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Research

Formulation and evaluation of mesalamine tablets for Colon drug delivery systems

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Abstract

Objective of the current study is to develop colon targeted drug delivery systems for Mesalamine. Eudragit S-100 and Ethyl cellulose is used as polymers in this drug delivery system. The colon targeted tablet was prepared by direct compression technique. Study of the preformulation characteristics and FTIR studies indicates that there was no interaction between Mesalamine and excipients used. 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. From among the entire batches, formulation F4 showed 98.90% 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 F4 was considered as best formulation.

Keywords: Mesalamine, Eudragit S-100, Ethyl cellulose, and colon targeted drug delivery systems.

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. 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 iswell 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.

Tablets [5]

Tablets are solid dosage forms each containing a unit dose of one or more medicaments. They are intended for oral administration. Some tablets are swallowed whole or after being chewed, some are dissolved or dispersed in water before administration and some are retained in the mouth where the active ingredient is liberated. Because of their composition, method of manufacture or intended use, tablets present a variety of characteristics and consequently there are several categories of tablets. Tablets are usually solid, the end surfaces of which are flat or convex and the edges of which may be bevelled. They may exist in other shapes like triangular, rectangular, etc also.They may have lines or break-marks and may bear a symbol or other markings. They are sufficiently hard to withstand handling without crumbling or breaking.

Advantages of Tablets [6]

- ✓ They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
- ✓ They are in general the easiest and cheapest to package and strip of all oral dosage forms.
- ✓ They may provide the greatest ease of swallowing with the least tendency for "hang-up" above the stomach, especially when coated, provided that tablet disintegration is not excessively rapid.
- ✓ They lend themselves to certain special release profile products, such as enteric or delayed release products.
- ✓ They are better suited to large-scale production than the other unit oral forms.
- ✓ They have the best-combined properties of chemical.
- ✓ Cost is low.
- ✓ Lighter and compact.
- ✓ Easy to swallowing with least tendency for hang-up.
- ✓ Sustained release product is possible by enteric coating.
- ✓ Objectionable odour and bitter taste can be masked by coating technique.
- ✓ Suitable for large scale production.
- ✓ Greatest chemical and microbial stability over all oral dosage form.
- ✓ Product identification is easy and rapid requiring no additional steps whenemploying an embossed and or monogrammed punch face.

Disadvantages of the tablets

- ✓ Some drugs resist compression in to dense particles, owing to their amorphous nature or flocculent, low density character.
- ✓ Drugs with poor wetting, slow dissolution properties, intermediate to large dosages, optimum absorption high in the GIT or any combination of these features are very challenging for the formulators.
- ✓ Difficult to swallow in case of children and unconscious patients.
- ✓ Bitter tasted drugs, drugs with an objectionable odour or drugs that are sensitive to oxygen may require encapsulation or coating. In such cases, capsule may offer the best and lowest cost.

Pharmaceutical ingredients used in the formulation of tablets

Active ingredients

A drug substance is the Active Pharmaceutical Ingredient (API) or component that produces pharmacological activity.

Fillers/diluents

Diluents are used as excipients for direct compression formulas have been subjected to prior processing to give them flow ability and compressibility.

Eg: Lactose, Dibasic calcium phosphate, Dextrose, Calcium carbonate, Magnesium carbonate, Starch, Sucrose, Mannitol.

Binders

Binders are agents which are used to impart cohesive qualities to the powdered material. Binders are added either dry or in liquid form during wet granulation to form granules or to promote cohesive compacts for directly compressed tablets.

Eg: Povidone, Acacia, Gelatin, HPMC, Polyvinyl pyrrollidone, Hydroxypropyl cellulose.

Disintegrants

Disintegrants are substances or a mixture added to a tablet formulation to facilitate its breakup or disintegration of the tablet after administration. The active ingredient must be released from the tablet matrix as efficiently as possible to allow rapid dissolution.

Eg: Microcrystalline cellulose, Starch, Crosscarmellose sodium, Sodium starch glycolate.

