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Research

Formulation Optimization and Characterization of Colon Specific Delivery System for Effective Management of Inflammatory Bowel Disease

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Abstract

The purpose of the study was To design, formulate and evaluate Colon Specific Delivery System tablets of Mesalamine which is effective in Management of Inflammatory Bowel Disease. The present work is aimed at preparation and evaluation of Colon Specific Delivery System tablets of Mesalamine using using HPMC K 100, Eudragit S 100 as polymers in varying ratios. The tablets were evaluated for its Thickness, Hardness, Friability, Friability, Disintegration and in vitro drug release studies. The FTIR studies revealed no chemical interaction between the drug molecule and polymers and found that drug was compatible with used polymer. In vitro drug release study confirms that formulation F9 was the best formulation as it releases 98.81 % at the end of 10 hr. This confirms the developed Mesalamine tablet is promising for Colon Specific Delivery System.

Keywords: Mesalamine, Disintegration, Management, Eudragit S, Hydroxy Propyl Methyl Cellulose.

INTRODUCTION

In the area of targeted delivery, the colonic region of the GI tract is the one that has been embraced by scientists and is being extensively investigated over the past two decades. Targeted delivery to the colon is being explored not only for local colonic pathologies, thus avoiding systemic effects of drugs or inconvenient and painful trans-colonic administration of drugs, but also for systemic delivery of drugs like proteins and peptides, which are otherwise degraded and or poorly absorbed in the stomach and small intestine but may be better absorbed from the more benign environment of the colon. The treatment of disorders of the large intestine, such as irritable bowel syndrome (IBS), colitis, crohn's disease and colon disease, where it is necessary to attain a high concentration of the active agent, maybe efficiently achieved by colon-specific delivery.

The colon, as a site for drug delivery, offers distinct advantages on account of a near neutral pH, a much longer transit time, relatively low proteolytic enzyme activity, and a much greater responsiveness to absorption enhancers. These criteria favour this distal part of the gastrointestinal tract (GIT) as a site for the delivery of various drug molecules, including proteins and peptides. Colon-specific delivery systems should prevent the release of the drug in the upper-part of GIT and require a triggering mechanism to affect an abrupt release on reaching the colon. In the past, various primary approaches for colon specific delivery, such as pro-drugs, pH sensitive polymers, timed release delivery systems, and microbially degraded delivery systems, have achieved limited success. The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and / or targeting the drug to desired site. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. There is a continuously growing interest in the pharmaceutical industry for sustained release oral drug delivery systems.

There is also a high interest for design a dosage formulation that allows high drug loading, particularly for actives with high water solubility. Oral route has been the most popular and successfully used for sustained delivery of drugs because of convenience and ease of administration, greater flexibility in dosage form design and ease of production and low cost of such a system.

MATERIALS AND METHODS

Material

Mesalamine was obtained as gift- sample from Sun Pharma, Pvt. Ltd. Dewas M.P. and Ethyl cellulose, HPMC of pharmaceutical grade were procured from Oxford Laboratories, Mumbai and Talc, Magnesium stearate, Micro crystalline Cellulose from SD Fine chemicals.

Pre-formulation studies

Pre- formulation is considered as important phase where researcher characterizes the physical and chemical properties of drug substance which helps to develop stable, effective and safe dosage forms and also check possible interaction with various excipients. The absorbance of above solutions was recorded at λ max (232 nm) of the drug using double beam UV-Visible spectrophotometer.

Compatibility Study FT-IR Spectra Analysis

The FTIR analysis of Mesalamine the was carried out for qualitative compound identification. The FTIR spectra for pure drug and with other excipients was obtained by placing the drug directly into the cavity and was determined by FTIR spectrophotometer in the wave number region of 4000-400 cm-

Preparation of tablet

All ingredients were weighed separately. Accurately weighed quantity of drug, and polymers (Eudragit S100 and HPMC K100) are mixed thoroughly in mortar and granulated using 5% w/v starch solution as a binder as given in Table No 3.The granules so obtained are placed in oven at 60ºC for 2 hr. These granules are again passed through 22 mesh sieve after getting dry. The fine granules formed are then lubricated with 0.5% w/w Magnesium stearate. The flow properties are determined. These granules were then compressed into tablet (each 600mg) using 11.7mm concave punch of 10 station shiv pharma ETBC 1974 compression machine.

