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Formulation and Evaluation of Controlled Drug Delivery System of Isometheptene mucate for Enhanced Therapeutic Efficacy

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Abstract: In the present study isometheptene mucate is formulated into gastro retentive floating tablets, which is a thiophene derivative; it acts as a serotonin and adrenaline selective neurotransmitter uptake inhibitor. Based on the FTIR compatibility between the drug and polymers and review of literature an attempt was made to prepare floating tablets of the drug, where sodium alginate, Klucel HXF, Methocel K100 were selected as release retarding agents. Total 9 trials were made, of which sodium alginate and Klucel HXF were used till trial F-3, and then only eudragit was used till trial F-09 with varying concentrations. Drug release was satisfactory in trial T-06. F-4 to F-6, proportional increase of hydrophilic polymer Klucel was taken, in same ratio lag phase and floating time were attaining satisfying timings. Physical characterization of all trials for F-4 to F-6 were showing good results and are within the limits according to standard specification. A further attempt in formulation of floating tablets of Isometheptene mucate was carried out by taking MCC from F-4 to F- 6 in increasing proportionate. The drug release obtained was taken for determination of release rate kinetics by interpreting the data in different kinetic models.

INTRODUCTION

Oral route is the effective and mostly easily accepted route to administer the therapeutic agents due to its features like its low cost therapy, easily it can be handled and administered, flexibility in preparation of formulation and best patient compliance. ODDS is the safest secure and satisfactory means of administration due to its simplicity and appropriateness kind of administration.

The basic aim of CRDDS should be to optimize the pharmacokinetic, pharmacodynamics and biopharmaceutics properties of a drug. Thus, the drug is used to its maximum due to reduction seen in side effects occurred and treatment of disease in possible shortest time when administered by the most suitable route in smallest quantity of drug.

The delivery system chosen should be able to capable of delivering the drug taken in it at a rate of the need of body over a specified time period of treatment.

The important objective of CRDDS is to decrease the dose and its frequency to give a uniform or constant drug delivery.

The rate at which the gastric emptying which is quite different and unpredictable from person to person, GI transit time (8-12h) and due to absorption window in upper part of small intestine for results in the need to design or prepare delivery system that can be in seen in stomach for a predictable and prolonged period.

For this the approach is "Gastro retentive drug delivery systems" (GRDDSs) which are developed form of dosage that can be remain in stomach for the desired longer period of time.

Potential drug candidates for GRDDS:

1. *Acting drugs locally in the stomach* - E.g. Misoprostol, Antacids etc.
2. *Primarily absorbed drugs in the stomach* - E.g. Albuterol, Amoxicillin.
3. *Poorly soluble at a basic pH* - E.g. Diazepam, Chlordiazepoxide, Verapamil HCl etc.
4. *Drugs absorbed in Narrow absorption window* - E.g. L-Dopa, p- aminobenzoic acid, Furosemide, Ranitidine HCl etc.
5. *Drugs absorbed rapidly in GI tract.*
6. *Drugs Degraded in the colon* - E.g. Ranitidine HCl, etc.

MATERIALS AND METHODS

Composition of the formulations

Table 1: Formulations of GRDDS tablets F1 to F9

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Isometheptene mucate	20	20	20	20	20	20	20	20	20
Klucel HXF	30	36	45	-	-	-	-	-	-
HPMC K100	-	-	-	30	36	45	-	-	-
Eudragit	-	-	-	-	-	-	30	36	45
Lactose	120	100	110	120	100	110	120	100	110
MCC	79	93	74	79	93	74	79	93	74
Sodium Bicarbonate	45	45	45	45	45	45	45	45	45
Magnesium Stearate	3	3	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3	3	3
Total Weight	300	300	300	300	300	300	300	300	300

