



Received on 03 February, 2013; received in revised form, 18 April, 2013; accepted, 18 May, 2013

AN *IN VITRO* INVESTIGATION OF SUITABILITY OF PRESS-COATED TABLETS WITH HYDROXYPROPYLMETHYLCELLULOSE ACETATE SUCCINATE (HPMCAS) AND SODIUM ALGINATE IN OUTER SHELL FOR COLON TARGETING

Krishnakumar Devrao Lone*¹ and Jyoti Arjunrao Dhole ²

JSPM's Rajarshi Shahu College of Pharmacy and Research ¹, Tathawade, Pune, Maharashtra, India
Department of Botany, Yeshwant Mahavidyalaya ², Nanded, Maharashtra, India

Keywords:

Press coated tablet, Mesalazine, ulcerative colitis. HPMCAS, Granulation

Correspondence to Author:

Krishnakumar Devrao Lone
Lecturer in Pharmaceutics, JSPM's Rajarshi Shahu College of Pharmacy and Research, Tathawade, Pune, Maharashtra, India
E-mail: krishnalone@gmail.com

ABSTRACT: The aim of present study was to develop a new colon targeting formulation, which can minimize the escape of Mesalazine completely in upper gastro-intestinal tract and ensure availability of maximum amount of drug to achieve the desired site i.e. distal colon. The use of press coated tablets with Hydroxypropylmethylcellulose acetate succinate (HPMCAS) and sodium alginate in outer shell was investigated. Two coats (upper and lower) were compressed onto the core tablets of Mesalazine using varying quantities of coating composition i.e. 100mg and 150mg each for lower and upper coat. The Mesalazine tablets coated by compressing 100 mg of HPMCAS each as upper and lower coat did not maintain integrity of the coats and released almost 100% of drug within 3 hrs. The tablets coated by compressing 150 mg of HPMCAS on the core tablets maintained good integrity during the dissolution test and prevented escape of Mesalazine totally in acid stage and buffer stage 1. However, the release of Mesalazine in subsequent buffer stage 2 was also affected. Mesalazine tablets coated with 1:1 blends of HPMCAS and sodium alginate could maintain good mechanical strength in acid stage and buffer stage 1 and released 81.65 % of drug within 5 hrs. While the tablets with higher proportion of Sodium alginate in coat although possessed good mechanical strength indicated slower release of drug. The amount of Mesalazine released from the tablets coated with higher proportion of HPMCAS alone was comparable to that released from the tablets coated with equal proportions of two pH sensitive polymers. These release indicating the usefulness of press coated tablets.

QUICK RESPONSE CODE	DOI: 10.13040/IJPSR.0975-8232.4(6).2244-51
	Article can be accessed online on: www.ijpsr.com

INTRODUCTION: Colonic drug delivery has gained increased importance not just for the delivery of drugs for the treatment of local diseases of colon such as irritable bowel syndrome (IBS), inflammatory bowel disease (IBD) including Crohn's disease and ulcerative colitis (UC) but also for its potential for the delivery of proteins and therapeutic peptides like insulin ¹.

Inflammatory Bowel Diseases (IBD) includes two conditions Ulcerative colitis and Crohn's disease. Ulcerative colitis (UC) is a condition that affects a part of large intestine- the rectum and the colon ². The affected part becomes inflamed and develops ulcers, causing symptoms that include bloody diarrhoea, abdominal pain and fever.

Mesalazine is considered to be the “Gold standard” drug for treatment of ulcerative colitis and it is available as delayed released tablets, controlled released capsules, enteric coated tablets for oral use and rectal suppositories, enema suspension for rectal use³.

In present study, press coated tablets were prepared using Hydroxypropylmethylcellulose acetate succinate (HPMCAS) as a basic enteric material in the outer shell, and their functions were examined by in vitro dissolution test. In addition the effects of addition of sodium alginate to HPMCAS were investigated to improve the acid resistance and time released function of press coated tablet using HPMCAS⁴.

MATERIAL AND METHODS: Mesalazine was obtained from Sari Overseas, Mumbai, India, Sodium alginate from Alembic Pharmaceuticals Ltd., Baroda. HPMCAS, povidone (PVP-K30) and microcrystalline cellulose were obtained from Signet Chemical Corporation, Mumbai for free of cost. Talc and Magnesium stearate were procured from Emcure House M.I.D.C. Pune. All the other chemicals and reagents used were of analytical grade. The commercially available Mesalazine product, Asacol was procured from A. Birla hospital (Pune).