Table 1: Formulation Designs of Sustained Release Tablets of Mesalamine

S. No.	Ingredients	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
1.	Mesalamine	250	250	250	250	250	250	250	250	250
2.	HPMC K 100	150	150	150	150	150	150	150	150	150
3.	Eudragit S 100	40	45	50	50	40	50	40	46	42
4.	DCP	100	100	100	100	100	100	100	108	108
5.	Cross Povidone	30	30	30	25	30	25	30	30	30
6.	Magnesium stearate	30	25	20	25	30	25	30	25	25
	Total weight	600	600	600	600	600	600	600	600	600

Evaluation of Tablet

The evaluation of tablet was carried out on different parameter.

Angle of Repose

The angle of repose of granules was determined by the funnel-method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone measured and angle of repose was calculated using the following equation.

$\tan \theta = h/r$

Determination of Bulk Density and Tapped Density

An accurately weighed quantity of the granules/ powder (W) was carefully poured into the graduated cylinder and volume (V_0) was measured. Then the graduated cylinder was closed with lid and set into the tap density tester (USP). The density apparatus was set for 100 tabs and after that the volume (V_f) was measured and continued operation till the two readings were equal.

The bulk density and the tapped density were calculated using the following formula.

Bulk density = $\mathbf{W/V_0}$

Tapped density = $\mathbf{W/V_f}$

Compressibility Index (Carr's Index)

Carr's index (CI) is an important measure that can be obtained from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is.

CI = (TD-BD) x 100/TD

where, TD is the tapped density and BD is the bulk density

Table 2: In Process Evaluation of Granules

S. No.	Formulation	Angle of repose	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index (%)	Hausner's ratio
1	F1	27.20	0.214	0.451	14.74	1.17
2	F2	28.20	0.308	0.464	15.38	1.18
3	F3	29.04	0.276	0.522	14.28	1.16
4	F4	27.88	0.341	0.488	12.11	1.13
5	F5	28.44	0.324	0.476	13.82	1.16
6	F6	29.61	0.320	0.597	15.39	1.24
7	F7	29.86	0.264	0.532	13.24	1.11
8	F8	28.86	0.282	0.498	16.75	1.21
9	F9	29.74	0.362	0.567	14.32	1.19

RESULT AND DISCUSSION

Compatibility Study FT-IR Spectra Analysis

The comparative FTIR studies of Drug and excipients combination revealed that no chemical interaction between the drug molecule and polymers and found that drug was compatible with used polymer. The FTIR spectra of pure drug and drug with excipients are shown in the Fig 1.

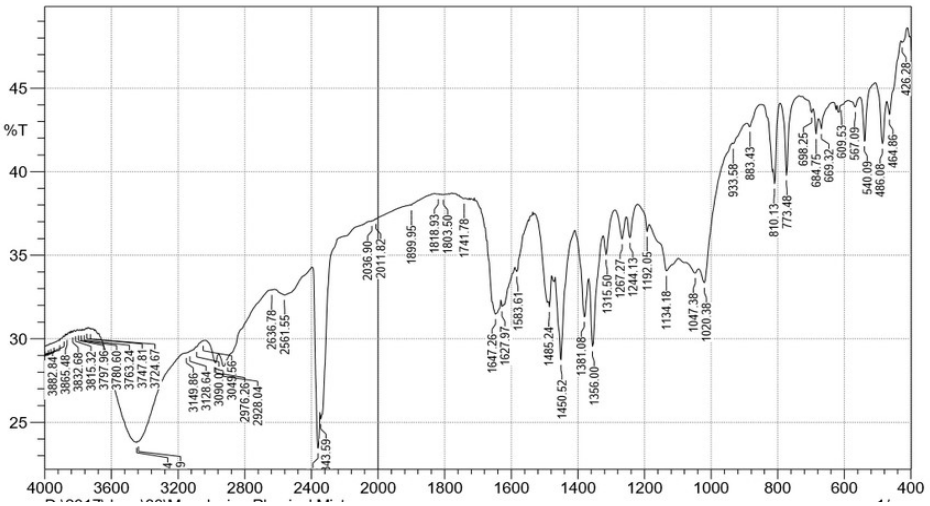

Fig 1: FT-IR Spectra of Pure drug (Mesalamine)

Evaluation of Prepared Tablets

The Evaluation of tablet carried out on thickness, Hardnesss, Friability and weigh Variation. The Parameter of evaluation are given in table no.3

