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RESEARCH ARTICLE

Formulation and *in-vitro* evaluation of Propantheline Bromide tablets for colon targeted drug delivery system

CH. Ramadevi, Dr. V. Anjaneyulu*, Dr. Gampa Vijay Kumar

Department of Pharmacy, KGR Institute of Technology and Management, Rampally, Kesara, Medchal, Telangana, India

ABSTRACT

In the present research work colon formulation of Propantheline Bromide targeted to colon by using various polymers developed. To achieve pH-independent drug release of Propantheline Bromide, pH modifying agents (buffering agents) were used. Colon targeted tablets were preparedin two steps. Initially core tablets were prepared and then the tablets were coated by using different pH dependent polymers. Ethyl cellulose, Eudragit RLPO and L100 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 F4 formulation was found to be optimized as it was retarded the drug release up to 18 hours and showed maximum of 98.73% drug release. It followed zero order kinetics mechanism.

Keywords: Propantheline Bromide, Colon targeted drug delivery system, Ethyl cellulose, Eudragit RLPO, Eudragit L 100

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Corresponding Author

Dr.V.Anjeneyulu

Department of Pharmacy,

KGR Institute of Technology and Management,

Rampally, Kesara, Rangareddy, Telangana, India

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CONTENTS

1. Introduction

The challenge of targeting drugs to the colon part of the GI tract has been embraced by scientists over the past two decades. The research on colon targeting has been driven primarily by the need to improve the treatment of the colonic pathologies. These disease states range in severity from constipation and diarrhoea, to irritable bowel syndrome, ulcerative colitis and Crohn's disease, through to infection and colon carcinoma.

2. Materials and methods

Propantheline Bromide

Ethyl Cellulose, Eudragit RLPO, Eudragit L-100, Cross carmellose sodium, Magnesium stearate Micro crystalline cellulose, Talc all the chemicals were laboratory grade.

Formulation:

Formulation development of Tablets:

Propantheline Bromide 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 8 mg of drug molecule, Cross carmellose sodium 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.

Table 1: Composition of core tablet

Ingredient Name	Quantity (mg)
Propantheline Bromide	15
Cross carmellose sodium	15
Talc	3
Magnesium stearate	3
MCC pH102	Q.S
Total weight	100

Total weight of core tablet was fixed as 100 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 RLPO as coating materials the composition of coating layer is given in below table Compression coating layer was divided into two equal portions i.e., 100mg of each quantity .Half of the quantity of powder blend was placed in the die cavity, core tablet was placed exactly in the middle of die cavity and then remaining quantity of powder blend was placed over the core tablet so that the powder blend should cover all the sides and top side of core tablet uniformly. Then the tablets are compressed by using 10mm flat surfaced punch using 8 station tablet punching machine with the hardness of 4-4.5 kg/cm^2.Then the prepared compression coted tablets are evaluated for various post compression parameters as per standard specifications

Evaluation of post compression parameters for prepared Tablets: The designed formulation compression coated tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

3. Results and discussion

Standard Calibration curve of Alosetron: Graphs of Propantheline Bromide was taken in Simulated Gastric fluid (pH 1.2) and Simulated Intestinal Fluid (pH 6.8 and 7.4).

Table 3: Observations for graph of Propantheline Bromide in 0.1N HCl (254 nm)

S.No.	Conc	abs
1	0	0
2	2	0.144
3	4	0.279
4	6	0.394
5	8	0.523
6	10	0.652

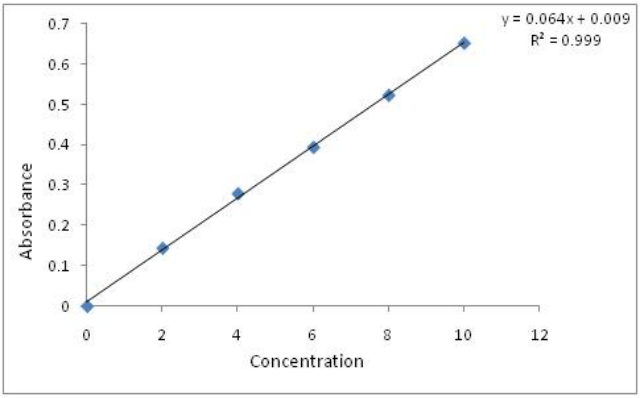

Figure 1: Standard graph of Propantheline Bromide in 0.1N HCl

Table 4: Observations for graph of Propantheline Bromide in 6.8 pH (256 nm)

