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Research Article

FORMULATION AND INVITRO EVALUATION OF COMPRESSION COATED MESALAMINE TABLETS FOR COLON SPECIFIC DRUG DELIVERY

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Abstract: The present study has been aimed at developing a compression coated tablets of Mesalamine with a view of minimizing the drug release in the physiological environment of stomach and small intestine and to ensure maximum drug release in the physiological environment of colon with an improved patient compliance, least side effects, better drug therapy and all aspects of an ideal drug delivery system. Mesalamine is one of the most popular drug used in the treatment of Inflammatory Bowel Disease (IBD). Here direct compression method was used for the preparation of Mesalamine core tablets and the Compression coating technique was used for coating of core tablets. Guargum alone and in the combination with HPMCK4M was used in the coating formulations. All the formulations were evaluated for the hardness, friability, thickness, weight variation, drug content, and *in vitro* drug release studies. In vitro drug release studies have in presence and absence of rat caecal content shown that guar gum in the combination with HPMC K4M is promising system for colon targeting

Key words: Mesalamine, Guar gum, HPMC K4M, colon targeting, compression coating tablets

1. INTRODUCTION

Colonic delivery refers to targeted delivery of drugs into the colon. Targete drug delivery in to the colon is highly desirable for local treatment of a several colonic diseases such as ulcerative colitis, crohn's disease and colonic cancer[1].

Now a days, various routes of administration have been explored for the effective delivery of the drug to the colon. The oral route is considered to be most convenient for the administration of drugs to patients. Rectal administration offers the shortest route for targeting the drug to the colon. However, reaching the proximal part of colon via rectal administration is difficult. Rectal administration can also be uncomfortable for patients and compliance may be less. Hence oral route is preferred route of drug administration[19].

Although oral delivery has become a widely accepted route of administration of therapeutic drugs, the gastro intestinal tract presents several barriers to drug delivery. On oral administration of conventional dosage forms drug normally dissolves in the gastro intestinal fluids and is absorbed from these regions of the gastrointestinal tract (GIT) which depends upon the physicochemical properties of the drug. It is a serious drawback in condition where localized delivery of drugs in the colon is required, or in conditions where drug needs to be protected from the hostile environment of upper GIT[9].To achieve successful colonic delivery, a drug needs to be protected from absorption and or the environment of the upper gastrointestinal tract (GIT) and then be abruptly released into the proximal colon, which is considered the optimum site for colon targeted delivery of drugs[9,26].

In the present study, Mesalamine is formulated in to the compressed coated tablet. This drug is selected because, Mesalamine is one of the most popular drug used in the treatment of Crohn's disease and ulcerative colitis[22].

2. MATERIALS AND METHODS

2.1 Materials:- Mesalamine, Guar gum, Hydroxypropylmethylcellulose K4M (HPMCK4M), Cross povidone, Microcrystalline cellulose, Talc, Magnesium stearate were obtained from Bright labs Hyderabad.

2.2 Method

Preparation of compression coated Mesalamine tablets

A. Preparation of Mesalamine core tablets

Core tablets of Mesalamine was prepared by Direct compression technique[4,15,39].. Cross povidone included in the formulation to obtain the Mesalamine tablets with fast disintegrating characteristics (disintegrating time < 1min). All the ingredients were weighed and thoroughly mixed and passed through a mesh no 60 to ensure complete mixing. The thoroughly mixed materials

were then directly compressed into tablets using 6 mm round, flat and plain punches on a single station tablet machine. Tablet quality control tests such as weight variation, hardness, friability, thickness, and dissolution in different media were performed on the core tablets. The composition of core tablets of Mesalamine given in table 1.

Table 1: Composition of core tablet

Ingredients	Quantity (mg)		
	C1	C2	C3
Mesalamine	100	100	100
Microcrystalline cellulose	38	35	32
Cross povidone	6	9	12
Talc	3	3	3
Magnesium stearate	3	3	3
Total Weight	150	150	150

B. Compression coating of core tablets[4,5,15,20,21,23,32]

The core tablets were compression coated with different quantities of coating material containing of Guar gum/ hydroxypropyl methylcellulose (HPMC) with different coat weights (i.e. the coat weights were either 200 or 175 mg). Microcrystalline cellulose was included in the coat formulations to impart enough hardness, since guar gum alone gave very soft coats. Half the quantity of the coating material was placed in the die cavity the core tablet was carefully placed in the centre of the die cavity and was filled with the other half of the coating material[20,21]. The coating material was compressed using 9 mm round, flat and plain punches. In this study, HPMC in combination with guar gum was used to enforce the mechanical resistance of the tablet during its transit in the GI tract. Tablet quality control tests such as weight variation, hardness, friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

Table 2. Composition of guar gum coats used to cover Mesalamine core tablets

Ingredients	Quantity (mg) present in the coat formulation					
	F1	F2	F3	F4	F5	F6
Guar gum	160	150	140	120	110	100
Microcrystalline cellulose	35	45	55	50	60	70
Talc	3	3	3	3	3	3
Magnesium stearate	2	2	2	2	2	2
Total Weight	200	200	200	175	175	175

