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FORMULATION AND EVALUATION OF COLON TARGETED MATRIX TABLETS OF IBUPROFEN

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ABSTRACT

Ulcerative colitis is a chronic condition of inflammation and ulcers in colon and rectum, the present study aim was to developed Ibuprofen colon targeted matrix tablet for the effective treatment of Ulcerative colitis. Formulation of Ibuprofen matrix tablets was prepare by using different polymers such as Eudragit S 100 and Ethyl cellulose (as carriers) in different ratios. Ibuprofen tablet were prepared by direct compression method. Based on FT-IR study drug and excipient compatibility was checked and confirmed the nil interactions. The prepared tablets were coated with an enteric polymer and were evaluated for the physicochemical parameters such as hardness, thickness, content uniformity, drug content and in vitro-drug release studies. Among the six formulation F6 showed better drug release 98.51% of Ibuprofen. The stability study was also conducted, the results showed there is no significant changes of drug content and other parameter, which make a clearance of Ibuprofen matrix tablet formulation.

Key words: *Colon targeted, Enteric polymer, FT-IR, Ibuprofen, Matrix and Ulcerative colitis.*

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INTRODUCTION

The effective and safe therapy for colonic disorders, colon specific drug delivery is necessary. The colon targeted tablets drug release and absorption should not occur in the stomach as well as the small intestine, and neither the bioactive agent should be degraded in either of the dissolution sites but only released and absorbed once the system reaches the colon. Nowadays colon specific drug delivery is challenging task to pharmaceutical technologist. The colon is to be a suitable absorption site for peptides and protein drugs for the reasons of less diversity and Intensity of digestive enzymes[1].Comparative proteolytic activity of colon mucosa is much less than that observed in the small intestine, thus Colon targeted drug delivery system protects peptide drugs from hydrolysis, and enzymatic degradation in duodenum and jejunum, and eventually releases the drug into ileum or colon which leads to greater systemic bioavailability[2]. The concentration of drug reaching the colon depends on formulation factors, the extent of retrograde spreading and the retention time[3]. Coating of the drugs with pH-sensitive polymers provides simple approach for colon-specific drug delivery[4].

The medicament should be absorbed once the reaches the colon. To reach the colon has a long residence time 72 hours and having high water content it favors absorption of poorly absorbed drug molecule may have an improved bioavailability. Colon targeted drug delivery system has the advantage of

- Controlled / Sustained release thus reduce dosing frequency

- Targeted delivery of drug to achieve high concentration in treatment of disease of distal gut
- Deliver drug to that region that is less hostile metabolically, drug which is acid and enzyme labile such as proteins[5].

A glance of colonic absorption and disease

The absorption capacity of colon is very high which is attributed to the colon transit time, which can be as long as 20-35 hours, hence it is ideally suited for absorption. The absorption is influenced by the transport of water, electrolytes and ammonia across the mucus and it is more in the proximal colon than the distal colon. Drug molecules pass from the apical to basolateral surface of epithelial cells byPassing through colonocytes (trans cellular transport), or Passing between adjacent colonocytes (para cellular transport)

Inflammatory bowel disease

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. It affect the small intestine and large intestine, it can also affect the mouth, esophagus, stomach and the anus whereas ulcerative colitis primarily affects the colon and the rectum[6].

Ulcerative colitis

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. Bloody diarrhoea is the characteristic symptom of the disease.Ulcerative colitis is a nonspecific inflammatory bowel disease of unknown etiology that effects the mucosa of the colon and rectum. The treatment of ulcerative colitis depends on the amount of the large bowel affected and the severity of the inflammation. Ulcerative colitis most often begins gradually and can become worse over time. Symptoms can be mild to severe. The goal of care is to keep people in remission long term[7].

MATERIALS AND METHODS

Materials and source

Ibuprofen was obtained as a gift sample from FourrtsIndia Laboratory, Eudragit S100, Eudragit FS 30D-Vikram Thermo (India) Ltd, Ethyl cellulose - Jalan cellulose. Co, Lactose (DCL 21) - Cabot sanmar, Talc-Abishek organics. Magnesium stearate - Amishi Drugs & Chemical, & Co. Tri Ethyl Citrate- Chemtrec – International Ltd, all the above excipients and other chemicals used in these formulations are of analytical grade.

Method of matrix tablet preparation

The formula was designed as 450 mg tablet. There was six formulas (F1 to F6) ware developed. The various ratios of polymers and other additives in the formula ware mentioned in table 1.

