FORMULATION AND IN-VITRO EVALUATION OF FAST DISSOLVING TABLETS OF NIMESULIDE MICROPELLETS

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ABSTRACT

The notion of the Fast-Dissolving Drug Delivery System (FDTs) developed from the need to provide patients with a conventional means of taking their medication. FDTs are solid unit dosage forms that dissolve or disintegrate swiftly without the use of chewing or water. Nimesulide is a crystalline medication with low bioavailability due to its strong hydrophobicity and low water solubility. One such technology is spherical micropelletization, which provides maximum dissolution with improved wettability as well as uniform and spherical pellet size to guarantee smooth drug transit through the stomach. The goal of this research was to create an uncoated Nimesulide micropellets with improved bioavailability and micromeritic characteristics that may be utilised to construct rapid dissolving tablets. FDTs were created using the formulated Nimesulide micropellets. All formulations were subjected to general physical properties and in vitro dissolution tests. To investigate the efficacy of super disintegrants such as sodium starch glycolate and croscaramellose sodium, many combination ratios were created at various concentration levels. There were several tablet evaluation parameters used. In terms of in vitro dispersion time and drug release, tablets containing the above super disintegrants outperformed other formulations.

Key words: Nimesulide, micropellets, FDTs, Super disintegrants and Bioavailability.

INTRODUCTION

Nimesulide, also known as N-(4-Nitro-2-phenoxyphenyl) methane sulphonamide, is a non-steroidal anti-inflammatory medication that targets COX-2. It is a derivative of p-nitro phenyl methane sulphonamide. When taken orally, rectally, or topically, it belongs to a class of selective COX-2 inhibitors having significant analgesic action. According to the literature, Nimesulide Pka levels range from 5.9 to 6.56. This molecule is easily soluble in organic polar solvents but sparingly soluble in aqueous solution (0.01 mg/ml), indicating that it has low bioavailability and so belongs to BCS class II (Biopharmaceutical classification system).[1-2] It is commonly utilised for the treatment of numerous inflammatory disorders due to its analgesic and antipyretic effects. Furthermore, it is better tolerated and has fewer side effects than other nonsteroidal anti-inflammatory medications now in use. There are less digestive side effects. This chemical is structurally distinct from the coxibes, a novel class of COX-2 inhibitors.[3]

Because of its ease of self-administration, compactness, and ease of manufacture, the tablet is the most extensively used dosage form. Traditional tablets, on the other hand, are difficult to swallow for geriatric and paediatric patients, resulting in low patient compliance. To address this flaw, scientists have created "melt in mouth" or "mouth dissolving (MD)" tablets, which are novel drug delivery techniques. These are unique tablets that disintegrate, dissolve, and disperse in saliva. Their unique benefits, such as the ability to administer them without water, anywhere, at any time, make them ideal for elderly and paediatric patients. They're also good for people who are mentally sick, immobile, or don't have easy access to water. These tablets are popular as a dosage form of choice in the present market due to their benefits in terms of patient compliance, rapid onset of action, enhanced bioavailability, and superior stability.[4-5]

In order to create acceptable FDTs, taste masking is essential. In terms of clinical practise, NSAIDs are the most frequently prescribed medications by doctors for inflammatory conditions. Cyclooxygenase-II, the primary isozyme linked to inflammation, is inhibited by NSAIDs, which then has an anti-inflammatory effect. However, the concurrent inhibition of cyclooxygenase I and the resulting renal and gastrointestinal problems limit their regular use. Model active pharmaceutical ingredient nimesulide only affects cyclooxygenase-II while having no effect on cyclooxygenase-I. Simultaneously with nimesulide's anti-inflammatory effects, gastrointestinal tolerability noticeably improves, and the likelihood of renal failure is reduced. Nimesulide is also well tolerated by asthmatic patients due to its added effect of preventing the respiratory burst of phagocytosing neutrophils. In order to treat a variety of inflammatory illnesses such tonsillitis, pharyngitis, stomatitis, rheumatoid arthritis, osteoarthritis, low back pain, etc., it is one of the most frequently prescribed NSAIDs. Because of its high hydrophobicity and poor water solubility, nimesulide has a poor bioavailability when taken as traditional tablets.[6-9]