Table 3. Composition of Guar gum and Hpmc K4M coats used to cover Mesalamine core tablets

Ingredients	Quantity (mg) present in the coat formulation			
	F7	F8	F9	F10
Guar gum	80	85	90	95
Hydroxypropylmethyl cellulose (HPMC K4M)	20	15	10	5
Microcrystalline cellulose	70	70	70	70
Talc	3	3	3	3
Magnesium stearate	2	2	2	2
Total Weight	175	175	175	175

C. Determination of drug content

Core tablets of Mesalamine were tested for their drug content.Ten tablets were finely powdered, quantities of the powder equivalent to 100 mg of Mesalamine were accurately weighed, transferred to a 100 mL volumetric flask containing 50 mL Phosphate buffer pH 6.8 and methanol was added to ensure complete solubility of the drug. The solution was made up to volume with Phosphate buffer pH 6.8. The solution was suitably diluted and the absorption was determined by UV-Visible spectrophotometer at 333nm. The drug concentration was calculated from the calibration curve.

2.3. In vitro drug release studies:-

Drug release studies of Mesalamine core tablets

The core tablets containing 100 mg of mesalamine were tested in SIF (pH 6.8), for their dissolution rates. Dissolution studies were performed using USP dissolution test apparatus (Apparatus 2, 100 rpm, 37±0.5 °C). At various time intervals, a sample of 5 ml was withdrawn and replaced with equal volume of fresh medium. The samples were analyzed spectrophotometrically at 333 nm.

Drug release studies of compression coated Mesalamine tablets

The release of Mesalamine from compression coated tablets was carried out using USP basket -type dissolution apparatus at a rotation speed of 100 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 without pepsin (SGF, pH 1.2) for the first 2 h as the average gastric emptying time is about 2 h. Then, the dissolution medium was replaced with enzyme-free simulated intestinal fluid (SIF, pH 7.4) and tested for drug release for 3 h, as the average small intestinal transit time is about 3 h, and finally enzyme-free simulated intestinal fluid (SIF, pH 6.8) was used for 19 h to mimic colonic pH conditions.

Drug release was measured from compression coated mesalamine tablets, added to 900mLof dissolution medium. Samples withdrawn at various time intervals were analyzed spectrophotometrically at 333 nm. All dissolution runs were performed in triplicate.

Drug release studies in the presence of rat caecal contents[4]

Dissolution study procedure:

Drug release studies were carried out using USP dissolution rate test apparatus (Apparatus 1, 50 rpm, 37±0.5 °C) for 2 h in SGF (900 mL). Then the dissolution medium was replaced with SIF (pH 7.4) (900 mL) and tested for drug release for another 3 h. Then the dissolution medium was replaced with SIF (pH 6.8) containing rat caecal contents. The experiment was carried out with continuous CO_2 supply into the beakers to simulate anaerobic environment of the caecum. The drug release studies were continued for 24h (usual colonic transit time is 20–30 h).At different time intervals, 1ml sample was withdrawn and replaced with 1ml of fresh SIF (pH 6.8) bubbled with CO2 and the experiment was continued upto 24h. One milliliter of methanol was added to the samples to ensure solubility of finely suspended drug particles released due to the erosion of guar gum by caecal enzymes and the volume was made up to 10ml with PBS and the samples was analyzed for Mesalamine content at 333nm using a double beam UV spectrophotometer[4,15]

3. RESULTS AND DISCUSSION

The powder mixtures of different formulations were evaluated for angle of repose, bulkdensity, tapped density and compressibility index and their values were shown in Table 4.

Table 4: Characterization of core powder mixtures

Formulation code	Angle of Repose (^{0})	Bulk density (g/ml)	Tapped density (g/ml)	% Carr's Index
C1	27.91±0.13	0.35±0.03	0.42±0.21	16.6±0.54
C2	26.23±0.24	0.37±0.23	0.41±0.32	9.7±0.43
C3	25.34±0.32	0.34±0.43	0.40±0.12	15±0.76

The physical mixtures of the formulations C_1, C_2 and C_3 evaluated The apparent bulk density and Tapped bulk density values for core powder mixture is ranging from 0.34±0.43 to 0.377±0.23

and 0.40±0.12 to 0.42±0.21 respectively. The angles of repose and compressibility index (%) values are ranging from 25.34^0±0.32 to 27.91^0±0.13 and 9.7±0.43 to 16.6±0.54 respectively. These results show that the core powder mixture has good flow properties.