No.	Conc	Abs
1	0	0
2	1	0.103
3	2	0.234
4	3	0.359
5	4	0.474
6	5	0.587

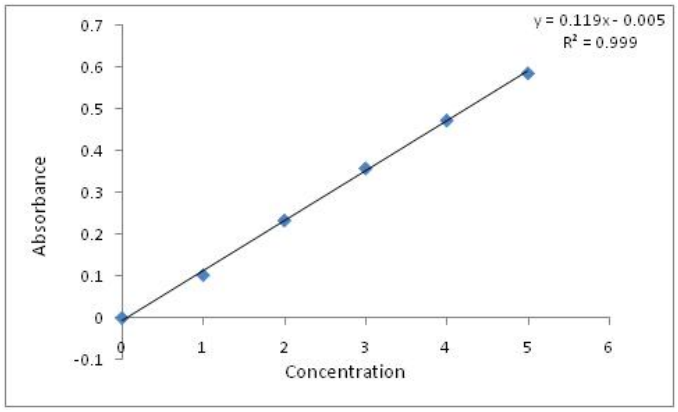

Figure 2: Standard graph of Propantheline Bromide in 6.8 pH

Table 5: Observations for graph of Propantheline Bromide in 7.4 pH (257 nm)

No.	Conc	Abs
1	0	0
2	0.5	0.129
3	1	0.265
4	1.5	0.374
5	2	0.485
6	2.5	0.618

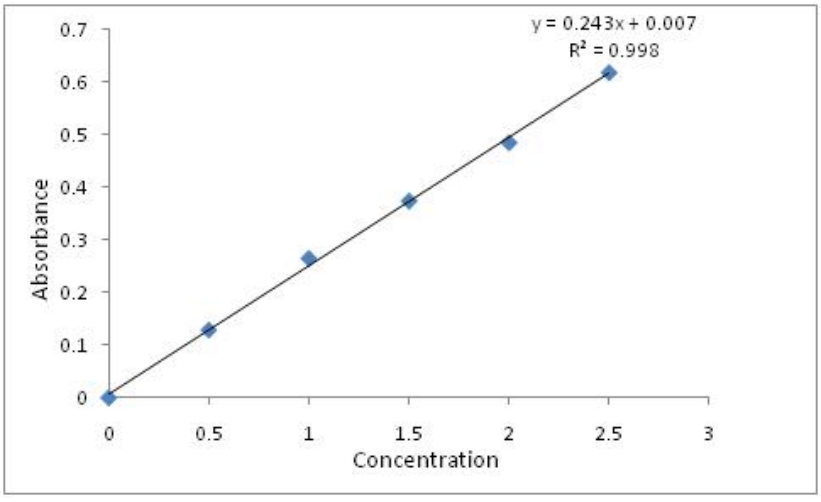

Figure 3: Standard graph of Propantheline Bromide in 7.4 pH preformulation parameters of coating material

Table 6: Pre-formulation parameters of core blend Preformulation parameters of coating material

Preformulation parameters	Core material
Angle of Repose	20.87
Bulk density (gm/ml)	0.53
Tapped density (gm/ml)	0.60
Carr's index (%)	14.16
Hausner's Ratio	0.83

