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Formulation and evaluation of colon targeted matrix tablet of ibuprofen

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Abstract

The present work involves the formulation of colon targeted matrix tablet of Ibuprofen by using direct compression method. Literatures regarding, Ibuprofen tablet dosage form preparation, excipients selection, manufacturing method etc., has been collected and reviewed. In this work, selection of excipients was done based on a literature review. Excipients include Eudragit S100, Ethyl cellulose, Lactose, Talc, Magnesium stearate. Quantities of the excipients were selected performing FT-IR method which is an HIS of Fourrts India Laboratory. Preformulation studies have also been performed to study the nature of API and compatibility of API with excipients by physical observation and FT-IR studies. The result showed that API was compatible with all the excipients selected. The tablets were formulated by direct compression method using the selected excipient quantities. The formulated tablets were tested for both pre-compression parameters and post compression parameters as per requirements of standards. Pre-compression parameters such asbulk density, tapped density, compressibility index, Hausner's ratio and compressibility index. The results obtained indicate that it has good flow property for direct compression. The formulated Ibuprofen matrix tablets were coated with enteric polymer Eudragit FS30D by pan coating method. The prepared tablets were evaluated for weight variation, hardness, thickness, friability, drug content, and disintegration time and *in-vitro* dissolution studies. All these parameters were found to be within the standard limits. Comparative studies of coated Ibuprofen tablets and uncoated Ibuprofen tablets are evaluated for the hardness, thickness, *in-vitro* dissolution studies and disintegration time. Out of six formulations, the formulation F6 showed 98.51% drug release at 24 hrs. Since it provide greater protection to the core under acidic condition while at the same time show the fastest drug release under intestinal pH. So the formulation F6 was considered as the confirmatory trial and it was subjected for stability studies up to three months of accelerated stability $40^0C \pm 2C^0$, 75 %± 5 % RH and found to be within limits.

Keywords: Ibuprofen; Colon; Matrix; Eudragit S100; Ethyl cellulose; Lactose; Talc; Magnesium stearate

1. Introduction

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage forms [1]. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost effective manufacturing process. The reasons that the oral route achieved such popularity may bein part attributed to its ease of administration, belief that by oral administration of the drug is well absorbed. All the pharmaceutical products formulated for systemic delivery via the oral route of administration irrespective of the mode of delivery and the design of dosage forms must be developed within the intrinsic characteristics of GIT physiology, pharmacokinetics and pharmacodynamics and formulation design to achieve a systemic approach to the successful development of an oral pharmaceutical dosage form [2]. Colon Targeted Drug Delivery System (CTDDS) may be following the concept of Controlled or Sustained drug Delivery System. For CTDDS oral route of administration has

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received most attention. Inflammatory bowel disease (IBD) is a group of inflammatory conditions of the colon and small intestine. Crohn's disease and ulcerative colitis are the principal types of inflammatory bowel disease. Ulcerative colitis is an idiopathic, chronic inflammatory disorder of the colonic mucosa, which starts in the rectum and generally extends proximally in a continuous manner through part of or the entire colon however, some patients with proctitis or left-sided colitis might have a caecal patch of inflammation [3].

2. Material and methods

2.1. Materials

Ibuprofen is a gift sample from Shasun chemicals, Chennai. The other Excipients are Eudragit S100 is from Vikram Thermo (India) LTD Ahmedabad, and Ethyl cellulose is from Jalan cellulose. Co, India, also used diluents and lubricants such as Lactose (DCL 21) (Diluent Cabot sanmar LTD, Chennai), Talc (Abishek organics, Mumbai), Magnesium stearate (Amishi Drugs and Chemicals,Gujarat).

2.2. Methods

2.2.1. Preformulation Studies

Pre formulation is the first step in the rational development of dosage form of a substance and is defined as an investigation of physical and chemical properties of drug substance alone and when combined with excipients [4]. This initial learning phase is known as pre formulation. The basic purpose of the pre formulation activity is to provide a rational basis for the formulation approaches, to minimize the chances of success in formulating an acceptable product and to ultimately provide a basis for optimizing drug product quality and performance. The first step in any formulation activity is careful consideration of a complete physicochemical profile of the active ingredients available, prior to initiating a formulation development activity [5].

2.3. Important Parameters Evaluated During Pre formulation Studies

2.3.1. Evaluation of API

The Evaluation of Ibuprofen was done according to IP. Following are some of the important parameters evaluated during pre formulation studies [6].

2.3.2. Solubility

Aqueous solubility is an important physicochemical property of drug substance, which determines its systemic absorption and in turns its therapeutic efficacy [7].

Table 1 Solubility Specifications

Descriptive terms	**Approximate volume of solvent in Milli liters per gram of solute**
Very soluble	Less than 1
Freely soluble	From1 to10
Soluble	From10 to30
Sparingly soluble	From30 to100
Slightly soluble	From100 to1000
Very slightly soluble	From1000 to10,000
Practically insoluble	More than 10,000

2.3.3. Melting point

The temperature at which the first particle of the substance completely melts is regarded as melting point of the substance. The temperature at which the first particle start to melt and last particle completely melts is regarded as melting range. Melting point of Ibuprofen was conducted as per monograph [8].

2.3.4. Loss on drying

The loss on drying test is designed to measure the amount of water and volatile matters in a sample when the sample is dried under specified conditions. Loss on drying of Ibuprofen was measured by using moisture balance. Weigh approximately 2gm of Ibuprofen and placed into a plate of moisture balance. Set the temperature to 29°C. Measure the moisture content of drug in percentage [9].

