International Journal of Chemistry and Pharmaceutical Sciences

Journal Home Page: www.pharmaresearchlibrary.com/ijcps

RESEAECH ARTICLE

Formulation and *In-vitro* Evaluation of Colon Targeted Drug Delivery of Dicyclomine Tablets

D. Keerthi Raj*, B. Ramya Sree, S. Anusha, T. Anil Goud

Assistant Professor, Department of Pharmaceutics, Vijay College of Pharmacy, Nizamabad, Telangana, India

ABSTRACT

In the present research work sustained release matrix formulation of Dicyclomine targeted to colon by using various polymers developed. 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 F3 formulation was found to be optimized as it was retarded the drug release up to 18 hours and showed maximum of 98.09% drug release.

Keywords: Dicyclomine, colon, Ethyl cellulose, Eudragit L100 and S100

ARTICLE INFO

***Corresponding Author**
D. Keerthi Raj
Assistant Professor,
Department of Pharmaceutics,
Vijay College of Pharmacy,
Nizamabad, Telangana, India
MS-ID: IJCPS3600

PAPER QR-CODE

Article History: Received 19 December 2017, **Accepted** 28 January 2018, **Available Online** 27 February 2018

Citation: D. Keerthi Raj*, et al.* Formulation and In-vitro Evaluation of Colon Targeted Drug Delivery of Dicyclomine Tablets. *Int. J. Chem, Pharm, Sci..*, 2018, 6(2): 75-80.

CONTENTS

1. Introduction. 75
2. Materials and Methods. 76
3. Results and Discussion. 76
4. Conclusion. 77
5. References 80

1. Introduction

Colon targeted drug delivery is used to deliver the substances that are degraded by the digestive enzymes in the stomach such as proteins and peptides. It is also used for the treatment of various diseases like ulcerative colitis, crohn's disease, intestinal cancer, diarrhoea, for the treatment of diseases sensitive to circadian rhythms like Asthma, Angina, for the delivery of steroids, etc. colon targeted drug delivery of drugs reduces the systemic side. Dicyclomine hydrochloride is an anticholinergic agent having direct smooth muscle relaxant action, and in addition to being a weak anticholinergic, it exerts antispasmodic action. Its plasma

half-life is 4 - 6 hours 14. It is commonly used for the treatment of irritable bowel syndrome. It is rapidly absorbed after oral administration with peak plasma concentration occurring in 60-90 minutes. Conventional therapy of Dicyclomine hydrochloride requires multiple daily administrations (3- 4 times daily) . Therefore it was felt that inclusion into a colon release dosage form may be beneficial in terms of increasing patient compliance through twice daily dosing, and thereby improving therapeutic outcomes.

2. Materials and Methods

Dicyclomine, Sodium starch glycollate, Talc, Magnesium stearate, MCC pH102, Ethyl cellulose, Eudragit S100, Eudragit L100 chemicals were Laboratory grade made of SD Fine chemicals Pvt Ltd

Formulation of core tablet: The core tablets are formulated by using 20mg 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.

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.

3. Results and Discussion

Analytical Method: Graphs of Dicyclomine was taken in Simulated Gastric fluid (pH 1.2) and Simulated Intestinal Fluid (pH 6.8 and 7.4)