Furthermore, it is better tolerated and has fewer side effects than other NSAIDs now in use. Nimesulide uncoated micropellets were manufactured utilising the spherical agglomeration technique for the formulation of fast dissolving tablets in this study. FDTs were created employing superdisintegrants such as microcrystalline cellulose (Avicel PH-101), Crosscarmellose Sodium [Ac Di Sol], Sodium starch Glycolate, and Crospovidone, with granules prepared using a dry granulation process. This technology also opens up new economic opportunities, such as product differentiation, promotion, and patent extension. For

increased patient compliance, an ideal FDT must disintegrate quickly without water and be tasty.[10]

The primary goal of this research is to create Nimesulide uncoated micropellets in order to improve bioavailability and micromeritic characteristics, which would be advantageous during the processing of such crystalline drugs. These Nimesulide micropellets were then included into the FDTs. The Nimesulide micropellets based formulations disintegration time and dissolution rate were compared to normal conventional plain Nimesulide formulations.

Materials and Methods:

Nimesulide was obtained as gift sample from JNTU Kakinada, Andhra Pradesh (India). Croscarmellose sodium, Crospovidone, sodium starch glycolate, and Avicel-PH101 (Microcrystalline cellulose) were obtained as gift samples from JNTU Kakinada, Andhra Pradesh (India). Magnesium stearate, and Mannitol was used in the laboratory of SVU College of Pharmaceutical sciences, SV University, Tirupati, (India). All reagents and chemicals used were of AR grade.

Physical characterization studies (Drug-excipient compatibility study)

The physical and chemical properties of drug compounds alone and when coupled with excipients were investigated during preformulation testing. It was the first step toward logical dosage form development. By triturating together in a mortar and pestle and sifting through a sieve no 20 and keeping at room temperature in a glass container, drug alone and mixtures consisting of drug with various excipients at a 1:5 ratio were formed. This was done in open and closed glass vials for a month. The samples were taken out at 2 and 4 weeks of intervals and physical parameters such as colour change, if any, were noted. Finally, the mixtures are examined.

PREFORMULATION STUDIES

It is the first step in rational development of dosage forms of drug substance. 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.

Bulk Density (BD)

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, was poured into a measuring cylinder, and the starting weight was recorded. The bulk volume is the original volume. Using this information, the bulk density is computed using the formula below. It is expressed in g/ml and is given by

$$\mathbf{BD = M/Vb}$$

Where,

M is the mass of powder

Vb is the bulk volume of the powder.

Tapped Density (TD)

It is the ratio of total mass of the powder to the tapped volume of the powder. The powder was tapped 750 times to determine its volume, and if there was a variation of less than 2% between the two volumes, it was documented. If the percentage is greater than 2%, tapping is repeated 1250 times, and the volume of taps is recorded. Tapping was kept up until the volume difference between each successive reading was under 2% in a bulk density apparatus. It is expressed in g/ml and is given by

$$TD = M/Vt$$

Where,

M is the mass of powder

Vt is the tapped volume of the powder.

Carr's index (or) % compressibility

The parameters of powder flow are indicated. It is expressed in percentage and is give

$$\text{Compressibility Index (\%)} = [(TD-BD) \text{ X } 100]/TD]$$

Where,

TD is the tapped density of the powder and

BD is the bulk density of the powder

Table 1: Relationship between % compressibility and flowability

% Compressibility	Flowability
5-12	Excellent
12-16	Good
18-21	Fair passable
23-35	Poor
33-38	Very poor
>40	Very very poor

Hausner ratio

Hausner ratio is an indirect index of case of powder flow. It is calculated by the following formula.

$$\text{Hausner's ratio} = (\text{Tapped density x } 100)/ (\text{Poured density})$$

Where

TD is the tapped density.

BD is the bulk density.

Better flow qualities are indicated by hausner ratios below 1.25 than those over 1.25.

Angle of Repose

The friction forces in a loose powder can be measured by the angle of repose. It is an indicative of the flow properties of the powder. It is described as the greatest angle that can be formed between the powder pile's surface and the horizontal.

$$\mathbf{Tan\ \theta = h/r}$$

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

Where

'**θ**' is the angle of repose.

h is the height in cms

r is the radius in cms.

