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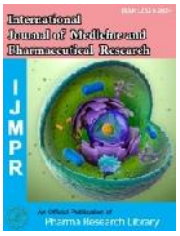

Research Article Open Access

Formulation and *In-Vitro* Evaluation of Colon Targetted Drug Delivery System of Olsalazine Tablets

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A B S T R A C T

In the present research work colon formulation of Olsalazine targeted to colon by using various polymers developed. To achieve pH-independent drug release of Olsalazine, pH modifying agents (buffering agents) were used. Colon targeted tablets were prepared in two steps. Initially core tablets were prepared and then the tablets were coated by using different pH dependent polymers. Ethyl cellulose, Eudragit RLPO and S100 were used as enteric coating polymers. The precompression blend of all formulations was subjected to various flow property tests and all the formulations were passed the tests. The tablets were coated by using polymers and the coated tablets were subjected to various evaluation techniques. The tablets were passed all the tests. Among all the formulations F6 formulation was found to be optimized as it was retarded the drug release up to 18 hours and showed maximum of 98.45% drug release. It followed first order kinetics mechanism.

Keywords: Olsalazine, Colon targeted drug delivery system, Ethyl cellulose, Eudragit RLPO, Eudragit S100

A R T I C L E I N F O

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1. Introduction

Now a days a novel oral colon-specific drug delivery system (CDDS) has been developed as one of the site-specific drug delivery systems. This delivery system, by means of combination of one or more controlled release mechanisms, hardly releases drug in the upper part of the gastrointestinal (GI) tract, but rapidly releases drug in the

colon following oral administration. First as for treating localized colonic diseases, i.e. ulcerative colitis, Crohn's disease and constipation etc., the optimal drug delivery system, such as CDDS, should selectively deliver drug to the colon, but not to the upper GI tract1 . Second, the colon is referred to as the optimal absorption site for protein and polypeptide after oral administration, because of the existence of relatively low proteolytic enzyme activities and quite long transit time in the colon. Finally, CDDS would be advantageous when a delay in absorption is desirable from a therapeutically point of view, as for the treatment of diseases that have peak symptoms in the early morning and that exhibit circadian rhythms, such as nocturnal asthma, angina and rheumatoid arthritis . There were currently a few strategies to achieve colonic specificity, such as use of pH sensitive polymers and pressure-controlled CDDS.

Topically active olsalazine sodium was, recognizing the need for treating colon cancer (COX-2 may be involved in the adenoma to carcinoma sequence, and that both highly potent and selective COX-2 inhibitors) in a manner that results in a minimal number of systemic side effects, and cognizant of the problem of delivering efficacious levels of drugs to the colonic environment, This research carried out the methods by which therapeutic levels of drugs might be presented to the colonic environment.

2. Materials and Methods

Olsalazine, Ethyl Cellulose, Eudragit RLPO, Eudragit L-100, Cross carmellose sodium, Magnesium stearate, Micro crystalline cellulose, Talc chemicals were Laboratory grade made of SD Fine chemicals Pvt Ltd

Formulation development of Tablets:

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

Tablets are developed in two stages

- Preparation of core tablet containing drug and super disintegrate.
- Compression coating of prepared core tablets.

Formulation of core tablet:

The core tablets are formulated by using 250 mg of drug molecule, sodium starch glycollate as super disintegrate, Micro crystalline cellulose as diluent, talc and magnesium stearate as Glidant and Lubricant respectively. The composition of core tablet was given in below table. Total weight of core tablet was fixed as 7.5 mg. The tablets are prepared by using 6mm flat punch. Then the prepared core tablets are subjected to compression coating by using various compositions of polymers.

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

Evaluation of prepared tablets

The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability, *In-vitro* release and drug content.

3. Results and Discussion

The present study was aimed to developing compression coated Olsalazine formulations for colon targeting using ethyl cellulose and enteric coating polymers like Eudragit RLPO and Eudragit L 100. All the formulations were evaluated for physicochemical properties and *in-vitro* drug release studies.

