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Formulation and Evaluation of Colon Targeted Matrix Tablets of Mesalazine

Jaiswal Anamika*, Koshta Ashok, Malviya Sapna, Kharia Anil
Modern Institute of Pharmaceutical Sciences, Indore MP, India (453111)

ABSTRACT

The present work involves the formulation of colon targeted matrix tablet of Mesalazine by using direct compression method. Excipients including in the formulation are Eudragit S100, Ethyl cellulose, Lactose, Talc, Magnesium stearate. Preformulation studies have also been performed to study the nature of API and compatibility of API with excipients by physical observation and TLC 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 as bulk 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 Mesalazine matrix tablets were coated with enteric polymer Eudragit FS 30D by pan coating method. The prepared tablets were evaluated for weight variation, hardness, thickness, friability, drug content, disintegration time and *in-vitro* dissolution studies. All these parameters were found to be within the standard limits. Comparative studies of coated Mesalazine tablets and uncoated Mesalazine tablets were 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 16 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: Matrix Tablet, Mesalazine, direct compression method.

*Corresponding Author Email: anamikajaiswal61997@gmail.com
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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 time3. Coating of the drugs with pH-sensitive polymers provides simple approach for colon-specific drug delivery4. 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 by Passing through colonocytes (transcellular 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 METHOD

Materials and source

Mesalazine was gift sample, provided by Modern laboratories Pvt Ltd, Indore. Other excipients are procured from Modern Institute of Pharmaceutical Sciences Indore. All chemicals and reagents used in the research work are of analytical grade.

Preformulation Studies [8]

Preformulation 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. This initial learning phase is known as preformulation.

Parameters evaluated during preformulation studies:

Evaluation of API

The Evaluation of Mesalazine was done according to IP. Following are some of the important parameters evaluated during preformulation studies.

Description:

It is the initial evaluation during preformulation studies which assess the colour of the substance. This was only a descriptive test.

Solubility:

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

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 Mesalazine was conducted as per monograph.

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 Mesalazine was measured by using moisture balance. Weigh approximately 2gm of Mesalazine and placed into a plate of moisture balance. Set the temperature to 45°C. Measure the moisture content of drug in percentage.

Flow Properties

(Angle of Repose)[8]:

Angle of repose is defined as the maximum angle possible between the surface of the pile of the powder and horizontal plane.

Bulk density:

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.

Tapped density:

Tapped density is achieved by mechanically tapping a 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.

Measurement of Powder Compressibility

Carr's Compressibility Index:

Compressibility index are a measure of the tendency for arch formation and the ease with which the arches will fail.

Hausner's ratio:

Hausner found that the ratio ρ_t / ρ_{bulk} was related to interparticle friction and, as such could be used to predict powder flow properties.

Particle Size Analysis:

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.

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 therefore very useful to the formulator in selecting appropriate excipients. It is done by two methods, Physical & Chemical

Preparation of Granules for Compression

Matrix tablet of Mesalazine was prepared by direct compression method. All tablet ingredients was accurately weighed. The average weight of each uncoated tablet was 450 mg.

Formulation of colon targeted matrix tablet of Mesalazine

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

Table 1: Formulation Trial Batches

Ingredients	Quantity of Ingredients (mg/tab)					
	F1	F2	F3	F4	F5	F6
Mesalazine	250	250	250	250	250	250
Eudragit S-100	80	60	50	35	20	14
Ethyl cellulose	60	55	40	25	15	10
Lactose (DCL 21)	50	75	100	130	154	165
Talc	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	6	6
Total weight (mg)	450	450	450	450	450	450

Coating Formula:

6% coating has been given for all the formulations to protect the drug from acidic environment.

Table 2: Composition of Ingredient for Enteric Coating

Ingredients	Quantity/1000 Tablet (gm)
Eudragit FS 30 D	125
Triethyl citrate	1.875
Talc	18.75
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. Finally the volume were make up to required quantity with purified water**.** Filtered the above solution with #100 mesh.

Evaluation of Powder Blend:

The powder blends were evaluated for the following parameters before compression into tablets. Angle of repose, Bulk density, Tapped density, Compressibility index, Hausner's ratio &

Moisture content.

Evaluation of Post-Compression Parameters:

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.

Hardness:

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging, and shipping. Tablet hardness of all the formulations was measured using a Monsanto hardness tester.

Thickness:

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. Thickness of all the formulations was measured using a Vernier caliper.

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.

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 37^0C 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 37^0C 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.

***In-Vitro* Dissolution Studies:**

The release rate of Mesalazine from tablets were determined using USP Dissolution Testing

Apparatus 2 (paddle method).The test was performed using 900ml of 0.1N HCL at $37^0 \pm 0.5^0$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.