The funnel was set up on a stand at a specific height (h), and the powder mixture was allowed to flow through it. The height and radius of the newly created pile of powder were then measured to determine the angle of repose. Care was taken to see that the powder particles slip and roll over each other through the sides of the funnel. Angle of repose and powder flow characteristics are related.

Table 2: Angle of Repose as an Indication of Powder Flow Properties

S.No	Angle of repose	Type of flow
1	<20	Excellent
2	20 – 30	Good
3	30 – 34	Passable
4	>34	Very Poor

Preparation of Nimesulide micropellets:

The spherical agglomeration process was used to make Nimesulide uncoated micropellets. The medication solution was made by dissolving 1.5g of Nimesulide in 20ml acetone and slowly pouring it into 100ml of demineralized water at room temperature while swirling continuously at 400-500 rpm with a magnetic stirrer. In order to produce spherical micropellets with a mean diameter of 100-200 m, 6 mL of bridging liquid chloroform (10% v/v) was dropwise added to the crystallisation media after 20 minutes of continuous stirring. To obtain stable and spherical micropellets, the stirring was continued for 2 hours. Filtration was used to separate the spherical micropellets, which were then dried in a hot air oven at 45°C for 24 hours.

Preparation of fast dissolving tablets (FDTs):

Dry granulation was used to make FDTs of Nimesulide uncoated micropellets. Table.1 shows the formulation of Nimesulide uncoated micropellets based FDTs. Nimesulide, Sodium starch Glycolate, Croscarmellose sodium, Microcrystalline cellulose, and D-Mannitol were sieved 40

and thoroughly combined for 30 minutes in a plastic bag to ensure equal mixing. The power blend was gradually supplemented with the granulating fluid Alcoholic solution of PVP (10% w/v), which was then thoroughly blended to produce wet mass. This wet mass was then kneaded for a few minutes till a moist mass was formed. Sodium Saccharin and Powder Vanilla flavour were added to the aforesaid blend by co-sifting via sieve 40, and the mixture was weighed using diluent (DCP or lactose) and Avicel, which were fully combined in mortar using the geometric dilution technique and blended in a poly bag for 10 minutes (Addition of the artificial sweetener and the flavour for improving the palatability of the tablet). Re sieved through a # 20 sieve, the dry granules were then thoroughly combined with the lubricants. A single station tablet punching machine with flat facing punches was used to crush the lubricated granules. Plain Nimesulide were also made for comparison with Nimesulide uncoated micropellets FDTs.

In vitro drug release study of FDTs:

In vitro drug release was investigated using the USP 2 equipment, with 900 ml of saline phosphate buffer pH 7.4 dissolving media kept at 37 ± 0.5°C for 1 hour at 50 rpm. After proper dilution of the samples, 5ml of sample was taken at specified time intervals and replaced with an equal volume of fresh dissolution medium of the same pH, and the dissolved medication was assessed using UV spectrophotometer at max 300nm.

Evaluation of FDT tablets

Weight variation, hardness (Monsanto Hardness tester), thickness (Vernier callipers), friability (Roche friabilator), Disintegration and wetting times in vitro and in vivo, water absorption ratio, in vitro dispersion time, drug content, and in vitro dissolution were all evaluated.

Tablet Hardness

The Monsanto Hardness Tester was used to determine the hardness of the tablets. It's measured in kilogrammes per square metre. The mean and standard deviation values were determined after three tablets were randomly selected from each formulation.

Tablet Friability

The Roche Friabilator was used to determine the friability of the tablets. It's measured in percentages (%). Initially, ten pills were weighed W1(initial) and placed in the friabilator. For 4 minutes, the friabilator was spun at 25 rpm. W2 weighed the tablets once again (final). Percentage friability was then calculated using the formula:

$$\text{Friability (\%)} = \frac{\text{Initial Weight (W1)} - \text{Final Weight (W2)}}{\text{Initial Weight (W1)}} \times 100$$

Tablets with a friability of less than 1% are regarded acceptable.

Weight variation of tablets

To verify for weight variance, pills were chosen at random from each formulation and weighed individually. The United States Pharmacopoeia allows for some variance in pill weight.