Formulation of compression coated tablets of Mesalazine: The formulation was developed in two stages. Initially the core tablets (weight 300mg) of Mesalazine were prepared using following formula. (Table 1) Subsequently two coatings were compressed onto these cores (upper layer and lower layer) using S.S. punches (diameter 13 mm flat surface) on rotary tablet press. The compression force was maintained in such a way that the hardness of resulting core tablets ranged between 2-3 kg/m²⁵.

Preparation of Core tablets of Mesalazine: The physical mixtures of polymers and excipients were prepared by blending the accurately weighed quantities of each of them with Mesalazine in geometric proportions in glass mortar for 15 minutes. Ethnolic solution of PVP K-30 (3% w/v) was used as binder which was added gradually to powder blends with trituration until a coherent moist mass was formed. This mass was passed through screen (22#) to get moderately coarse granules. The wet granules were dried at 50°C for 1 hour. The dried granules were again passed through screen (44#) to obtain fine granules. The resulting granules were lubricated with magnesium stearate (Table 1). For the preparation of Core tablets (300 mg), tableting was performed under compression force of 1030kg/cm² and punch speed of 10 mm/min, with a multi station rotary punch tablet compression machine. A flat faced punch 8 mm in diameter was used⁶.

TABLE1: FORMULAE FOR MESALAZINE CORE TABLETS

Formulation code	Tablet excipients (%w/w)			
	Povidone (PVP K-30)	Ac-Di-Sol	Magnesium stearate	Talc
C1	3	0	1	12.67
C2	3	1	1	11.67
C3	3	2	1	10.67
C4	3	3	1	9.67
Total weight of core tablet= 300mg				

The drug contents were maintained at 250 mg for all the formulations

Evaluation of core tablets: The core tablets were evaluated for various tablet characterization viz;

Tests for physical evaluation

- Appearance & dimensions
- Weight variation
- Hardness
- Friability

Tests for performance evaluation

1. Test for % drug content
2. *In-vitro* drug release

Test for physical evaluation of core tablets were carried out by the procedure described in standard text book Liberman, 2001⁷.

***In vitro* release of Mesalazine from Core tablets:**

The test was conducted using three tablets of each type of formulation using USP (23) dissolution

apparatus (Apparatus I) ⁸. The test was performed using 900 ml of phosphate buffer (pH 7.2). Aliquots were withdrawn at time intervals of 5 minutes carefully over a period of 60 minutes.

Every time the equal volume of fresh dissolution medium, (maintained at same temperature) was added to the bulk to maintain sink conditions.

Samples were filtered through Whatman filter paper (No. 41) and their absorbances were recorded at λ_{\max} 303.5nm ⁹.

Coating of core tablets using different polymer compositions: The coating formulae were prepared using HPMCAS (HF) alone, and combination with sodium alginate in different proportions (**Table 2**).

TABLE 2: COMPOSITION OF COMPRESSION COATED TABLETS

Code for coated Tablets	Coating layer composition	Proportion of HPMCAS: Sodium alginate
CHA1	100 mg each layer	1: Nil
CHA2	150 mg each layer	1: Nil
CHS1	150mg each layer	1:1
CHS2	150mg each layer	1:2
CHS3	150mg each layer	2:1

Compression of Coats on Core tablets of Mesalazine: Two coats (upper and lower) were compressed onto the core tablets of Mesalazine using varying quantities of coating composition i.e. 100mg each for lower and upper coat; 150mg each for lower and upper coat.

Evaluation of Coated tablets of Mesalazine: The coated tablets were evaluated for the various physical and performance characteristics similar to the core tablets of Mesalazine.

- **In vitro release of Mesalazine from Press Coated Tablets:** The test was conducted using three tablets of each type of formulation using USP (23) dissolution apparatus (Apparatus I) ⁸.

Procedure: The tablets of each type of formulations were kept in baskets which were placed successively in above mentioned dissolution media. The dissolution apparatus was run maintaining above stated test conditions (**Table 3**).