Lubricants 8
During compression lubricants acts as to reduce the interface between the face of the die and the surface of the tablet and act to reduce the friction at this interface during ejection of the tablet from the tablet press. Inadequate lubrication of this interface results in the production of tablets with a pitted surface and is due to their ability of the tablet surface to detach from the surface of the tablet die. There are two main categories of lubricants: (1) insoluble and (2) soluble. Insoluble lubricants are added to the final mixing stage prior to the tablet compression.
Eg: Magnesium stearate, Stearicacid, Glycerylpalmitostearate.
Soluble lubricants are principally employed to overcome the possible deleterious effects of their insoluble counterparts on the time required for tablet disintegration and drug dissolution. Eg: Polyethylene glycol, Polyethylene stearate, Lauryl sulphate salt.

Glidants 9
Glidants are added to the formulation in order to improve the flow properties of the material to be fed into the die and sometimes aid in particle rearrangement within the die during the early stages of compression. They may act by interposing their particles between those of the other components and so, by virtue of their reduced adhesive tendencies, lower the overall interparticulate friction of the system.
Eg: Talc, Colloidal silicon dioxide.

Adsorbents
Adsorbents are used whenever it is required to include a liquid or semisolid component, e.g. a drug or a flavour, within the tablet formulation. As the production of tablets requires solid components, the liquid/semisolid constituent is adsorbed on to a solid component which, in many cases, may be one of the other components in the tablet formulation (e.g. diluent) during mixing. If this approach is not possible, an adsorbent is specifically included in the formulation.
Eg: Magnesium oxide/Carbonate, kaolin/Bentonite.

Sweetening agents/flavours
Sweetening agents and flavours (in accordance with other dosage forms) are employed to control the taste and hence the acceptability of tablets. These agents are of particular importance if the conventional tablet contains a bitter drug or, more importantly, if the tablet is a chewable tablet.
Eg: Aspartame, Sucralose, Sucrose, Glycerine, Mannitol, Sorbiltol, Acesulfame potassium. Flavouring agents are incorporated into the formulation to give the tablet a more pleasant flavouror mask an unpleasant one. Eg: Chocolate, Peppermint, Pineapple and Vanilla flavour.

Colours
Colorants do not contribute to the therapeutic activity and to improve the product bioavailability or stability. Their main role is to facilitate identification and to enhance the aesthetic appearance of the product. All colorants used in pharmaceuticals must be approved and certified by the FDA. Some commonly used Pharmaceutical colorants are,
Eg: Erythrosine, Tartrazine, Sunset Yellow, Brilliant blue.

MATERIALS AND METHODS

Mesalamine-Provided by SURA LABS, Dilsukhnagar, Hyderabad, Eudragit S-100-Merck Specialities Pvt Ltd, Mumbai, India, Ethyl cellulose-Merck Specialities Pvt Ltd, Mumbai, India, Lactose -Merck Specialities Pvt Ltd, Mumbai, India, Talc-Merck Specialities Pvt Ltd, Mumbai, India, Magnesium stearate-Merck Specialities Pvt Ltd, Mumbai, India.

Methodology

Preformulation studies

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. The basic purpose of the preformulation 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.

Contents of preformulation studies
Organoleptic properties – Appearance, colour and odour.
Microscopic examination – Crystal habit, crystal shape and size.
Physical properties – Density, particle size, surface area, flow properties, hygroscopicity. Solvent properties – pH of solution, solubility and dissolution rate, drug excipient¬ compatibility study.

Important parameters evaluated during preformulation studies
Evaluation of API
The Evaluation of Mesalamine was done according to IP. Following are some of the important parameters evaluated during Preformulation studies and results are tabulated in Table.

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

Determination of Mesalamine Solubility: Determination of solubility of drug by visual observation. An excess quantity of Mesalamine was taken separately and adds in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the Table.