2.3.5. Flow Properties (Angle of Repose)[10]

Angle of repose is defined as the maximum angle possible between the surface of the pile of the powder and horizontal plane. The angle of repose of the powder or granules was determined by fixed funnel method. To assess the flow property of the powder granules, the height of the funnel was adjusted in such a way that the tip of the funnel just touches the apexof the heap of the powder or granules above a paper that was placed on a flat horizontal surface.Accurately weighed powder blend was taken in a beaker. It was allowed to flow through the funnel freely on the surface of the paper to form a cone shaped pile. The diameter of the cone (d) and the height (h) of the pile was noted. From the diameter, radius (r) was calculated. The angle of repose (θ) was calculated using the following formula.

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

Table 2 Angle Of Repose of Powder Flow Property

Flow properties	Angle of repose(degree)
Excellent	25-30
Good	31-35
Fair	36-40
Passable	41-45
Poor	46-55
Very poor	56-65
Extremely poor	>66

2.3.6. Bulk density [11]

Bulk density is a characteristic of a powder rather than individual particles and is given by the mass M, of the powder occupying a known volume, Vo. It is expressed in g/ml. An accurately weighed quantity of granules was transferred into a 50 ml measuring cylinder with the aid of the funnel. The unsettled apparent volume, to the nearest graduated unit occupied by the granules was measured. Bulk density was determined using the formula.

$$\rho \text{ bulk} = m/v0$$

Where,
ρ bulk = Bulk density; m = Mass of the blend Vo = Untapped Volume

2.3.7. Tapped density

Tapped density is achieved by mechanically tapping a measuring cylinder containing a powder sample [12]. After observing the initial volume, the cylinder is mechanically tapped, and volume readings are taken until little further volume change is observed. The measuring cylinder containing a weighed quantity of granules (after measurement of bulk density) was subjected to 500 taps in tapped density tester (Electro Lab USP II). The tapped density was calculated by using the formula.

$$\rho t = m/ Vt$$

Where,
ρ t = Tapped density;
m = Mass of the granules Vt = Final tapped volume.

2.4. Measurement Of Powder Compressibility

2.4.1. Carr's compressibility index [13]:

Compressibility index are a measure of the tendency for arch formation and the ease with which the arches will fail. Table No: 3 show the relationship between compressibility index and flowability.

$$CI = \rho t - \rho bulk / \rho t \times 100$$

Where,
CI = Compressibility index
ρ bulk = Bulk density
ρ t = Tapped density

Table 3 Carr's Compressibility Index

S. No.	Compressibility index (%)	Flow characters
1	<10	Excellent
2	11-15	Good
3	16-20	Fair
4	21-25	Passable
5	26-31	Poor
6	32-37	Very poor
7	>38	Extremely poor

2.4.2. Hausner's ratio [14]

Hauser found that the ratio ρ t / ρ bulk was related to interparticle friction and, as such could be used to predict powder flow properties. He showed that powders with low interparticle friction, such as coarse spheres, had ratios of approximately 1.2; whereas more cohesive, less free flowing powders such as flakes have values greater than 1.6. Table No: 4 shows the flow characters and corresponding Hauser's ratio.

$$\text{Hauser's Ration} = \rho t / \rho bulk$$

Where,
ρ bulk = Bulk density
ρ t = Tapped density

Table 4 Hauser's ratio

S.No.	Hauser's ratio	Type of flow
1	1.0 –1.11	Excellent
2	1.12 –1.18	Good
3	1.19 – 1.25	Fair
4	1.26 – 1.34	Passable
5	1.35– 1.45	Poor
6	1.46 -1.59	Very poor
7	>1.60	Extremely poor

2.4.3. Particle Size Analysis[15-16]

In case of tablets, size influences the flow and the mixing efficiency of powders and granules. Size can also be a factor in stability. Fine materials are relatively more open to attack from atmospheric oxygen, the humidity and interacting excipients than are coarse materials.

Particle size distribution of the drug was estimated by sieving method. The sieves are stacked on top of one another in ascending degrees of coarseness. The test powder, for example 10gm, was placed on the top sieve. The nest of sieves was subjected to a standard period of agitation. The weight of material retained on each sieve was accurately determined. Percentage of powder retained on each sieve was calculated by using the following formula.

2.4.4. Drug-Excipient Compatibility Studies [17-19]

In the tablet dosage form the drug is in intimate contact with one or more excipients; the latter could affect the stability of the drug. Knowledge of drug- excipient interactions is therefore very useful to the formulator in selecting appropriate excipients. This information may be present for known drugs. For new drugs or new excipients, the pre formulation scientist must generate the needed information.

Physical observation

Active ingredient was mixed well with all excipients in binary ratio and small portion of this mixed powder was placed in a 2ml of cleaned and dried vial. This vial was kept for observation in stability chamber at 40°C ± 2°C / 75 ± 5% RH. Mixtures were also placed at 2°C -8°C, 50°C and room temperature (Control). Physical observation has been carried out visually at the initial stage, after 15 days and after 1 month at 40°C ± 2°C / 75 ± 5% RH.

Table 5 Drug-Excipient Compatibility Studies

S.No	Drug and excipients	Parameter
1	Ibuprofen	Colour change
2	Ibuprofen + Excipients	Colour change

Chemical compatibility studies by FT- IR:
Physical compatibility studies were assured by FT-IR studies. The pure drug sample, drug-excipient mixtures of the formulation were chosen for the study. The FT-IR spectra's of the above samples were studied after a period of 30 days from preparation of the mixtures, to facilitate prompt detection of incompatibility. The spectra's were obtained by preparing Potassium bromide pellets under dry condition by using pellet press.

