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(Research Article)

Formulation and *in vitro* evaluation of compression coated mebeverine HCl tablets for colon targeting

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Abstract

The aim of the study was to develop colon targeted compression coated Mebeverine HCl (MEB) tablets using pH dependent, swellable and rupturable polymers for effective treatment of irritable bowel syndrome (IBS). The MEB loaded core tablets were prepared by direct compression method using CCM and CP as super disintegrating agents at different concentrations and evaluated for pre compression and post compression parameters. The optimized core tablets were further used to fabricate compression coated tablets using different ratios of Eudragit L100, Eudragit S100 as pH- dependent polymers, Keltone and Ethocel as swellable and rupturable polymers by modified compression method. Drug compatibility with excipients was checked by FTIR studies and results indicate no interaction. The precompression and post compression studies were within acceptable limits. *In vitro* dissolution studies were done for compression coated tablets to find out the lag phase, burst drug release and retard drug release The findings of this study concludes that the lag time of compression coated tablet can be modulated by combining with EL 100, ES 100, Keltone and Ethocel in different weight ratio. These designed tablet system was found to be satisfactory in terms of release of the drug after the predetermined lag time, thus the system can be target to release in the colon proximity. The compression coating technique can be successfully applied for MEB for colon targeting to treat IBS.

Keywords: Mebeverine HCl; Eudragit; Cross povidone; Croscarmellose; Compression coating

1. Introduction

Colon targeted drug delivery systems offers to treat various colonic diseases like ulcerative colitis, amoebiasis, colonic cancer, inflammatory bowel disease (IBD) by delivering drugs directly to the colon region due to its longer transit time1. Colonic route of drug administration is not only used for the local treatment of colonic diseases but also be used for the systemic delivery of protein and peptide drugs2 and treat diseases which are sensitive to the circadian rhythms such as angina, asthma, arthritis etc. Various approaches are developed for colon targeting by considering the physiological characteristics such as gastric emptying, pH gradient and peristaltic moment of the GIT. The present study developed pH dependent colon targeting compression coated tablets loaded with Mebeverine HCl to treat IBD. Mebeverine is an antispasmodic drug that is claimed to act directly on the colonic muscle and is virtually free of systemic adverse reactions and has been used to treat IBD, it has direct effect on colonic muscle activity.

2. Materials and methods

2.1. Materials

Mebeverine HCl (MEB) obtained from Magnus Pharma Pvt.Ltd, Nepal. Croscarmellose sodium (CCM), Crospovidone (CP), Eudragit S100 (ES100), Eudragit L100 (EL100) obtained from Yarrow Chem Products, Mumbai. Galen IQ720

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(GQ720) procured from Beneo-Palatinite, Germany. Keltone, Ethocel, Magnesium stearate and Talc from SD Fine Chem limited, Mumbai.

2.2. Methods

Preparation of the Core Tablet: MEB core tablets were prepared by direct compression method using two super disintegrants viz., CCM, CP at 4, 8 and 12% w/w and GQ720 as directly compressible carrier. All the ingredients as per the table 1 were weighed and blend with GQ720 and shaken in a polybag for prescribed time to get uniform mixing, further this blend was subjected for precompression studies viz., bulk density, compressibility index, angle of repose by standard procedure3-5. The powder blend was further compressed into tablets using 8 mm punch in Cadmach 10 station rotary tablet punching machine.

Table 1 Formulae of MEB core tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	Plain
MEB	130	130	130	130	130	130	130
CCM	7.2	14.4	21.6	-	-	-	-
CP	-	-	-	7.2	14.4	21.6	--
GIQ	42.8	35.6	28.4	42.8	35.6	28.4	50
Total weight	180	180	180	180	180	180	180

2.2.1. Preparation of compression coated tablets

The B-1 to B-8 batches of compression coated tablets were designed as per table 2 by one step dry coating technique[6] using optimized core tablets viz., F-3 and F-6 as shown in figure 1. In each case impermeable ethocel was applied under the bottom of the die cavity and core tablet was placed carefully at the center of die. Core tablet was slightly pressed to fix, above it the mixture of pH dependent (ES100, EL100), rupturable and swelling polymers (Keltone, Ethocel) were filled and manually lowered the lower punch slowly and compressed by using 13 mm flat faced punch.