Determination of Mesalamine Melting point : The melting point of Mesalamine was determined by capillary tube method according to the USP. A sufficient quantity of Mesalamine powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Mesalamine in the tube passed into liquid phase**.**

Analytical method development
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 solutions.

Determination of absorption maxima:
A solution containing the concentration 10 µg/ mL drug was prepared in 0.1N HCL UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 800 nm.

Preparation calibration curve:
10mg Mesalamine pure drug was dissolved in 10ml of methanol (stock solution1) from stock solution 1ml of solution was taken and made up with10ml of 0.1N HCL (100µg/ml). From this 1ml was taken and made up with 10 ml of 0.1N HCL (10µg/ml). The above solution was subsequently diluted with 0.1N HCL to obtain series of dilutions Containing 2, 4, 6, 8, 10 µg /ml of per ml of solution. The absorbance of the above dilutions was measured at 230 nm by using UV-Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis.

Flow Properties
Measurement of Micromeritic properties of powders
Angle of repose
The angle of repose of API powder is determined by the funnel method. The accurately weighed powder blend is taken in the funnel. The height of the funnel is adjusted in a way that the tip of the funnel just touched the apex of the powder blend. The powder blend is allowed to flow through the funnel freely on o the surface. The diameter of the powder cone is measured and angle of repose is calculated using the following equation.

$\tan \Theta = h/r$ ……(1)
Where , h and r are the height and radius of the powder cone.

Table 1: Flow Properties and Corresponding Angle Of Repose

Flow Property	Angle of Repose (^{0})
Excellent	25-30
Good	31-35
Fair- aid not needed	36-40
Passable-may hang up	41-45
Poor-must agitate, Vibrate	46-55
Very Poor	56-65
Very, very Poor	>66

Bulk density

The powder sample under test is screened through sieve No.18 and the sample equivalent to 25 gm is weighed and filled in 100 ml graduated cylinder and the powder is leveled and the unsetled volume , V_0 is noted . The bulk density is calculated in g/cm^3 by the formula.

Bulk density = M/V_0 ……. (2)

V_0 = apparent unstirred volume

M= Powder mass

Tapped density

The powder sample under test is screened through sieve No. 18 and the weight of the sample equivalent to 25 gm filled in 100ml graduated cylinder. The mechanical tapping of cylinder is carried out using tapped density tester at a nominal rate for 500 times initially and the tapped volume V_0 is noted. Tappings are preceded further for an additional tapping 750 times and tapped volume, V_b is noted. The difference between two tapping volume is < 2%, V_b is considered as a tapped volume V_f. The tapped density is calculated in g/cm^3 by the formula.

Tapped density = M/V_f …… (3)

M = weight of sample powder taken

V_f = Tapped volume

Compressibility index

The compressibility index of the powder blend is determined by Carr's index to know the flow character of a powder. This formula for Carr's index is as below:

Carr's Index (%) = [(TD-BD)/TD] x100 …… (4)

Hausner's ratio

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material. The ratio of tapped density to bulk density of the powders is called the Hausner's ratio. It is calculated by the following equation.

H = Pt / ρB ……..(5)

where ρT= tapped density, ρB = bulk density

Table 2: Scale of Flowability

Compressibility index (%)	Flow character	Hausner Ratio
≤ 10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59
> 38	Very, very Poor	> 1.60

Formulation of colon targeted matrix tablet of Mesalamine

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

- **Weighing:** A required quantity of raw materials was weighed accurately.
- **Sifting:** The Mesalamine, Eudragit S100 and Ethyl cellulose were sifted using 60 # mesh. Lactose (DCL 21) sifted through 40 # mesh.
- **Mixing:** The sifted powders were mixed in polythene bag for ten minutes.