Table .1: Formula of Ibuprofen Matrix Tablets

S.No	Ingredients	Quantity of ingredients (mg/tab)					
		F1	F2	F3	F4	F5	F6
1	Ibuprofen	250	250	250	250	250	250
2	Eudragit S-100	80	60	50	35	20	14
3	Ethyl cellulose	60	55	40	25	15	10
4	Lactose (DCL 21)	50	75	100	130	154	165
5	Talc	5	5	5	5	5	5
6	Magnesium stearate	5	5	5	5	6	6
Total weight (mg)		450	450	450	450	450	450

Preformulation studies:

The basic purpose of the preformulation study was to provide a rational basis of the formulation and maximize the chances of formulation success and thus optimizing drug product quality and performance.[8]

Evaluation of Active pharmaceutical ingredient:

The evaluation of ibuprofen was done according to Indian Pharmacopoeia standard.

Melting point

Determining the melting point of a compound is of one the purity evaluation. Melting-point apparatus was used to determine the melting point of an ibuprofen.

Loss on drying

The loss on drying test is designed to measure the substance weight and volatile matters in a sample when

Physical character Description

It is the initial evaluation in preformulation studies, which assess the colour, solubility, melting point and moisture content.

Solubility

Aqueous solubility is an important physicochemical property of drug substance, which determines its systemic absorption and in turns its therapeutic efficacy. As per the solubility specifications mentioned in table no.2.

the sample is dried under specified conditions. Loss on drying of Ibuprofen was measured by using moisture balance. Approximately 2gm of Ibuprofen was placed into a plate of moisture balance and set the temperature to 45°C. Measured the moisture content of drug in percentage.

Table .2: Solubility Specifications

Descriptive terms	Approximate volume of solvent in milliliters per gram of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10,000
Practically insoluble	More than 10,000

Table : 3 Angle of repose powder flow property description

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

Flow Properties (Angle of Repose)[8]

To assess the flow property powder by angle of repose funnel method. 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.

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

Bulk density

Bulk density is an indicator of compaction. It is defined as the weight of powder occupying a unit volume and is expressed in g/ml. Bulk density depends on the particle size distribution. It is expressed in g/ml. An accurately weighed quantity of granules was transferred into a 50 ml measuring cylinder. The unsettled apparent volume, to the nearest graduated unit occupied by the powder was measured. Bulk density was determined using the formula.[10]

$\rho bulk = m/Vo$

Where,

ρbulk = Bulk density;

m = Mass of the blend

Vo = Untapped Volume

Tapped density:

Tapped density was measured by mechanically tapping of measuring cylinder containing a powder sample. 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 powder (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,

ρt = Tapped density

m = Mass of the granules

Vt = Final tapped volume.

Measurement of powder compressibility

Carr's compressibility index:

The Carr index or Carr's Compressibility index is an indication of the compressibility of a powder. The Carr index is frequently used as an indication of the flowability of a powder. Ibuprofen cars was calculated by using the formula.[11]The compressibility description index was shown in table number 4.

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

Where,

CI = Compressibility index

ρbulk = Bulk density

ρt = Tapped density

Table. 4. 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

Table .5 Hausner's ratio as an indication of powder flow

S. No.	Hausner'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

Hausner's ratio:
Hausner's ratio is simply the tapped density divided by the bulk density. Compressibility and Hausner ratio parameters are influenced by variables such as particle size and shape and cohesivity, since they essentially reflect the impact of tapping on the particle packing. Hausner's ratio description are mentioned in table no. 5It was calculated using the formula.[12]
Hausner's Ratio = ρt / ρbulk
Where,
ρbulk = Bulk density
ρt = Tapped density

Particle Size Analysis
In case of tablets, particle size influences the flow and the mixing efficiency of powders. Particle 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, 10gm, was placed on the top sieve. The next 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. The powder category was classified as per the table number 6 description

$$\text{Percentage retained} = \frac{\text{Mass retained on each seive}}{\text{Total weight}} \text{ X } 100$$

Table no.6 Classification of powder based on particle size

Sl. No.	Nature of sample	Result of determination
1	Coarse powder	Not less than 95% of the sample mass pass through #14
2	Moderately coarse powder	Not less than 95% of the sample mass pass through #25
3	Moderately fine powder	Not less than 95% of the sample mass pass through #36
4	Fine powder	Not less than 95% of the sample mass pass through #100
5	Very fine powder	Not less than 95% of the sample mass pass through #150 and not more than 40% pass
6	Super fine powder	Not less than 90% by number of particles are less than

Preformulation studies
Drug-excipient compatibility studies
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 essential and very useful to the formulator in selecting appropriate excipients.