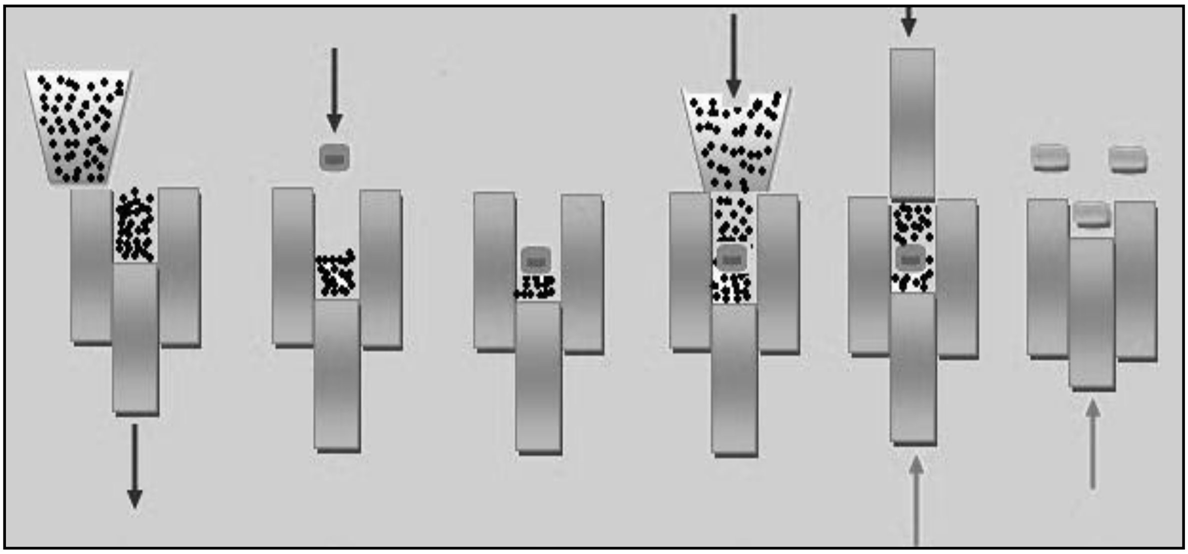

Figure 1 Scheme represent One step compresion coating of tablets

Table 2 Formulae of compression coated MEB tablets

Ingredients (mg)	F-3 core tablet				F-6 core tablet			
	B-1	B-2	B-3	B-4	B-5	B-6	B-7	B-8
Core tablet	180	180	180	180	180	180	180	180
pH dependent and rupturable and swelling polymers								
Eudragit S 100	175	175	-----	-----	175	175	-----	----
Eudragit L 100	---	----	175	175	---	----	175	175
Keltone	75	50	75	50	75	50	75	50
Ethocel	100	125	100	125	100	125	100	125
Impermeable Ethocel layer								
Ethocel	170	170	170	170	170	170	170	170
Total weight (mg)	700	700	700	700	700	700	700	700

2.3. Evaluation

2.3.1. FTIR studies

The FTIR spectra for MEB, and optimized core and compression coated tablets were recorded using BRUKER-FTIR spectrophotometer in the wave number region from 4000 cm^{-1} to 500 cm^{-1}. The KBr press was used to prepare potassium bromide pellets loaded with samples under the study. Samples and KBr were mixed in a ratio of 1:100 and pellets were prepared by finely grinding the mixture in a mortar. Finely grinded mixture was introduced into a stainless steel die and pellets were prepared by pressing the die between polished steel anvils at a pressure of $10t/in^2$.

2.3.2. Postcompression evaluation

The developed core and compression coated tablets were studied for post compression parameters viz., thickness, diameter, friability, hardness, drug content, weight variation as per standard procedures and conditions.

2.3.3. Disintegration

Disintegration test is carried out by using USP apparatus, introduce one tablet into each tube and, add a disc to each tube. Suspend the assembly in the beaker containing phosphate buffer pH 7.4 and operate the apparatus for the specified time. Note down the time taken for tablet to disintegrate, triplicate readings were taken and data was computed.

2.4. *In vitro* release study

2.4.1. For core tablets

In vitro dissolution study core tablets were conducted by using USP Type II Paddle apparatus. Place the stated volume about 900 ml of the dissolution medium viz., phosphate buffer pH 7.4, free from dissolved air, into the vessel of the apparatus. Assemble the apparatus and warm the dissolution medium to 37°C. Place one core tablet in the apparatus, allow the tablet to sink to the bottom of the vessel prior to the rotation of the paddle. Operate the apparatus immediately at the 50 rpm. At specified time interval withdraw the 5 ml sample and add a volume of fresh dissolution medium equal to the volume of the samples withdrawn to maintain sink condition. Filter the sample solution through Whatman filter 44, and measure at 263 nm for MEB content using a double beam UV spectrophotometer. The study was conducted in triplicate and data were computed by using dissolution software PCP Disso V3.0.

2.4.2. For compression coated tablet

In vitro drug dissolution studies were carried out for compression coated tablets using USP Type II Paddle apparatus. The drug release was studied in three different medium to simulate GIT proximity. Initially the dissolution was carried out in 0.1N HCl for first 2 h to mimic the simulation of gastric fluid. After replace the 0.1N HCl with phosphate buffer pH 7.4 and continue the dissolution for 6 h. Replace the phosphate buffer pH 7.4 with phosphate buffer pH 6.8 and continue the dissolution for 12 h to mimic small intestine and colon pH. In each case at different intervals of time specified volume was withdrawn and same was replaced with fresh dissolution medium to maintain the sink conditions. Filter the sample solution through Whatman filter 44, and measure at 263 nm for MEB content using a double beam UV spectrophotometer. The study was conducted in triplicate and data were computed by using dissolution software PCP Disso V3.0.