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

Formulation chart

S. No	INGREDIENTS	QUANTITY OF INGRIDIENTS (mg/tab)					
		F1	F2	F3	F4	F5	F6
1	Mesalamine (g)	0.375	0.375	0.375	0.375	0.375	0.375
2	Eudragit S-100	100	200	300	-	-	-
3	Ethyl cellulose	-	-	-	100	200	300
4	Lactose	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
5	Talc	15	15	15	15	15	15
6	Magnesium stearate	20	20	20	20	20	20
Total weight (mg)		800	800	800	800	800	800

RESULT AND DISCUSSION

The present study was carried out to formulate colon targeted matrix tablet of Mesalamine using direct compression method. In this method, the powder blend was subjected to various evaluation studies such as bulk density, tapped density, compressibility index and hausner'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 stability studies. 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. The results are presented in appropriate tables and figures.

Evaluation of ibuprofen (api)

Table 3: PHYSICAL CHARACTERISTICS OF API

S.No	Tests	Specification	Results
1	Colour	off-white to tan powder	off-white to tan powder
2	Solubility	Practically insoluble in water, freely solublein Acetonitrile and methanol.	Complies
3	Melting point	260-280 °C	265°C
4	Moisture content	NMT 0.2 w/w%	0.2% w/w

The colour, solubility, melting point and moisture content of the API were evaluated. It was found to be within the range of the monograph. Formulation and evaluation of Mesalamine tablets for colon drug delivery systems.

Analytical Method

Graphs of Mesalamine were taken in 0.1N HCL and in pH 6.8 phosphate buffer at 230 nm and 232 nm respectively.

Table 4: Observations for graph of Mesalamine in 0.1N HCL

Concentration (µg/ml)	Absorbance
0	0
5	0.125
10	0.231
15	0.334
20	0.458
25	0.561

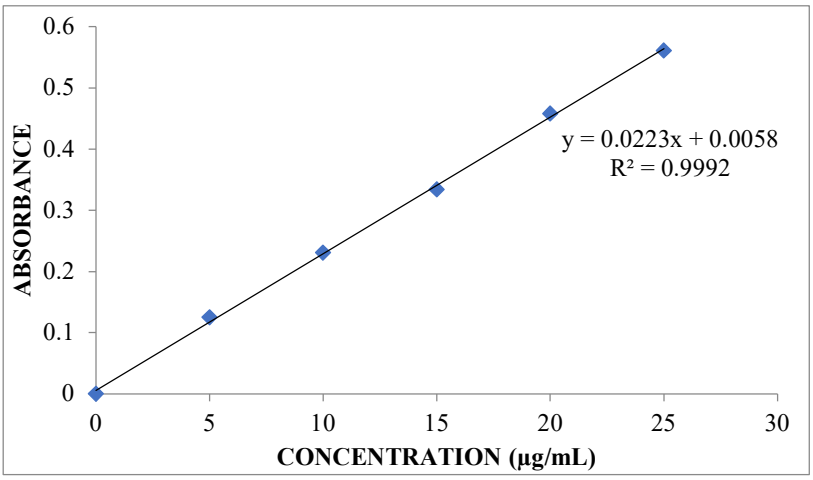

Fig 1: Standard curve of Mesalamine

Table 5: Standard graph values of Mesalamine at 232 nm in pH 7.4 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
5	0.134
10	0.252
15	0.357
20	0.492
25	0.599