Drug Content Uniformity

Five tablets were chosen at random, weighed correctly, and the average weight per tablet was computed. Individually, the tablets were ground to a fine powder. A 100 mL volumetric flask was filled with accurately weighed tablet powder equivalent to 100 mg of nimesulide. Up to the mark, add methanol. The solution was filtered after a few minutes, with the first few ml of the filtrate being rejected. In a 50 ml volumetric flask, 5 ml of filtrate was diluted up to the mark with methanol. The solution was filtered after a few minutes, with the first few ml of the filtrate being rejected. 5 mL of the filtrate was placed in a 50 mL volumetric flask, diluted to the desired concentration with methanol, and spectrophotometrically examined at 300 nm. The following formula was used to compute the content:

$$\text{Absorbance} = 0.0376 \times \text{Concentration} - 0.0094$$

Wetting time

The approach was used to calculate the time it took for tablets to moisten. The amount of time it took for a tablet to completely wet was determined by placing it on a piece of tissue paper that had been folded twice in a micro petri dish (i.d. = 6.5 cm). Each batch was subjected to three trials, with the standard deviation calculated as well. Yunxia Bi re-reported the procedure.

Water Absorption Ratio

The tablet's water absorption ratios were measured in Petri plates with a pH 6.8 phosphate buffer. The tablets were periodically removed from the petri plates and weighed on an electronic balance after surface water was removed by light blotting with a lab tissue for change of weight until a constant weight was achieved.

In-vitro Disintegration Time

One tablet was inserted in each of the basket's six tubes, and the apparatus was run with pH 6.8 (simulated saliva fluid) as the immersion liquid at 37°±1°C. At a rate of 100 cycles per minute, the assembly should be raised and lowered. The time in seconds it took for the tablet to completely disintegrate and leave no palpable mass in the instrument was measured and recorded.

In-vitro Dissolution Studies

Using the Electrolab Dissolution Test device, USP TDT 06P, the release rate of Nimesulide from mouth dissolving tablets was determined. The dissolution test was carried out with 900 ml of 6.8 phosphate buffer and 100rpm at 37±5°C. Every 5 minutes, aliquot (1 ml) of the solution was collected from the dissolving equipment and replaced with fresh dissolution medium for 60 minutes. Whatman filter paper no. 41 was used to filter the aliquots. These solutions' absorbance was measured at 391nm. Using an equation derived from a standard curve, the cumulative percentage drug release was computed.

Stability Studies

According to ICH recommendations, stability tests were carried out for the chosen formulations at 40°C and 75% relative humidity for a specific time period of up to 30 days in order to evaluate their stability with regard to their physical attributes and release characteristics.

Results and Discussion

The formulated FDTs complied with the pharmacopoeial criteria for weight homogeneity. According to I.P., all of the tablets met the assay requirements.

The hardness, percent friability, disintegration time, diameter, and thickness of the material were all well within acceptable standards.

The drug content of Nimesulide uncoated micropellet based formulation was determined to be between 98.45 and 103.51% (acceptable limit), and the tablet hardness was found to be between 3.53 and 4.06 kg/cm^2. The tablet's friability was found to be less than 1%, suggesting strong mechanical resistance. The average disintegration time for all batches was 9.34-14.25 seconds. The drug content of ordinary Nimesulide based formulations was determined to be between 96.40 and 100.25% (acceptable limit), while the tablet hardness was found to be between 3.23 and 4.1 kg/cm^2. The tablet's friability was found to be less than 1%, suggesting strong mechanical resistance.

Batches F15 and F18 were chosen as the best, as they included Crosscarmellose Sodium, crospovidone, Sodium starch Glycolate as a superdisintegrants. It disintegrates after 10.44 seconds and 14.30 seconds, respectively. The dissolving investigation revealed that F15 released 98.30% of its medicine while F18 released 99.52 percent of its drug after 30 minutes. The Nimesulide uncoated micropellet based formulation F15 had a better dissolving profile than the plain Nimesulide based formulation. The formulations all had excellent organoleptic qualities, a comfortable tongue feel, and no gritty taste. According to the findings of this study, FDTs of Nimesulide uncoated micropellet may be effectively made utilising various superdisintegrants, and they take less time to disintegrate and have a quicker dissolving rate than plain Nimesulide formulations.