Analytical Method

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

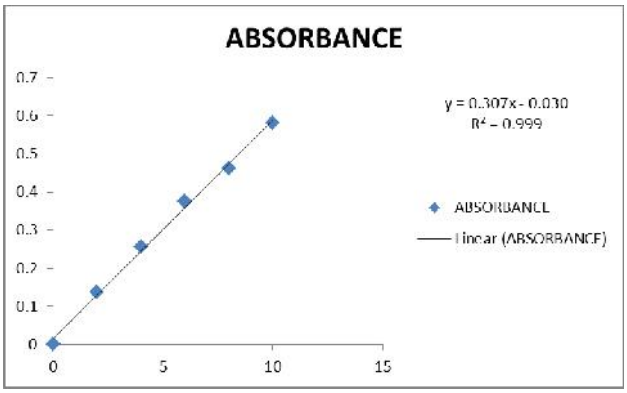

Figure 1: Standard graph of Olsalazine in 0.1N HCl

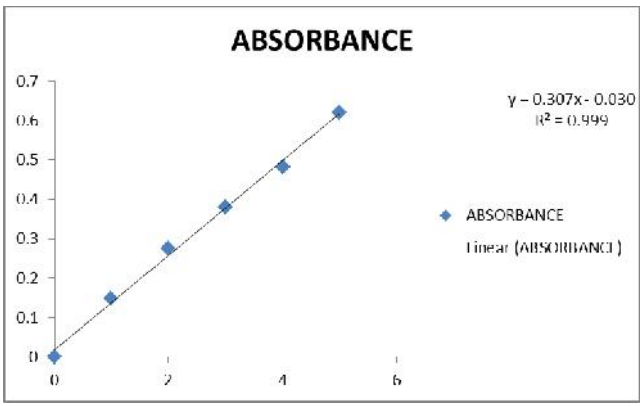

Figure 2: Standard graph of Olsalazine in 6.8 pH

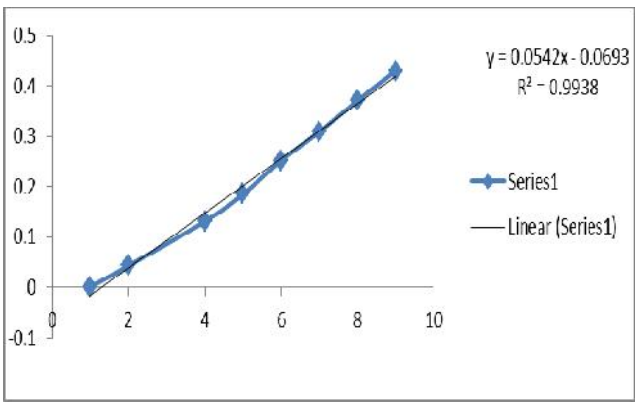

Figure 3: Standard graph of Olsalazine in7.4 pH

Olsalazine blend was subjected to various pre-formulation parameters. The apparent bulk density and tapped bulk density values ranged from 0.52 to 0.581 and 0.606 to 0.671 respectively. According to Tables 6, the results of angle of repose and compressibility index (%) ranged from 32.74±0.12 to 37.08±0.96 and 13.37±0.38 to 14.72±0.62 respectively. The results of angle of repose (<35) and compressibility index (<23) indicates fair to passable flow properties of the powder mixture. These results show that the powder mixture has good flow properties. The formulation blend was directly compressed to tablets and *in-vitro* drug release studies were performed.

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

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

The compression coated tablets containing 7.5 mg of Olsalazine were tested in 6.8 pH phosphate buffer solution for their dissolution rates. The release of Olsalazine from compression coated tablets was carried out using USP paddle-type dissolution apparatus at a rotation speed of 50 rpm, and a temperature of 37±0.5 °C. For tablets, simulation of gastrointestinal transit conditions was achieved by using different dissolution media. Thus, drug release studies were conducted in simulated gastric fluid (SGF, pH 1.2) for the first 2 hours as the average gastric emptying time is about 2 hours. Then, the dissolution medium was replaced with enzyme- free simulated intestinal fluid (SIF, pH 6.8) and tested for drug release upto 12 hours, as the average small intestinal transit time is about 3 hours, and finally enzyme-free simulated intestinal fluid (SIF, pH 7.4) was used upto 18 hours to mimic colonic pH conditions.

Drug release was measured from compression coated Olsalazine tablets, added to 900 ml of dissolution medium. 5 ml of sample was withdrawn every time and replaced with fresh medium, samples withdrawn at various time intervals were analyzed spectrophotometrically at 275 nm ,319 and 320 nm respectively. All dissolution runs were performed for six batches.