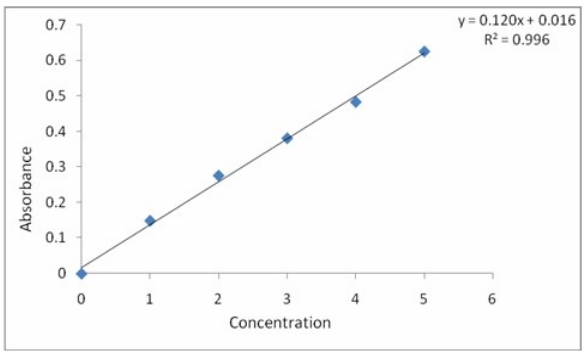

Figure 1: Standard graph of Dicyclomine in 0.1N HCl

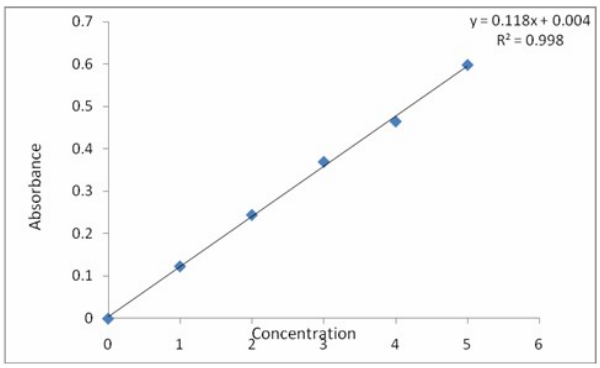

Figure 2: Standard graph of Dicyclomine in 7.4 pH

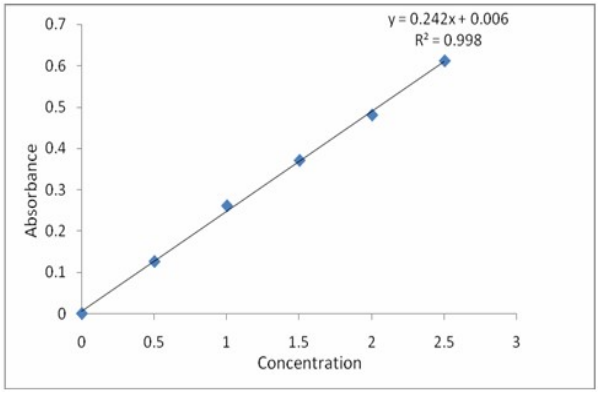

Figure 3: Standard graph of Dicyclomine in 6.8 pH

Quality Control Parameters For compression coted 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 12mg of Dicyclomine were tested in 6.8 pH phosphate buffer solution for their dissolution rates. The release of Dicyclomine 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 7.4) and tested for drug release for 3 hours, as the average small intestinal transit time is about 3 hours, and finally enzyme-free simulated intestinal fluid (SIF, pH 6.8) was used upto 18 hours to mimic colonic pH conditions. Drug release was measured from compression coated Dicyclomine 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 ,272 and 271 nm respectively. All dissolution runs were performed for six batches.

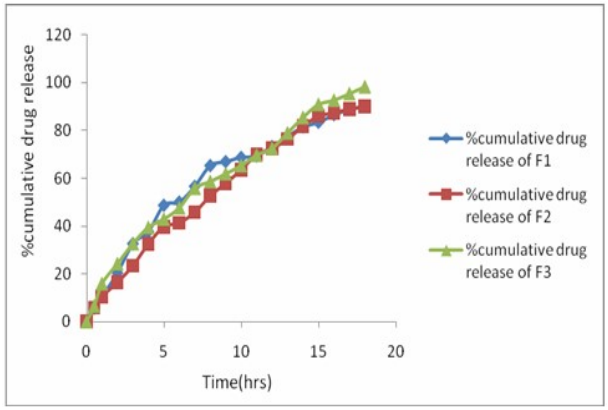

Figure 4: Dissolution profile of F1, F2, F3 formulations.

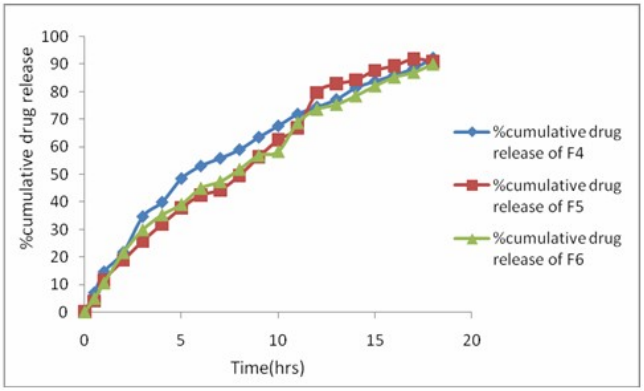

Figure 5: Dissolution profile of F4, F5, F6 formulations.

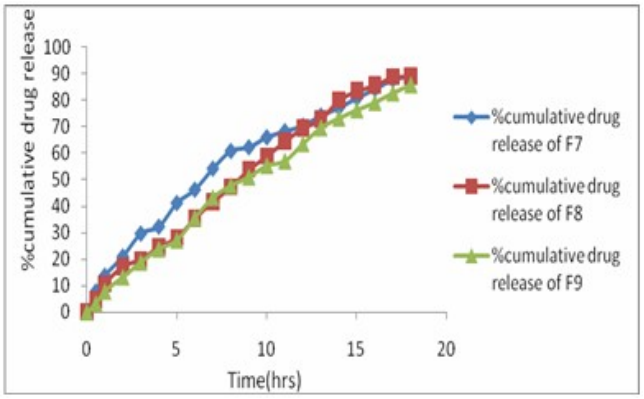

Figure 5: Dissolution profile of F4, F5, F6 formulations.