(a) Physical observation:
Active ingredient was mixed well with all excipients in binary ratio and small portion of this mixed powder was placed in cleaned and dried vial. This vial was kept for observation in stability chamber at 40oC ± 2oC / 75 ± 5% RH. Mixtures were also placed at 2^0C -8^0C, 50^0C and room temperature (Control). Physical observation has been carried out visually at the initial stage, after 15 days and after 1 month at 40^0C ± 2^0C / 75 ± 5% RH.

(b) Chemical compatibility studies by FT- IR:
Chemical 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.

Formulation of colon targeted Ibuprofen matrix tablet:
Ibuprofen colon targeted matrix tablet was prepared by direct compression method. All tablet ingredients was accurately weighed as mentioned in Table number 1. The average weight of each uncoated tablet was 450 mg.
A required quantity of raw materials was weighed accurately. The Ibuprofen, eudragit S100 and ethyl cellulose were sifted using 60 # mesh. Lactose (DCL 21) sifted through 40 # mesh. The sifted powders were mixed in polythene bag for ten minutes. The above dried powder blend were lubricated by using Talc. Talc was sifted through 40# mesh and magnesium stearate was sifting through 60# mesh. Then the lubricated blend was compressed at an average weight of 450 mg using punch size 14.2 mm.

Coating formula:
6% coating has been given for all the formulations to protect the drug from acidic environment. The coating formula was shown in table number 7.

Table No: 7 Coating formula

S. No	Ingredients	Quantity/1000 Tablet (gm)
1	Eudragit FS 30	125
2	Triethyl citrate	1.875
3	Talc	18.75
4	Purified water	120

Preparation of Enteric Coating solution:
A required quantity of Eudragit FS 30 D was weighed accurately and stirred. Meanwhile Triethylcitrate was added to it, purified talc were triturated separately in a mortar and added to the solution and stirred well. Finally the volume were make up to required quantity with purified water. Filtered the above solution with #100 mesh.
Weight built up calculation for enteric coating: [6 %]
450(Tablet weight) X 6 % (Coating) =27 g
The weight of enteric coated tablet = (450 + 27) = 477 477mg.
Coating was done in following specification, speed of revolution 10-12 rpm, spray rate 1.5 – 2 ml per minute, dry air temperature $50^0 \pm 5^0$ C / 30 minutes, coating time 4 hour and bed temperature 30^0-40^0

Evaluation of compressed tablet
The compressed tablets were evaluated for the following parameters.

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. The above quality parameter was checked in all formulated batch.

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 test. Tablet hardness of all the formulations was measured using a Monsanto hardness tester.[13]

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%

The percentage of deviation for weight variation description shown in table number 8

In-vitro dissolution studies:
The release rateof Ibuprofenmatrix tablets were determined using USP Dissolution
Testing Apparatus II (paddle method).The test was performed using 900ml of 0.1N HCL at 37^0+0.5^0C and 100 rpm for first 2 hours then medium replaced with 7.4

Table No.8 Percentage deviation for weight variation

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

variation of a standard value.[12] Thickness of all the formulations was measured using a digital vernier 76 tandar.

Friability:
Friability is a measure of the resistance of the tablet to abrasion. The measure is useful to determine the ability of the tablet to withstand abrasion during handling, coating, packing and transport. Friability was measured by using 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.[14]

$$\text{Friability (F)\%} = \frac{\text{Weight loss}}{\text{Initial weight}} \text{ X } 100$$

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 370C for a period of time limit specified in the monograph.[15]

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.

$$\text{Percentage deviation} = \frac{\text{Weight of tablets} - \text{Average weight of tablets}}{\text{Average weight of tablets}} \text{ X } 100$$

pH phosphate buffer and continued for 22 hours. A liquid 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.

