nm wavelength [6].

SR.NO	CONCENTRATION IN PPM	ABSORBANCE	WAVELENGTH
1)	5 ppm	0.099	259 nm
2)	10 ppm	0.146	259 nm
3)	15 ppm	0.232	259 nm
4)	20 ppm	0.305	259 nm
5)	25 ppm	0.382	259 nm

Table- 1 : Readings of UV spectrophotometer

Figure- 4: UV spectrophotometer

(B)Infrared spectroscopy: In this the nimesulide and other polymers HPMCK30, and eudragitrs100 were individually exposed to IR radiation with a 1:1 proportion and the IR spectra were compared and interpreted by the functional groups [7].

Figure- 5: Infrared spectrometer

STABILITY TEST: It Is a Major Part to Determine the Stability of The Substances to Be Used in Formulation Because Sometimes the Substances Change Their Behavior After the Exposure to External Environment, Sunlight.

So, The Nimesulide Drug and Polymers HPMCK30, and Eudragitrs100 Were Mixed in 1:1:1 Concentration in The Vial Bottle. Then The Vial Bottle Was Kept in The Environmental Chamber For 15 Days [8].

UTILIZATION OF FBP IN THE MICROENCAPSULATION

Microencapsulation is the process in which small droplets or patches of liquid or solid material are girdled or coated by a continuous film of polymeric paraphernalia as shown in Figure 6[9].

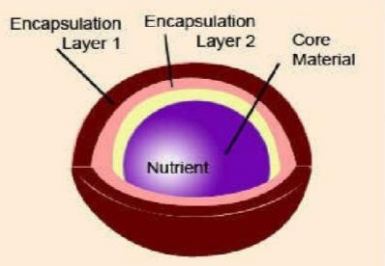


Figure- 6: Microencapsulation

Materials Used for Microencapsulation

- Core Materials: The core material is defined as the specific material to be coated which can be liquid or solid. The liquid core can include dispersed and dissolved paraphernalia. The solid core may be active constituents, stabilizers, diluents, excipients, and release-rate retardants or accelerators [10].
- Coating Materials: The coating material should be suitable for forming a film that is cohesive with the core material. The coating material should be chemically compatible and non-reactive with the core material and give the asked coating parcels, analogous to strength, strictness, impermeability, optical parcels, and stability [10].

PREPARATION OF POLYMERS SOLUTION

A) Eudragit RS100: It is taken as per the batch's concentration mentioned in table no.2.
They then poured in acetone quantity while continuously stirring at 600-800 rpm with a magnetic stirrer and after completely soluble the coloring agent was added quantity.

B) HPMCK30: It is taken as per the batch's concentration mentioned in table no.
Then pour in chloroform quantity while continuously stirring at 600-800 rpm with a magnetic stirrer till completely soluble.

SR.NO	INGREDIENTS	F1	F2	F3	F4
1)	Nimesulide	2 gm	2 gm	2 gm	2 gm
2)	Eudragit RS100	1.5 gm	2 gm	2.5 gm	3 gm
3)	HPMC k100	1.5 gm	2 gm	2.5 gm	3 gm
4)	Lactose	10 gm	10 gm	10 gm	10 gm
5)	Ethanol	q. s	q. s	q. s	q. s
6)	Chloroform	q. s	q. s	q. s	q. s

Table 2 : Master Formula of Nimesulide

3. MICROENCAPSULATION OF NIMESULIDE DRUG BY FBP PROCEDURE

According to the batches, the 2 gm nimesulide with 10 gm lactose was taken and transferred into the expansion or product chamber. The nozzle position was downside spray. the tubes for coating and air were fixed properly in FBP. The FBP machine was started at a time interval of 30 minutes the air force was adjusted sufficiently with optimum temperature and the lamp was on with the process on as well as spray test was started after all parameters were set. First, the HPMC K30 was coated after complete coating the next polymer was used Eudragit RS100 With 30-minute time intervals. The continuous observation has to be taken after the completion of coating the product is taken out and dried in the oven machine. after the formation of microspheres of nimesulide drug, it is filled into capsules 100 mg per capsule [12].