TABLE 3: THE EXPERIMENTAL CONDITIONS USED FOR IN VITRO RELEASE OF MESALAZINE FROM PRESS COATED TABLETS

Phases	Type and volume of Dissolution medium	Speed of Rotation (rpm)	Duration (min)	λ_{\max} used for recording absorbance	Volume withdrawn & frequency of withdrawn of aliquots
Phase I Acid stage	0.1N HCl 500ml pH- 3	100 rpm	120	303.0	10ml at intervals of 30min
Phase II Buffer stage-1	Phosphate buffer 900ml pH- 6	100 rpm	60	330.0	10ml at intervals of 30min
Phase III Buffer stage-2	Phosphate buffer 900ml pH-7.2	50 rpm	90	331.0	10ml at intervals of 30min

- In the phase I, the test was performed using 0.1N HCL.10 ml aliquots were withdrawn at time intervals of 30 minutes carefully over a period of 120 minutes. Every time the equal volume of fresh dissolution medium, (maintained at same temperature) was added to the bulk to maintain sink conditions. Samples were filtered through Whatman filter paper (No. 41) and their absorbances were recorded at λ_{\max} 303.5nm.
- In the phase II i.e. buffer stage-1, 900 ml of phosphate buffer (pH 6) was transferred into each of the dissolution vessels. Apparatus was run maintaining test conditions as mentioned for buffer stage-1. Aliquots (10ml) were removed after 30 minutes carefully over a period of 60 minutes and were filtered and absorbances were recorded at λ_{\max} 330.0nm. Equal volume of phosphate buffer (pH 6) was added into the vessels after each withdrawal.

- In the phase III i.e. buffer stage-2, 900 ml of phosphate buffer (pH 7.2) was transferred into each of the dissolution vessels. Apparatus was run again maintaining test conditions as mentioned for buffer stage 2. Aliquots (10 ml) were withdrawn at time intervals of 30 minute carefully over a period of 90 minutes. Every time the equal volume of fresh dissolution medium, (maintained at same temperature) was added to the bulk. These samples were filtered through Whatman filter paper (No. 41) and their absorbances were recorded at λ_{\max} 331.0 nm.

RESULT AND DISCUSSION:

TABLE 4: FLOW PROPERTIES OF GRANULES OF MESALAZINE

Code	LBD (g/ml)	TBD (g/ml)	Carr's C.I. (%)	Angle of Repose (θ)
C1	0.22±0.04	0.26±0.03	15.38±0.42	24.22
C2	0.24±0.05	0.29±0.01	17.24±0.56	24.32
C3	0.24±0.03	0.28±0.05	14.28±0.54	24.69
C4	0.21±0.02	0.25±0.02	16.00±0.40	25.40

All values are expressed as mean± SD, n=3

TABLE 5: CHARACTERIZATION OF CORE TABLETS OF MESALAZINE

Code	Avg. Weight (mg)	Diameter (mm)	Thickness (mm)	Hardness (Kg/cm ²)	Friability (%)	Drug Content (%)
C1	299±1.56	8.09	3.12	2.0	0.83	99.42±0.123
C2	300±0.85	7.96	3.10	2.0	0.88	99.45±0.066
C3	297±1.92	7.90	3.13	2.5	0.76	98.35±0.107
C4	300±2.25	8.02	3.10	3.0	0.74	98.26±0.126

The core tablets possessed acceptable values for tablet characteristics.

- Effect of varying concentrations of superdisintegrant on *in vitro* release of Mesalazine from Core tablets:** *In vitro* dissolution data of Mesalazine from the control tablets i.e. tablets prepared without addition of superdisintegrant indicated complete release of the drug within 65 minutes in the buffer stage 2 while the core tablets containing increasing concentrations of superdisintegrant released the contents in shorter span of time period. Thus, the tablets containing highest % (3% w/w of tablet weight) amounts of Ac-di-Sol released Mesalazine within 40 minutes in the buffer stage 2 (Table 6; Fig. 1).

Characterization of Lubricated granules of Mesalazine used for Core Tablets: The values for loose bulk density, tapped bulk density, compressibility index and angle of repose of granules of Mesalazine prepared with PVP K-30 as binder for core tablets indicated good flow properties (Table 4).

Values of loose bulk density and tapped bulk density for Mesalazine granules ranged between 0.21±0.02-0.24±0.05 and 0.25±0.02- 0.29±0.01 g/ml. Similarly values of Carr's index ranged between 15.38±0.42-16.00±0.40. Angle of repose values ranged between 24.22-25.40 suggesting good flow properties of granules (table 5).