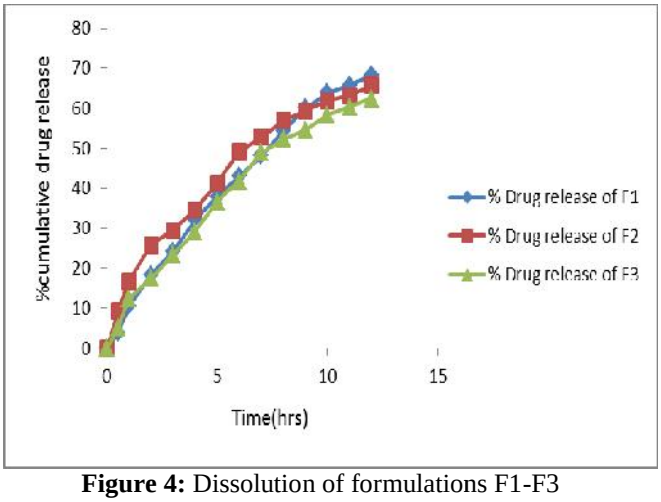

Figure 4: Dissolution of formulations F1-F3

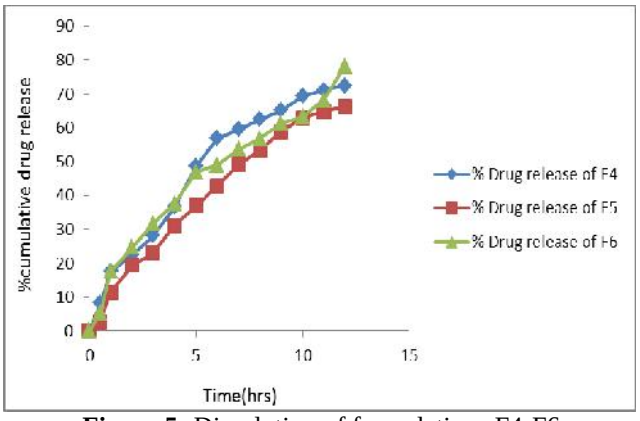

Figure 5: Dissolution of formulations F4-F6

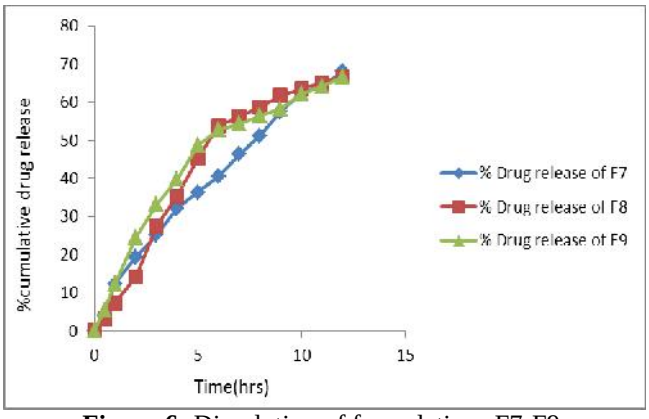

Figure 6: Dissolution of formulations F7-F9

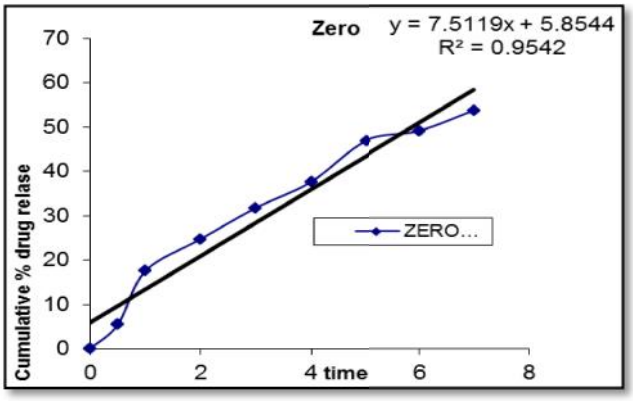

Figure 7: Zero order release kinetics graph

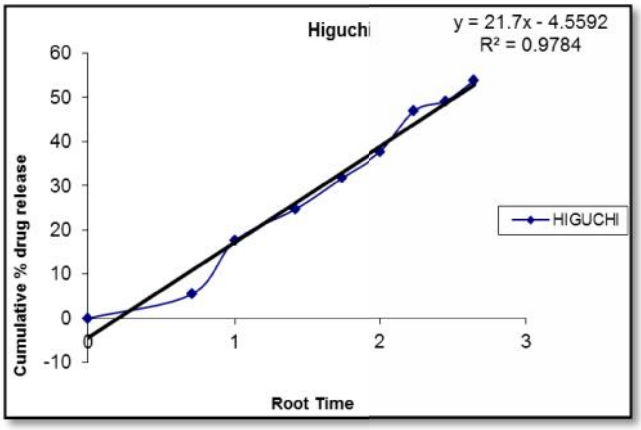

Figure 8: Higuchi release kinetics graph

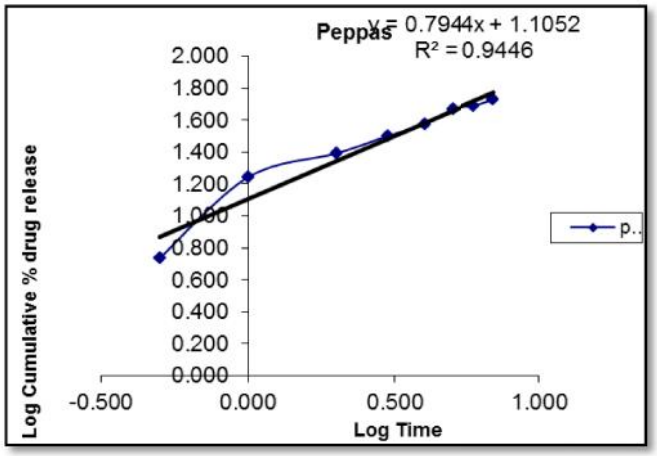

Figure 9: Kars mayer peppas graph

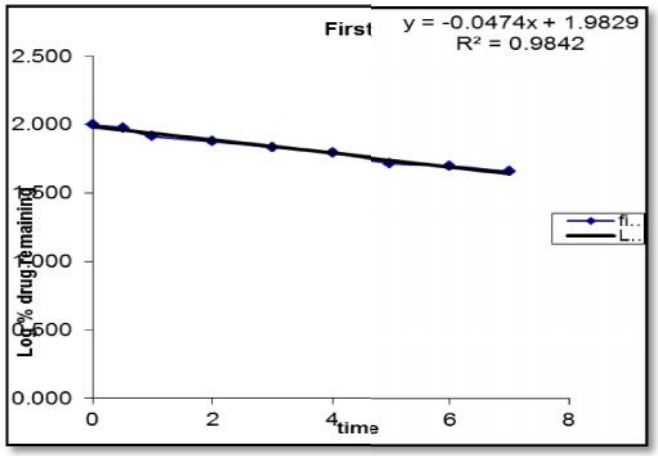

Figure 10: First order release kinetics graph

Table 1: Composition of core tablet

Ingredient Name	Quantity (mg)
Olsalazine	50
Cross carmellose sodium	30
Talc	3
Magnesium stearate	3
MCC pH102	QS
Total weight	120

Table 2: Composition of coating layer

Ingredient name	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ethyl cellulose (mg)	50	100	-	-	-	-	50	-	50
Eudragit RLPO (mg)	-	-	50	100	-	-	50	50	-
Eudragit L 100 (mg)	-	-	-	-	50	100	-	50	50