Figure No. 1. Standard calibration curve of Nimesulide

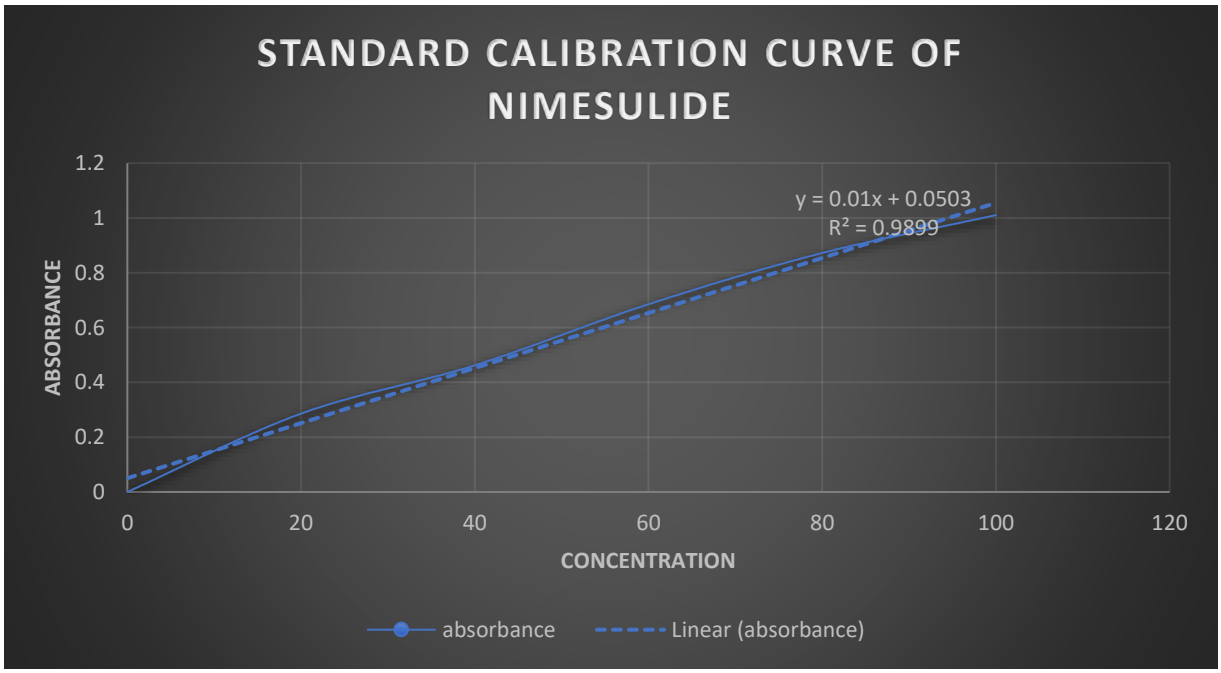


Table 3: Formulations of Nimesulide uncoated micropellets based FDTs

Ingredients (Quantity in mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20
Nimesulide uncoated micropellets	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Croscarmellose sodium	4.8	9.6	14.4	19.2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sodium starch glycolate	-	-	-	-	4.8	9.6	14.4	19.2	-	-	-	-	-	-	-	-	-	-	-	-
Crospovidone	-	-	-	-	-	-	-	-	4.8	9.6	14.4	19.2	-	-	-	-	-	-	-	-
Croscarmellose sodium + Crospovidone	-	-	-	-	-	-	-	-	-	-	-	-	4.8	9.6	14.4	19.2	-	-	-	-
Sodium starch glycolate + Crospovidone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4.8	9.6	14.4	19.2
Avicel-PH101	30	29.8	28.4	20.6	25	20.4	17	20	30	29.8	28.4	20.6	25	20.4	17	20	30	29.8	28.4	20.6
Lactose monohydrate	25	20.4	17	20	30	29.8	28.4	20.6	25	20.4	17	20	30	29.8	28.4	20.6	25	20.4	17	20
Mannitol	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30	30
Colloidal Silica	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2	1.2
Magnesium stearate	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0
Talc	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0	6.0
Tablet weight	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200