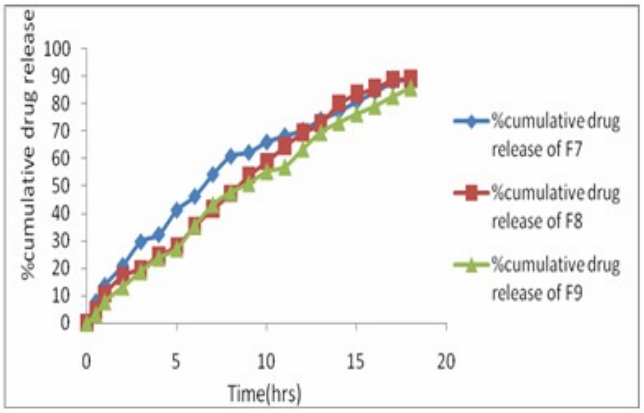

Figure 6: Dissolution profile of F7, F8, F9 formulations.

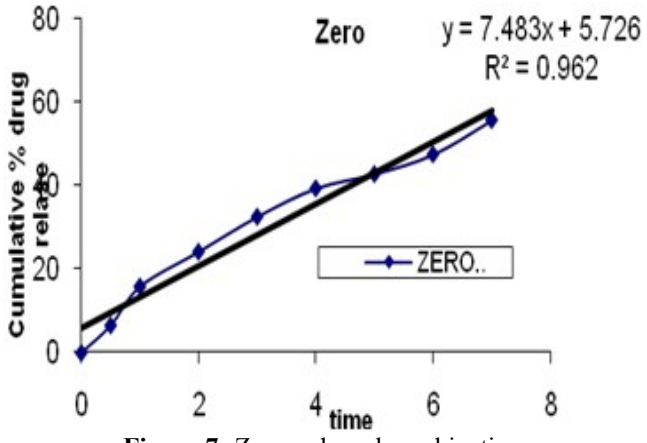

Figure 7: Zero order release kinetics

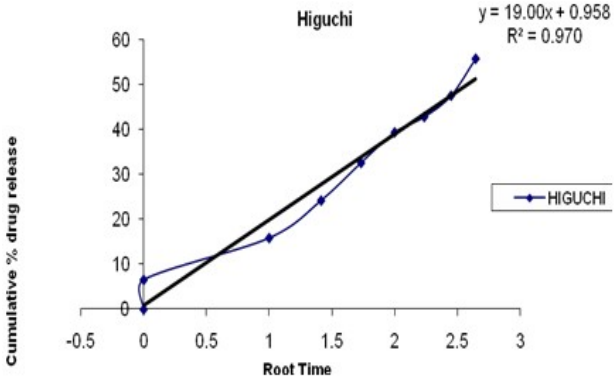

Figure 8: Higuchi release kinetics

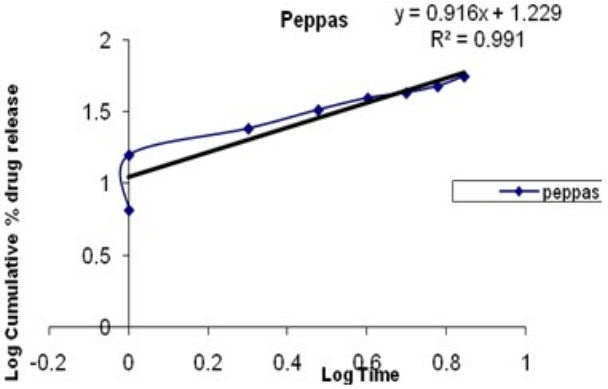

Figure 9: Kars mayer peppas

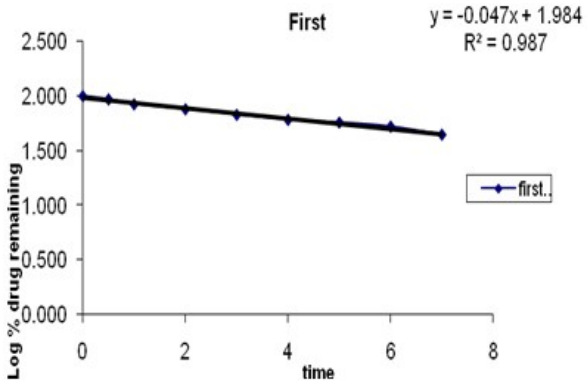

Figure 10: First order release kinetics

4. Conclusion

In the present research work sustained release matrix formulation of Dicyclomine targeted to colon by using various polymers developed. 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 F3 formulation was found to be optimized as it was retarded the drug release up to 18 hours and showed maximum of 98.09% drug release.

Table 1: Composition of core tablet

Ingredient Name	Quantity (mg)
Dicyclomine	20
Sodium starch glycollate	20
Talc	2
Magnesium stearate	2
MCC pH102	Qs
Total weight	100

Total weight of core tablet was fixed as 100 mg. The tablets are prepared by using 5mm flat punch. Then the prepared core tablets are subjected to compression coating by using various compositions of polymers.

Table 2: Composition of coating layer

Ingredient name	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ethyl cellulose (mg)	25	50	100						
Eudragit S100 (mg)				25	50	100			
Eudragit L100 (mg)							25	50	100
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	200	200	200	200	200	200	200	200	200

Weight variation test, Hardness, Thickness, Friability, Determination of drug content, *In-vitro* drug release studies are the various evaluation tests performed for the prepared tablets

Table 3: Observations for graph of Dicyclomine in 0.1N HCl

No.	Conc [mg/l]	abs
1	1	0.149
2	2	0.276
3	3	0.381
4	4	0.483
5	5	0.625

Table 4: Observations for graph of Dicyclomine in 7.4 pH

S. No.	Conc [mg/l]	Abs