3. Results and discussion

3.1. FTIR studies

The comparative FTIR data and specters were shown in table 3 and figure 2. The FTIR spectra of MEB shows characteristic absorption bands appeared at 2959.06 cm^{-1} for Ar-CH=CH-, 2837.27cm^{-1} for -CH_2-,1714.33 cm^{-1} for C=O, 1510.11 cm^{-1} for Ar-CH=CH- and 1339.31 cm^{-1} for -C-N-. MEB loaded core tablets and compression coated tablets shows all the characteristic bands of MEB which clearly indicate that there is no interaction between the MEB and polymers used in the preparation of core and compression coated tablets.

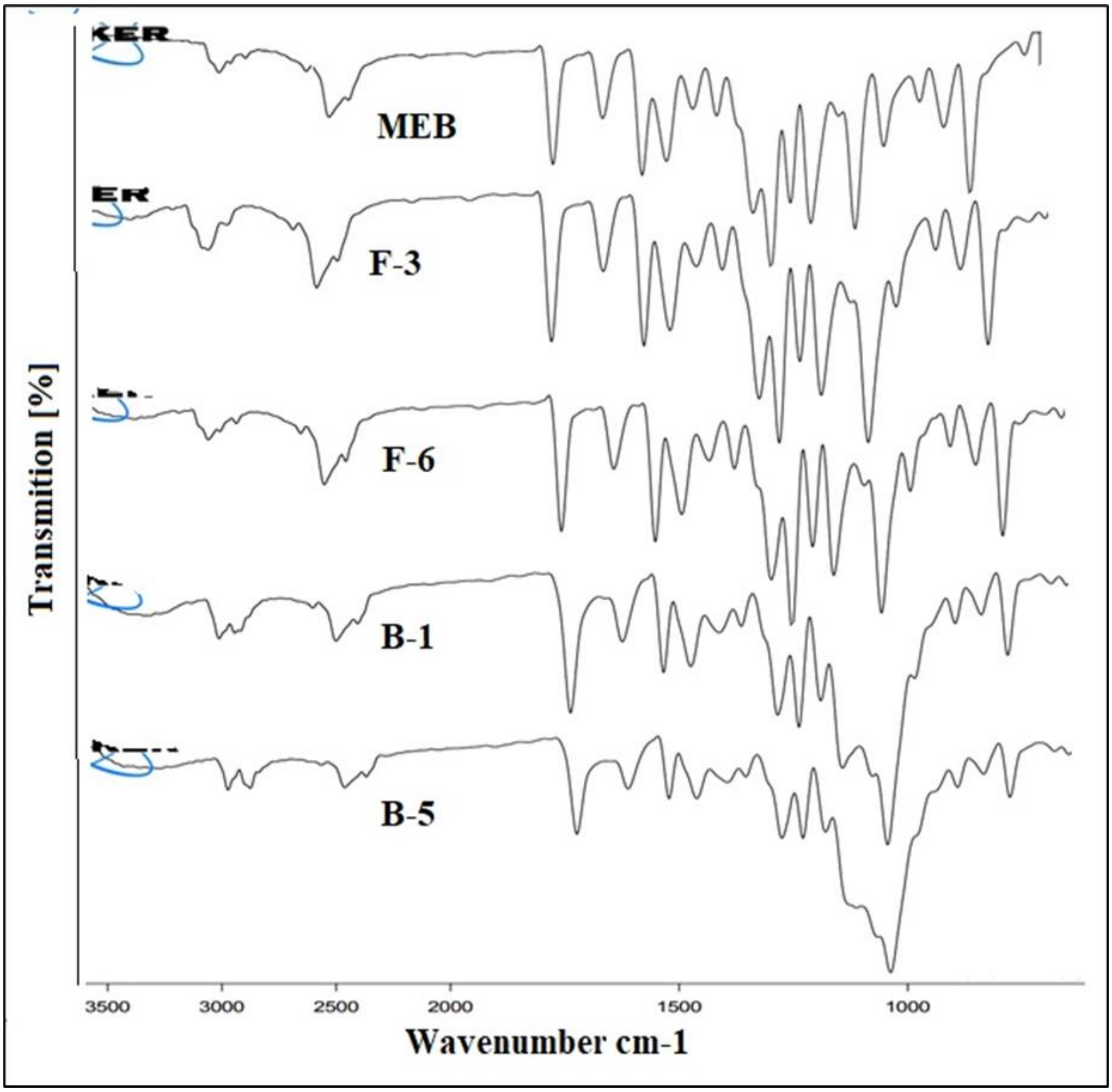

Figure 2 FTIR spectra of MEB and MEB loaded core and compression coated tablets

Table 3 FTIR data of MEB and MEB loaded core and compression coated tablets

Batches	Ar CH=CH Stretching cm^{-1}	Aliphatic $-CH_2-$ Stretching cm^{-1}	C=O Stretching absorption cm^{-1}	Ar C=C ring stretching cm^{-1}	C-N stretching cm^{-1}
MEB	2959.06	2837.27	1714.33	1510.11	1339.31
F-3	2930.78	2848.05	1714.11	1511.61	1340.38
F-6	2959.08	2837.77	1715.20	1511.91	1340.65
B-1	2968.53	2874.94	1715.54	1512.14	1342.12
B-5	2972.30	2874.18	1715.78	1512.28	1342.91

3.1.1. Pre compression studies

The bulk density was found to be in the range of 0.279±0.107 to 0.321±0.002 g/cm^3; compressibility index value 20.4±5.67 to 27.3±0.01 and Hauser's value 1.19±0.122 to 1.36 ±0.03 for F-1 to F-6 and plain tablets indicates a powder with good compressibility and flowability can be used for direct compression. The angle of repose was found to be in the range of 28.34±1.76 to 36.4±0.4 for F-1 to F-6 and plain tablets showing that the blends of powder were free flowing.

3.1.2. Post compression studies

The post compression data for core and compression coated tablets were given tables 4 and 5**.** The core tablet results were within the limits and are in accordance with pharmacopoeial standards. The hardness and friability data indicates that tablets have sufficient mechanical integrity and strength. The weight variation results revealed good uniformity of the tablets and were found to be within acceptable limits as per the pharmacopoeial specifications, the disintegration time was below 3 min in core tablets and is the determinant factor in the designing of compression coated tablets where burst release after lag time is in question. The results suggest the disintegration time decreases with increase in concentration of super disintegrants, among the super disintegrants the tablets prepared with CCM shows better disintegration time. In both the case the mechanism of disintegration was due to swelling and hydrophilic wicking property. In case of compression coated tablets the hardness of the tablets was found