The spectra of the pure drug sample and that of the drug-excipient mixtures were compared to check the incompatibility problems. If there are no changes in peaks of mixture when compared to pure drug, it indicates the absence of chemical interaction.

2.5. Preparation of Granules for Compression

Matrix tablet of Ibuprofen was prepared by direct compression method. All tablet ingredients was accurately weighed as mentioned in Table No. 16. The average weight of each uncoated tablet was 450 mg [20].

2.6. Formulation of colon targeted matrix tablet of Ibuprofen [21].

The method used in the formulation of colon targeted matrix tablet of Ibuprofen was direct compression method. All the batch formulations in these studies are formulated by direct compression method.

2.6.1. Weighing

A required quantity of raw materials was weighed accurately.

2.6.2. Sifting

The Ibuprofen, eudragit S100 and ethyl cellulose were sifted using 60 # mesh. Lactose (DCL 21) sifted through 40 # mesh.

2.6.3. Mixing

The sifted powders were mixed in polythene bag for ten minutes.

2.6.4. Lubrication

The above dried granules were lubricated by using Talc. Talc is sifted through 40# mesh and magnesium stearate, sifting through 60# mesh after that mixed for 5 minutes in polythene bag.

2.6.5. Compression

Then final lubricated blend was compressed at an average weight of 450 mg using punch size 14.2 mm.

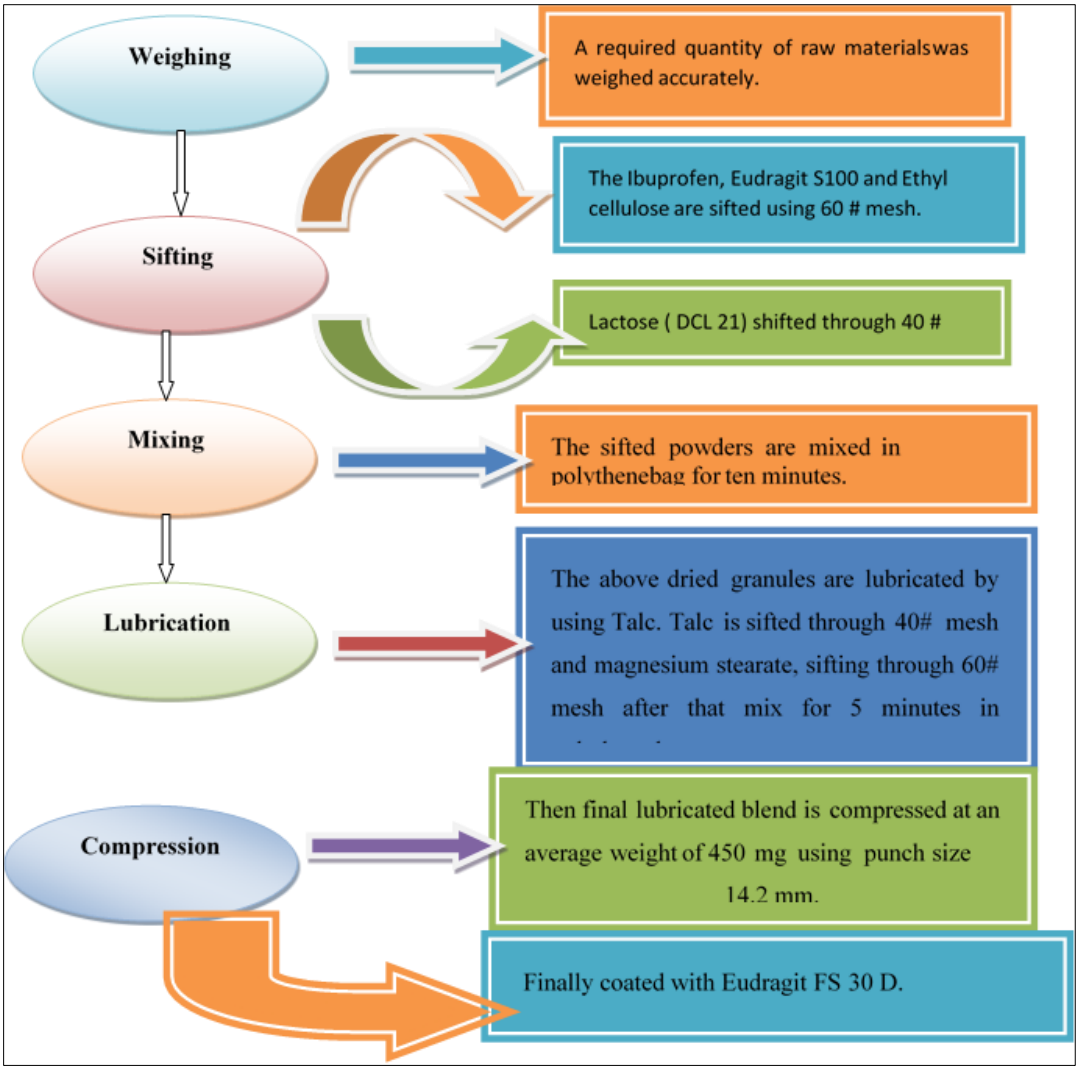

Figure 1 Formulation Flowchart of Ibuprofen Matrix Tablets by Direct Compression Method

2.7. Evaluation of Powder Blend [22]

The powder blends were evaluated for the following parameters before compression into

- Angle of repose
- Bulk density
- Tapped density
- Compressibility index and Hausner's ratio.
- Moisture content.

These procedures are discussed earlier in pre formulation studies.

