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Formulation and Evaluation of Mesalazine Colon Targeted Matrix Tablets

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A B S T R A C T

In the present study Mesalazine colon targeting was done by suing various polymers. To achieve pH-independent drug release of Mesalazine, pH modifying agents (buffering agents) were used. Colon targeted tablets were prepared in two steps. Initially core tablets were prepared and then the tablets were coated by using different pH dependent polymers. Ethyl cellulose, Eudragit L100 and S100 were used as enteric coating polymers. The precompression blend of all formulations was subjected to various flow property tests and all the formulations were passed the tests. The tablets were coated by using polymers and the coated tablets were subjected to various evaluation techniques. The tablets were passed all the tests. Among all the formulations F7 formulation was found to be optimized as it was retarded the drug release up to 12 hours and showed maximum of 97.87% drug release. It followed first order kinetics mechanism. Stability studies was Performed no chemical changes was occurred.

Keywords: Mesalazine, Colon drug delivery

A R T I C L E I N F O

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1. Introduction

The oral route is considered to be most convenient for administration of drugs to patients. Oral administration of conventional dosage forms normally dissolves in the stomach fluid or intestinal fluid and gets absorbed from these regions of the gastrointestinal tract (GIT) depending upon the physicochemical properties of the drug[1]. Numerous drug entities based on oral delivery have been successfully commercialized, but many others are not readily available by oral administration, which are incompatible with the physical and/or chemical

environments of the upper gastrointestinal tract (GIT) and/or demonstrate poor uptake in the upper GIT. Due to the lack of digestive enzymes, colon is considered as suitable site for the absorption of various +-drugs. Over the past two decades the major challenge for scientist is to target the drugs specifically to the colonic region of GIT. Previously colon was considered as an innocuous organ solely responsible for absorption of water, electrolytes and temporary storage of stools. But now it is accepted as important site for drug delivery.

Factors to be considered in the design of colon specific drug delivery system

To reach the colon and to be able to specifically deliver and absorb the drug there, the dosage forms must be formulated taking into account the obstacles of the gastrointestinal tract. The various strategies developed to achieve this goal have used the specific characteristics of this organ, i.e. transit time, pH, microflora, enzymes disease and the colonic environment. Nevertheless, these parameters can vary from one individual to the next and also according to the pathological condition and diet documented that gastric emptying varies with different types of dosage forms[2].

Physiological Factors:

a) Gastrointestinal transit [3]
b) Colonic Transit [4]
c) pH in the Colon
d) Colonic microflora [5].
e) Volume of the ascending colon
f) Disease and the Colonic Environment

Drugs Suitable For Colonic Drug Delivery

A number of drugs available as sustained release or delayed release or timed release tablets or capsules for oral administration are anti-inflammatory drugs, anti-hypertensive drugs, etc. Unless these drugs have good absorption characteristics in the colon, their intended use in the management of respective disorder s through sustained release or timed release formulations will be in question. The drugs that are having good absorption properties from the colon include theophylline, glibenclamide and oxeprenolol. Diclofenac, ibuprofen, nitrenidipine, isosorbide, metoprolol (anti-hypertensive), nifedipine etc. and hence can be investigated for better bioavailability through colon specific drug delivery[6].

Approaches to colon-specific drug delivery

In recent years, a large number of solid formulations targeting the lower parts of the Gastro Intestinal Tract, especially the colon, have been reported. These formulations may be broadly divided into four types, which are:

- pH- dependent system designed to release a drug in response to change in pH
- Time controlled (or Time-dependent) system designed to release a drug after a predetermined time.
- Microbially-controlled system making use of the abundant entero-bacteria in the colon.
- Enzyme- based system. Prodrug.
- Pressure-dependent system making use of luminal pressure of the colon.

Among these, first three are most widespread formulation technologies being developed for pharmaceutical market[7].

- pH-Dependent Systems [8].
- Time-controlled (or time-dependent) systems [9].
- Microbially-Controlled Systems [10].
- Enzyme- based systems – prodrug [11].
- Pressure-dependent system

2. Materials and Methods

Analytical method development:

Determination of absorption maxima:

A solution of containing the concentration 10 µg/ ml was prepared in 0.1N HCl , 7.4 pH & phosphate buffer 6.8pH respectively, UV spectrum was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400.