Table 4: Physical properties of Nimesulide uncoated micropellets

Formulation Code	Drug content (%)	Friability (%)	Hardness (kg/cm^2) ±SD	Diameter (mm) ±SD	Thickness(mm) ±SD	Disintegration time (sec)±SD
F1	93.45	0.32	4.12±0.01	9.03±0.02	4.45±0.03	16.52±0.02
F2	95.32	0.405	3.95±0.05	9.15±0.03	4.69±0.01	12.62±0.05
F3	94.40	0.15	4.02±0.03	9.16±0.02	4.77±0.02	14.32±0.02
F4	93.23	0.20	4.11±0.01	9.21±0.01	4.35±0.01	16.60±0.02
F5	95.50	0.31	4.19±0.03	9.46±0.03	4.44±0.03	20.32±0.01
F6	92.48	0.18	4.06±0.02	9.35±0.02	4.75±0.01	14.64±0.02
F7	91.67	0.29	3.85±0.05	9.18±0.01	4.59±0.02	11.44±0.01
F8	95.20	0.30	4.21±0.05	9.13±0.03	4.49±0.03	10.65±0.02
F9	94.80	0.015	3.72±0.01	9.56±0.01	4.75±0.02	20.17±0.01
F10	94.45	0.099	3.24±0.06	9.94±0.02	4.94±0.03	12.46±0.01
F11	96.33	0.16	3.76±0.04	9.46±0.03	4.85±0.01	13.89±0.01
F12	98.74	0.023	3.54±0.02	9.57±0.02	4.68±0.02	12.78±0.02
F13	96.31	0.11	4.02±0.01	9.43±0.01	4.46±0.03	11.80±0.02
F14	98.50	0.34	4.36±0.02	9.15±0.03	4.77±0.01	14.65±0.01
F15	101.68	0.012	4.28±0.06	9.38±0.01	4.69±0.03	09.37±0.02
F16	97.72	0.089	4.64±0.05	9.29±0.02	4.59±0.02	16.38±0.01
F17	98.46	0.12	3.7±0.04	9.56±0.03	4.46±0.03	14.98±0.02
F18	103.20	0.018	3.98±0.01	9.72±0.01	4.82±0.03	09.32±0.01
F19	99.48	0.098	3.12±0.06	9.39±0.03	4.71±0.02	11.49±0.01
F20	99.32	0.24	3.95±0.03	9.16±0.03	4.94±0.01	13.26±0.01

Table no.5: Preformulation studies

S. No	Formulation	Angle of repose (θ)	Loose bulk density(gm/cm^3)	Tapped bulk density(gm/cm^3)	Carr's Index
1	F1	24º22´	0.481	0.624	22.91
2	F2	23º13´	0.475	0.526	9.69
3	F3	20º32´	0.461	0.526	12.35
4	F4	23º54´	0.476	0.540	11.85
5	F5	23º68´	0.478	0.555	13.87
6	F6	25º44´	0.492	0.605	18.67
7	F7	24º75´	0.485	0.625	22.4
8	F8	22º81´	0.465	0.588	20.91
9	F9	24º69´	0.482	0.526	8.36
10	F10	25º78´	0.500	0.625	20.00
11	F11	24º63´	0.487	0.625	22.08
12	F12	25º95´	0.465	0.540	13.9
13	F13	24º71´	0.500	0.555	10.0
14	F14	25º13´	0.476	0.588	19.08
15	F15	23º43´	0.476	0.526	9.56
16	F16	25º21´	0.476	0.555	14.33
17	F17	25º36´	0.487	0.555	12.25
18	F18	20º53´	0.465	0.526	11.65
19	F19	22º53´	0.476	0.526	9.56
20	F20	25º37´	0.487	0.606	19.6