1	1	0.123
2	2	0.244
3	3	0.369
4	4	0.464
5	5	0.597

Table 5: Observations for graph of Dicyclomine in 6.8 pH (320)

No.	Conc [mg/l]	Abs
1	0.5	0.126
2	1	0.261
3	1.5	0.371
4	2	0.481
5	2.5	0.612

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	32.74	0.53	0.606	14.19	0.858
F4	35.33	0.531	0.613	13.37	0.866
F5	36.24	0.549	0.641	14.35	0.856
F6	36.12	0.564	0.666	15.31	0.846
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	312.5	4.5	0.52	4.8	99.76
F2	305.4	4.2	0.54	4.9	99.45
F3	298.6	4.4	0.51	4.9	99.34
F4	310.6	4.5	0.55	4.9	99.87
F5	309.4	4.4	0.56	4.7	99.14
F6	310.7	4.2	0.45	4.5	98.56
F7	302.3	4.1	0.51	4.4	98.42
F8	301.2	4.3	0.49	4.7	99.65

All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

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	5.67	5.87	6.58	6.98	3.98	4.88	7.83	4.63	3.25
1	10.45	10.53	15.88	14.56	11.56	10.54	13.81	10.75	7.85
2	20.46	16.45	24.22	21.67	18.75	21.56	21.02	17.18	13.29
3	32.65	23.42	32.61	34.62	25.75	29.87	29.7	19.89	18.87
4	37.72	32.53	39.39	39.86	31.84	35.27	32.32	24.64	23.87
5	48.71	39.63	42.83	48.43	37.74	39.1	41.25	28.04	27.19
6	50.08	41.28	47.55	52.98	42.35	44.98	46.28	35.43	35.66
7	56.62	45.71	55.76	55.78	44.21	47.36	54.25	41.65	43.32
8	65.32	52.56	58.47	58.92	49.54	51.84	60.92	47.18	47.83
9	66.98	57.84	61.73	63.43	56.27	56.92	62.31	53.81	51.06
10	68.76	63.43	65.18	67.52	62.46	58.32	66.08	58.89	55.43
11	69.35	69.87	69.54	71.83	66.75	68.77	68.36	64.53	57.13
12	73.32	72.31	72.36	74.38	79.63	73.65	70.44	69.43	63.63
13	77.51	76.31	78.79	77.13	82.75	75.42	74.25	72.83	69.71
14	81.54	81.67	85.27	81.34	84.17	78.56	77.22	79.98	73.34
15	83.45	85.91	90.69	83.76	87.65	82.19	80.9	83.52	76.43
16	86.59	87.31	92.45	85.98	89.32	85.35	84.26	85.65	79.27
17	88.82	88.86	95.19	88.42	91.85	87.12	87.83	88.73	82.86
18	90.13	89.97	98.09	92.18	90.89	90.16	89.25	89.03	85.97