Table 5:Characterization of coating powder mixtures

Formulation code	Angle of Repose (^{0})	Bulk density (g/ml)	Tappeddensity (g/ml)	% Carr's Index
F1	28.23±0.23	0.38±0.12	0.46±0.23	17.3±0.34
F2	29.34±0.32	0.36±0.23	0.46±0.22	10±0.76
F3	30.71±0.35	0.39±0.87	0.45±0.54	13.33±0.65
F4	26.34±0.46	0.42±0.35	0.51±0.32	17.64±0.34
F5	29.23±0.13	0.46±0.45	0.55±0.32	16.3±0.23
F6	29.34±0.35	0.36±0.14	0.43±0.96	16.2±0.23
F7	28.78±0.84	0.39±0.45	0.47±0.65	17±0.21
F8	30.34±0.35	0.45±0.35	0.51±0.87	11.7±0.56
F9	29.56±0.86	0.47±0.23	0.55±0.67	14.5±0.11
F10	31.12±0.23	0.39±0.87	0.48±0.12	18.75±0.54

The physical mixtures of the coat formulations F1 to F10 evaluated (Table 5). The apparent bulk density and tapped bulk density values ranged from 0.36±0.23 to 0.47±0.23and 0.43±0.96 to 0.55±0.67 respectively. The results of angle of repose and compressibility index (%) ranged from 26.34^0±0.46 to 31.12±0.23 and 10±0.76 to 18.75±0.54 respectively. These results show that all the formulation exhibited good flow properties.

Evaluation of Mesalamine core and coated tablets

The tablets of different formulations were evaluated for Hardness, Weight variation, Friability, Drug content, and their values were shown in Table 6 & 7

Table 6. Physical properties of Mesalamine core tablets

Formulation Code	Hardness (Kg/cm^2)	Weight variation (mg)	Friability (%)	Drug Content (%)
C1	2.2±0.41	150.5±0.68	0.40±0.12	99.2±0.76
C2	2.4±0.21	152.65 ± 0.52	0.35±0.23	98.1±0.50
C3	2.3±0.11	148.25±0.20	0.45±0.34	99.5±0.30

Table 7: Physical properties of Mesalamine coating tablets

Formulation Code	Hardness (Kg/cm^2)	Weight variation (mg)	Friability (%)
F1	5.0±0.61	324.2±0.56	0.25±0.32
F2	5.2±0.35	326.4±0.12	0.33±0.21
F3	5.1±0.42	352.6±0.54	0.17±0.45
F4	4.6±0.70	351.2±0.45	0.64±0.78
F5	4.4±0.58	355.5±0.63	0.54±0.23
F6	4.8±0.46	356.7±0.22	0.58±0.87
F7	5.0±0.86	358.1±0.36	0.45±0.76
F8	5.2±0.46	359.6±0.74	0.38±0.32
F9	5.0±0.76	358.0±0.12	0.68±0.65
F10	5.5±0.62	362.5±0.56	0.46±0.34

The various formulations of tablets were evaluated. The percent drug content of the Mesalamine core tablets was found to be in the range of 98.1±0.50 to 99.5±0.30 of the labeled amount indicating uniformity of drug content in the formulation. The hardness of the core tablets of Mesalamine was found to be 2.2±0.41 to 2.4±0.21 kg/cm^2. The core tablets of Mesalamine were also found to comply with the friability test since the weight loss was found to be in the range of 0.35±0.23 to 0.45±0.34. The weight variation of core tablets was found to be in the range of 148.25±0.20 to 152.65 ± 0.52mg. The tablets thickness was found to be 2.2±0.12mm.

The hardness of the coated tablets of Mesalamine was found to be 4.4±0.58 to 5.5±0.62 kg/cm^2. The coated tablets of Mesalamine were also found to comply with the friability test since the weight loss was found to be in the range of 0.17±0.45 to 0.68±0.65. The weight variation of coated tablets was found to be in the range of 326.4±0.12 to 362.5±0.56mg. The coated tablets thickness was found to be 4.2±0.23 to 4.8±0.43mm.

Table 8:Percent drug release of Mesalamine core tablets(C1,C2,C3) in SIF (PH 6.8)

Time(min)	C1	C2	C3
0	0	0	0
5	52.34±0.45	50.65±0.43	55.67±0.54
10	65.43±0.43	68.45±0.54	72.34±0.34
15	85.67±0.23	88.45±0.43	95.76±0.12
20	92.23±0.54	94.23±0.56	98.32±0.32

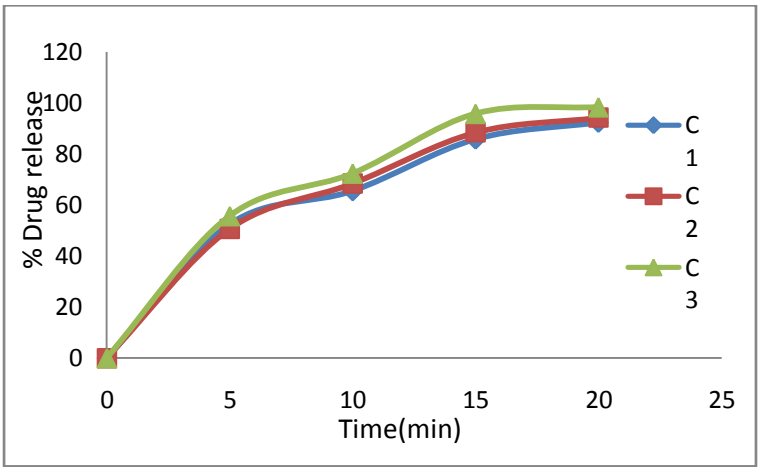

Figure 7: Dissolution profiles of Mesalamine core tablets(C1,C2,C3)

The dissolution results of Mesalamine core tablets in SIF (pH 6.8) were shown Figure7. The core tablets dissolved faster in SIF pH 6.8 and the C3 formulation reached 95% in 15min when compared to C1 and C2 formulations. Hence C3 formulation selected as a optimized formulation.