Table 3: Evaluation of Prepared Tablets

S. No.	Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight Variation (mg)
1	F1	6.22	5.50	0.36	349.8±1.48
2	F2	6.37	5.50	0.39	350± 0.54
3	F3	6.14	5.58	0.12	349.6±0.41
4	F4	6.20	5.66	0.41	348.8±1.64
5	F5	6.08	4.25	0.54	348.6±1.14
6	F6	6.33	4.08	0.58	349.2±0.83
7	F7	6.13	4.12	0.34	347.2±0.12
8	F8	6.21	5.42	0.46	348.9±0.23
9	F9	6.25	5.31	0.51	349.3±0.39

In vitro dissolution study

The dissolution rate studies were performed to evaluate the dissolution character of the mesalamine from the colon targeted tablets. Figure 5 shows release profile of all batches. The dissolution study of all formulations shows the percentage drug release were found to be in between 88% to 99% in within given time period. From the data F9 shows the faster drug release compare to any other batch and F1 batch shows the lowest drug release and hence F9 was considered as the best formulation based on its kinetic release characteristic. The cumulative % drug release of drug is given in table no 7.5.

Table 4: In vitro release of Cumulative % Drug Release Vs Time

Time	Cumulative % drug release								
(in min)	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
0	0	0	0	0	0	0	0	0	0
30	0.24	0.30	0.34	0.38	0.45	0.68	0.90	0.96	0.98
60	1.83	1.86	1.98	2.12	2.25	2.29	2.34	3.40	3.56
120	4.00	4.20	3.50	4.80	5.90	6.10	6.30	7.60	6.90
180	11.63	12.34	13.76	15.80	16.90	17.00	18.96	20.00	20.22
240	17.18	18.78	19.70	19.90	20.00	21.21	22.45	23.46	23.98
300	24.78	25.61	26.71	26.80	27.71	28.81	29.01	30.00	30.67
360	26.71	27.56	28.99	29.00	29.00	30.00	32.00	34.50	35.50
420	44.51	46.81	48.90	48.99	45.00	46.08	47.89	49.80	50.98

480	80.16	67.28	69.28	69.84	69.90	70.00	72.00	75.00	79.80
540	85.12	88.00	88.90	88.12	88.19	89.12	89.15	89.90	90.00
600	90.19	90.17	91.23	92.22	92.43	93.00	93.32	95.62	98.81

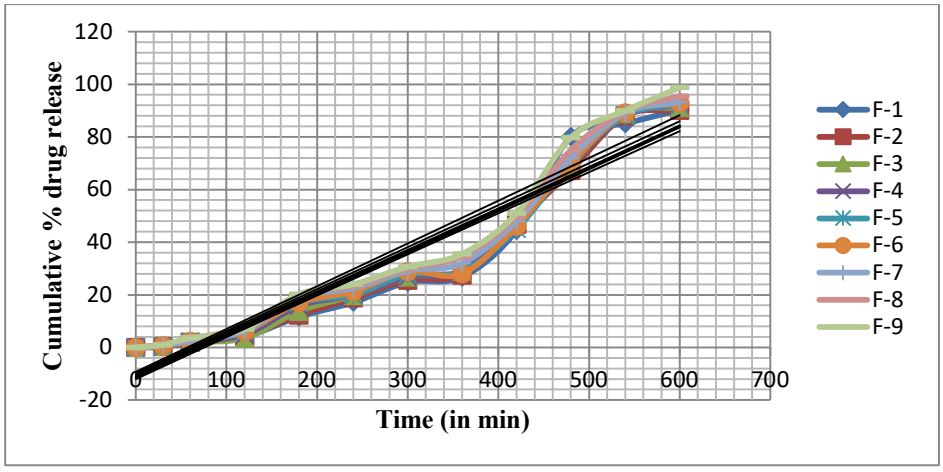

Fig 3: In vitro release of Cumulative % Drug Release Vs Time

CONCLUSION

The development of colon-targeted oral drug delivery systems has gained increasing interest among formulation scientists in recent years. As discussed above, colon-specific drug delivery systems provide significant therapeutic benefits to the patients in terms of safety, efficacy, and patient compliance. The formulation with Ethyl Cellulose has shown low drug release and has the problem of dose dumping.

The dissolution rate studies were performed to evaluate the dissolution character of the mesalamine from the colon targeted tablets. Figure 3 shows release profile of all batches. The dissolution study of all formulations shows the percentage drug release was found to be In between 88% to 99% in within given time period. From the data F9 shows the faster drug release compare to any other batch and F1 batch shows the lowest drug release and hence F9 was considered as the best formulation based on its kinetic release characteristic.

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