Assay (By UV method) Preparation of standard solution:

Weigh accurately 100.0 mg of Mesalazine 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 50ml with phosphate buffer.

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. The ICH guideline recommends the following storage conditions for stability studies:

RESULTS AND DISCUSSION

Preformulation studies:

Evaluation of Mesalazine (API):

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

Table 3: Physical Characteristics of API

Tests	Specification	Results
Color	White or off white powder	White or off white powder
Solubility	Practically insoluble in water, freely soluble in acetone, methanol & in methylene chloride. It dissolves in dilute solution of alkali hydroxide & carbonates.	Complies
Melting point	282.0° -285.0°C	284.4°C
Moisture content	NMT 0.5 w/w%	0.3% w/w

Angle of Repose of Mesalazine:

The angle of repose of API was found to be $28^0.56' \pm 0.69$. Hence the drug belongs to fair flow and requires glidants to improve the flow property.

Table 4: Results of Angle of Repose

Raw material (API)	Angle of repose (Degree)	Average
Mesalazine	$28^0.14'$	$28^0.56' \pm 0.69$
Mesalazine	$29^0.36'$	
Mesalazine	$28^0.12'$	

Bulk Density and Tapped Density of Mesalazine:

The average bulk density and tapped density was found to be 0.453 ± 0.01 and 0.614± 0.003 g/ml respectively.

Table 5: Results of Bulk Density and Tapped Density of Mesalazine

Raw material (API)	Bulk density (g/ml)	Average bulk density (g/ml)	Tapped density (g/ml)	Average tapped density (g/ml)
Mesalazine	0.459	0.453 ± 0.01	0.612	0.614± 0.003
Mesalazine	0.452		0.614	
Mesalazine	0.448		0.618	

Powder Compressibility and Hausner's Ratio:

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

Table 6: Compressibility Index and Hausner's Ratio

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

Particle Size Distribution:

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

Table 7: Particle Size Distribution of Mesalazine

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

Drug - Excipients Compatibility Studies:

From the drug excipients compatibility study, it was observed that there was no characteristic change or interaction between drug and excipients.

Table 8: Drug - Excipients Compatibility

Composition	Initial	After 15days	After 30days	Conclusion
Mesalazine	White	NCC	NCC	Complies
Mesalazine + Excipients	White	NCC	NCC	Complies

NCC- No Characteristic Change.

Thin Layer Chromatography (TLC):

Pure Mesalazine shows Rf value of 0.63. These are also prominent in the physical mixtures containing Mesalazine and other excipients in the final formula. This indicates that there is no interaction between the drug and excipients.

Table 9: Chemical Compatibility of Mesalazine and Excipients

S. No.	Mesalazine +Excipients	Room Temperature 40°C & 75% RH in days						Result
		Initial		15th		30th		
		Rf_1	Rf_2	Rf_1	Rf_2	Rf_1	Rf_2	
1.	Mesalazine	0.63	0.61	0.61	0.56	0.61	0.58	NC
2.	*D + $NaHCO_3$	0.56	0.55	0.62	0.60	0.59	0.63	NC
3.	D + Na alginate	0.62	0.61	0.50	0.36	0.53	075	NC
4.	D + Chitosan	0.58	0.56	0.63	0.61	0.61	0.50	NC
5.	D + Carbopol	0.62	0.66	0.52	0.65	0.61	0.50	NC
6.	D + MCC	0.60	0.61	0.50	0.56	0.55	0.68	NC
7.	D + Xanthan gum	0.61	0.56	0.55	0.59	0.56	0.60	NC
8.	D + Lactose	0.56	0.53	0.53	0.52	0.61	0.63	NC
9.	D + Adipic Acid	0.52	0.55	0.58	0.53	0.55	0.62	NC
10.	D + Talc	0.56	0.52	0.55	0.61	0.58	0.59	NC
11.	D + Mg stearate	0.52	0.59	0.60	0.52	0.60	0.53	NC

Rf_1* = standard value & Rf_2* = sample value. D*= Mesalazine, NC* - No Change

Evaluation of Lubricated Powder Blend:

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

Table 10: Results of Precompressional Parameters

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	29.05°±0.53	1.15 ± 0.05
F2	0.31±0.03	0.35 ± 0.05	12.10±0.54	1.13 ±0.28	33.02°±0.35	1.28 ± 0.02
F3	0.37 ± 0.01	0.42 ± 0.06	13.63±0.38	1.13 ±0.12	30.09°±0.19	1.42 ± 0.02
F4	0.38 ± 0.07	0.40 ± 0.08	11.57±1.05	1.14± 0.85	31.02°±0.60	1.21 ± 0.06
F5	0.35 ± 0.10	0.44 ± 0.06	12.60±0.86	1.12 ±0.74	29.03°±0.48	1.33 ± 0.03
F6	0.41± 0.06	0.46± 0.01	12.98±0.65	1.13 ±0.24	31.05°±0.25	1.15 ± 0.02

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

- 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 within 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 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.
- If the angle of repose is within 35^0, it indicates good flow property of the granules. The result 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.