to be in the range of 6.08±0.39 to 6.67±0.13kg/cm^2 friability in the range of 0.39±0.019 to 0.564±0.08% which were below 1% indicating the sufficient mechanical integrity and strength of the prepared compression coated tablets. All other parameters were found to be within specified limits and are complying with pharmacopoeial standards. The % drug content of MEB loaded core tablets and plain tablets were found to be 98.12±1.87 to 99.12±1.27, low SD values indicate uniformity in drug distribution and method adapted was reproducible.

Table 4 Postcompression data for core tablets

Batches	Thickness (mm)*	Diameter (mm)*	Weight Variation (mg)**	Hardness (kg/cm^2)***	Friability (%)**	Disintegration time in sec***
F-1	3.73±0.01	8.01±0.01	180±1.01	3.42±0.16	0.39±0.12	68±0.65
F-2	3.95±0.03	8.04±0.01	179±2.87	3.93±0.03	0.54±0.04	42±0.24
F-3	3.81±0.02	8.01±0.01	180±0.89	3.61±0.23	0.61±0.46	26±0.41
F-4	3.87±0.03	8.01±0.01	180±1.67	4.01±0.02	0.41±0.29	56±0.35
F-5	4.03±0.07	8.01±0.02	182±2.16	3.91±0.04	0.52±0.35	49±0.84
F-6	3.85±0.03	8.01±0.02	179±1.14	3.86±0.15	0.62±0.35	30±0.32
Plain	3.92±0.05	8.01±0.02	179±1.78	3.94±0.65	0.43±0.22	90±0.62
n = 10*/20**/6***						

Table 5 Postcompression data for compression coated tablets

Batches	Thickness (mm)*	Diameter (mm)*	Weight Variation (mg)**	Hardness (kg/cm^2)***	Friability (%)**
B-1	4.94±0.05	13.10±0.01	696.6±3.84	6.32±0.15	0.56±0.081
B-2	4.94±0.08	13.00±0.02	694.6±4.82	6.13±0.31	0.49±0.031
B-3	4.94±0.05	13.10±0.01	699.4±2.51	6.41±0.22	0.39±0.019
B-4	4.92±0.04	12.90±0.03	698.6±1.51	6.24±0.19	0.54±0.018
B-5	5.02±0.08	13.00±0.01	698.6±4.33	6.19±0.08	0.48±0.012
B-6	4.98±0.04	13.10±0.01	695.2± 5.26	6.39±0.61	0.42±0.061
B-7	5.12±0.10	13.00±0.02	699.8±3.83	6.08±0.39	0.50±0.091
B-8	5.04±0.05	13.12±0.04	699.4±0.11	6.67±0.13	0.47±0.652
n = 10*/20**/6***					

3.2. Disintegration studies

The disintegration test for compression coated tablets was carried out for 12 hr in order to check the influence of pH dependent, swellable and rupturable polymers on tablet integrity and the results suggest that the disintegration was time dependent and type of polymers. The disintegration time directly related to the lag period of the study is depends on swelling and bursting nature of the swellable and rupturable polymers and impermeable behavior of ethocel used in outer shell of the tablet and superdisintegrants in the inner shell core tablet. Swellable and rupturable polymer, ethocel in outer shell delayed the disintegration rate to great extent and super disintegrants in the inner core increases the faster disintegration and facilitate faster drug release. The sequential changes during disintegration of compression coated tablets were shown in the figure 3.