Table 7: Pre-formulation parameters of compression blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	26.01	0.55	0.64	14.72	0.85
F2	24.8	0.57	0.66	13.63	0.86
F3	26.05	0.53	0.60	14.19	0.83
F4	24.19	0.53	0.61	13.37	0.86
F5	26.24	0.54	0.64	14.35	0.85
F6	23.25	0.56	0.66	15.31	0.85
F7	27.08	0.58	0.67	13.41	0.86
F8	25.12	0.56	0.65	13.12	0.84
F9	25.45	0.57	0.68	13.28	0.85

Propantheline Bromide blend was subjected to various pre-formulation parameters. The apparent bulk density and tapped bulk density values ranged from 0.53 to 0.58 and 0.60 to 0.68 respectively. According to Tables 4.4, the results of angle of repose and compressibility index (%) ranged from 23.25 to 27.08 and 13.12 to 14.72respectively. 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 core tablets

Table 8: In-vitro quality control parameters for compression coated tablets

Quality Control parameters	Core material
Weight variation(mg)	99
Hardness(kg/cm2)	2.5
Friability (%loss)	0.50
Thickness (mm)	2.5
Drug content (%)	99.04
Disintegration Time(mins)	1.37

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.

Table 9: In-vitro quality control parameters for compression coated tablets In-Vitro Drug Release Studies

Formulation codes	Weight variation(mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	302.5	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
F9	298.3	4.5	0.55	4.6	99.12

Table 10: 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	6.98	6.58	3.98	4.88	7.83	4.63	3.25
1	10.45	10.53	14.56	15.88	11.56	10.54	13.81	10.75	7.85
2	20.46	16.45	21.67	20.22	18.75	21.56	21.02	17.18	13.29
3	32.65	23.42	34.62	32.61	25.75	29.87	29.7	19.89	18.87

4	37.72	32.53	39.86	39.39	31.84	35.27	32.32	24.64	23.87
5	48.71	39.63	48.43	42.83	37.74	39.1	41.25	28.04	27.19
6	50.08	41.28	52.98	47.55	42.35	44.98	46.28	35.43	35.66
7	56.62	45.71	55.78	55.76	44.21	47.36	54.25	41.65	43.32
8	65.32	52.56	58.92	58.47	49.54	51.84	60.92	47.18	47.83
9	66.98	57.84	63.43	61.73	56.27	56.92	62.31	53.81	51.06
10	68.76	63.43	67.52	65.18	62.46	58.32	66.08	58.89	55.43
11	69.35	69.87	71.83	69.54	66.75	68.77	68.36	64.53	57.13
12	73.32	72.31	74.38	72.36	79.63	73.65	70.44	69.43	63.63
13	77.51	76.31	77.13	78.79	82.75	75.42	74.25	72.83	69.71
14	81.54	81.67	81.34	85.27	84.17	78.56	77.22	79.98	73.34
15	83.45	85.91	83.76	90.69	87.65	82.19	80.9	83.52	76.43
16	86.59	87.31	85.98	92.45	89.32	85.35	84.26	85.65	79.27
17	88.82	88.86	88.42	95.19	91.85	87.12	87.83	88.73	82.86
18	90.13	89.97	92.18	98.73	90.89	90.16	89.25	89.03	85.97

From the dissolution values it was evident that the formulations F4 shown maximum drug release of 98.73 in 18hours hence it was considered as the optimized formulation.