2.7.1. Evaluation of Post-Compression Parameters [23]:

General appearance

The tablets should be free from cracks, depression, pinholes etc. the color and polish of the tablets should be uniform on whole surface. The surface of the tablets should be smooth.

Hardness

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging, and shipping. Tablet hardness has been defined as, the force required to break a tablet in a diametric compression test81.Tablet hardness of all the formulations was measured using a Monsanto hardness tester.

Thickness

Tablet thickness is an important parameter to be controlled to facilitate packaging. Tablet thickness, at constant compressive load, varies with changes in die fill, with particle size distribution and packing of the particle mix being compressed; whereas at constant die fill, thickness varies with variations in compressive load. Tablet thickness must be controlled within a ±5% variation of a standard value. Any variation within a particular lot should not be apparent to the unaided eye of the consumer.

Friability

Friability is a measure of the resistance of the tablet to abrasion. Tablets are generally subjected to a standardized level of abrasion for a given time and the friability is expressed as a % weight loss. The measure is useful to determine the ability of the tablet to withstand abrasion during handling, coating, packing and transport. The laboratory friability tester is known as the Roche friabilator. This device subjects the tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that rotates at 25 rpm, dropping the tablets form a height of 6 inches with each revolution. Twenty tablets were weighed accurately and placed in the friabilator and was operated for 100 revolutions or 4 minutes. The tablets were then de dusted and weighed. The weight loss of 0.5 to 1% is considered as acceptable limits for conventional uncoated tablets. The weight loss was calculated using the formula.

$$Friability, F(5) = \frac{Weight\ loss}{Initial\ weight}$$

Disintegration Test

USP disintegration test specifies that one tablet is added to each of the six tubes in the USP disintegration apparatus. The apparatus is operated without disks, using simulated gastric fluid (pH 1.2) at 370C for 2 hrs. The tablets are then removed and must show no evidence of disintegration, cracking or softening. Disks are then added and the apparatus is operated using simulated intestinal fluid (pH 7.4) at 37°C for a period of time limit specified in the monograph. The product passes the test if all tablets are disintegrated.

Weight Variation Test

Twenty tablets were selected randomly and weighed individually. Calculate average weight and compare the individual tablet weight to the average. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in and none deviate by more than twice the percentage.

Table 6 Percentage Deviation for Weight Variation Test

S.No	Average weight of tablet (mg)	Percentage deviation
1	80 mg or less	± 10.0
2	More than 80 mg but less than 250 mg	± 7.5
3	250 mg or more	± 5.0

In-Vitro Dissolution Studies

The release rate of Ibuprofen from tablets were determined using USP Dissolution Testing Apparatus 2 (paddle method). The test was performed using 900ml of 0.1N HCL at 37°+0.5°C and 100 rpm for first 2 hrs. Then replaced with 7.4 pH phosphate buffer and continued for 24 hrs. A liquot volume of 5ml was withdrawn at regular intervals and replaced with fresh buffer diluted. The samples were replaced with fresh dissolution medium. The drug release is determined from the absorbance of the sample and standard.

Dissolution media Preparation:

Preparation of 0.1N HCl - 8.5 ml of concentrated HCl was added to 1000 ml of purified water and the pH is 1.2. Preparation of pH 7.4 phosphate buffer - Dissolved 6.8g of potassium Dihydrogen phosphate in 1000 ml of purified water and adjusted the pH to 7.4 by using 0.1 N sodium hydroxide solution.

Test A

Dissolution at Acid stage medium:
Dissolution Medium: 900 ml of 0.1 N HCL
Apparatus: USP Type II (Paddle)
Rotation: 100 rpm
Duration: 2 hours
Temperature: 37˚C ± 0.5˚C

Standard Preparation

Weigh accurately about 27.0 mg of Ibuprofen working standard in to 100ml volumetric flask, add 50ml of methanol, shake for 5 minutes and make up to volume with methanol. Pipette out 10ml of the solution in to 100ml volumetric flask and make up to volume with dissolution medium. Further dilute 5ml of this solution to 10ml volumetric flask and make up to volume with dissolution medium.

Test preparation

Withdraw 20ml of sample from each bowl and filter. Measure the absorbance of both standard and Test preparation at 222 nm using dissolution medium as blank and calculate the content of Ibuprofen per tablet.

2.8. ASSAY (By UV method)

2.8.1. Preparation of standard Solution

Weigh accurately 100.0 mg of Ibuprofen working standard in a clean, 100 ml volumetric flask and 10ml of Acetonitrile. Shake well to dissolve and make up the volume to 100ml with phosphate buffer. Mix well and dilute 5ml with of this solution to 50ml with Phosphate buffer. Further dilute 5ml of the resulting solution to 100ml with phosphate buffer.

2.8.2. Preparation of sample solution

Weigh accurately about 190 mg of crushed tablet powder in a clean, 200 ml volumetric flask and add 10ml of acetonitrile. Shake well and make up the volume to 200 ml with Phosphate buffer. And dilute 5ml with of this solution to 50ml with Phosphate buffer. Further dilute 5ml of the resulting solution to 25ml with phosphate buffer

Procedure

Measure the absorbance of both the standard and sample preparation at 222 nm using Phosphate buffer as blank. Assay was calculated from the following formula.