Figure 3 Sequential changes observed during disintegration of optimized compression coated tablet

3.3. *In vitro* dissolution studies

The *in vitro* dissolution studies were carried out for both core and compression coated tablets using USP Type II apparatus and the results were computed and analyzed by using dissolution software PCP Disso V3. The results were given tables 6, 7 and comparative dissolution profiles were shown in figure 4 and 5.

3.3.1. Core tablets

Total seven formulations F-1 to F-3 and F-4 to F-6 core tablets were prepared with CCM and CP at 4%, 8%, 12% w/w concentrations respectively, and Plain core tablets were prepared without any superdisintegrants. The cumulative percentage drug release at 30 min was found to be 82.79±0.67, 87.69±0.45, 90.29±0.46, 82.87±0.93, 85.76±0.68, 89.03±0.45, 50.96±0.59; and at 60 min 88.01± 0.22, 93.59 ± 0.56, 94.61 ± 0.44, 93.51±0.22, 94.54±0.34, 95.72±0.22, 69.08±0.58 for F-1 to F-6 and plain core tablets respectively. CCM decreases the disintegration time and increases drug release because it accelerates disintegration of tablets by virtue of its ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration occurs. This disintegration is reported to have an effect on dissolution characteristics as well. It was found that the F-3 core tablet containing CCM 12% w/w as a superdisintegrant have lower disintegration time and higher drug release than that of other CCM formulations, F-6 core tablets prepared with 12% w/w CP as superdisintegrant have lower disintegration time and higher drug release than other CP formulations, which may be due to that CP is a cross linked polymer of povidone and this cross linking makes it an soluble, hydrophilic, highly absorbent material, resulting in excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities, so CP provides superior drug dissolution and disintegration characteristics. Based on the *in vitro* results F-3 and F-6 core tablets were chosen for compression coating.

Table 6 *In vitro* dissolution data of MEB core tablets

Time in min	Cumulative percentage drug release						
	F-1	F-2	F-3	F-4	F-5	F-6	Plain
5	31.88±0.35	34.55±0.23	40.58±0.35	28.21±0.48	30.88±0.61	34.24±0.35	25.62±0.46
10	41.04±0.47	45.89±0.35	48.86±2.90	30.94±0.68	34.13±0.68	41.95±0.35	30.86±0.57
15	64.72±0.60	67.30±0.47	75.38±0.60	54.77±0.23	58.85±0.45	65.64±0.23	33.33±0.69
20	74.28±0.23	77.81±0.57	81.71±0.68	68.35±0.69	71.58±0.45	77.74±0.69	39.23±0.34
25	76.77±0.37	83.12±0.34	87.82±0.47	77.52±0.34	81.85±0.56	85.66±0.47	46.99±0.22
30	82.79±0.67	87.69±0.45	90.29±0.46	82.87±0.93	85.76±0.68	89.03±0.45	50.96±0.59
45	84.98±0.38	91.25±0.56	93.24±0.34	86.75±0.44	89.55±0.68	92.80±0.26	62.77±0.46
60	88.01±0.22	93.59±0.55	94.61±0.44	93.51±0.22	94.54±0.34	95.72±0.22	69.08±0.58