Preparation calibration curve:

10mg of drug was accurately weighed and dissolved in 10ml of 0.1N HCl, 7.4 PH, and 6.8 PH in 10 ml volumetric flask, to make (1000 µg/ml) standard stock solution (1). Then 1 ml stock solution (1) was taken in another 10 ml volumetric flask to make (100 µg/ml) standard stock solution (2), then again 1 ml of stock solution (2) was taken in another 10 ml volumetric flask and then final concentrations were prepared 2, 4,6, 8, 10, 12, 14, 16, 18 ,and 20µg/ml with 0.1N HCl, 7.4 pH, and 6.8 pH. The absorbance of standard solution was determined using UV/ VIS spectrophotometer at 273nm. Linearity of standard curve was assessed from the square of correlation coefficient (r2) which determined by least-square linear regression analysis[12].

Analytical Method

Graphs of Mesalazine was taken in Simulated Gastric fluid (pH 1.2) and Simulated Intestinal Fluid (pH 6.8 and 7.4)

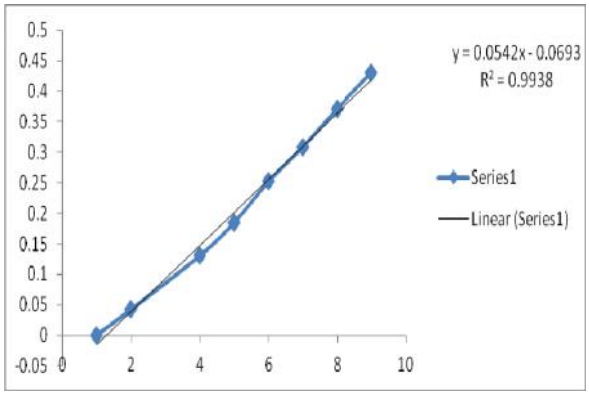

Figure 1: Standard graph of Mesalazine in 0.1N HCl

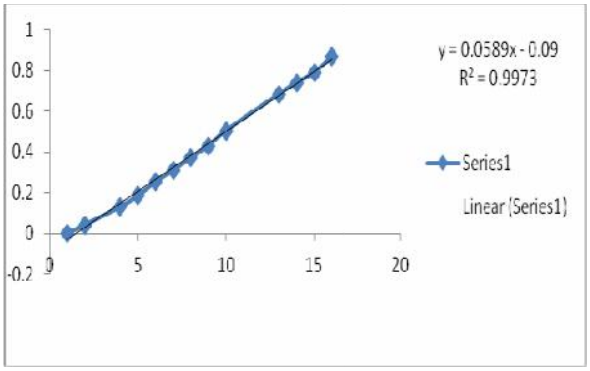

Figure 2: Standard graph of Mesalazine in 6.8 pH

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy:

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes[13]. By the application of the release kinetics to the drug release data we have observed which order of release kinetics optimised formulation follows From the above graphs it was observed that the first order release has the highest R^2 (0.993) value. Then it is evident that the formulation F7 was followed first order kinetics.