Table No. 6: Wetting time and water absorption study

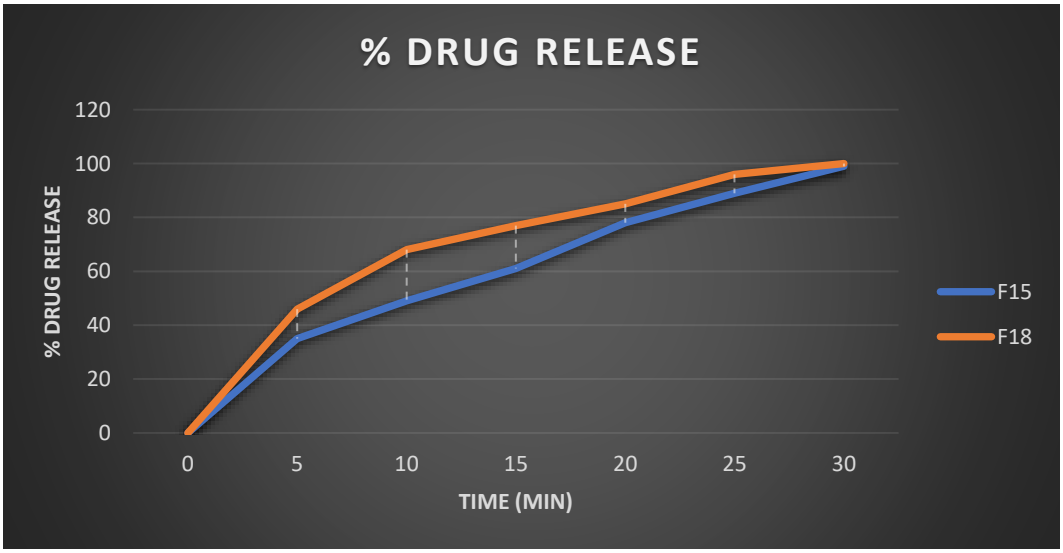
Formulation Code	Wetting Time (n=3)	Water Absorption Ratio (n=3)
	Mean ± SD	Mean ± SD
F1	31 ± 1.45	41.04 ± 0.51
F2	25 ± 0.27	39.81 ± 0.14
F3	21 ± 0.19	40.42 ± 0.08
F4	52 ±0.75	41.33 ±1.29
F5	39 ±1.08	39.92 ±0 .82
F6	115 ± 0.85	42.11 ± 0.18
F7	109 ±0.45	41.02 ± 1.28
F8	99 ± 0.91	38.27 ± 0.17
F9	91 ±0.07	39.39 ± 1.47
F10	75±1.34	38.03±1.25
F11	84 ± 1.52	43.23±1.25
F12	91 ± 0.17	42.29 ± 1.47
F13	105 ± 0.09	40.33 ±1.29
F14	98 ±0.71	41.37 ± 0.17
F15	108 ±1.09	39.14 ± 0.51

F16	117 ± 0.81	39.11 ± 0.18
F17	103 ±0.39	40.81 ± 0.14
F18	95 ± 0.81	40.28 ± 1.28
F19	93 ±0.09	41.51 ± 0.08
F20	84±2.34	39.87 ±0 .82

Table No.7: In-vitro Disintegration Time, Drug Content Uniformity

Formulation Code	In-vitro Disintegration Time In seconds	Drug Content Uniformity (n=5) (mg)
F1	33 ± 0.63	93.80 ± 0.01
F2	26 ± 0.32	95.45 ± 0.02
F3	29 ± 0.34	94.25 ± 0.06
F4	45 ± 0.45	92.35 ± 0.03
F5	38 ± 0.41	93.50 ± 0.04
F6	94 ± 0.79	91.00 ± 0.01
F7	95 ± 0.65	90.85 ± 0.004
F8	97 ± 1.02	93.45 ± 0.05
F9	93 ± 0.26	94.30 ± 0.85
F10	88 ± 0.85	92.25± 0.83
F11	98 ± 0.72	96.65 ± 0.01
F12	94 ± 0.36	97.05 ± 0.02
F13	95 ± 0.29	95.15 ± 0.06
F14	101 ± 0.64	96.65 ± 0.03
F15	106± 0.46	98.50 ± 0.04
F16	97 ± 0.78	97.20 ± 0.01
F17	100 ± 075	97.85 ± 0.004
F18	112± 0.49	99.05 ± 0.05
F19	95 ± 0.36	97.30 ± 0.85
F20	84 ± 0.89	96.27± 0.83

Figure No. 2. % Drug Release of Nimesulide Micropellets FDTs



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