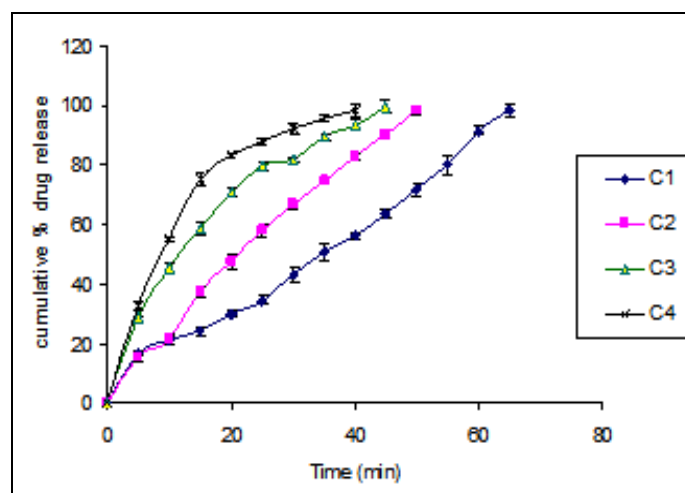


FIG. 1: *IN VITRO* RELEASE OF MESALAZINE FROM CORE TABLETS.

TABLE 6: DISSOLUTION DATA MESALAZINE FROM THE CORE TABLETS

Time (min)	Cumulative (Avg.) % drug release from core tablets			
	C1	C2	C3	C4
0	0	0	0	0
5	16.83±0.98	15.358±1.36	28.52 ±1.06	32.55±1.77
10	21.21±1.23	24.74±1.46	45.27 ±1.53	55.09±0.89
15	24.16±1.52	21.40±1.82	58.67 ±2.25	75.16±2.13
20	29.99±1.36	37.46±2.01	70.70 ±1.51	83.43±0.79
25	34.56±1.63	47.66±2.75	79.64 ±1.90	87.86±1.18
30	43.08±2.35	58.16±2.17	81.71 ±0.88	92.33±1.57
35	50.65±3.01	66.65±1.35	89.44 ±1.46	95.42±1.11
40	56.28±1.42	74.53±1.21	93.717±1.99	98.54±2.20
45	63.54±1.49	82.89±1.02	99.63 ±2.38	--
50	71.81±2.31	90.03±0.99	--	--
55	80.21±3.08	98.34±1.46	--	--
60	91.51±1.35	--	--	--
65	98.56±2.11	--	--	--

Characterization of Coated tablets of Mesalazine:

TABLE 7: TABLET CHARACTERISTICS OF COATED TABLETS OF MESALAZINE WITH VARYING AMOUNTS OF COATING FORMULAE

Code	Avg. Weight (mg)	Diameter (mm)	Thickness (mm)	Hardness (Kg/cm ²)	Friability (%)
CHA1	499±1.56	12.67	3.37	8.0	0.52
CHA2	600±0.85	12.73	3.64	8.0	0.58
CHS1	600±1.32	12.78	3.54	7.5	0.36
CHS2	599±1.30	12.92	3.56	8.0	0.35
CHS3	600±1.10	12.90	3.60	7.5	0.31

- The pharmacopoeial specifications for deviation in weight from average weight for tablets weighing more than 250 mg are $\pm 5\%$. The percentage deviation in the weight of prepared tablets (weighing 600 mg except CHA1 weighing 500 mg) was within the specified limits for all the formulations and hence they complied with the test for weight variation
- There was obvious increase in diameter, thickness and hardness of the coated tablets as compared with core tablets.
- The friability of all the coated formulations was lower than the core tablets and complied with the specified limits.
- **In vitro release of Mesalazine from prepared compression coated tablets:** The Mesalazine tablets coated by compressing 100 mg of HPMCAS each as upper and lower coat did not maintain integrity of the coats and released almost 100% of drug within 3 hrs. This performance is not useful to qualify these tablets as colon targeted formulations (Table 8).
- The tablets coated by compressing 150 mg of HPMCAS on the core tablets maintained good integrity during the dissolution test and prevented escape of Mesalazine totally in acid stage and buffer stage 1. However, the release of Mesalazine in subsequent buffer stage 2 was also affected (Table 8; Fig. 2).