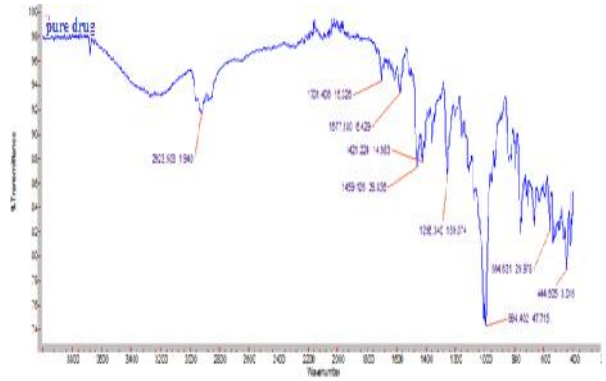

Figure 3: FTIR Spectrum of pure drug

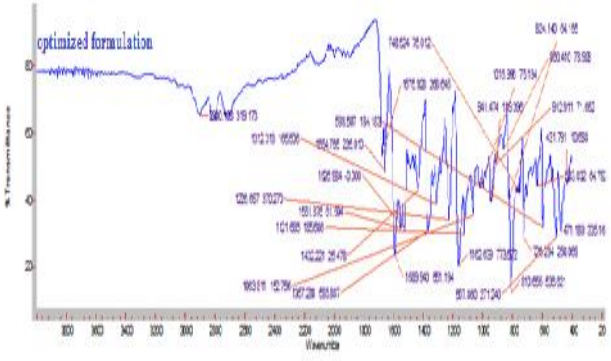

Figure 4: FTIR Spectrum of optimized formulation

By observing the above spectrums it was shown that there is not any change in the characterestic peaks of the drug and polymer it shows the compatability between the drug and polymer.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose:

A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula[14]:

$\tan \theta = h / r$ $\tan \theta$ = Angle of repose

h = Height of the cone, r = Radius of the cone base

Table 1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density: Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend[20]. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:

$$\text{Bulk Density} = M / V_o$$

Where, M = weight of sample

V_o = apparent volume of powder

Tapped density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated[21], in gm per L, using the formula[15]:

Tap = M / V

Where, Tap= Tapped Density

M = Weight of sample

V= Tapped volume of powder

Measures of powder compressibility:

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value[16]. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

Carr's Index = [(tap - b) / tap] × 100

Where, b = Bulk Density, Tap = Tapped Density

Table 2: Carr's index value (as per USP)

Carr's index	Properties
5 – 15	Excellent
12 – 16	Good
18 – 21	Fair to Passable
2 – 35	Poor
33 – 38	Very Poor
>40	Very Very Poor

Formulation development of Tablets:

Mesalazine colon targeted tablets were prepared by using compression coating technology. Initially internal core tablet containing drug and super disintegrate was formulated. For the prepared core tablet compression coating is done by using various compositions of polymers. Ethyl cellulose, Polymethacrylate polymers such as Eudragit L100 and Eudragit S100 are used as polymers for compression coating[17].

- Tablets are developed in two stages
- Preparation of core tablet containing drug and super disintegrate.
- Compression coating of prepared core tablets.

Formulation of core tablet:

The core tablets are formulated by using 250 mg of drug molecule, sodium starch glycollate as super disintegrate, Micro crystalline cellulose as diluent, talc and magnesium stearate as Glidant and Lubricant respectively. The composition of core tablet was given in below table[18-19].

Table 3: Composition of core tablet

Ingredient Name	Quantity (mg)
Mesalazine	250
Sodium starch glycollate	31.25
Talc	5
Magnesium stearate	5
MCC pH102	108.75
Total weight	400

Total weight of core tablet was fixed as 400 mg. The tablets are prepared by using 9mm flat punch. Then the prepared core tablets are subjected to compression coating by using various compositions of polymers.

Formulation of compression coated tablets:

The prepared core tablets were subjected to compression coating by using various compositions of polymers such as Ethyl cellulose, Eudragit L 100 and Eudragit S 100 as coating materials. The composition of coating layer is given in below table.

Compression coating layer was divided into two equal portions i.e., 50mg of each quantity .Half of the quantity of powder blend was placed in the die cavity, core tablet was placed exactly in the middle of die cavity and then remaining quantity of powder blend was placed over the core tablet so that the powder blend should cover all the sides and top side of core tablet uniformly. Then the tablets are compressed by using 10mm flat surfaced punch using 8 station tablet punching machine with the hardness of 4-4.5 kg/cm^2.Then the prepared compression coted tablets are evaluated for various post compression parameters as per standard specifications.

Evaluation of post compression parameters for prepared Tablets

The designed formulation compression coated tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula[21].

% Deviation = (Individual weight – Average weight / Average weight) × 100

Hardness:

For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation[22].

Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation[23].

Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = [(W1-W2) / W] × 100

Where, W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

Determination of drug content:

Both compression-coated tablets of were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Mesalazine were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve[24].