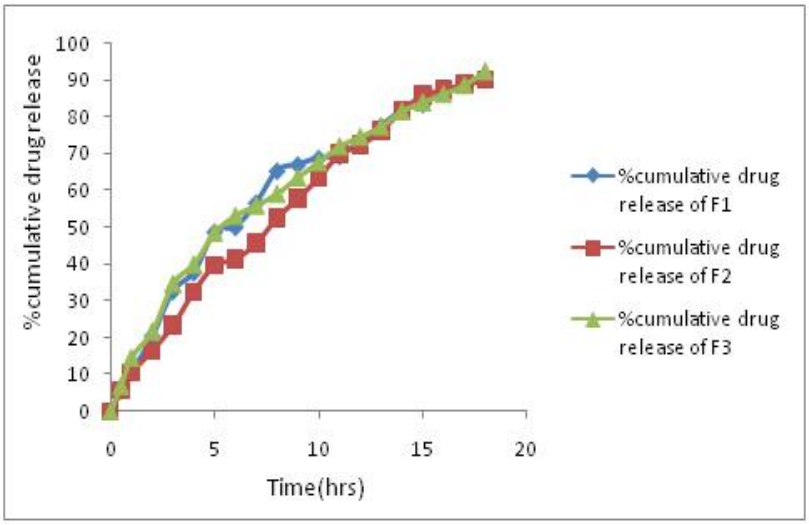

Figure 4: Dissolution of formulations F1-F3

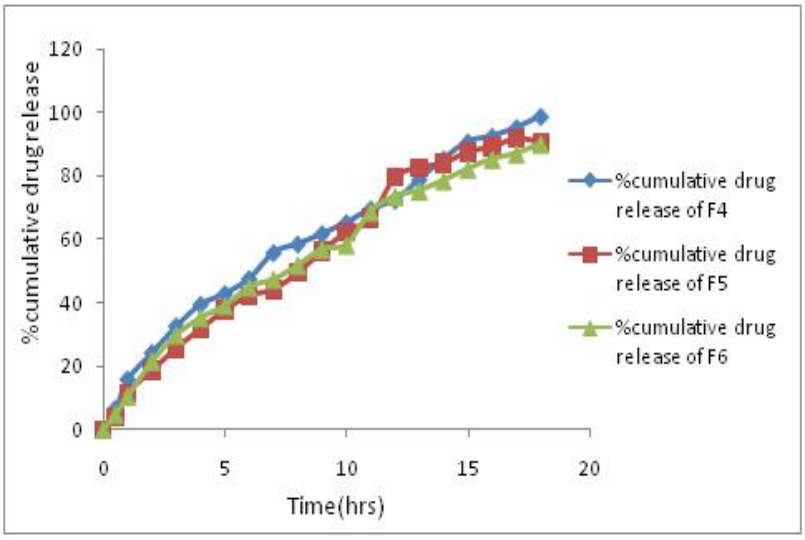

Figure 5 : Dissolution of formulations F4-F6

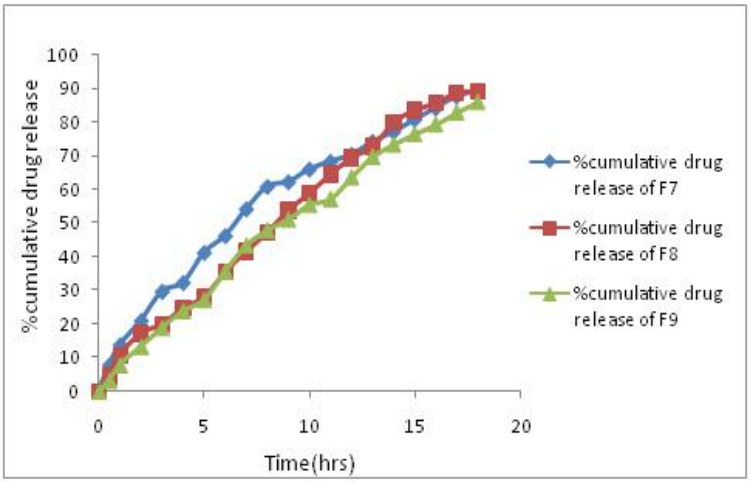

Figure 6: Dissolution of formulations F7-F9

Application of Release Rate Kinetics to Dissolution Data:

Table 10: Release kinetics data for optimised 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
98.73	18	4.243	1.994	1.255	0.104