Stability studies
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. Stability analysis was done by accelerated stability study method. The ICH guideline recommends the following storage conditions for stability studies.[16,17,18]

Table. 9: Stability conditions according to ICH guidelines

S. No.	Study	Storage Condition
1.	Long term	25°C±2°C / 60%RH±5%RH
2.	Intermediat	30°C±2°C / 65%RH±5%RH
3.	Accelerated	40°C±2°C / 75%RH±5%RH

Table .10: Physical character of Ibuprofen

S. No	Evaluation	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 methylene 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	Not more than 0.5 w/w%	0.3% w/w

Table No.11. Ibuprofen angle of repose

S. No	Raw material (API)	Angle of repose (Degree)	Average
1	Ibuprofen	$38^0.14'$	$38^0.56' \pm 0.69^0$
2	Ibuprofen	$39^0.36'$	
3	Ibuprofen	$38^0.12'$	

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

RESULTS AND DISCUSSION

Preformulation studies:
The preformulation study results were shows Ibuprofen and excipients have a adaptability for make Colon targeted matrix tablets the results are tabulated in following tables.

Physical characteristics of Ibuprofen
The colour, solubility, melting point and moisture content of the Ibuprofen was found to be within the range of the monograph, the results are shown in table no.10

Flow property-angle of repose
The angle of repose of Ibuprofen was found to be 380.56′± 0.690. Hence the drug belongs to fair flow and requires glidants to improve the flow property. The results were tabulated in table number 11.

Bulk density and tapped density of Ibuprofen
The average bulk density and tapped density was found to be within a range 0.453 ± 0.01 and 0.614± 0.003 g/ml respectively. The evaluation values ware showed in table no. 12

Table No.12 Ibuprofen bulk density and tapped density

Sl. No	Raw material	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	

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

Table No 13 Compressibility and Hausner ratio of Ibuprofen

Raw material (API)	Compressibility index (%)	Hausner's ratio
Ibuprofen	26.22	.35

Compressibility Index and Hausner's Ratio
Based on Compressibility index and Hausner's ratio indicates the Ibuprofen (API) belongs to poor flow property. So need to enhance flow property by adding glitants. The results are shown in table no. 13

Particle size distribution particle size distribution of ibuprofen
The particle size analysis was concluded that the particles size of the Ibuprofen (API) was found to be moderately coarse powder.

Table No. 14 Particle size distribution

Sieve No	Empty weight of sieve	Quantity retained (gm)	Mass retained (gm)	Cumulative mass retained	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

Drug - excipients compatibility studies:

Physical character

The drug excipients compatibility study 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. Table no:15 illustrates drug excipient physical compatability.

Table No: 15 Drug - excipients physical compatibility

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

FT-IR spectral analysis:

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 there is no interaction between the drug and excipients from both Physical observation and FT-IR studies. It is shown in table No. 16 and figure No. 1.

Table .16 FT-IR Spectra of pure ibuprofen

S. No	Wave No. (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	CH2 bending vibration of alkane

Table. 17 FT-IR spectra of Ibuprofen physical mixtures

S. No	Wave No. (cm^{-1})	Functional Group
1.	1720.0	C=O Stretching of carboxylic acid
2.	1420.0	C=C Stretching of Benzene
3.	1321.0	Methyl of 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