2.9. Stability studies [24]

Stability of a formulation can be defined as the time from the date of manufacture of the formulation until its chemical or biological activity is not less than a pre-determined level of labeled potency and its physical characteristics have not changed appreciably or deleteriously. Formulation and the development of pharmaceutical products are not complete without proper stability analysis. It is carried out to assess the physical and chemical stability and safety use of the product. The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug products varies with the time under the influence of a variety of environmental factors such as temperature, humidity, and light

enabling recommended for storage conditions and shelf life. The ICH guideline recommends the following storage conditions for stability studies:

Table 7 Stability conditions according to ICH guidelines

S.No.	Study	StorageCondition
1.	Longterm	25°C±2°C / 60%RH±5%RH
2.	Intermediate	30°C±2°C / 65%RH±5%RH
3.	Accelerated	40°C±2°C / 75%RH±5%RH

2.9.1. Accelerated stability studies

Generally the observation of the rate at which the product degrades under normal room temperature requires a long time. The International Conference of Harmonization (ICH) Guidelines titled "Stability testing for new drug substances and product" (Q1A) describes the stability test requirements for drug registration application in the European Union, and United States of America [25]. The accelerated stability was carry out by ICH guidelines. The formulation F6 was packed in high density polyethylene container and kept at 40^0C ± 2^0C and 75% ± 5% RH. Samples were analyzed for drug content and *in-vitro* dissolution studies in the intervals of 1, 2, 3 months.

3. Results and discussion

The present study was carried out to formulate colon targeted matrix tablet of Ibuprofenusing direct compression method. In this method, the powder blend was subjected to variousevaluation studies such as bulk density, tapped density, compressibility index and Hauser's ratio and was compressed into tablets. The compressed tablets were evaluated such as thickness,hardness, friability, weight variation, assay, *in-vitro* dissolution studies, and accelerated stabilitystudies. The tablets are coated using Enteric coating polymers (Eudragit FS 30 D) to target the release of pH 7.4. The uncoated and coated tablets are evaluated for *in-vitro* dissolution studies and the tablets are packed in bluster pack and were subjected to accelerated stability studies.

3.1. Preformulation Studies

The following pre formulation studies were performed on Ibuprofen and excipients.

3.1.1. Evaluation of Ibuprofen (API)

Table 8 Physical Characteristics of API

S. No	Tests	Specification	Results
1	Colour	White or off white powder	White or off white powder
2	Solubility	Practically insoluble in water, freely soluble in acetone, methanol and in ethylene chloride. It dissolves in dilute solution of alkali hydroxide and carbonates	Complies
3	Melting point	75.0°-78.0°C	76.4°C
4	Moisture content	NMT0.5 w/w%	0.3%w/w

The color, solubility, melting point and moisture content of the API were evaluated. It was found to be with in the range of the monograph.

Table 9 Angle Of Repose of Ibuprofen

S. No	Raw material(API)	Angle of repose (Degree)	Average
1	Ibuprofen	$38^0.14'$	$38^0.56' \pm 0.69$
2	Ibuprofen	$39^0.36'$	
3	Ibuprofen	$38^0.12'$	

The angle of repose of API was found to be $38^0.56' \pm 0.69$. Hence the drug belongs to fair flow and requires glidants to improve the flow property.

Table10 Bulk Density and Tapped Density of Ibuprofen

S. No	Raw material (API)	Bulk density (g/ml)	Average bulk density (g/ml)	Tapped density (g/ml)	Average tapped density (g/ml)
1	Ibuprofen	0.459	0.453 ± 0.01	0.612	0.614± 0.003
2	Ibuprofen	0.452		0.614	
3	Ibuprofen	0.448		0.618	

The average bulk density and tapped density was found to be 0.453 ± 0.01 and0.614±0.003 g/ml respectively.

3.1.2. Powder Compressibility and Hauser's Ratio

Table 11 Compressibility Index and Hauser's Ratio

Raw material (API)	Compressibility index (%)	Hausner's ratio
Ibuprofen	26.22	1.35

Based on Compressibility index and Hausner's ratio, it indicates the Ibuprofen (API) belongs to poor flow property.

3.1.3. Particle Size Distribution

Table12 Particle Size Distribution of Ibuprofen

Sieve no	Empty weight of sieve	Quantity retained (gm)	Mass retained (gm)	Cumulative mass retained (gm)	Cumulative % retained	Percentage passing %
#20	367.8	368.55	0.75	0.75	4.34	95.66
#30	417.65	417.85	0.2	0.95	5.5	94.5
#40	358.05	365.65	7.6	8.55	49.56	50.44
#60	343.45	343.65	0.2	8.75	50.72	49.28
#80	340.75	340.9	0.15	8.9	51.59	48.41
#100	332.5	332.85	0.35	9.25	53.62	46.38
Base	540.45	548.45	8	17.25	100	0

From the particle size analysis it was concluded that the particles size of the API was found to be moderately coarse powder.

Drug-Excipients Compatibility Studies:

It was determined as per procedure given in material and method part. The following Table No:12 illustrates,

Table13 Drug-Excipients Compatibility

S.No	Composition	Initial	After 15days	After 30days	Conclusion
1	Ibuprofen	White	NCC	NCC	Complies
2	Ibuprofen +Excipients	White	NCC	NCC	Complies

NCC – No Characteristic Change.

From the drug excipients compatibility study, it was observed that there was no characteristic change or interaction between drug and excipients. Thus it was concluded that the excipients selected for the formulation were compatible with Ibuprofen.

3.1.4. IR Spectral Analysis:

The FTIR studies of Ibuprofen and Ibuprofen with Excipients. The results are shown in Table No: 14, 15 Figure No: 2,3.