***In vitro* drug release studies**

Drug release studies of Mesalazine core tablets:

The core tablets containing 15mg Mesalazine of were tested in (pH 6.8), for their dissolution rates. Dissolution studies were performed using USP paddle type sample of 5 ml was withdrawn and replaced with equal volume of fresh medium. The samples were analyzed spectrophotometrically

at respective 270 nm[25-26].

Drug release studies of Compression coated Mesalazine tablets: The release of Mesalazine from coated tablets was carried out using USP paddle-type dissolution apparatus at a rotation speed of 50 rpm, and a temperature of 37±0.5 °C. For tablets, simulation of gastrointestinal transit conditions was achieved by using different dissolution media. Thus, drug release studies were conducted in simulated gastric fluid (SGF, pH 1.2) for the first 2 hours as the average gastric emptying time is about 2 hours. Then, the dissolution medium was replaced with enzyme- free simulated intestinal fluid (SIF, pH 7.4) and tested for drug release for 3 hours, as the average small intestinal transit time is about 3 hours, and finally enzyme- free simulated intestinal fluid (SIF, pH 6.8) was used upto 12 hours to mimic colonic pH conditions. Drug release was measured from compression coated Mesalazine tablets, added to 900 ml of dissolution medium. 5 ml of sample was withdrawn every time and replaced with fresh medium, samples withdrawn at various time intervals were analyzed spectrophotometrically at 275 nm and 270 nm respectively. All dissolution runs were performed for nine batches. The results were given with deviation[27-28].

Application of Release Rate Kinetics to Dissolution Data: Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data ar e fitted to the following equation.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$\text{Log } (100\text{-}F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model:

To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$$F = k\ t1/2$$

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t/ M_\infty = K\ t^n$$

Where, M_t/ M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for super case II transport, n > 1. In this model, a plot of log (M_t/ M_∞) versus log (time) is linear.

Hixson-Crowell release model:

$$(100\text{-}Q_t)^{1/3} = 100^{1/3} – K_{HC}.t$$

Where, k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

The present study was aimed to developing compression coated Mesalazine formulations for colon targeting using ethyl cellulose and enteric coating polymers like Eudragit L100 and Eudragit S 100. All the formulations were evaluated for physicochemical properties and *invitro* drug release studies.

Pre-formulation parameters of Core blend

Mesalazine blend was subjected to various pre-formulation parameters. The apparent bulk density and tapped bulk density values ranged from 0.52 to 0.581 and 0.606 to 0.671 respectively. According to Tables 7.3, the results of angle of repose and compressibility index (%) ranged from 32.74±0.12 to 37.08±0.96 and 13.37±0.38 to 14.72±0.62 respectively. The results of angle of repose (<35) and compressibility index (<23) indicates fair to passable flow properties of the powder mixture. These results show that the powder mixture has good flow properties. The formulation blend was directly compressed to tablets and *in-vitro* drug release studies were performed.

Quality Control Parameters For compression coted tablets: Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet. Total weight of tablet including core is 300 mg.

3. Results and Discussion

The present study was aimed to developing compression coated Mesalazine formulations for colon targeting using ethyl cellulose and enteric coating polymers like Eudragit L100 and Eudragit S 100. All the formulations were evaluated for physicochemical properties and *invitro* drug release studies.

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***In-Vitro* Drug Release Studies**

The compression coated tablets containing 250mg of Mesalazine were tested in 6.8 pH phosphate buffer solution for their dissolution rates. The release of Mesalazine from compression coated tablets was carried out using USP paddle-type dissolution apparatus at a rotation speed of 50 rpm, and a temperature of 37±0.5 °C. For tablets, simulation of gastrointestinal transit conditions was achieved by using different dissolution media. Thus, drug release studies were conducted in simulated gastric fluid (SGF, pH 1.2) for the first 2 hours as the average gastric emptying time is about 2 hours. Then, the dissolution medium was replaced with enzyme- free simulated intestinal fluid (SIF, pH 7.4) and tested for drug release for 3 hours, as the average small intestinal transit time is about 3 hours, and finally enzyme-free simulated intestinal fluid (SIF, pH 6.8) was used upto 12 hours to mimic colonic pH conditions. Drug release was measured from compression coated Mesalazine tablets, added to 900 ml of dissolution medium. 5 ml of sample was withdrawn every time and replaced with fresh medium, samples withdrawn at various time intervals were analyzed spectrophotometrically at 275 nm ,319 and 320 nm respectively. All dissolution runs were performed for six batches.