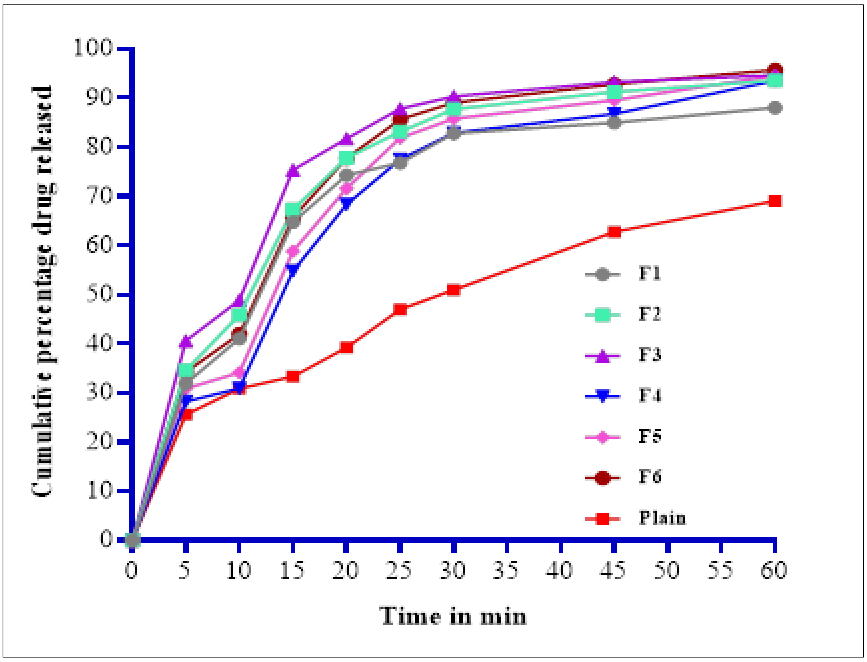

Figure 4 Comparative *in vitro* dissolution profile of F-1 to F-6 and plain core tablets

Table 7 *In vitro* dissolution data of MEB compression coated tablets

Time in (hr)	Cumulative percent drug released Mean* ± SD							
	B-1	B-2	B-3	B-4	B-5	B-6	B-7	B-8
0.25	0.734±0.35	1.039±0.58	1.116±0.46	0.887±0.46	1.803±0.46	1.803±0.46	2.032±0.46	2.261±0.46
0.5	1.196±0.57	1.427±0.87	1.656±0.58	1.579±0.46	2.042±0.46	2.271±0.46	2.730±0.46	2.960±0.46
0.75	1.737±0.48	1.740±0.27	3.040±0.48	1.511±0.95	2.282±0.46	2.741±0.45	2.974±0.46	3.206±0.46
1	2.358±0.58	1.979±1.18	3.973±0.58	2.741±0.46	2.982±0.47	2.986±0.46	3.220±0.45	3.682±0.46
1.5	2.676±0.48	2.753±1.83	4.376±0.24	3.214±0.45	4.143±0.23	3.689±0.46	3.695±0.46	4.618±0.47
2	3.607±0.35	3.990±0.53	4.629±0.83	3.232±0.46	4.929±0.36	3.938±0.46	4.632±0.46	6.246±0.47
2.5	5.077±0.46	5.767±0.46	5.341±0.23	4.623±0.46	5.872±0.34	3.960±0.46	6.031±0.46	11.090±0.47
3	6.937±0.23	8.165±0.33	7.279±0.72	19.764±0.46	16.134±0.45	17.264±0.45	16.522±0.58	23.976±0.47
3.5	10.257±0.35	11.340±0.45	9.075±0.45	22.621±0.46	21.948±0.46	20.795±0.46	23.789±1.61	26.398±0.45
4	11.535±0.47	31.098±0.48	10.956±0.46	28.700±0.46	31.459±0.46	24.115±0.46	31.020±0.45	33.948±0.47
4.5	16.026±0.69	36.613±0.35	51.628±0.58	36.186±0.46	33.006±0.46	33.408±0.46	34.167±0.46	37.951±0.47
5	28.40S4±0.35	41.471±0.33	58.936±0.45	42.339±0.45	39.370±0.47	40.233±0.46	41.454±0.45	41.364±0.48
6	62.073±0.23	45.591±0.37	64.299±0.46	60.892±0.46	48.287±0.45	45.949±0.47	47.329±0.69	44.566±0.44
7	64.629±0.36	54.161±0.68	64.651±0.46	70.615±0.45	62.291±0.46	64.063±0.47	59.801±0.47	62.290±0.48
8	71.166±0.13	66.594±0.44	66.607±0.70	79.245±0.46	65.150±0.47	67.161±0.47	64.249±0.47	67.285±0.58
9	81.403±0.35	71.537±0.44	79.106±0.47	81.737±0.45	73.290±0.46	72.106±0.47	69.101±0.49	71.924±0.70
10	93.221±0.35	77.268±0.47	86.710±0.36	91.111±0.45	75.824±0.26	77.306±0.44	74.818±0.47	77.275±0.47
11	97.468±0.57	86.999±0.48	94.278±0.73	95.726±0.45	90.356±0.46	90.777±0.47	77.512±0.45	86.622±0.46
12	98.988±0.45	93.499±0.35	96.618±0.34	98.073±0.46	95.652±0.44	96.152±0.68	92.356±0.45	90.752±0.44