Table 9: Cumulative percent drug release of F1-F6 formulations containing guar gum

Time (hr)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	0.95±0.56	1.16±0.45	0.82±0.54	1.08 ±0.02	2.62±0.79	1.93 ±0.02
2	1.55±0.02	1.48±0.86	1.28±0.02	2.27±0.79	5.13 ±0.87	4.06±0.46
3	3.10±0.02	3.48±0.02	3.02±0.02	5.34±0.95	6.93±0.79	5.98 ±0.87
4	3.59±0.02	4.47±0.95	4.72±0.65	7.26 ±0.02	7.86±0.46	7.37±0.68
5	4.33±0.86	5.21±0.95	5.29±0.86	8.22 ±0.45	10.32±0.68	10.28±0.79
6	5.50±0.02	6.74±0.02	6.58±0.65	10.90±0.13	11.41±0.79	12.24±0.02

8	5.86±0.95	7.10±0.55	7.92±0.02	11.96 ±0.45	12.91±0.13	15.79±0.68
10	6.10±0.45	7.59±0.02	9.04±0.55	13.62 ±0.02	13.95±0.95	16.24±0.13
14	6.59±0.86	8.08±0.45	11.94±0.86	14.56±0.95	15.79±0.79	17.04±0.87
18	7.32±0.95	9.05±0.55	12.66±0.95	21.01±0.68	24.43±0.68	29.39±0.02
24	11.62±0.65	13.39±0.02	15.97±0.65	31.16 ±0.45	36.15±0.87	38.11±0.79

Data represents mean ± SD, n = 3

Table 10: Cumulative percentage drug release of F7-F10 formulations containing guar gum

Time (hr)	F7	F8	F9	F10
0	0	0	0	0
1	1.84±0.65	1.67±0.68	1.32±0.55	1.88±0.02
2	3.01±0.65	2.80 ±0.56	2.40±0.68	3.02±0.02
3	5.10 ±0.13	4.91±0.75	3.76±0.46	4.72±0.65
4	6.77±0.86	5.18±0.68	4.96±0.55	5.79±0.86
5	7.91 ±0.13	7.11±0.75	6.70±0.46	12.18±0.65
6	11.03±0.86	11.97 ±0.13	11.59±0.86	15.92±0.02
8	12.44 ±0.56	13.18±0.14	14.83±0.65	19.04±0.55
10	13.14±0.65	15.36 ±0.87	16.87 ±0.13	24.94±0.86
14	15.49 ±0.13	16.20 ±0.56	20.11±0.86	36.66±0.95
18	18.07±0.65	20.67 ±0.87	23.22 ±0.56	48.97±0.65
24	26.07±0.75	29.69±0.86	37.46±0.14	61.07±0.54

Data represents mean ± SD, n = 3

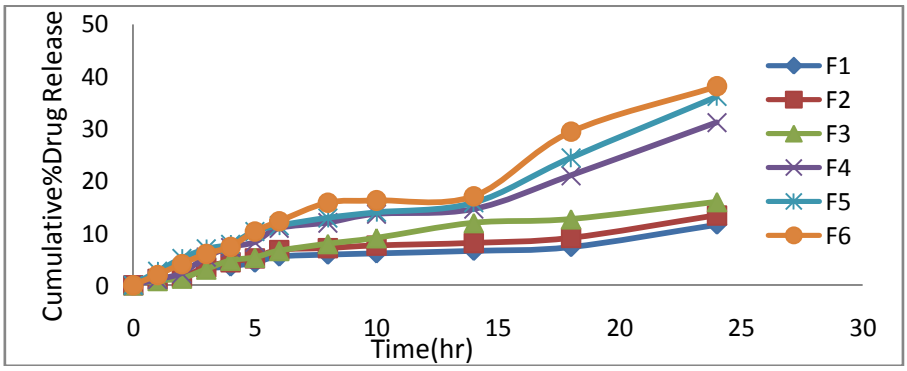

Figure 8: Dissolution profiles of F1-F6 formulations containing guar Gum.