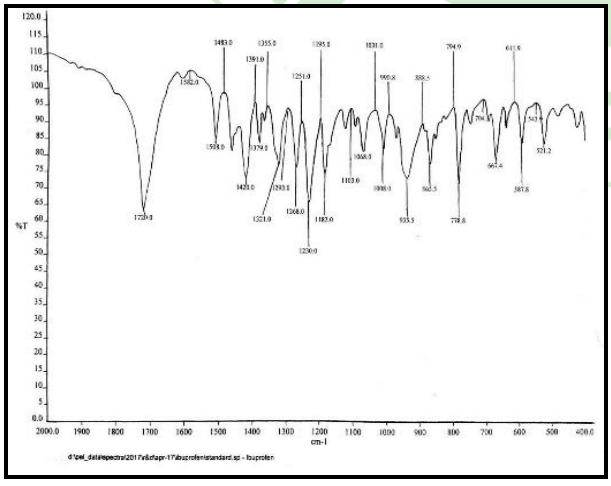

Fig. 1 FT-IR pure Ibuprofen

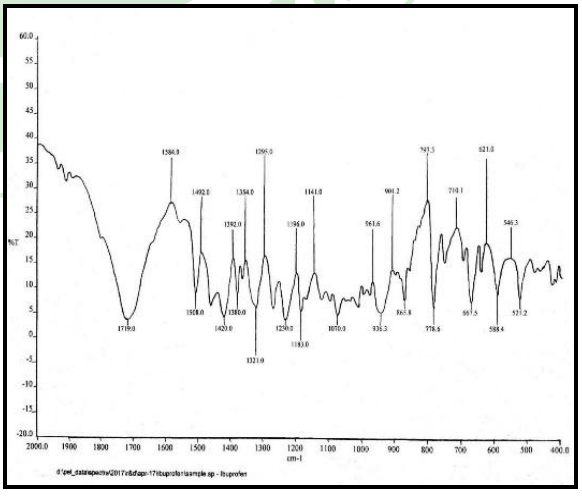

Fig.2 FT-IR Ibuprofen physical mixtures

Evaluation of pre compression parameter for lubricated powder blend

The lubricated powder blends was evaluated for different parameters and the results are given in Table no: 18. The bulk density was found in the range of 0.31- 0.41gm/cm3. The tapped density was between 0.35-0.46 gm/cm3. Both are within the acceptable limits. The compressibility index of the powder is between 11 and 15%, it shows good flow character, and 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 Hausner 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. The angle of repose is within 350, it indicates good flow property of the granules. The result showed that the angle of repose of all the formulations was between 290-330.It proved that the flow properties of all formulations are good.

Table No: 18 Pre compression evaluation

Formulation Code	Bulk density (gm/cm3)	Tapped density (gm/cm3)	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	30096'±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

Evaluation of finished uncoated tablet

The prepared uncoated tablets are evaluated for different parameters are given in Table no: 19. The thickness of the tablets was in the range of 3.4 to 5.9 mm. 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/cm2.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 450mg. It is within 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 within the acceptable limits. Based on the above said parameters F-6 was selected as best one.

Table. 19 Evaluation of uncoated tablet

Parameters	F1	F2	F3	F4	F5	F6
Average weight	450±1.18	450±0.89	450±2.0	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/cm2)	12.6	9.4	6.2	5.2	6.0	5.8
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''
Drug content (%)	99.34	99.2	98.51	99.85	99.53	100.21

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

In-vitro dissolution profile of enteric coated tablets

F1: The concentration of Eudragit S 100 used was 80mg/unit, Ethyl cellulose concentration was 60mg/unit. Lactose DCL 21 was50mg/unit. And the concentration of Talc and magnesium stearate used was 5mg/unit. The hardness of the tablet were crossed the specification limit. So it was rejected for dissolution study.

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 diluent concentration increased to 75mg/unit. The hardness of this formulation were better than F1 formulation but the time required to disintegrate tablets were crossed the specification limit. So this formulation also not to consider for dissolution study.

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 diluent 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 24 hrs.

F4: The concentration of Eudragit S100 and Ethyl cellulose was further decreased to 35mg/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 15mg/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 toin-vitro dissolution study. The percentage of drug release showed98.51±0.78 at 24 hrs. This trial was taken as confirmatory trial and subjected as stability studies.

Table No. 20 Drug release profile for coated tablet

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

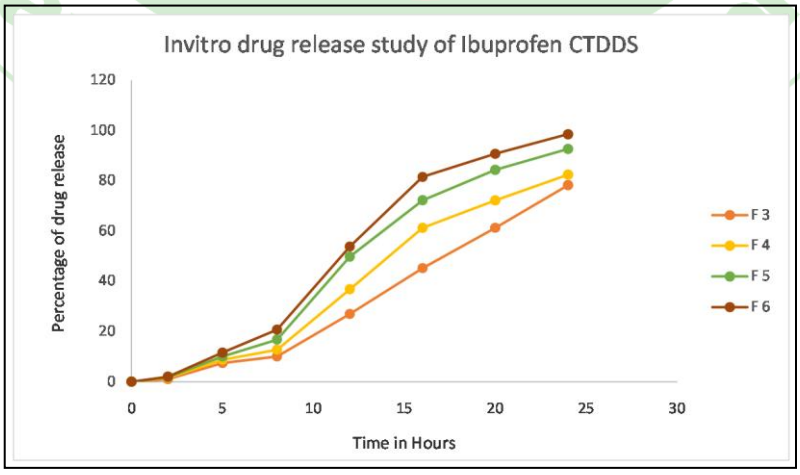

Fig. : 3 Graphical representation of in-vitro drug release

Other evaluation of best release Ibuprofen enteric coated tablet:

Coated Ibuprofen tablet of the trial (F6) was satisfied of all the parameters. It was coated by using enteric coating method. The F6 evaluation reports are tabulated in the table No.21.