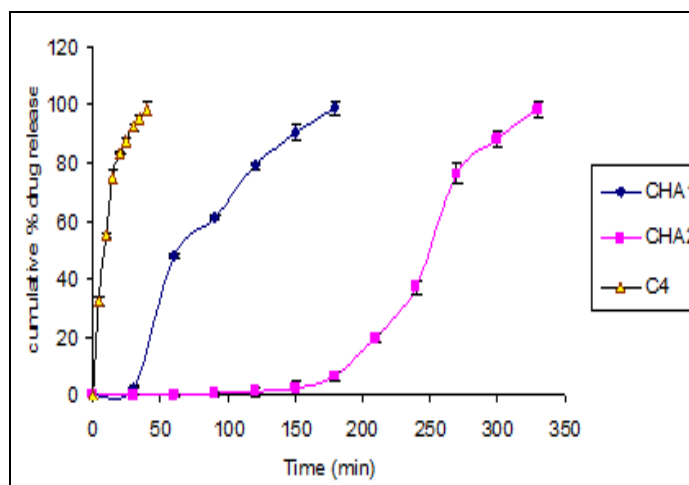


FIG. 2: IN VITRO DISSOLUTION PROFILES OF MESALAZINE FROM EXPERIMENTAL COATED TABLETS

TABLE 8: IN VITRO RELEASE DATA OF MESALAZINE FROM EXPERIMENTAL COATED TABLETS WITH HPMCAS

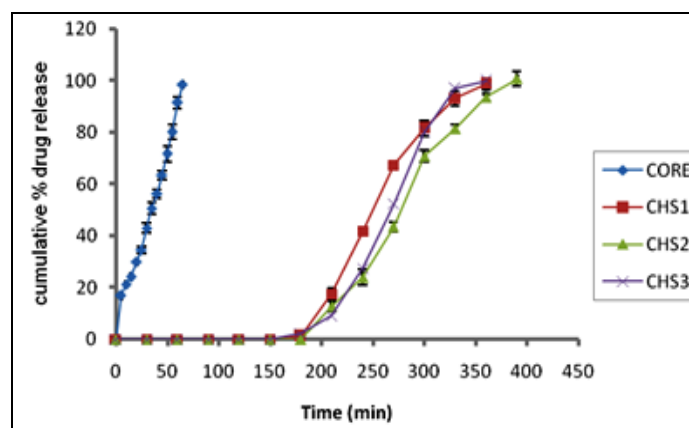
Time (min)	C4 (Core Tablet)	Dissolution phase	Cumulative % drug release		
			Time (min)	CHA1	CHA2
0	0	Acid stage pH 3	0	0	0
5	32.55±1.77		30	2.501±0.38	0.025±0.21
10	55.09±0.89		60	47.88±0.86	0.034±0.58
15	75.16±2.13		90	61.34±0.98	0.45±0.094
20	83.43±0.79		120	79.27±1.28	0.98±1.28
25	87.86±1.18	Buffer stage 1 pH 6.0	150	90.61±2.54	2.198±1.11
30	92.33±1.57		180	98.87±2.14	6.451±2.14
35	95.42±1.11	Buffer stage 2 pH 7.2	210	-	19.73±2.84
40	98.54±2.20		240	-	37.21±3.10
--	--		270	-	76.37±2.14
--	--		300	-	88.12±1.47
--	--		330	-	98.47±1.34

- In vitro release data of Mesalazine from tablets coated with combinations of HPMCAS and Sodium alginate:** *In vitro* dissolution data of Mesalazine from core tablets, from press coated tablets with combination of HPMCAS

and Sodium alginate at different proportions viz CHS1 (1:1), CHS2 (1:2) and CHS3 (2:1) (total coat weight 300mg) is presented in **Table 9** and **Fig. 3**.

TABLE 9: DISSOLUTION DATA OF PRESS COATED TABLETS OF MESALAZINE WITH COMBINATION OF HPMC-AS AND SODIUM ALGINATE.