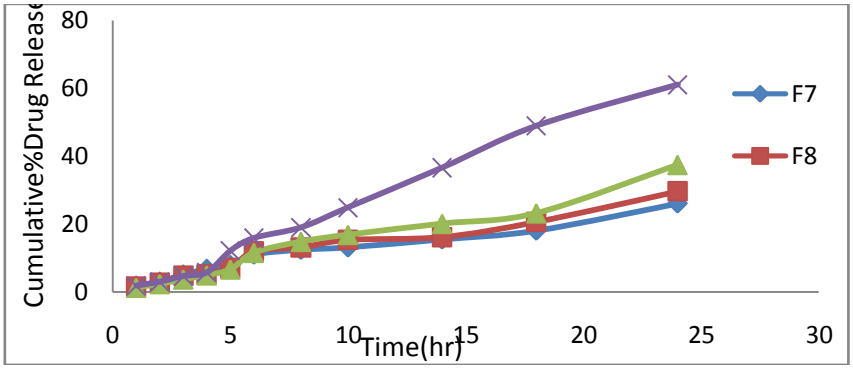

Figure 9: Dissolution profiles of F7-F10 formulations containing combination of guar gum and HPMC K4M

The cumulative mean percent of Mesalamine released from tablets coated with 200 mg coat weights of formulations containing varying amounts of guar gum (from F1 to F3) was found to vary from 4.33±0.86 to 5.29±0.86 after 5 h of testing in simulated gastric and intestinal fluids. The percent of drug released from tablets coated with 175 mg coat weights of formulations containing varying amounts of guar gum (from F4 to F6) was found to vary from 8.22 ±0.45 to 10.32±0.68 after 5 h of testing. The cumulative mean percent drug released from F7, F8 and F9 formulation containing different amounts of combination of guar gum and HPMC K4M was found to vary from 6.70±0.46 to 7.91±0.13after 5 h dissolution testing. Thus, guar gum in the form of coat is capable of protecting the drug from being released completely in the physiological environment of stomach and small intestine.

The drug release studies were further continued for 19 h by replacing the dissolution medium with SIF (pH 6.8). At the end of the experiment, the cumulative mean percent drug released from coat formulations F1, F2 and F3 was between 11.62±0.65 and 15.97±0.65 and the coats were intact. This indicates that the guar gum will not permit the release of the bulk of the drug core until the coat is broken. The percent drug release for the formulations F4, F5, and F6 was found between 31.16 ±0.45 and 38.11±0.79 after 24h study.

However, the tablets with coat formulation F10 found to release 12.18±0.65 after 5h and 61.07±0.54 after 24 h study. This may be due to lesser gum content of the coat which was unable to remain intact and not protecting the drug from being released.

This F10 was not studied further in rat caecal contents. The formulations F1andF2 were not studied in the rat caecal contents because very less amount of drug released after 24 h study. Even though F3 formulation releasing tiny amount (15.97±0.65 percent) of drug after 24 h, it was further studied in caecal contents to know the effect of coat thickness 200 mg coat weight compared with 175 mg coat weight.

Table 11: Cumulative percentage drug release of F3, F4, F5, F6 formulations in presence of rat caecal contents

Time (hr)	F3	F4	F5	F6
0	0	0	0	0
1	0.87±0.98	1.08 ±0.12	2.82±0.59	1.93 ±0.02
2	1.48±0.87	2.27±0.78	5.23 ±0.88	4.16±0.56
3	4.24±0.12	5.34±0.75	6.63±0.89	5.68 ±0.27
4	5.32±0.96	7.26 ±0.02	7.86±0.46	7.37±0.18
5	6.55±3.32	8.72 ±0.45	10.22±0.38	10.18±0.29
6	10.99±0.46	11.46±0.65	12.32±0.24	20.58±0.46
8	14.59±0.65	15.34±0.02	21.62±0.24	27.10±0.02
10	19.19±0.02	25.76±0.46	32.31±0.14	34.52±0.14
14	20.30±0.46	32.98±0.87	48.14±0.23	40.27±0.45
18	29.63±0.87	58.34±0.55	65.24±0.54	79.97±0.65
24	41.84±0.55	74.23±0.24	85.94±0.13	90.45±0.55

Data represents mean ± SD, n = 3

Table 12: Cumulative percentage drug release of F7, F8, F9 formulations in presence of rat caecal contents

Time (hr)	F7	F8	F9
0	0	0	0
1	1.94±0.65	1.67±0.43	1.12±0.65
2	3.11±0.55	2.80 ±0.54	2.10±0.28
3	5.60 ±0.53	4.71±0.85	4.60±0.54
4	6.27±0.76	6.28±0.28	5.56±0.75
5	8.23±0.44	7.65±0.55	6.85±0.95

6	17.24±0.87	15.23±0.45	18.79±0.46
8	28.23±0.46	23.32±0.45	27.29±0.55
10	39.23±0.68	39.23±0.78	44.89±0.46
14	44.54±0.55	55.32±0.36	68.43±0.87
18	68.07±0.87	76.47±0.45	83.12±0.65
24	86.52±0.46	91.95±0.32	96.53±0.46