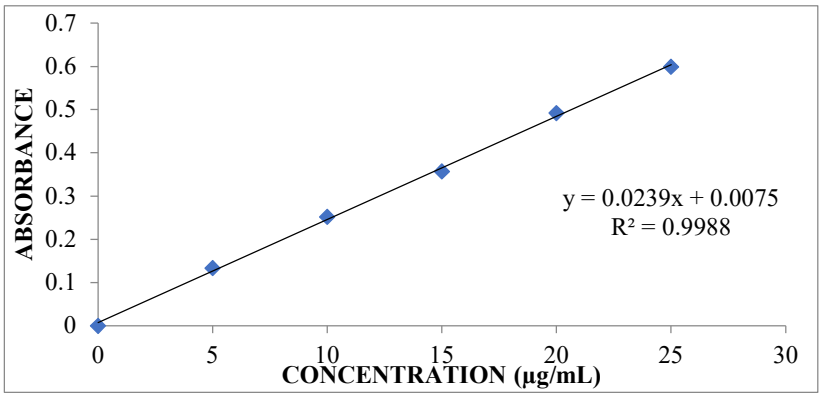

Fig 2: Standard curve of Mesalamine

Drug - excipients compatibility studies

It was determined as per procedure given in material and method part

Table 6: Drug - Excipients Compatibility

Composition	Initial	After 15days At 25°C	After 30days At 25°C	Conclusion
Mesalamine	off-white to tan powder	NCC	NCC	Complies
Mesalamine + Excipients	off-white to tan powder	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 Mesalamine.

IR spectral analysis

The FTIR studies of Mesalamine and Mesalamine with Excipients

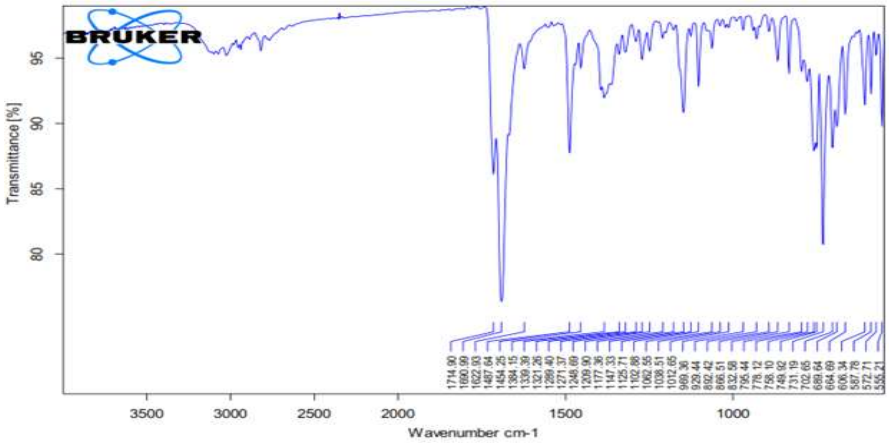

Fig 3: FT-TR Spectrum of Mesalamine pure drug

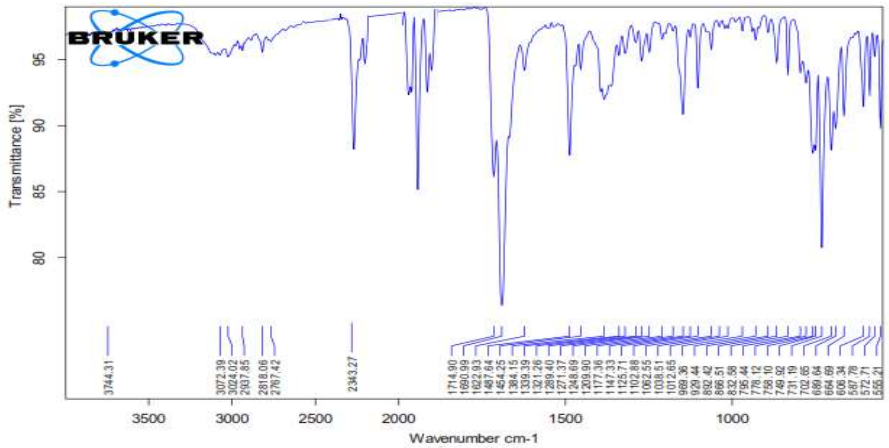

Fig 4: FT-IR Spectrum of Optimised Formulation

Pure Mesalamine spectra showed sharp characteristic peaks. These peaks are also prominent in the FTIR spectra's of the physical mixtures containing Mesalamine 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.