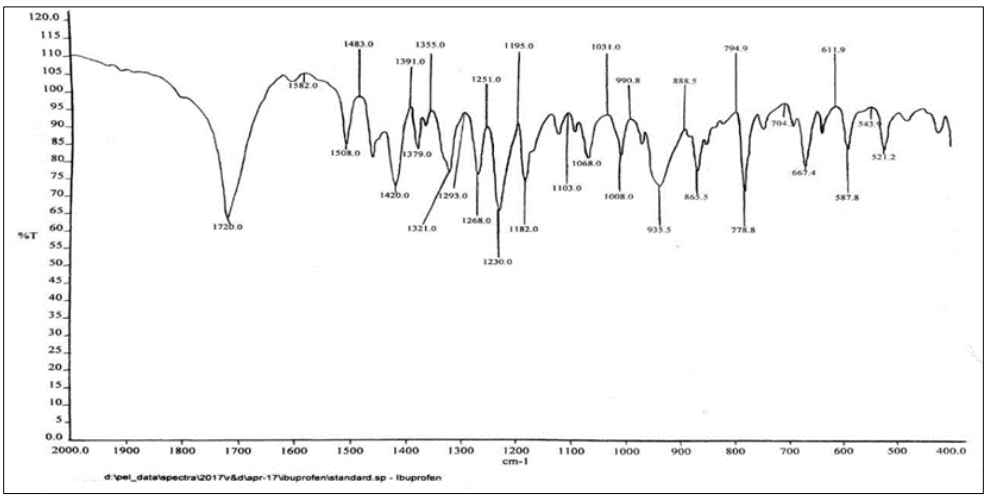

Figure 2 FT-IR Spectra of Pure Ibuprofen

Table 14 FT-IR Spectral Values of Pure Ibuprofen

S.No	Wave Number (cm^{-1})	Functional Group
1.	1720.0	C=O Stretching of carboxylic acid
2.	1420.0	C=C Stretching of Benzene
3.	1321.0	Methylof alkane
4.	1230.0	Methylene of Benzene ring
5.	1068.0	C-O of carboxylic acid
6.	935.5	CH_2 bending vibration of alkane

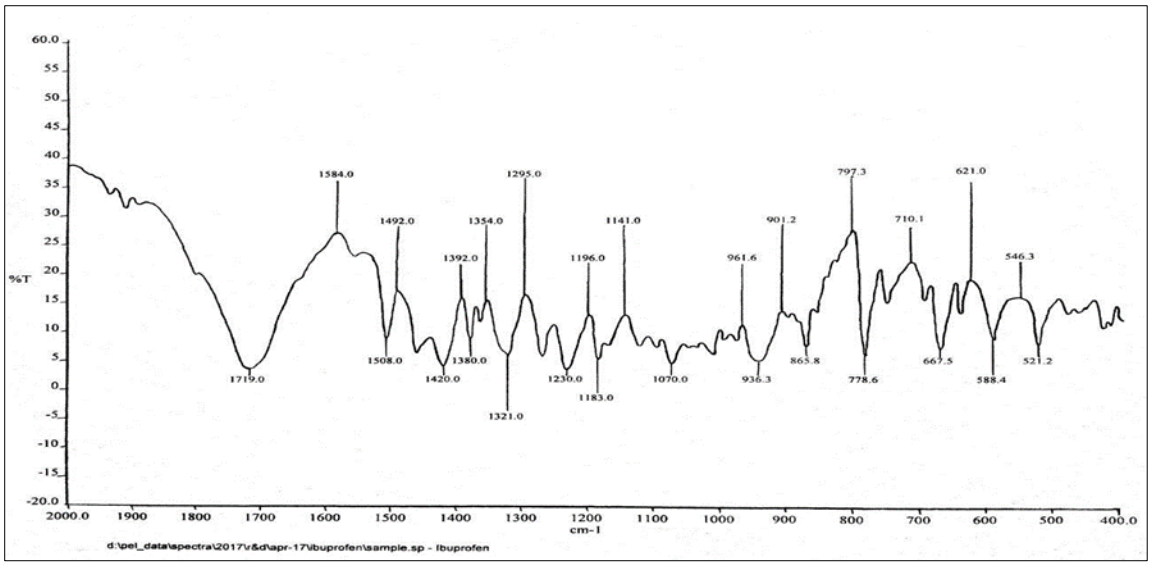

Figure 3 FT – IR Spectra Of Ibuprofen With Excipients

Table 15 FT-IR Spectral Values of Ibuprofen with Excipients

S.No	Wave Number(cm^{-1})	Functional Group
1.	1719.0	C=O Stretching of carboxylic acid
2.	1420.0	C=C Stretching of Benzene
3.	1380.0	Methyl of alkane
4.	1230.0	Methylene of Benzene ring
5.	1070.0	C-O of carboxylic acid
6.	936.3	CH_2 bending vibration of alkane

Pure Ibuprofen spectra showed sharp characteristic peaks at 1720.0, 1420.0, 1321.0, 1230.0, 1068.0, 935.5 cm^{-1}. These peaks are also prominent in the FTIR spectra's of the physical mixtures containing Ibuprofen and other excipients in the final formula. This indicates that thereis no interaction between the drug and excipients from both Physical observation and FT-IR studies.