Data represents mean ± SD, n = 3

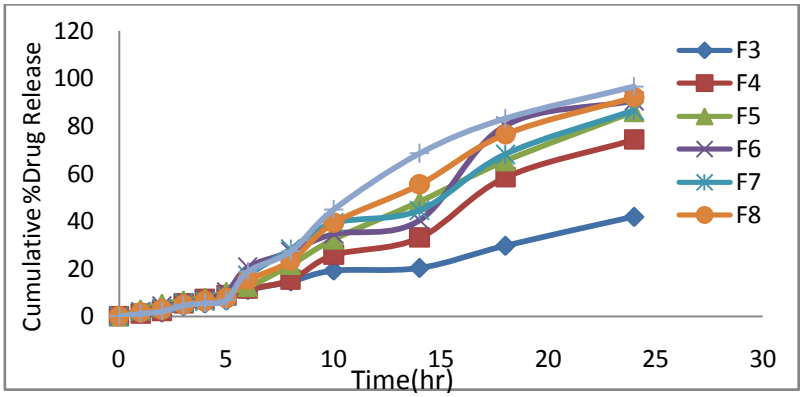

Figure 10: Dissolution profiles of F3 to F9 formulations in presence of rat caecal content

Dissolution results of compression coated Mesalamine tablets in rat caecal contents

The drug delivery systems targeted to the colon should not only protect the drug from being released in the physiological environment of stomach and small intestine, but also release the drug in colon after enzymatic degradation by colonic bacteria[39]. Hence, in vitro drug release studies were carried out for selected formulations in SIF (pH 6.8) containing 4% w/v of rat caecal contents. At the end of 24 h of testing which includes testing in simulated gastric and intestinal fluids, the percent drug released from Mesalamine tablets coated with coat formulation F3 was found to be only 41.41±2.68. The presence of higher amount of guar gum (200 mg) in the coat with resultant thicker coat might not have allowed the disintegration of the coat during the time period of testing. This also indicates that the drug will not be released unless the coat is broken.

The percent drug released from tablets coated with coat formulation F4,F5,F6, was found to be 74.23±0.24, 85.94±0.13, 90.45±0.55 respectively. The coat was completely degraded by the rat caecal enzymes thereby releasing the drug into the dissolution medium. Since the coat weight and thickness of coat formulations F4, F5 and F6 were lesser (175 mg) compared to coat formulation F3 (200 mg) the coat might have been completely hydrated and subsequently degraded by the caecal enzymes at a faster rate.

To improve the mechanical strength it was mixed with HPMC K4M polymer. The percent drug release from F7, F8 and F9 formulation at the end of 24 h study in presence of rat caecal content was found to be 86.52±0.46, 91.95±0.32, 96.53±0.46. Better release profile was observed in the system containing Guar gum and HPMC K4M[15,31].

It is evident from the results of the drug release studies in the presence and absence of rat caecal contents that the drug release occurred by the degradation of guar gum coats by the enzymes present in the caecal matter. And the tablet containing two polymeric systems shows much more promising release than the single polymeric system. From this we concluded that by taking single hydrophilic polymer also release can be retarded but addition of another polymer which can control its release is necessary. Thus the F9 formulation was considered better among other formulations to produce colon specific drug delivery of Mesalamine.

Kinetic results

The mechanism and kinetics of drug release of Mesalamine is determined by the application of korsmeyer-peppas model, higuchi's model, zero order and first order. Most of the tablet formulation follows the zero order release as their r^2 values are between 0.964 and 0.986.

The mechanisms of drug release was best fitted well with Korsmeyer–Peppas[3] models as their r^2 values in the range of 0.931-0.989.

Table 13:Drug release kinetics

Formulation Code	Zero order	First order	Higuchi	Korsmeyer & Peppas
F3	0.985	0.977	0.892	0.978
F4	0.974	0.919	0.827	0.989
F5	0.986	0.914	0.852	0.945
F6	0.964	0.886	0.839	0.961
F7	0.982	0.923	0.866	0.931
F8	0.979	0.915	0.852	0.943
F9	0.966	0.909	0.856	0.968

4. CONCLUSION

The study was undertaken with an aim to formulate and evaluate Mesalamine compression coated tablets to deliver the drug in the colon. The *invitro* dissolution studies shows that Guar gum and HPMC K4M in combination, in the form of compression coated tablets is capable of protecting Mesalamine from being released in the upper region of GI system, i.e. stomach and small intestine. The in vitro drug release studies indicated that formulation F9 was a promising system to provide targeting of Mesalamine to the colon. The release pattern of the above formulation was best fitted to Korsmeyer-Peppas model and zero-order model. FT-IR spectral studies showed that there is no interaction between the drug and excipients.