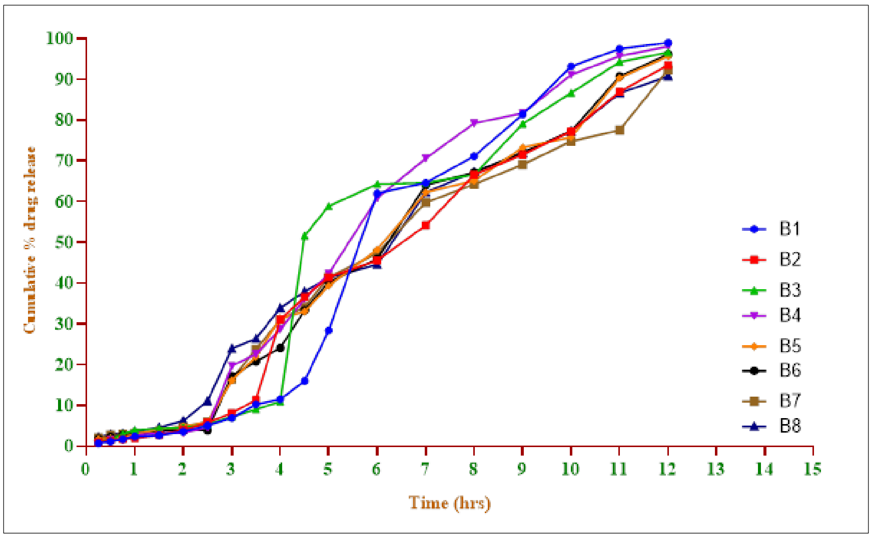

Figure 5 Comparative *in vitro* dissolution profile of B-1 to B-8 compression coated tablets

3.3.2. Compression coated tablets

The developed compression coated tablets consist of three components, the central core tablet made up pure drug MEB and different concentrations CCM, CP super disintegrants and GQ720 as carrier; the impermeable layer Ethocel; and barrier layer consist of mixture of pH dependent swellable and rupturable polymers viz., Keltone, ES100, EL100. B-1, B-2 compression coated tablets prepared using ES100 at different concentrations of Keltone and Ethocel using F-3 as core tablet; B-5 and B-6 compression coated tablets prepared using ES100 at different concentrations of Keltone and ethocel using F-6 core tablet respectively. Similarly B-3, B-4 compression coated tablets prepared using EL100 at different concentrations of Keltone and Ethocel using F-3 as core tablet; B-7 and B-9 compression coated tablets prepared using EL100 at different concentrations of Keltone and Ethocel using F-6 core tablet respectively.

Lag time: Lag time is the time before the drug release started or the time in which less than 10 % of the drug released. Incorporation of core tablet into compression coated tablet produce a lag time prior to drug release. The lag time (t10) was in the range of 2.5 hr to 4 hr and t50 was in the range of 4.6 hr to 6.8 hr, cumulative amount of drug release after 12 hr was in the range of 90.752±0.44 % to 98.988±0.45 % for B-1 to B-8 compression coated tablets. Lag time i.e., t10 was found to be 3.5 hr, 3.5 hr, 4 hr, 2.5 hr, 2.6 hr, 2.5 hr, 2.8 hr, 2.5 hr; t50 was found to be 6 hr, 6.5 hr, 6.8 hr, 4.6 hr, 5.9 hr, 6.4 hr, 6.2 hr, 6.1 hr; and cumulative drug release after 12 hr was found to be 98.988±0.45%, 93.499±0.35%, 96.618±0.34%, 98.073±0.46 %, 95.652±0.44 %, 96.152±0.68%, 92.356±0.45% , 90.752±0.44% respectively for B-1 to B-8 compression coated tablets. The tablets prepared with higher concentrations of EL100, ES100, Keltone and Ethocel shows increase lag time (2.5 to 3.5 hr), which clearly indicates the drug release was restricted in acidic environment, a small amount drug release within lag time is may be due to solution of adhered drug particles. The t50 results show similar results and can be due the rupturing and swelling property of polymer and influence of polymers on environmental pH at intestine and colon proximity with EL100 and ES100.

3.3.3. Mechanism of drug release from compression coated tablets

In compression coated tablets, drug containing core compressed with the outer barrier layer, it prevents the rapid drug release from core tablets. The drug will not be released unless the coat is broken. When the dissolution medium reaches the core after eroding or rupturing the outer barrier layer rapid drug release was observed. The release profile of compression coated tablet exhibited lag time followed by burst release, in which the outer shell swells and ruptured followed by exposure of core tablets to the medium. When the dissolution medium come in contact with compression coated tablet, the barrier consisting of pH dependent (ES 100 and EL 100), swelling and rupturing polymers (Keltone and Ethocel) starts absorbing dissolution medium as a consequence the polymer swells and expanded and bursting of the layer. As the time passes the swelling process acts as disintegrating force which facilitates the destabilization of the barrier layer itself and additionally rupturing property of the polymer prone to disintegration of the tablet. Finally depending on the nature of the swelling and rupturing polymers the top layer is completely removed i.e., lag time, as a result the dissolution of drug increases sharply due to increased access of dissolution medium into the core of the tablet. Barrier layer intended to regulate the function of the system and modify the release of drug and the polymers present in the core tablet regulate drug release in burst release followed by controlled manner. This type of tablet could be described as a compression coated systems in which the top cover layer consists of swellable and rupturable polymer layer and the inner part of a conventional tablet acting as a drug reservoir. The possible sequential changes observed during dissolution studies for the compression coated tablet was depicted in the figure 6.