Preformulation parameters of powder blend

Table 7: Pre-formulation parameters of Core blend

Formulation code	Angle of repose (Ɵ)	Bulk density (gm/cm^3	Tapped density(gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	26.05±0.65	0.307	0.444	13.46	1.16
F2	25.94±0.56	0.384	0.434	17.85	1.22
F3	26.02±0.61	0.267	0.307	13.33	1.15
F4	26.21±0.93	0.346	0.404	14.35	1.16
F5	26.28±0.33	0.323	0.376	14.09	1.16
F6	25.81±0.61	0.393	0.453	13.24	1.15

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range showing that the powder has good flow properties. The tapped density of all the formulations powders has good flow properties. The compressibility index of all the formulations was found to be below 17.85 which show

that the powder has good flow properties. All the formulations have shown the Hausner ratio below 1.22 indicating the powder has good flow properties.

Evaluation of finished product (uncoated)

Table 8: Evaluated for different parameters

Formulations	Parameters					
	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Disintegration time (min)	Assay (%)
F1	798.15	6.92	5.6	0.26	6.54	96.18
F2	799.25	6.69	5.3	0.32	8.21	99.82
F3	801.39	6.87	5.0	0.46	15.37	97.60
F4	797.52	6.35	4.9	0.51	4.42	99.72
F5	800.10	6.16	5.2	0.63	6.09	100.05
F6	801.57	6.61	4.8	0.72	10.72	98.76

✓ The thickness of the tablets was in the range of 6.16 to 6.92 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 4.8 to 5.6 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 weight variation of all the formulations was found to be within the permissible range.
✓ The percentage of drug content was found among different batches of the tablets and ranged from 96.18 to 100.05 which were within the acceptable limits.

Evaluation parameters of mesalamine enteric coated tablets

Formulation	Thickness (mm)	Weight variation(mg)	Disintegration time(min)	Assay (%)
F4	6.51 ± 0.03	821.12±0.42	210.41±2.14	99.48 ± 0.06

Mesalamine tablet of the above trial (F4) 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, weight variation, Disintegration assay and *in-vitro* studies.

Comparative datas of uncoated and enteric coated mesalamine tablets

Formulation	Thickness (mm)	Weight variation (mg)	Assay (%)
F4 Un coated	6.35± 0.10	797.52	99.72±0.12
F4 Enteric coated	6.51 ± 0.03	821.12	99.48 ± 0.06

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

Mesalamine Enteric coated tablets were compared with the same trial of uncoated Mesalamine 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 9: *In-Vitro* Dissolution profile of Enteric coated Tablets

TIME (H)	CUMULATIVE % OF DRUG RELEASE					
	F1	F2	F3	F4	F5	F6
In dissolution media 0.1 N HCL						
0	0	0	0	0	0	0
2	1.05	1.68	1.25	2.31	1.84	1.23

In dissolution media Simulated Intestinal Fluid (7.4pH Phosphate buffer)						
5	6.71	8.03	10.85	12.58	14.10	10.28
8	10.14	13.96	16.96	28.76	21.65	18.10
12	28.89	31.24	45.69	57.18	50.96	43.37
16	46.63	49.73	51.52	64.44	60.25	57.05
20	63.56	70.19	76.07	91.16	86.79	82.83
24	76.12	82.88	83.61	98.90	96.91	91.95