REFERENCES

1. Mohit Khandelwal, Ankit Ahlawat and Ram Singh. Polysaccharides and Natural Gums for Colon Drug Delivery.*The Pharma Innovation*,**2012**;1(1):9-13
2. Hemant H.Gangurde, Mayur A, Chordiya, Tamizharasi S, and Sivakumar T, A review on Diseases, approaches and evaluation parameterrs for colon specific drug delivery, *International Journal of Drug Research and Technology,***2012;** 2(3):239-262
3. Thiruganesh Ramasamy, Umadevi Subbaih Khandasamy ,Suresh Shanmugam and Himabindhu Ruttala, Formulation and Evaluation of Chondroitin Sulphate Tablets of Aceclofenac for Colon Targeted Drug Delivery, *Iranian Journal of Pharmaceutical Research,***2012**; 11(2):465-479
4. Mounika. B, Appa Rao. A, Prabhakar Reddy. V. Formulation and evaluation of compression coated meloxicam tablets for colon drug delivery**.** *International Journal of Pharmacy and Biological Sciences,***2012;**2(3):131-143
5. Bharani S. Sogali, Mohammed Yousuff and Shashank Nayak. Influence Of Natural Gums For Effective Colon Targeting Of Methotrexate For The Treatment Of Colorectal Cancer. *Int Journal of Pharmacy,***2012;**2(3): 498-506
6. M Manikandan,K Kannan, R Manavalan1, N Junior Sundresh. Design of Nanoparticles for Colon Target Drug Delivery – A Review. *Research Journal of Pharmaceutical, Biological and Chemical Sciences,* **2011;**2(4):128-139
7. Tarak Jayraj Mehta,A.D.patel,Mukesh R.Patel,N.M.patel. Need Of Colon Specific Drug Delivery System:A Review on primary and novel Approaches. *International journal of Pharma.Research & Development* ,**2011;**3(1):134-153.
8. Shailendra wasnik, poonam parmar. The design of colon-specific drug delivery system and different approaches to treat colon disease. *International journal of pharmaceutical sciences review and research,***2011**;6(2):167-177.
9. Jitender Mor.Recent Advances in colonic Targeted Drug Delivery Systems. *International Journal of Pharma Proffessional's Research,***2011;**.2(4):497-501.
10. K.Chandramohan, B.Rajkapoor, Development and *invitro* evaluation of Colon Specific Delivery System of Tinidazole, *jitps,***2011;**2 (4):111-121.
11. AO.Kabra, SS. Zavare and RS. Wanare, Hydrophilic polymers in formulation of sustained-release coated matrix tablets of 5-amino salicylic acid for targeting colon, International Journal of Research in Pharmaceutical and Biomedical Sciences,**2011;** Vol. 2 (1):224-230.

12. Negar Bashardoust, Josephine Leno Jenita, Parvin Zakeri-Milani. *Advanced Pharmaceutical Bulletin,***2011;**1(2):87-92.
13. Wycliffe Omwancha, Chahinaz Kouba, Satish Yelamanchili, and Steven H. Neau. Colon-specific drug delivery using ethylcellulose and chitosan in the coat of compression-coated tablets. *Drug Development and Industrial Pharmacy*,**2011**;37(8):945–953.
14. Thiruganesh Ramasamy**,** Uma Devi Subbaih Kandhasami, Himabindhu Ruttala, Suresh Shanmugam, Formulation and evaluation of xanthan gum based aceclofenac tablets for colon targeted drug delivery. *Brazilian Journal of Pharmaceutical Sciences,* **2011;**47(2):300-311.
15. Fahima M. Hashem, Dalia S. Shaker, Mohamed Nasr, Ibrahim E. Saad, Reem Ragaey. Guar gum and hydroxy propyl methylcellulose compressed coated tablets for colonic drug delivery: *in vitro* and *in vivo* evaluation in healthy human volunteers. *Drug Discoveries & Therapeutics,* **2011;**5(2):90-95.
16. R.Vijaya Muthumanikandar , Sudeesh Edavalath, Saravanakumar K. Design and Evaluation of Mesalamine Tablet for Colon Specific Drug Delivery. *International Journal of Drug Development & Research,***2011**;3(3):197-212.
17. Pragnesh Patel, Anupkumar Roy,Vinod kumar SM, Martand Kulkarni. Formulation and Evaluation Of Colon Targeted Tablets of Ornidazole For The Treatment of Amoebiasis. *International Journal of Drug Development & Research,***2011**;3(1).
18. Poonam kushwaha, sheeba fareed and sanju nanda. Promising approaches to target drug delivery to colon. International journal of pharmaceutical sciences,**2010**;2(3):669-679.
19. Anil K.Philip, Betty Philip.Colon Trgeted Drug Delivery Systems: A Review on primary and novel approaches. *Oman Medical Journa,***2010;**25(2).
20. J.Josephine Leno Jenita, Vijaya k, Suma .R, Bincy Raj and Ayesha Siddiqca. Formulation and Evaluation of Compression Coated Tablets of Mesalazine For Colon Delivery. *International Journal of PharmTech Reasearch,***2010;**2(1):535-541.
21. Chickpetty S. M,and Raga Baswaraj. Studies on Design and In Vitro Evaluation of Compression-Coated Delivery Systems for Colon Targeting of Diclofenac Sodium. *International Journal of PharmTech Research,***2010;**2(3):1714-1722.
22. Nirav V. Patel, Jayvadan K. Patel, Shreeraj H. Shah, Jagruti J Patel. Design, development and in vitro evaluation of Mesalamine tablets containing Pectin and Chitosan for colon-specific drug delivery**.** *Int. J. Res. Pharm. Sci,***2010;**194-102.
23. Rajesh kumar.R, Ramasamy.P, VengadeshPrabu.K. Formulation and Evaluation of Guar gum compressed tablets for colon targeted drug delivery. *Journal of Pharmacy Research,* **2010;**3(7):1538-1540.
24. G.Kishore, Somashekar shyale, K.srikanth,V.R.M.Gupta.Development and Evaluation of Colon targeted tablets of Praiquantel and its β-Cyclodextrin complex to treat Schistosomiasis. *Journal of Pharmaceutical Science and Technology,***2010***;*2(8):269-275.
25. Kinage Krishna, Nandgude Tanaji, Bhise Kiran, Deshmukh Pradeep. Studies on Development of oral colon targeted Drug Delivery Of Locust bean and Xanthan Gums *International Journal of Green Pharmacy,***2010**.
26. Tomuta,L.Vlase, Adina Popa,S.E.Leucuta. *Invitro –invivo* Evaluation of a Novel Drug Delivery System For Colonic Targeting.*Farmacia,***2010;**58(3):368-377.
27. Prabhakara prabhu, Nissara ahamed, Harish nairy matapady,Mohd. Gulzar ahmed, R. Narayanacharyulu, D. satyanarayana and EVS Subrahmanayam. Investigation and comparison of colon specificity Of novel polymer khaya gum with guar gum. *Pak. J. Pharm. Sci,***2010;** 23(3):259-265.
28. Raghavendra Rao NG, Pentewar Ram, Thube Ketan, Suryakar VB. Formulation and in vitro evaluation of gastric oral floating tablets of cefixime for controlled release. *RJPBCS,***2010;**1(3).
29. Sateesh Kumar Vemula, prabhakar reddy, Veera reddy. Different Approaches to design and evaluation of Colon specific Drug Delivery Systems. *International Journal of Phrmacy & Technology,***2009;**1(1):1-35.
30. Carien e. Beneke,Aalvaro m. Viljoen and josias h. Hamman . Polymeric plant-derived excipients in drugdelivery.*Molecules,***2009;**14:2601-2620.
31. A.V.Bhosale, Hardikar S.R, Naresh Patil1, Umang Patel, Yogesh Sumbe, Rajesh Jagtap. Formulation and In-vitro