Time (min)	C4 (core tablet)	Dissolution phase	Time (min)	Cumulative % drug release		
				CHS1	CHS2	CHS3
0	0	Acid stage pH 3	0	0	0	
5	32.55±1.77		30	0	0	0
10	55.09±0.89		60	0	0	0
15	75.16±2.13		90	0	0	0
20	83.43±0.79		120	0	0	0
25	87.86±1.18	Buffer stage 1 pH 6.0	150	0	0	0
30	92.33±1.57		180	1.321±1.36	0	2.213±1.26
35	95.42±1.11	Buffer stage 2 pH 7.2	210	17.54±1.84	12.78±1.96	9.153±1.78
40	98.54±2.20		240	45.71±1.15	24.05±3.02	27.43±2.14
--	--		270	67.34±2.16	43.55±1.88	52.41±1.74
--	--		300	81.65±2.46	70.83±2.30	80.21±1.32
--	--		330	93.34±1.66	81.48±1.67	97.38±1.86
--	--	360	98.25±1.71	93.72±1.37	99.91±1.16	
--	--	390	--	100.08±2.15	--	

**FIG. 3: IN VITRO DISSOLUTION PROFILES OF TABLETS OF MESALAZINE PRESS COATED WITH COMBINATION OF HPMC AS (HF) AND SODIUM ALGINATE**

Mesalazine tablets coated with 1:1 blends of HPMCAS and sodium alginate could maintain good mechanical strength in acid stage and buffer stage 1 and released 81.65 % of drug within 5 hrs. While the tablets with higher proportion of Sodium alginate in coat although possessed good mechanical strength indicated slower release of drug.

The amount of Mesalazine released from the tablets coated with higher proportion of HPMCAS alone was comparable to that released from the tablets coated with equal proportions of two pH sensitive polymers.

Comparative evaluation of drug release profiles of Mesalazine from press coated tablets with marketed formulation (Asacol): *In vitro* dissolution data of Mesalazine from marketed formulation and from press coated tablets with combination of

HPMCAS and Sodium alginate at different proportions viz CHS1 (1:1), CHS2 (1:2) and CHS3 (2:1) (total coat weight 300mg).is presented in **Table 10 and Fig. 4.**

TABLE 10: DISSOLUTION DATA OF PRESS COATED TABLETS OF MESALAZINE WITH COMBINATION OF HPMC-AS AND SODIUM ALGINATE.

Time (min)	Dissolution phase	Time (min)	Cumulative % drug release			
			Marketed formulation	CHS1	CHS2	CHS3
0	Acid stage pH 3	0	0	0	0	0
5		30	0	0	0	0
10		60	0	0	0	0
15		90	0	0	0	0
20		120	0	0	0	0
25	Buffer stage 1 pH 6.0	150	0.73	0	0	0
30		180	1.147	1.321±1.36	0	2.213±1.26
35	Buffer stage 2 pH 7.2	210	42.18	17.54±1.84	12.78±1.96	9.153±1.78
40		240	79.82	45.71±1.15	24.05±3.02	27.43±2.14
--		270	92.12	67.34±2.16	43.55±1.88	52.41±1.74
--		300	98.54	81.65±2.46	70.83±2.30	80.21±1.32
--		330	--	93.34±1.66	81.48±1.67	97.38±1.86
--		360	--	98.25±1.71	93.72±1.37	99.91±1.16
--		390	--	--	100.08±2.15	--

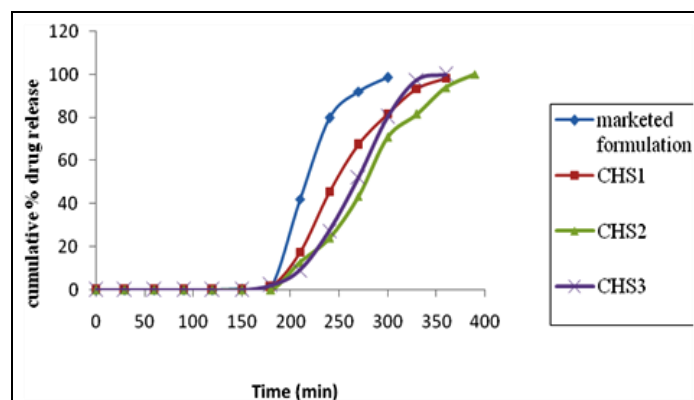


FIG. 4: COMPARATIVE EVALUATION OF MARKETED FORMULATION WITH PRESS COATED TABLETS

The comparative results indicated the usefulness of press coated tablets with desirable functions for colon targeting formulation.