Magnesium stearate (mg)	3	3	3	3	3	3	3	3	3
Talc (mg)	3	3	3	3	3	3	3	3	3
MCC pH 102 (mg)	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Total weight	280	280	280	280	280	280	280	280	280

Table 3: Observations for graph of Olsalazine in 0.1N HCl (270 nm)

No.	Conc [mg/l]	abs
1	0	0
2	2	0.138
3	4	0.256
4	6	0.376
5	8	0.461
6	10	0.582
7	12	0.824

Table 4: Standard graph of Olsalazine in 6.8 pH

No.	Conc [mg/l]	Abs
1	0	0
2	1	0.148
3	2	0.275
4	3	0.379

5	4	0.481
6	5	0.621
7	6	0.859

Table 5: Observations for graph of Olsalazine in 7.4 pH

S. No.	Conc [mg/l]	Abs
1	2	0.057
2	3	0.129
3	4	0.204
4	5	0.284
5	6	0.372
6	8	0.566
7	9	0.625
8	10	0.709
9	12	0.893

Table 6: Pre-formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	36.01	0.55	0.645	14.72	0.85
F2	34.8	0.57	0.66	13.63	0.86
F3	36.05	0.53	0.606	14.19	0.838
F4	34.19	0.531	0.613	13.37	0.866
F5	36.24	0.549	0.641	14.35	0.856
F6	33.25	0.564	0.666	15.31	0.854
F7	37.08	0.581	0.671	13.41	0.865
F8	35.12	0.567	0.654	13.12	0.845
F9	35.45	0.571	0.689	13.28	0.855