Table 16 Evaluation of Lubricated Powder Blend

Formulation Code	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Carr's Index (%)	Hausner's ratio	Angle of repose (degree)	Moisture content (%)
F1	0.35±0.02	0.40 ± 0.01	11.73±0.79	1.12 ±0.15	$29^0$58'±0.53	1.15 ± 0.05
F2	0.31±0.03	0.35 ± 0.05	12.10±0.54	1.13 ±0.28	$33^0$23'±0.35	1.28 ± 0.02
F3	0.37 ± 0.01	0.42 ± 0.06	13.63±0.38	1.13 ±0.12	$30^0$96'±0.19	1.42 ± 0.02
F4	0.38 ± 0.07	0.40 ± 0.08	11.57±1.05	1.14± 0.85	$31^0$26'±0.60	1.21 ± 0.06
F5	0.35 ± 0.10	0.44 ± 0.06	12.60±0.86	1.12 ±0.74	$29^0$35'±0.48	1.33 ± 0.03
F6	0.41± 0.06	0.46± 0.01	12.98±0.65	1.13 ±0.24	31^0.05'±0.25	1.15 ± 0.02

All values are expressed as mean ± standard deviation, n=3

The lubricated powder blends was evaluated for different parameters and the results are given in

The bulk density and tapped density of all formulations were measured by using graduated measuring cylinder. The bulk density was found in the range of 0.31-0.41gm/cm^3. The tapped density was between 0.35-0.46 gm/cm^3. Both are with in the acceptable limits.

If the compressibility index of the powder is between 11 and 15, it shows good flow character; here all the formulations exist in the range between 11.73-13.63. It indicates that the granules showed good flow character.

The result showed that the Hauser ratio of all the formulations was between 1.12-1.14, if the Hausner ratio lies between 1.12-1.18, it shows good flow behavior of the granules or powder. The result indicates good flow property of the granules.

If the angle of repose is within 35^0, it indicates good flow property of the granules. Theresult showed that the angle of repose of all the formulations was between 29^0-33^0. It proved that the flow properties of all formulations are good.

Table 17 Evaluation of Finished Product (Uncoated)

Parameters	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Average weight (mg)	450±1.18	450±0.89	450±2.00	450±0.61	450±2.68	450±0.21
Thickness (mm)	3.4± 0.16	4.2±0.09	4.7± 0.14	5.9± 0.12	5.7±0.01	5.9 ± 0.16
Hardness (kg/cm^2)	12.6(± 0.15)	9.4(±0.22)	6.2(±0.30)	5.2(±0.32)	6.0(±0.30)	5.8(±0.11)
Friability (%)	0.36	0.41	0.39	0.31	0.35	0.33
Disintegration Time (min)	-	24’46’’	17’42’’	14’45’’	8’42’’	7’18’’
Assay (%)	99.34	99.2	98.51	99.85	99.53	100.21

All values are expressed as mean ± standard deviation, n = 3

The tablets are evaluated for different parameters are given in Table no:18.

The thickness of the tablets was in the range of 3.4 to 5.9mm. This is due to the upper and lower punch adjustments during compression process. The prepared tablets in all the trials possessed good mechanical strength with sufficient hardness in the range of 12.6 to 5.2 kg/cm^2. The friability of the tablets was found to be within 1%. All the above trail formulations have passed the friability test. The average weight of all the formulations was found to be 450 mg. It is with in the permissible range. The percentage of drug content was found among different batches of the tablets and ranged from 98.5 to 100.21 which were with in the acceptable limits.

Table 18 Evaluation Parameters of Ibuprofen Enteric Coated Tablets

Trial	**Thickness(mm)**	**Weight variation(mg)**	**Disintegration time(min)**	**Assay (%)**	**Drugrelease(%)**
F6	6.0 ± 0.02	477±0.21	218’63’’±1.98	99.92 ± 0.08	98.51

Allv alues are expressed as mean± standard deviation,n=3

Ibuprofen tablet of the above trial (F6) was satisfied of all the parameters. It was coatedby using enteric coating method. The coated tablets were evaluated for the following parameters including thickness, disintegration test, weight variation, assay and *in-vitro* studies.

Table19 Comparative Datas of Uncoated and Enteric Coated Ibuprofen Tablets

Trial	**Thickness (mm)**	**Weight variation (mg)**	**Assay (%)**	**Drug release (%)**
F6 Uncoated	5.9 ± 0.16	451±5	100.21±0.12	99.69at 12 hrs
F6 Enteric coated	6.0±0.02	477±5	99.92 ± 0.08	98.51at 24 hrs

All values are expressed as mean ± standard deviation, n = 3

Ibuprofen Enteric coated tablets were compared with the same trial of uncoated Ibuprofen tablets. The thickness of Enteric coated tablets was found to be more than uncoated tablets. Weight variation was increased in Enteric coated tablets than the uncoated tablets. This is due to the coating of core tablet.

Table 20 *In-Vitro* Dissolution Profile of Enteric Coated Tablets

Dissolution Media	**Sampling time**	**Cumulative % drug release in different trials**			
		F3	**F4**	**F5**	**F6**
Simulated gastric fluid (0.1HCL)	2Hrs	1.07	1.60	1.83	2.00
Simulated Intestinal Fluid (7.4 pH Phosphate buffer)	5Hrs	7.43±0.32	8.804±0.13	10.09±0.78	11.58±0.13
	8Hrs	10.09±0.78	12.74±0.43	16.76±0.13	20.72±0.43
	12Hrs	26.97±0.52	36.82±1.35	49.76±0.57	53.80±0.78
	16Hrs	45.18±0.95	61.24±0.52	72.21±0.95	81.51±0.57
	20Hrs	61.24±0.57	72.19±0.43	84.31±0.57	90.71±0.95
	24Hrs	78.22±0.78	82.43±0.57	92.65±0.95	98.51±0.78