CONCLUSION: The applicability of press-coated tablets for colon targeting delivery systems, which suppress drug release totally in acid stage and buffer stage 1, was studied using hydroxypropylmethyl cellulose acetate succinate (HPMCAS) an enteric polymer alone and its combination with sodium alginate in various proportions in outer shell. The Mesalazine tablets coated by compressing 100 mg of HPMCAS each as upper and lower coat did not maintain integrity of the coats and released almost

100% of drug within 3 hrs. This performance is not useful for qualifying colon targeting drug delivery. The tablets coated by compressing 150 mg of HPMCAS on the core tablets maintained good integrity during the dissolution test and prevented escape of Mesalazine totally in acid stage and buffer stage 1.

The combination of HPMCAS with sodium alginate showed interesting effects on dissolution profile. The result indicate that these systems suppressed drug release completely in acidic stage 1 and the lag time could be controlled by adjusting mixing ratio of HPMCAS with sodium alginate. Comparative study of press coated tablets with marketed formulation (Asacol) indicated the usefulness of it for colon targeted delivery.

ACKNOWLEDGEMENT: The authors are thankful to Sarex Overseas Mumbai, India for providing sample of Mesalazine, Signet Chemical Corporation, Mumbai for sample of HPMCAS and Alembic Pharmaceuticals Ltd. Baroda for sample of Sodium alginate free of cost. Signet Chemical Corporation, Mumbai Authors wish to thank JSPM's Rajarshi Shahu college of Pharmacy and Research, Pune for providing necessary facilities to carry out the work.

REFERENCES:

1. Frieri G, Pimpo M, Galletti B. et al. Long-term oral plus topical mesalazine in frequently relapsing ulcerative colitis. *Digestive and Liver Disease* 2007; 37: 92-96.
2. Shanahan F. Probiotics in inflammatory bowel disease-therapeutic rationale and role. *Advance Drug Delivery Reviews* 2004; 56: 809-818.
3. Rudolph MW, Klein S, Beckert ET. A new 5 aminosalicylic acid multiunit dosage form for the therapy of ulcerative colitis. *Eur J Pharm and Biopharm* 2001; 51: 183-190
4. Fukui E, Miyamura N, Kobayashi M., An *in vitro* investigation of suitability of press-coated tablets with (HPMCAS) and Hydrophobic additives in outer shell for colon targeting. *Journal of Controlled Release*. 2001; 70: 97-107.
5. Fukui E, Miyamura N, Yoneyama T, Kobayashi M. Drug release from and mechanical properties of press coated tablets with hydroxypropylmethylcellulose acetate succinate and plasticizers in outer shell. *Int J Pharm*. 2001; 217: 33-43.
6. Fukui E, Miyamura N, Uemura K, Kobayashi M. Preparation of enteric coated timed-release press-coated tablets and evaluation of their function by *in vitro* and *in vivo* tests for colon targeting. *Int J Pharm*. 2000; 204: 7-15.
7. Lieberman H.A., Lachman L. and Kanig J.L.: The theory and practice of industrial pharmacy, 3rd ed. Bombay: Verghese publishing house.1990; 184.
8. The United States Pharmacopoeia, 27th revision and the national formulary 22nd edition. Vol. 2, the official compendia of standards, Asian edition published by the board of trustees 2004; 1165.
9. Schellekens RCA, Stuurman FE, Van der Weert FHJ. A novel dissolution method relevant to intestinal release behavior and its application in the evaluation of modified release mesalazine product. *Eur J Pharm Sci* 2007; 30: 15-20.
10. Aulton ME. 1998. *Pharmaceutics: The science of dosage form design*. 2nd ed. London, England: Churchill Livingstone, 208.
11. Sinha VR, Kumria R. Binders for colon specific drug delivery: an *in vitro* evaluation. *Int J Pharm* 2002; 249: 23-31.

How to cite this article:

Lone KD and Dhole JA: An *in vitro* investigation of suitability of Press-coated tablets with Hydroxypropylmethylcellulose acetate succinate (HPMCAS) and Sodium alginate in outer shell for Colon Targeting. *Int J Pharm Sci Res* 2013; 4(6); 2244-2251. doi: 10.13040/IJPSR.0975-8232.4(6).2244-51

All © 2013 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.