Table 7: In-vitro quality control parameters for compression coated tablets

Formulation codes	Weight variation(mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content(%)
F1	402.5	4.5	0.52	4.8	99.76
F2	405.4	4.2	0.54	4.9	99.45
F3	398.6	4.4	0.51	4.9	99.34
F4	410.6	4.5	0.55	4.9	99.87
F5	409.4	4.4	0.56	4.7	99.14
F6	410.7	4.2	0.45	4.5	98.56
F7	402.3	4.1	0.51	4.4	98.42
F8	401.2	4.3	0.49	4.7	99.65
F9	398.3	4.5	0.55	4.6	99.12

Table 8: In-vitro Drug Release profile for coated formulations (F1-F9)

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0.5	3.77	9.14	5.12	8.23	2.71	5.46	4.11	3.11	5.54
1	10.51	16.76	12.45	17.55	11.51	17.54	12.35	7.15	12.17
2	18.4	25.77	17.47	22.42	19.4	24.72	19.42	14.21	24.58

3	24.15	29.42	23.42	28.11	23.17	31.76	25.12	27.54	33.19
4	32.13	34.64	29.18	36.67	31.18	37.62	32.15	35.45	39.79
5	37.91	41.32	36.71	48.71	36.91	46.87	36.36	45.21	48.69
6	42.92	49.12	41.78	56.86	42.92	49.09	40.54	53.77	52.75
7	48.18	52.77	48.89	59.49	49.16	53.72	46.39	56.34	54.38
8	54.32	56.85	52.22	62.46	53.32	56.73	51.21	58.73	56.54
9	59.93	59.32	54.42	65.19	58.93	61.41	57.54	61.69	58.28
10	63.82	61.98	58.34	69.42	62.85	63.32	62.36	63.54	62.19
11	65.77	63.27	60.42	71.12	64.71	68.13	64.28	65.15	64.14
12	68.22	65.72	62.47	72.41	66.34	78.28	68.03	66.49	66.68
13	69.35	69.35	64.28	73.89	68.98	82.54	72.35	68.45	69.84
14	71.23	72.65	66.38	75.67	71.26	84.32	74.85	69.87	72.36
15	73.63	74.28	69.45	77.98	73.45	87.98	77.21	72.45	74.38
16	75.39	76.37	72.56	79.82	75.28	92.98	79.45	74.36	77.45
17	77.28	78.36	75.23	81.25	79.32	95.64	82.37	76.29	78.52
18	79.12	82.21	77.87	83.65	84.36	98.45	85.87	79.34	83.28

Table 9: Release kinetics data for optimised formulation

Cumulative (%) Release Q	Time (T)	Root (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN
0	0	0			2.000
5.46	0.5	0.707	0.737	-0.301	1.976
17.54	1	1.000	1.244	0.000	1.916
24.72	2	1.414	1.393	0.301	1.877
31.76	3	1.732	1.502	0.477	1.834
37.62	4	2.000	1.575	0.602	1.795
46.87	5	2.236	1.671	0.699	1.725
49.09	6	2.449	1.691	0.778	1.707
53.72	7	2.646	1.730	0.845	1.665
56.73	8	2.828	1.754	0.903	1.636
61.41	9	3.000	1.788	0.954	1.586
63.32	10	3.162	1.802	1.000	1.564
68.13	11	3.317	1.833	1.041	1.503
78.28	12	3.464	1.894	1.079	1.337
82.54	13	3.606	1.917	1.114	1.242
84.32	14	3.742	1.926	1.146	1.195
87.98	15	3.873	1.944	1.176	1.080
92.98	16	4.000	1.968	1.204	0.846
95.64	17	4.123	1.981	1.230	0.639
98.45	18	4.243	1.993	1.255	0.190

4. Conclusion

In the present research work of Olsalazine targeted to colon by using various polymers developed. To achieve pH-independent drug release of Olsalazine, pH modifying agents (buffering agents) were used. Colon targeted tablets were prepared in two steps. Initially core tablets were prepared and then the tablets were coated by using different pH dependent polymers. Ethyl cellulose, Eudragit L100 and S100 were used as enteric coating polymers. The precompression blend of all formulations was subjected to various flow property tests and all the formulations were passed the tests. The tablets were coated by using polymers and the coated tablets were subjected to various evaluation techniques. The tablets were passed all the tests. Among all the formulations F6 formulation was found to be optimized as it was retarded the drug release up to 18 hours and showed maximum of 98.45% drug release. It followed first order kinetics mechanism.

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