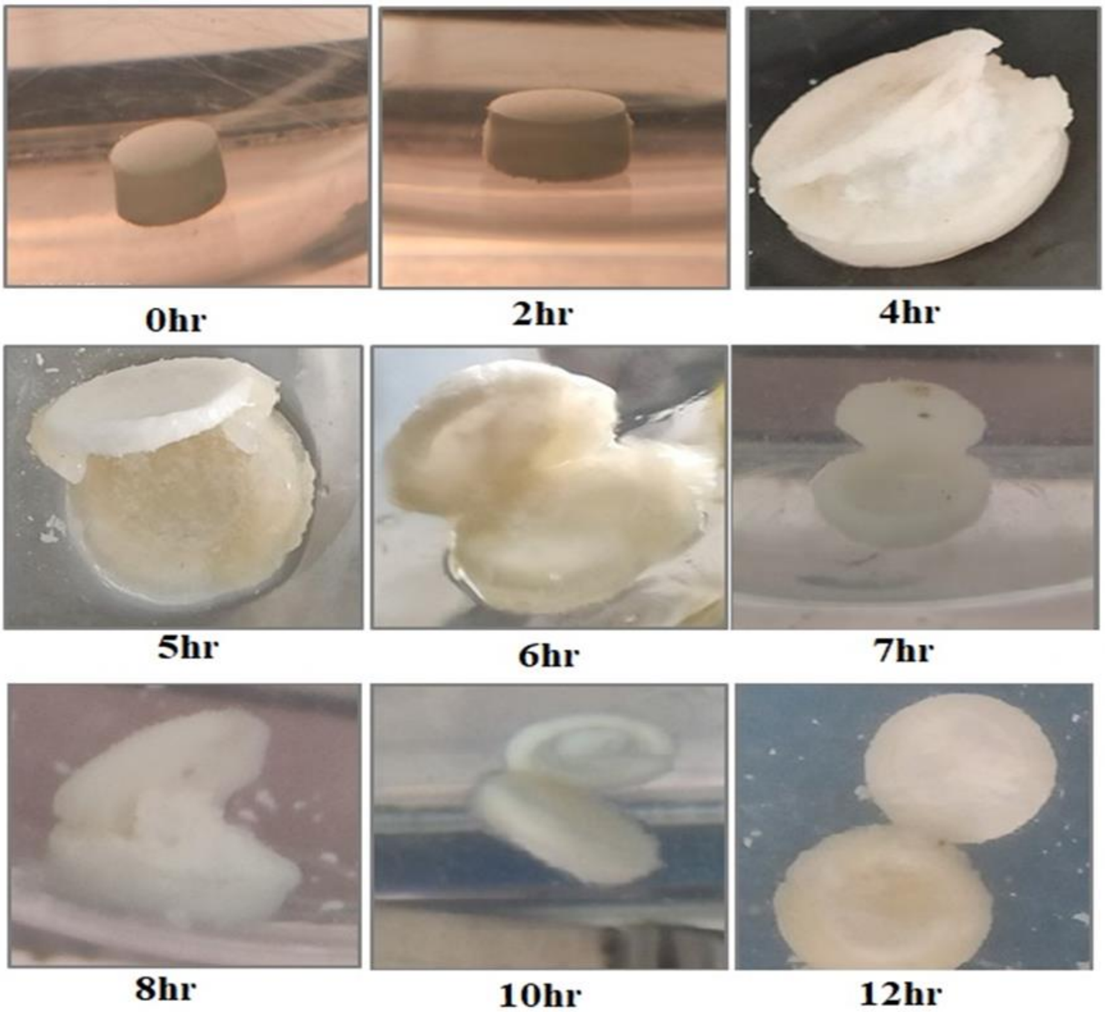

Figure 6 Sequential changes observed for compression coated tablets during dissolution studies

A similar behavior was noticed in all the formulations. The release profiles had a typical pulsatile shape. It is clear that in all cases minimum drug release occurs during the lag time followed by rapid drug release phase. At the stage of rapid release, the release of model drugs is faster and terminates from the systems. These results suggest that apart from the drug solubility the top cover layer also plays a significant role in modifying the lag time and the drug release. The polymer properties and the quantity of the polymer material contained in this layer control the performance and the function of the system. The best fit model was found to be korsemeyer peppas for all compression coated tablets and the exponential 'n' value greater than 1 suggest the drug release follows erosion followed super case II transport mechanism.

4. Conclusion

The compression coating technique can be successfully applied for colon targeting by using pH modulating, swellable and rupturable polymers. The findings of study concludes that the lag time of compression coated tablet can be modulated by combining with EL 100, ES 100, Keltone and Ethocel in different weight ratio. These designed tablet system was found to be satisfactory in terms of release of the drug after the predetermined lag time, thus the system can be target to release in the colon proximity.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

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