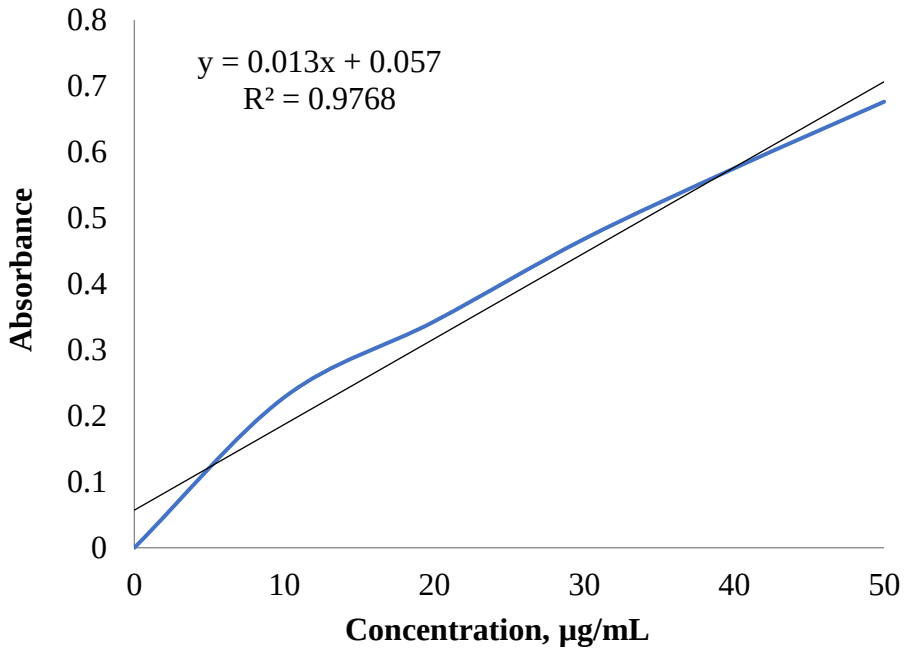

Fig 1: Calibration curve of Isometheptene mucate

FTIR Compatibility studies

In the present study, API Isometheptene mucate and polymers were studied for compatibility studies using FTIR techniques for the detection of any interference between the drug and polymers.