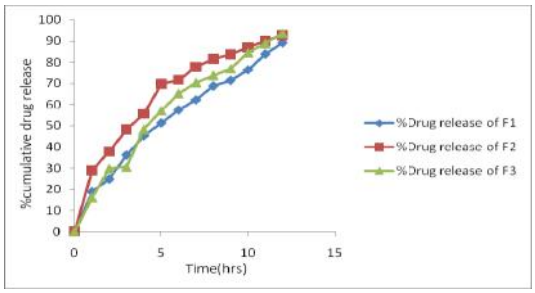

Figure 6: Dissolution of formulations F1-F3

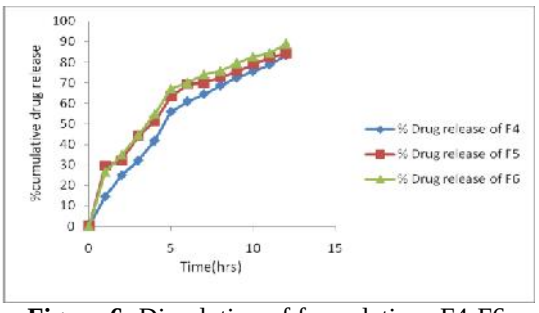

Figure 6: Dissolution of formulations F4-F6

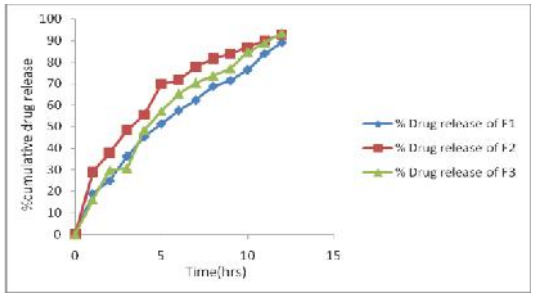

Figure 7: Dissolution of formulations F7-F9

By performing the *invitro* dissolution studies the drug release from the prepared formulations are observed that the formulation F7 showed the highest drug release(97.87%) in given time where F3,F8 showed significant drug release in given parameters.

Application of Release Rate Kinetics to Dissolution Data:

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

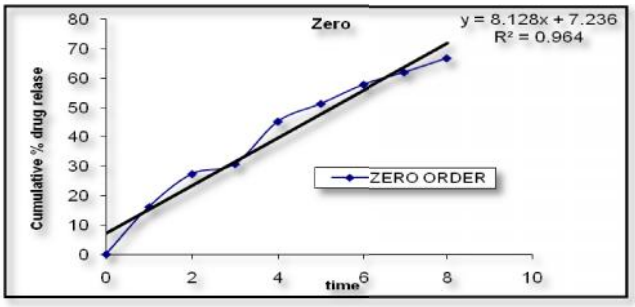

Figure 8: Zero order release kinetics graph

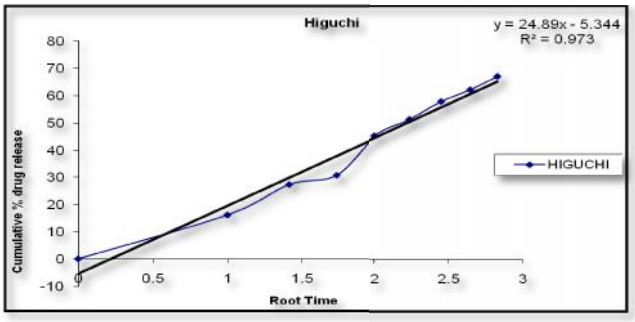

Figure 9: Higuchi release kinetics graph

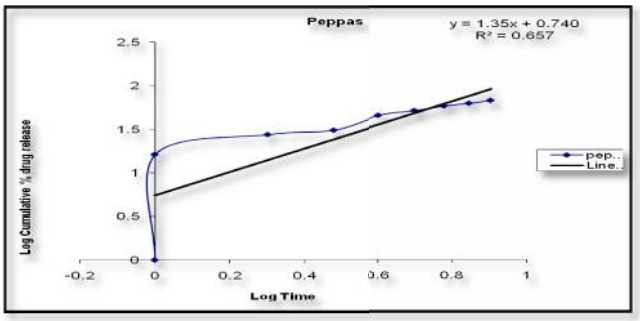

Figure 10: Korsmayer peppas graph

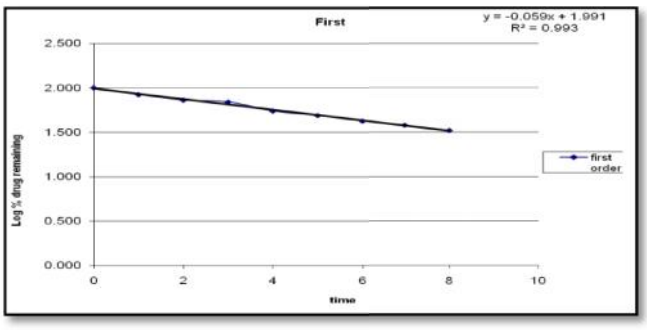

Figure 11: First order release kinetics graph

Table 1: Materials

Name of the material	Source
Mesalamine	Natco LABS
Ethyl Cellulose	Signet Chemical Corporation, Mumbai, India.
Eudragit L-100	Merck Specialities Pvt Ltd, Mumbai, India.
Eudragit S-100	Merck Specialities Pvt Ltd, Mumbai, India.
Hydroxy Propyl Methyl Cellulose K100M	Merck Specialities Pvt Ltd, Mumbai, India
Magnesium stearate	Merck Specialities Pvt Ltd, Mumbai, India
Micro crystalline cellulose	Merck Specialities Pvt Ltd, Mumbai, India
Talc	Merck Specialties Pvt Ltd, Mumbai, India

Table 2: Equipment

Name of the Equipment	Manufacturer
Weighing Balance	Sartourious
Tablet Compression Machine (Multistation)	Cemach Limited, India.
Hardness tester	Sisco, Mumbai, India.
Vernier calipers	Mitutoyo, Japan.
Roche Friabilator	Labindia, Mumbai, India
Dissolution Apparatus	Labindia, Mumbai, India
UV-Visible Spectrophotometer	Labindia, Mumbai, India
pH meter	Labindia, Mumbai, India
FT-IR Spectrophotometer	Per kin Elmer, United States of America.

Table 3: Observations for graph of Mesalazine in 0.1N HCl (275 nm)

No.	Conc.[mg/l]	Abs
1	1	0.001
2	3	0.075
3	4	0.128
4	5	0.199
5	6	0.280
6	7	0.343
7	8	0.397
9	11	0.557
10	12	0.623
13	21	0.823
14	22	0.87

Table 4: Standard graph of Mesalazine in 6.8 pH

S.No	Conc.[mg/l]	Abs
1	1	0.001
2	2	0.043
4	4	0.131
5	5	0.185
6	6	0.252
7	7	0.309
8	8	0.371
9	9	0.430
10	10	0.504
13	13	0.684
14	14	0.740
15	15	0.799
16	16	0.896

Table 5: Composition of coating layer

Ingredient name	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ethyl cellulose (mg)	25	50					25		25
Eudragit S100 (mg)			25	50			25	25	
Eudragit L100 (mg)					25	50		25	25
Magnesium stearate (mg)	3	3	3	3	3	3	3	3	3
Talc (mg)	3	3	3	3	3	3	3	3	3
MCC pH 102 (mg)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total weight	100	100	100	100	100	100	100	100	100

Table 6: Pharmacopoeial specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-250	130-324	7.5
More than	More than 324	5

Table 7: Preformulation parameters of core material

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	36.01	0.55	0.645	14.72	0.85
F2	34.8	0.57	0.66	13.63	0.86
F3	32.74	0.53	0.606	14.19	0.858
F4	35.33	0.531	0.613	13.37	0.866
F5	36.24	0.549	0.641	14.35	0.856
F6	36.12	0.564	0.666	15.31	0.846
F7	37.08	0.581	0.671	13.41	0.865
F8	35.12	0.567	0.654	13.12	0.845
F9	35.45	0.571	0.689	13.28	0.855