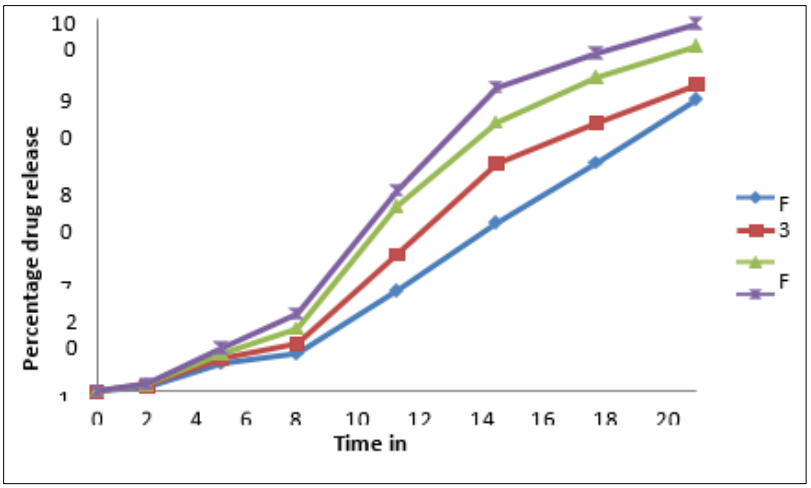

Figure 4 Graphical representation of *in-vitro* drug release

F1: The method used in this trial is direct compression. The concentration of Eudragit S 100 used was 80mg/unit, Ethyl cellulose concentration was 60mg/unit. Lactose DCL21 was 50mg/unit. And the concentration of Talc and magnesium stearate used was 5mg/unit. The hardness of the tablet were crossed the specification limit.

F2: Same as procedure of F1. But in this formulation the concentration of Eudragit S100 and Ethyl cellulose was decreased to 60 mg/unit and 55mg/unit. And diluents concentration increased to 75mg/unit. The hardness of this formulation were better than the above formulation but the time required to disintegrate tablets were crossed the specification limit.

F3: The hardness were achieved. But the time required to disintegrate tablets were crossed the specification limit. In this formulation the concentration of Eudragit S100 and Ethyl cellulose was decreased to 50 mg/unit and 40 mg/unit to reduce the hardness of the tablets. And the diluents concentration increased to 100mg/unit. This formulation was selected for coating. And the tablets were subjected to *in-vitro* dissolution study. The release was found to be 78.22±0.78 at 24hrs.

F4: In trial 4 the concentration of Eudragit S100 and Ethyl cellulose was further decreased to35mg/unit and 25mg/unit and increased the Lactose DCL21 concentration to 130mg/unit. The disintegration time of tablet was better than the above formulations but crossed the limits. The tablets were subjected to *in-vitro* dissolution study.

F5: The concentration of Eudragit S100 and Ethyl cellulose was further decreased to 20mg/unit and 15 mg/unit and increased the Lactose DCL21 concentration to 154mg/unit. The concentration of Magnesium stearate was increased to 6mg/unit to improve the lubrication of granules. The disintegration time of tablet was found to be within the limit. The triethyl citrate was used in the enteric coating part, to give better flexibility to the polymer. The tablets are subjected to *in-vitro* dissolution study. The percentages of drug release were found to be 92.65±0.95 at 24 hrs. It was better than the earlier trials.

F6: The concentration of Eudragit S 100 and Ethyl cellulose was further decreased to 14mg/unit and 10mg/unit and increased the Lactose DCL21 concentration to 165mg/unit. The tablets of this trial are subjected to *in-vitro* dissolution study. The percentage of drug release showed 98.51±0.78 at 24 hrs. This trial was taken as confirmatory trial and subjected as stability studies.

3.2. Stability Studies

3.2.1. Physical Parameters

Table 21 Stability studies for post compression parameters of (F-6) enteric coated tablets

Post compression Parameters	**Storage condition: $40^0C \pm 2^0C$ /75 ± 5% RH**			
	Initial	**1st month**	**2nd month**	**3rd month**
Description	White coloured Enteric coated tablet	White coloured Enteric coated tablet	White coloured Enteric coated tablet	White coloured Enteric coated tablet
Average weight(mg)	477±0.21	477.38 ± 0.003	477.52 ± 0.006	477.67 ± 0.04
Disintegration time(minutes)	219'63''±0.03	219'13''±0.08	220'38''±0.08	221'7''±0.05

*All the values are expressed as mean's, n=3.

The F-6 formulation of enteric coated tablets was carried out for the stability study. It was kept at 40^0C **±** 2^0C /75±5% RH. It revealed that there were no significant changes in color but slight increase in average weight and disintegration time. The sample was tested at one month interval.

Table 22 *In-Vitro* Drug Release and Assay

Formulation	**Time in hrs**	**Storage condition $40^0C \pm 2^0C$/75±5%RH**					
		***In-vitro* drug release (%)**				**Assay (%)**	
		Initial	**1 month**	**2 month**	**3 month**	**Initial**	**After Stability**
F6	24	98.51	98.31	97.42	97.28	100.21	100.1

The F6 formulation of enteric coated tablets was carried out for the stability study, it was kept in 40^0C**±** 2^0C /75±5% RH for the period of three months. Percentage of drug release and assay was determined. The data's does not showed much variation during stability studies. The results revealed that the product was stable.

4. Conclusion

Pre formulation studies were performed to study the nature of API and compatibility of API with excipients by physical observation and FT-IR studies. The results showed that there was no interaction between API and all the excipients selected. The Ibuprofen matrix tablets were successfully formulated by direct compression method using the selected excipient quantities. The formulated tablets were evaluated for both pre-compression and post-compression parameters as per requirements of standards. So the trial F6 was considered as best formulation. From the results obtained, it can be concluded that formulation F6 containing enteric coated matrix tablet of Ibuprofen would be a promising formulation to achieve the purpose which treat inflammatory bowel diseases (ulcerative colitis) without any gastric irritation or ulcers, which is useful for patients having pre history of ulcerative colitis.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest, financial or otherwise.

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