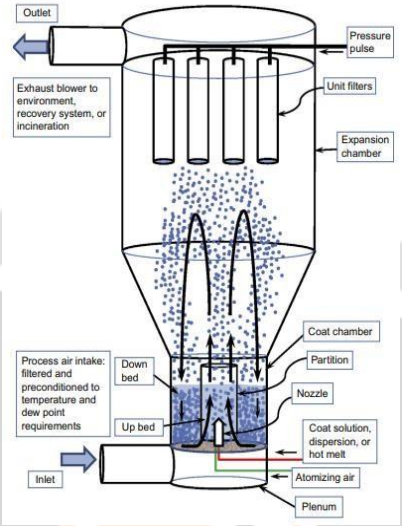


Figure -7: Microencapsulation method by FBP

The advantages of Microencapsulation Techniques are listed below

1. The important reason for microencapsulation is found to be either sustained or prolonged drug release.
2. This technique has been widely used for masking the taste and Odor of many drugs to improve patient compliance.
3. The drugs, which are sensitive to oxygen, moisture, or light, can be stabilized by Microencapsulation.
4. Many drugs have been microencapsulated to reduce toxicity and GI irritation for example ferrous sulphate and potassium chloride.
5. Alteration in the site of absorption can also be achieved by microencapsulation [11].

4. Evaluation parameters

1) ANGLE OF REPOSE: It determines the flow properties of powder; it is defined as the maximum angle possible between the surfaces of a pile of the powder and horizontal plane.

$$\Theta = \tan^{-1}(h/r)$$

Where 'θ' is the angle of repose, h is the height in cm, and r is the radius in cm [5].

Angle of repose	flow
< 25	Excellent
25-30	good
30-40	passable
>40	Very poor

Table- 3 : Angle of repose

2) PARTICLE SIZE DETERMINATION: The particle size was determined by the sieve method passing to different sizes. The particle size is in the range of 50-1500 nm [5].

3) **TAPPED DENSITY:** Density is defined as weight per unit volume (w/v). During tapping, particles gradually pack more efficiently, the powder volume decreases, and the tapped density increases.
Tapped density = weight of powder/ tapped volume of powder [5].

4) **BULK DENSITY:** It is the proportion of the powder's overall mass to its bulk volume. The weight powder, which had been put through a standard sieve #20, and #60 was poured into a measuring cylinder, and the starting weight was recorded [5].

Bulk density = mass of powder/volume of powder

5) **ELECTRON MICROSCOPE:** It is used to study the microstructure of nimesulide, check that the coating of the drug is properly done, and determine the particle size [5].

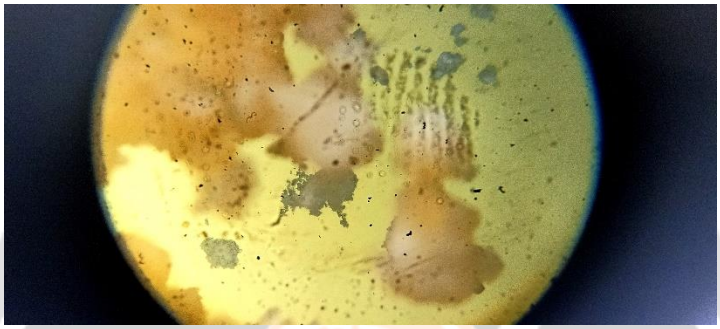


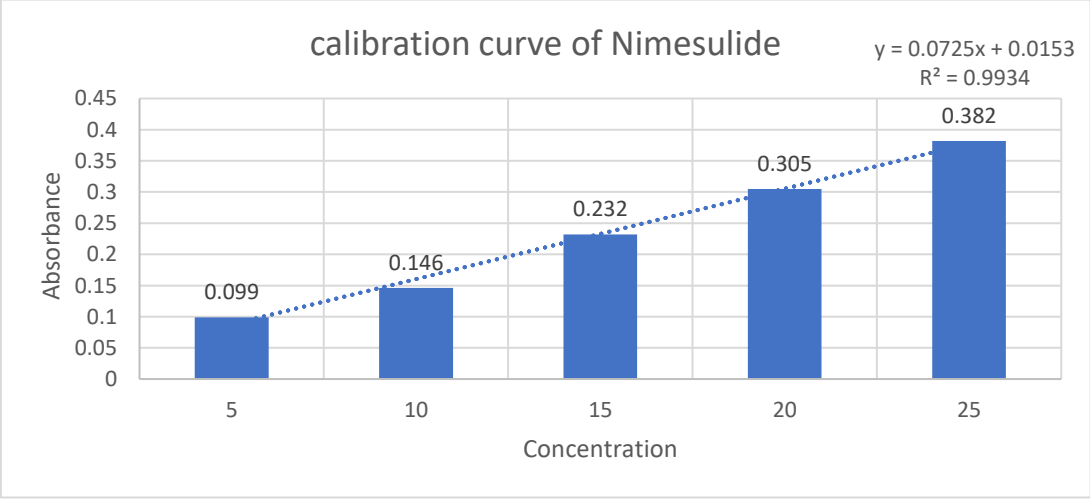
Figure-8: Nimesulide microencapsulation particles in electron microscope

6) **INVITRO DISSOLUTION TEST:** Dissolution medium for nimesulide taken 800 ml of 7.4 PH potassium phosphate buffer added tween 60 at 4 %.6 units of best two batches capsules taken for test at 36 c at 100 rpm with 1 hr interval. Nimesulide content determined by spectrophotometer [5].