Table 9: Release kinetics data for optimized formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN
0	0	0			2.000
6.58	**0.5**	0.000	0.818	0.000	1.970
15.88	1	1.000	1.201	0.000	1.925

24.22	2	1.414	1.384	0.301	1.880
32.61	3	1.732	1.513	0.477	1.829
39.39	4	2.000	1.595	0.602	1.783
42.83	5	2.236	1.632	0.699	1.757
47.55	6	2.449	1.677	0.778	1.720
55.76	7	2.646	1.746	0.845	1.646
58.47	8	2.828	1.767	0.903	1.618
61.73	9	3.000	1.790	0.954	1.583
65.18	10	3.162	1.814	1.000	1.542
69.54	11	3.317	1.842	1.041	1.484
72.36	12	3.464	1.859	1.079	1.442
78.79	13	3.606	1.896	1.114	1.327
85.27	14	3.742	1.931	1.146	1.168
90.69	15	3.873	1.958	1.176	0.969
92.45	16	4.000	1.966	1.204	0.878
95.19	17	4.123	1.979	1.230	0.682
98.09	18	4.243	1.992	1.255	0.281

5. References

[1] Pirjo Nykanen. Development of Multiple-Unit Oral Formulations for Colon-Specific Drug Delivery Using Enteric Polymers and Organic Acids as Excipients. Division of Biopharmaceutics and Pharmacokinetics Department of Pharmacy, University of Helsinki: Academic Dissertation 2003

[2] Sarasija S, Hota A. Colon specific drug delivery systems. Indian J. Pharm. Sci 200; 62(1): 1-8

[3] Howard NE Stevens, Clive G Wilson, Peter G. Welling, Alan C Perkins, Malcolm Frier. Evaluation of Pulsincap to provide regional delivery of Dofetilide to the Human GI tract. Int. J. Pharm., 2002; 236: 27 – 34.

[4] Rajesh Gandhi, Chaman Lal Kaul and Ramesh Panchagnula. Extrusion and spheronization in the development of oral controlled-release dosage forms. Pharmaceutical Science and Technology Today 1999; 2(4): 160-170.

[5] Krishnaiah YSR, Bhaskar Reddy PR, Satyanarayana V. Studies on the development of oral colon targeted drug delivery systems for Metronidazole in the treatment of amoebiasis. Int. J. Pharm 2002; 236: 43-55.

[6] Handbook of Pharmaceutical Excipients: Monographs. London: The Pharmaceutical press; 2000.

[7] Samanta MK, Suresh NV, Suresh B. Development of Pulsincap drug delivery of Salbutamol Sulphate for drug targeting. Indian J. Pharm. Sci 2000; 62(2): 102-07.

[8] Krishnaiah YSR, Dinesh Kumar B, Satyanarayana V, Karthikeyan RS. drug release studies on guar gum based colon targeted oral drug delivery systems of 5-fluorouracil. Euro. J. Pharm. Sci 2002; 16:185-192.

[9] Seshasayana A, Sreenivasa Rao B, Prasanna Raju Y, Ramana Murthy KV. Studies on release of Rifampicin from Modified Pulsincap Technique. Indian J. Pharm. Sci 2001; 337-39.

[10] Mishra B, Jayanth P, Sankar C. Development of Chitosan-Alginate microcapsules for colon specific delivery of Metronidazole. Indian Drugs.

[11] Zahirul M Khan, Zeljko Prebeg, Nevenka Kurjakovie. A pH dependent colon targeted oral drug delivery system using methacrylic acid copolymers.Manipulation of drug release using Eudragit L100-55 and Eudragit S100 combinations. J. Control. Rel

[12] Krishnaiah YSR, Satyanarayana V, Rama Prasad YV. Gamma Scintigraphy: An imaging technique for non- invasive evaluation of oral dosage forms. Indian Drugs 1998; 35(7): 387- 99.