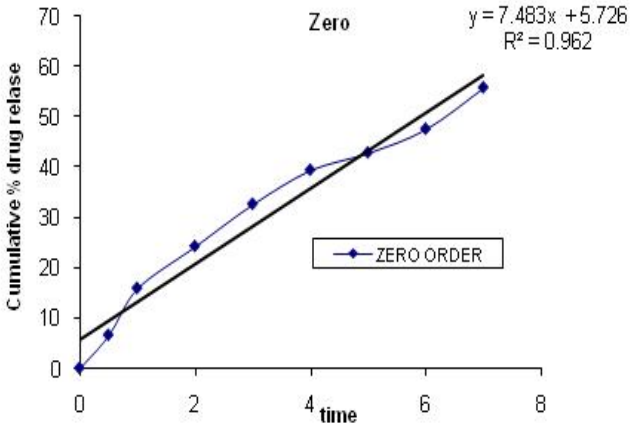

Figure 7: Zero order release kinetics graph

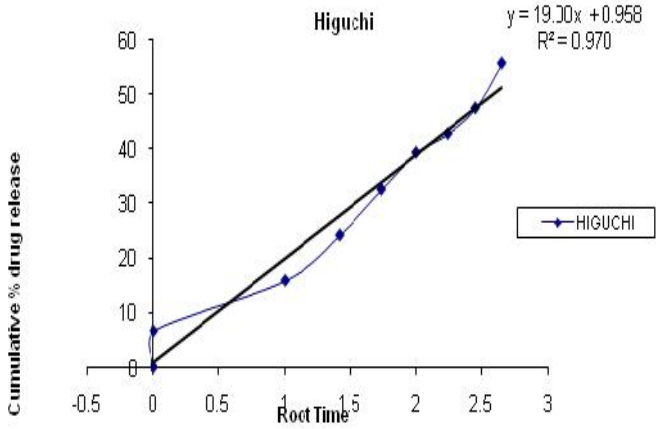

Figure 8: Higuchi release kinetics graph

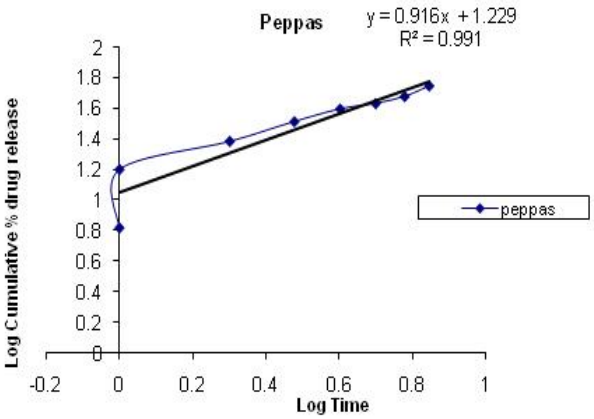

Figure 9: Kars mayer peppas graph

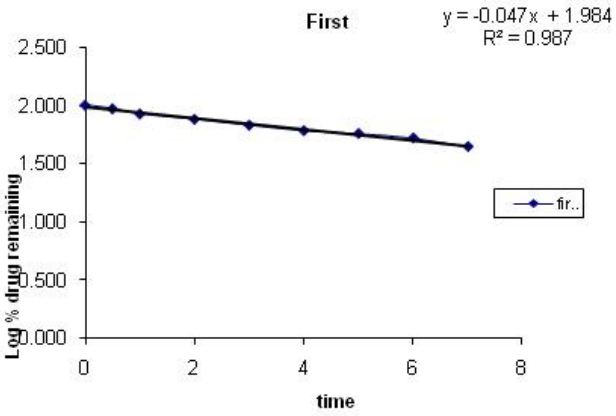

Figure 10: First order release kinetics graph

From the above graphs it was evident that the formulation F4 was followed peppas release kinetics.

4. Conclusion

In the present research work sustained release matrix formulation of Propantheline Bromide targeted to colon by using various polymers developed. To achieve pH-independent drug release of Propantheline Bromide, 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 L100 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 F4 formulation was found to be optimized as it was retarded the drug release up to 18 hours and showed maximum of 98.73% drug release. It followed peppas kinetics mechanism.

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