5. Result And Discussion

The formulated nimesulide capsules stand with the pharmacopeia standards with better results and quality products. U.V results of nimesulide from calibration curve method in chart no.1

We get the y-intercept of 0.0153, a slope of 0.0725, a regression coefficient of 0.9934, a correlation coefficient of 0.1, a standard deviation of 0.00215, % Relative standard deviation of 14.3%. the batch F1 and F2 were found to be optimum better-quality results at 259 nm absorbance.



The validation of Nimesulide drug **Chart -1 :** Calibration curve of Nimesulide

SR.NO	CONCENTRATION	ABSORBANCE	WAVELENGTH	STANDARD	% OF PURITY
1	10	0.149	259 NM	0.150	98.40
2	10	0.148	259 NM	0.152	98.80
3	10	0.150	259 NM	0.151	99.60
4	10	0.148	259 NM	0.150	98.80
5	10	0.150	259 nm	0.149	99.60

Table- 4 : precision

SR.NO	CONCENTRATION	ABSORBANCE	WAVELENGTH	STANDARD	% OF PURITY
1	10	0.150	259 NM	0.150	99.60
2	10	0.150	259 NM	0.152	99.60
3	10	0.148	259 NM	0.151	98.80
4	10	0.149	259 NM	0.150	98.40
5	10	0.146	259 NM	0.149	96.90

Table- 5 : Intermediate precision

SR.NO	VOL OF STOCK FROM SAMPLE	VOL OF STOCK FROM STD	ABSORBANCE	MEAN	RECOVERY %
1) 50 %	1.0 ML	0.5 ML	1.110	1.105	95 .24%
2) 50%	1.0 ML	0.5 ML	1.109		
3) 50%	1.0 ML	0.5 ML	1.098		
4) 100 %	1.0 ML	1.0 ML	1.460	1.463	95.63%
5) 100%	1.0 ML	1.0 ML	1.470		
6) 100 %	1.0 ML	1.0 ML	1.459		
7) 150 %	1.0 ML	1.5 ML	1.858	1.860	97.97
8) 150%	1.0 ml	1.5 ml	1.863		
9) 150 %	1.0 ml	1.5 ml	1.860		

Table- 6 : Accuracy

IR spectra of Nimesulide

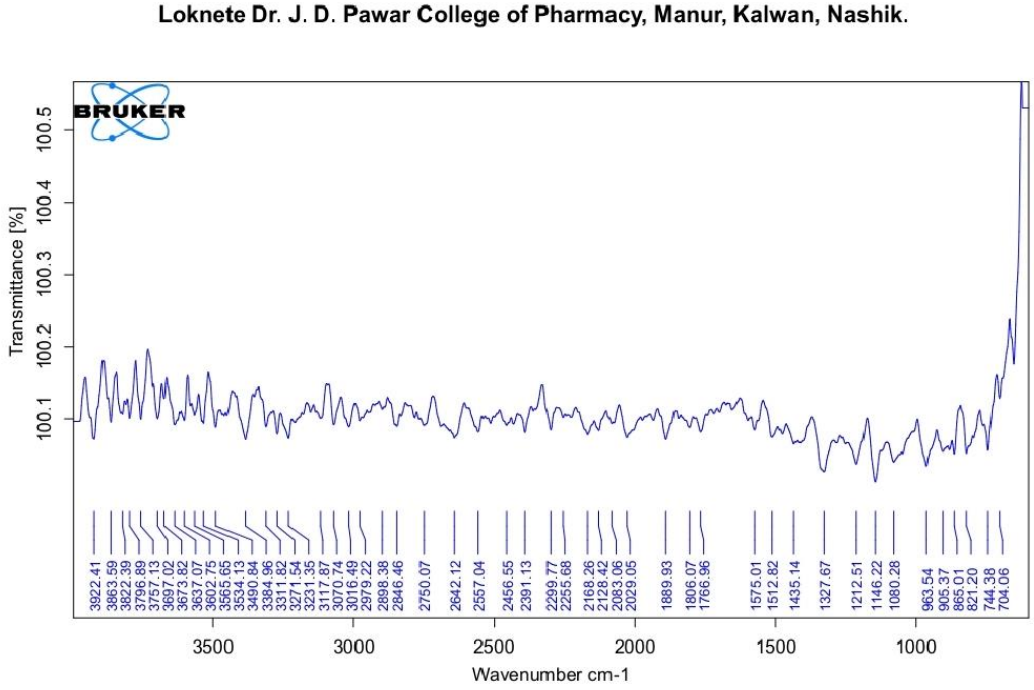


figure -9 : IR spectra of Nimesulide

IR spectra of nimesulide with Eudragit RS100 and HPMC K30 after environmental chamber to check the stability of the product was found to be no change in the physical nature and chemically stable store for 15 days in environmental chamber WITH ICH guidelines 40 C and relative humidity 75 %.