Evaluation of Microbially triggered Ibuprofen Delivery for Colon targetting. *International Journal of PharmTech Research,***2009;**1(2):328-333.

32. Soad A. Yehia,Ahmed H. Elshafeey,Ibrahim Sayed, and Ahmed H. Shehata. Optimization of Budesonide Compression-Coated Tablets for Colonic Delivery. *AAPS PharmSciTech,***2009;**10(1).
33. Santanu Ghosh and B. B. Barik. Preparation and evaluation of aceclofenac sustained release formulation and comparison of formulated and marketed product. *International Journal of Medicine and Medical Sciences,***2009;**1(9):375-382.
34. Naikwade Sonali R.,Kulkarni Pratibha P,Jathar Shripad R. Amrita N. Development of time and pH dependent Controlled Release Colon Specific Delivery of Tinidazole. *DARU,* **2008;**16(3):119-127.
35. Kishore Sahebrao Salunkh, Mohan Vinayak Kulkarni. Formulation and *Invitro* Evaluation of Dextrin Matrix Tablet of Ibuprofen for Colon Specific Drug Delivery. *J.Pharma.sci.,***2008;**21(1):17-20.
36. Timucin Ugurlu, Murat Turkogulu,Umran Soyogul Gurer, Burcak Gurbu Akarsu. Colonic delivery of Compression coated nisin tablets using pectin/HPMC polymer mixture. *European Journal of Pharmaceutics and Biopharmaceutics,***2007;**67:202-210.
37. J. Varshosaz, J. Emami and E. Jaffari. Comparison of hydrophilic natural gums and cellulosic polymers in formulation of sustained-release matrix tablets of terbutalin sulfate. *Reasearch in Pharmaceutical Sciences,***2006;**1:30-39.
38. Gang Cheng, Feng An, Mei-Juan Zou, Jin Sun, Xiu-Hua Hao, Yun-Xia He. Time- and pH dependent colon-specific drug delivery for orally administered diclofenac sodium and 5-aminosalicylic acid. *World Journal of Gastroenterology,***2004;**10(12):1769-1774.
39. Chellan vijaya Raghavan,Chithambaram Muthulingam, Joseph amaladoss josephine leno jenita and thengungal Kochupapy ravi. An *in Vitro* and *in Vivo* Investigation into the Suitability of Bacterially Triggered Delivery System for Colon Targeting. *Chem. Pharm. Bull,***2002;50**(7):892-895.
40. Y.S.R.Krishnaiah, P.Veer Raju,B.Dinesh Kumar,P.B haskar.Development of Colon targeted drug delivery systems for Mebendazole. *Journal of Controlled Release,***2001;**77:87-95.
41. Y.S.R.Krishnaiah,S.Satyanarayana,Y.V.R amaprasad, S.NarasimhaRao. Evaluation of Guargum as a Compression coat for drug targeting to colon.*International Journal of Pharmaceutics,***1998;**171:137-146.