Evaluation of Finished Product (Uncoated)

Table 11: Results of Finished Product (Uncoated)

Parameters	F1	F2	F3	F4	F5	F6
Average weigh(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)	25’59”	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.

- 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/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 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.

Evaluation Parameters of Mesalazine Enteric Coated Tablets:

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

Table 12: Results of Post Compressional Parameters

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

Comparative Data's of Uncoated and Enteric Coated Mesalazine Tablets:

Mesalazine Enteric coated tablets were compared with the same trial of uncoated Mesalazine 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 13: Results of Comparative Data

Trial	Thickness (mm)	Weight variation (mg)	Assay (%)	Drug release (%)
F6 Uncoated	5.9 ± 0.16	451±5	100.21±0.12	99.69 at 12 hrs
F6 Enteric coated	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

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

Table 14: Dissolution profile of enteric coated tablet

Dissolution Media	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	5 Hrs	10.09±0.78	12.74±0.43	16.76±0.13	20.72±0.43
Phosphate buffer)	8 Hrs	45.18±0.95	61.24±0.52	72.21±0.95	81.51±0.57
	12 Hrs	61.24±0.57	72.19±0.43	84.31±0.57	90.71±0.95
	16 Hrs	78.22±0.78	82.43±0.57	92.65±0.95	98.51±0.78

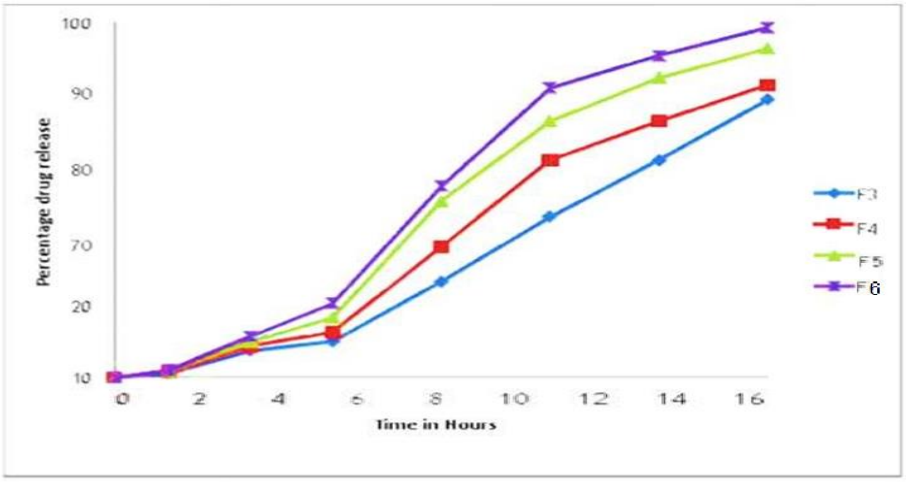

Figure 1: Graphical representation of *in-vitro* drug release

F1:

The method used in this trial is direct compression. The concentration of Eudragit S 100 used was 80 mg/unit, Ethyl cellulose concentration was 60mg/unit. Lactose DCL 21 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 diluent 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 was 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 16 hrs.

F4:

In trial 4 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 16 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 16 hrs. This trial was taken as confirmatory trial and subjected as stability studies.

Stability studies:

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 15: Stability studies for post compression parameters of (F-6) enteric coated tablets

Post compression Parameters	Storage condition: 40^0C± 2^0C /75±5%RH Initial	1st month	2nd month	3rd month
Description	White colored Enteric coated tablet	White colored Enteric coated tablet	White colored Enteric coated tablet	White colored 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.

***In-Vitro* Drug Release and Assay:**

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.

Table 16: *In-Vitro* Drug Release and Assay

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	16	98.51	98.31	97.42	97.28	100.21	100.1

CONCLUSION

Physical observation and TLC studies were used to determine API nature and excipient compatibility. API and all selected excipients exhibited no interaction. Direct compression method was used to successfully manufacture Mesalazine matrix tablets. The tablets were examined pre- and post-compression as per standards. Results met pharmacopoeia standards. Mesalazine matrix tablets were pan-coated with Eudragit FS 30D. F6 showed 98.51% drug release at 16 hours. Since it protects the core under acidic conditions while releasing drug quickly in the intestines. F6 was the best trial formulation. From the results, it can be concluded that formulation F6 containing enteric coated matrix tablet of Mesalazine is a promising formulation to treat inflammatory bowel diseases (ulcerative colitis) without gastric irritation or ulcers, which is useful for patients with a history of ulcerative colitis.

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