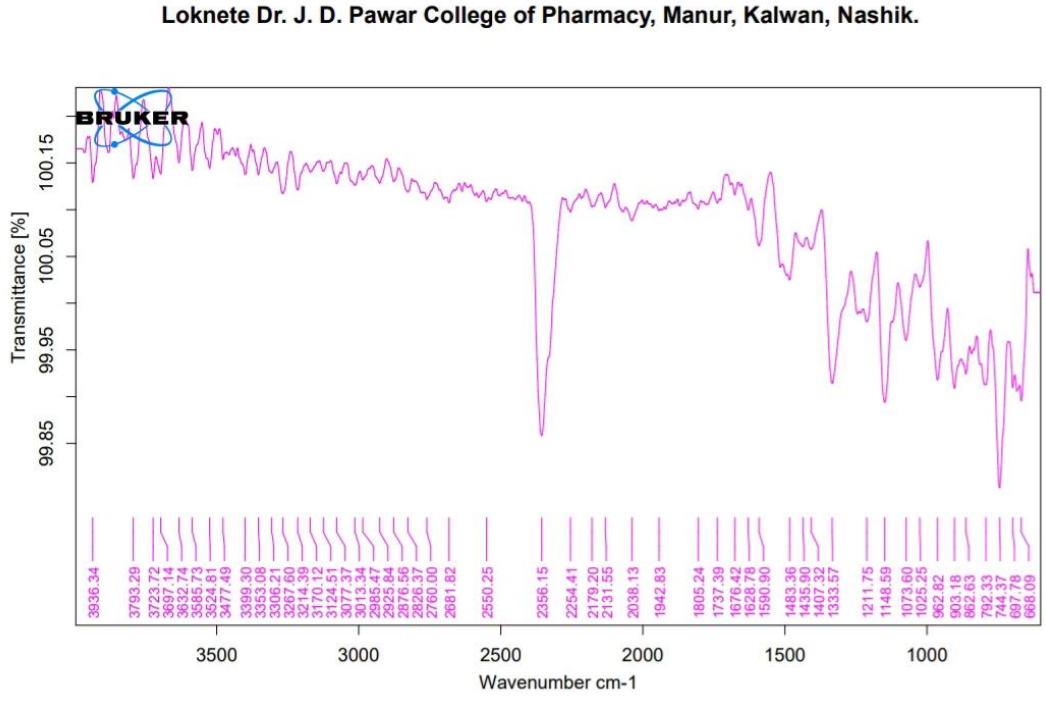


figure -10 : IR spectra of Nimesulide stability test

The flow properties of batches F1(22.67), and F2 (24.30) were found to be excellent angles of repose while batches F3 (26.46), and F4 (25.17) had good flow properties.

SR.NO	BATCHES	ANGLE OF REPOSE (Θ)	BULK DENSITY	TAPPED DENSITY
1.	F1	22.67	0.456	0.664
2.	F2	24.30	0.564	0.682
3.	F3	26.46	0.512	0.712
4.	F4	25.17	0.461	0.709

Table- 7: Flow property test

The invitro dissolution test for nimesulide was found to be equal to the standard as per the USP and the release of the drug through the capsules was sustained release at PH 7.4 with dissolution medium time interval of 1 hr.

Conclusion

This article aims to educate on fluidized bed technology. We attempt to cover the introduction and methods of formulation of nimesulide drug microencapsulation by polymers HPMC K30 and Eudragit RS100 in FBP. Various descriptions of the fluid bed process, including drying, granulation, coating (microencapsulation), and pelletization, are also provided. We concentrated on preformulation studies with validation tests by using various instruments such as UV spectrophotometer, IR spectroscopy, environmental chamber for stability test, and dissolution apparatus. FBP has significant benefits. High thermal efficiency drying and coating are made quick and simple by fluidization. So, the pharmaceutical business is currently seeing excellent outcomes from fluidized bed processing technologies.

Acknowledgment

I want to express my sincere appreciation and gratitude to our project guide, Mr. Rajendra Surawase, and our principal, Mr. Avish Maru, for their invaluable help and support in completing our project titled "Application of Fluidized Bed Processor in Pharmaceutical (Micro-Encapsulation)". The experience gained from this project was truly priceless, for his unwavering dedication and constant encouragement which enabled me to complete this project.

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