Comparative data's of uncoated and enteric coated Ibuprofen tablets

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. The comparative data was shown in table no. 22.

Table: 21 Evaluation parameter of coated tablet

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

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

Table: 22 Comparative data's of uncoated and enteric coated Ibuprofen tablets

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

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

Stability studies

Physical stability after 3 months

Stability studies for post compression parameters of (F-6) enteric coated tablets Table No: 23

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 No. 23 Stability study

Post compression Parameters	Storage condition: 400C± 20C /75±5%RH			
	Initial	1st month	2nd month	3rd month
Description	White colour	White colour	White colour	White colour
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.

In-vitro drug release and assay after 3 months

The F6 formulation of matrix enteric coated tablets was carried out for the stability study, it was kept in 40^0C± ^{20C} /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. The data's are shown in Table No:24

Table No. 24 Stability study- drug release

Formulation	Time in hrs	Storage condition 40^0C±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

SUMMARY AND CONCLUSION

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. And the results were complied with the pharmacopoeia specification. The formulated Ibuprofen matrix tablets were coated with enteric polymer Eudragit FS 30D by pan coating method.

From among the entire batches, 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 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.

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REFERENCE

1. *Akala E.O, Elekwachi O, Chase V, Johnson H, Lazarre M, Scott K. Organic Redox-initiate, Polymerization Process for the Fabrication of Hydrogels for Colon-specific Drug Delivery. Ind Pharm. 2003; 29(4): p.g 375-386.*
2. *Akala E.O, Elekwachi O, Chase V, Johnson H, Lazarre M, Scott K. Organic Redox-initiate, Polymerization Process for the Fabrication of Hydrogels for Colon-specific Drug Delivery. Ind Pharm. 2003; 29(4): p.g 375-386.*
3. *Wood E, Wilson C.G, Hardy J.G. The spreading of foam and solution enemas. International Journal of Pharmacy 1985; 25:p.g 191-197.*
4. *Singh N, Khanna R.C. Colon targeted drug delivery systems – A Potential Approach. The Pharma journal. Vol. 1 No. 1 2012.*
5. *QureshAltamash M, MominMunira, RathodSudha, DevAsish, KuteChaitrali. Colon targeted drug delivery system: A review on current approaches. Indian Journal of Pharmaceutical and Biological Research. 2013; 1(4):p.g 130-147.*
6. *Baumgart DC, Carding SR (2007). "Inflammatory bowel disease: cause and immunobiology." The Lancet. 369 (9573):p.g 1627–40.*
7. *Shanahan F. Ulcerative colitis. In: Hawkey C.J, Bosch J, Richter J.E, Garcia- Tsao G, Chan F.K.L,Textbook of Clinical Gastroenterology and Hepatology. 2nd edition. Oxford: Wiley- Blackwell; 2012:p.g 355–371.*
8. *Steele G. Preformulation as an aid to product design in early drug development. In Gibson M, editor. Pharmaceutical Preformulation and Formulation: A Practical guide from Candidate Drug Selection to Commercial Dosage Form.: p.g. 175.*
9. *Carr.R.L, Evaluation of flow properties of granules, Chem.Eng. 1965, p.g: 72,163- 168.*
10. *Bulk Density and Tapped Density. In USP 30 NF 25.; 2007. p.g. 643.*
11. *Powder Flow. In USP 30 NF 25.; 2007. p.g. 688-690.*
12. *Staniforth J. Powder Flow. In Aulton ME, editor. Pharmaceutics: The Science of Dosage Form Design. 2nd ed.: Churchill Livingstone. p.g. 207.*
13. *Powder Flow. In USP 30 NF 25.; 2007. p. 688-690. Banker GS, Anderson NR. Tablets. In Lachman L, Lieberman HS, Kanig JL, editors. The Theory and Practice of Industrial Pharmacy. Varghese Publishing House. p.g. 296-301.*
14. *Friability Test. In Indian Pharmacopoeia.: Government of India; 2010.*
15. *Weight Variation Test. In USP 30 NF 25; 2007.p.g.731.*
16. *Stability testing of active substance and pharmaceutical products. WHO Organization, 2006; p.g: 1211, 27:12-30.*
17. *Hadkar, U.B. Physical Pharmacy. NiraliPrakashan. Pune, 8th edition, 2008, p.g: 20.*
18. *ICH guideline, European Medicines Agency, 2003: CPMP/ICH/2736/99*