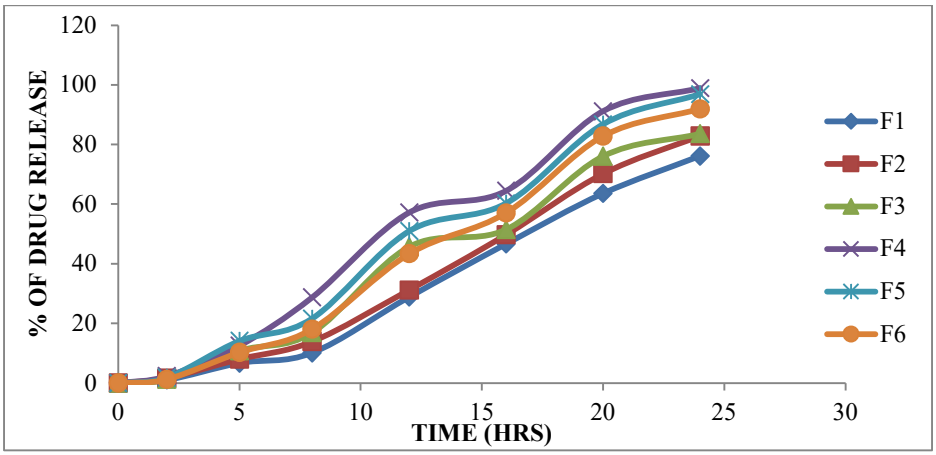

Fig 5: Graphical representation of *in-vitro* drug release

DISCUSSIONS

F1: The method used in this trial is direct compression. The concentration of Eudragit S 100 used was 100 mg/unit, and the concentration of Talc and magnesium stearate used. 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 was increased to 200 mg/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 was increased to 300 mg/unit.

F4: In trial 4 the concentration of Ethyl cellulose was further decreased to 100mg/unit and The disintegration time of tablet was better than the above formulations limits. The tablets were subjected to *in-vitro* dissolution study. The tablets are subjected to *in-vitro* dissolution study. The percentages of drug release were found to be 98.90 at 24 hrs. It was better than the earlier trials.

F5: The concentration of Ethyl cellulose was further increased to 200mg/unit. The disintegration time of tablet was found to be within the limit. The tablets are subjected to *in-vitro* dissolution study. The percentages of drug release were found to be 96.91 at 24 hrs. It was better than the earlier trials.

F6: The concentration of Ethyl cellulose was further increased to 300mg/unit. The tablets of this trial are subjected to *in-vitro* dissolution study. The percentage of drug release showed 91.95 at 24 hrs.

Hence from the above dissolution data it was concluded that F4 formulation was considered as optimised formulation because good drug release (98.90 %) in 24 hours.

Table 10: Release Kinetics

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
2.31	2	1.414	0.364	0.301	1.990	1.155	0.4329	-1.636	97.69	4.642	4.606	0.036
12.58	5	2.236	1.100	0.699	1.942	2.516	0.0795	-0.900	87.42	4.642	4.438	0.203
28.76	8	2.828	1.459	0.903	1.853	3.595	0.0348	-0.541	71.24	4.642	4.145	0.496
57.18	12	3.464	1.757	1.079	1.632	4.765	0.0175	-0.243	42.82	4.642	3.499	1.143
64.44	16	4.000	1.809	1.204	1.551	4.028	0.0155	-0.191	35.56	4.642	3.288	1.353
91.16	20	4.472	1.960	1.301	0.946	4.558	0.0110	-0.040	8.84	4.642	2.068	2.574
98.9	24	4.899	1.995	1.380	0.041	4.121	0.0101	-0.005	1.1	4.642	1.032	3.609

Optimised formulation F4 was kept for release kinetic studies. From the above graphs it was evident that the formulation F4 was followed **Zero order release** kinetics mechanism.

Summary

The present work involves the formulation of colon targeted matrix tablet of Mesalamine by using direct compression method. Literatures regarding, Mesalamine 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 by performing FT-IR method. 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 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 Mesalamine 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 Mesalamine tablets and uncoated Mesalamine tablets are evaluated for the hardness, thickness and disintegration time.

Out of six formulations, the formulation F6 showed 90.90 % 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 F4 was considered as the optimized formulation.

CONCLUSION

Preformulation studies were performed to study the nature of Mesalamine and compatibility of Mesalamine with excipients by physical observation and FT-IR studies. The results showed that there was no interaction between Mesalamine and all the excipients selected. The Mesalamine 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 Mesalamine matrix tablets were coated with enteric polymer Eudragit FS 30D and Ethyl cellulose by pan coating method. From among the entire batches, formulation F4 showed 98.90% 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 F4 was considered as best formulation. From the results obtained, it can be concluded that formulation F4 containing enteric coated

matrix tablet of Mesalamine would be a promising formulation to achieve the purpose which treat inflammatory bowel diseases (ulcerative colitis) without any gastric irritation.

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