Table 8: Quality Control Parameters For compression coated tablets

Formulation codes	Weight variation(mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	512.5	4.5	0.52	4.8	99.76
F2	505.4	4.2	0.54	4.9	99.45
F3	498.6	4.4	0.51	4.9	99.34
F4	510.6	4.5	0.55	4.9	99.87
F5	309.4	4.4	0.56	4.7	99.14
F6	510.7	4.2	0.45	4.5	98.56
F7	502.3	4.1	0.51	4.4	98.42
F8	501.2	4.3	0.49	4.7	99.65
F9	598.3	4.5	0.55	4.6	99.12

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

Table 9: *In-vitro* Drug Release profile for coated formulations (F1-F9)

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	18.8	28.94	16.1	14.47	29.42	26.56	16.14	11.12	11.52
2	24.87	37.88	29.74	24.89	32.05	34.92	27.35	33.45	29.36
3	36.12	48.2	30.56	32.11	44.1	44.52	30.73	45.62	35.2
4	45.25	55.45	48.29	41.82	51.25	54.85	45.24	58.73	49.65
5	51.24	69.52	57.1	56.01	63.33	67.21	51.27	62.64	61.1
6	57.35	71.53	65.25	60.98	69.24	70.05	57.83	70.43	68.99
7	62.17	77.56	70.32	64.55	70.01	74.16	62.19	76.21	72.58
8	68.65	81.45	73.65	68.76	72.44	75.87	67.02	81.26	79.56
9	71.26	83.65	76.98	72.43	75.76	79.61	72.01	85.76	82.95
10	76.25	86.77	84.56	75.66	78.97	82.83	79.58	89.75	86.25
11	83.76	89.87	88.76	78.98	82.44	84.55	87.76	92.89	89.76

12	88.98	92.54	93.55	83.44	84.29	89.21	97.87	93.65	92.45

Table 10: Release kinetics data for optimised formulation

Cumulative (%) Release Q	Time (T)	Root (T)	Log (%) Release	Log (T)	Log (%) Remain
0	0	0	0	0	2.000
16.14	1	1.000	1.208	0.000	1.924
27.35	2	1.414	1.437	0.301	1.861
30.73	3	1.732	1.488	0.477	1.841
45.24	4	2.000	1.656	0.602	1.738
51.27	5	2.236	1.710	0.699	1.688
57.83	6	2.449	1.762	0.778	1.625
62.19	7	2.646	1.794	0.845	1.578
67.02	8	2.828	1.826	0.903	1.518
72.01	9	3.000	1.857	0.954	1.447
79.58	10	3.162	1.901	1.000	1.310
87.76	11	3.317	1.943	1.041	1.088
97.87	12	3.464	1.991	1.079	0.328

Table 11: Stability studies for optimised formulation (F7)

S.No	Optimised formulation (F7) duration	25^0C (75%RH)	37^0C (75%RH)
1	1 MONTH	97.85%	97.92%
2	2 MONTH	97.35%	97.80%
3	3MONTH	97.10%	97.75%

By observing the stability studies it is concluded that the optimised formulation is stable through the entire period of 3 months and the drug release profile is also intact throughout the time being.

4. Conclusion

The present research work focuses on development of sustained release matrix formulation of Mesalazine targeted on colon by using various polymers developed. To achieve pH-independent drug release of Mesalazine, pH modifying agents (buffering agents) were used. Colon targeted tablets were prepared in two steps. Initially core tablets were prepared and then the tablets were coated by using different pH dependent polymers. Ethyl cellulose, Eudragit L100 and S100 were used as enteric coating polymers. The precompression blend of all formulations was subjected to various flow property tests and all the formulations were passed the tests. The tablets were coated by using polymers and the coated tablets were subjected to various evaluation techniques. The tablets were passed all the tests. Among all the formulations F7 formulation was found to be optimized as it was retarded the drug release up to 12 hours and showed maximum of 97.87% drug release. It followed first order kinetics mechanism. Stability studies was Performed no chemical changes was occurred.

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