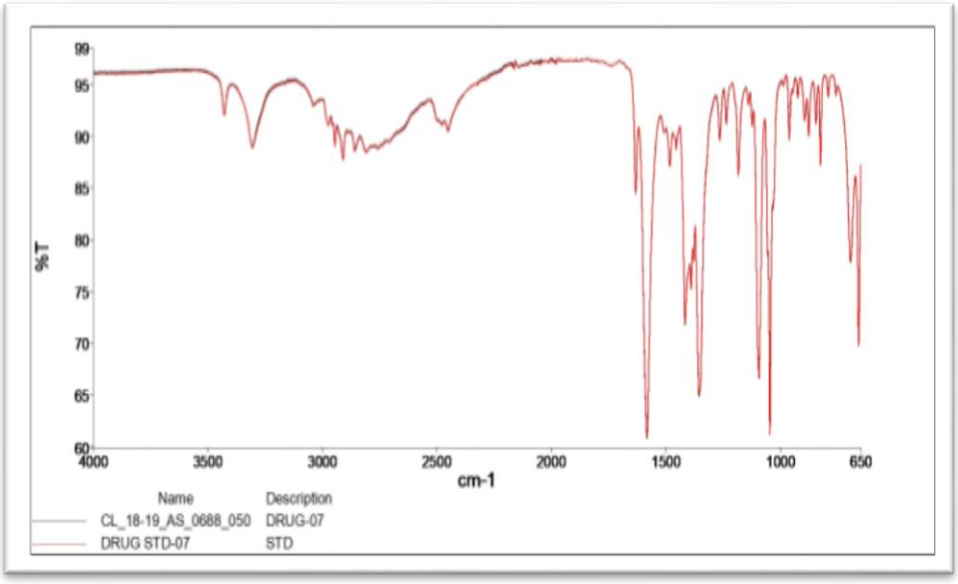

Fig 2: FTIR spectra of Isometheptene mucate

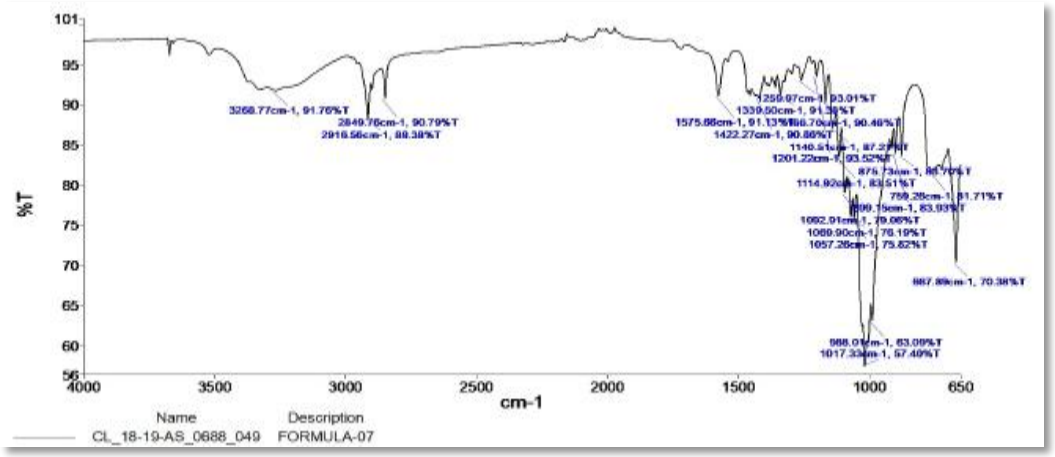

Fig 3: FTIR spectra of formula of drug

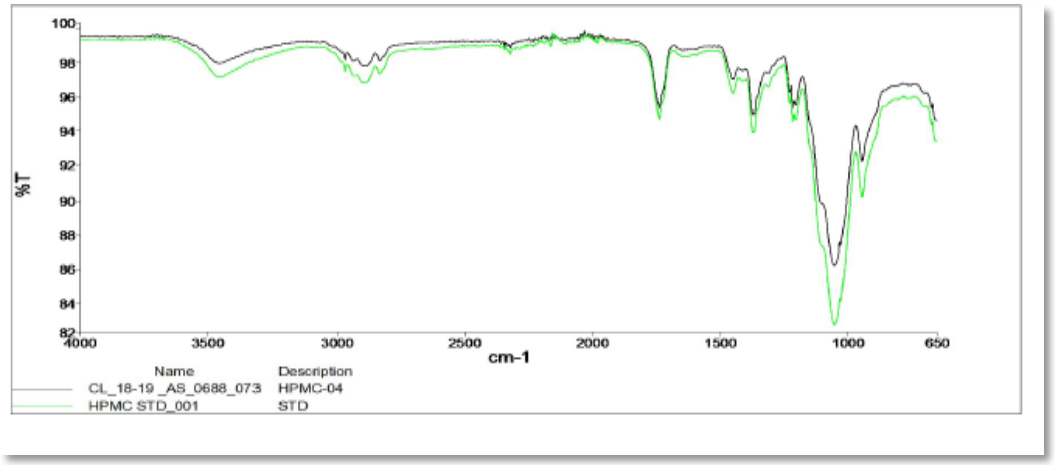

Fig 4: FTIR spectra of HPMC

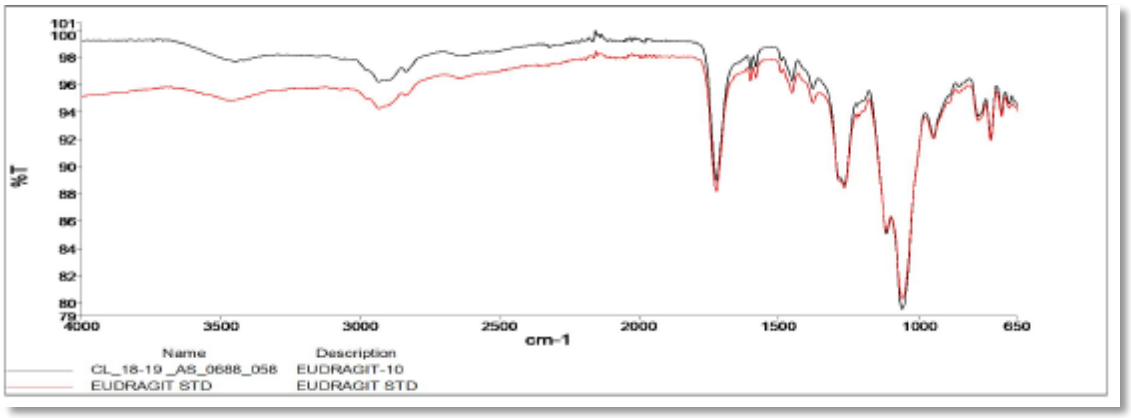

Fig 5: FTIR spectra of Eudragit

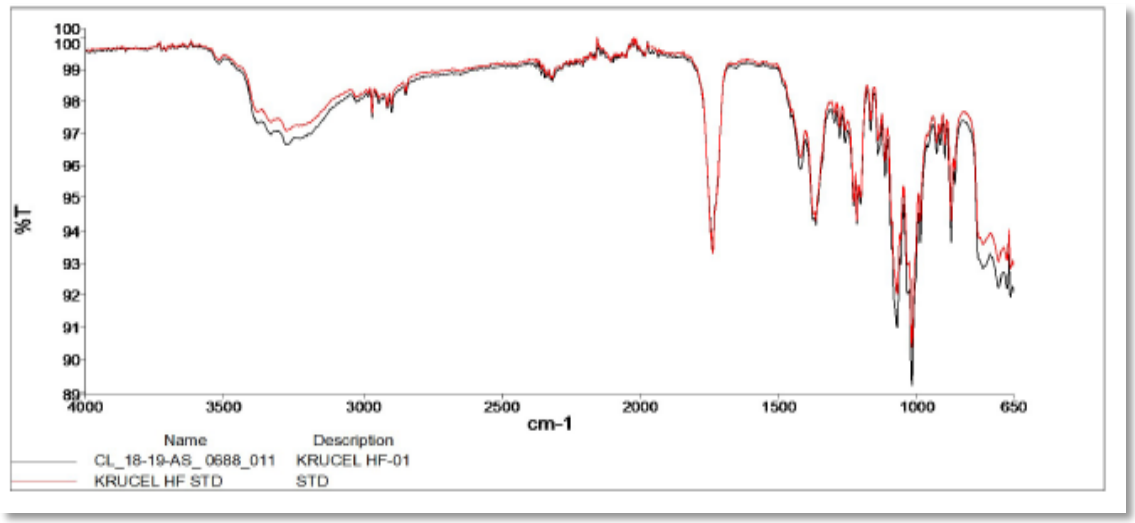

Fig 6: FTIR spectra of Klucel HXF

RESULTS

In Vitro Evaluation:

Characteristic properties of Blend

Table 2: Micrometrics properties of final blend of F1 to F9

Trial	Carr's index	Tan Ø	Hausner's ratio	Bulk Density
F1	6.25	25.25	1.08	0.25
F2	8.73	26.32	1.04	0.65
F3	6.97	23.82	1.03	0.46
F4	9.75	29.5	1.02	0.65
F5	7.67	27.2	1.15	0.77
F6	8.65	28.73	1.12	0.87
F7	10.47	29.73	1.02	0.65
F8	9.73	22.17	1.18	0.77
F9	8.49	27.62	1.15	0.87

Table 3: Evaluation of tablets from trial F1 to F9

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Weight Variation, mg	300.1	301.3	301.4	301.5	301.6	301.8	301.9	301.6	301.6
Friability, %	0.18	0.23	0.17	0.22	0.37	0.27	0.25	0.24	0.23
Hardness, Kg/Cm^2	5.3	5.4	5.6	5.2	5.4	5.6	5.2	5.4	5.6
Thickness, mm	4.0	4.1	4.2	4.4	4.8	4.9	4.4	4.6	4.2
Content Uniformity, %	99.25	100.3	101.8	98.2	98.2	99.37	99.28	101.38	100.38

Table 4: Lag phase and Floating time of trials F-1 to F-9

Formulation	Buoyancy Lag Time, Sec	Floating Time, h
F1	70	>10
F2	72	11.1
F3	74	11.24
F4	76	11.54
F5	78	11.60
F6	80	12.22
F7	82	12.32
F8	86	12.42
F9	78	12.22

Table 5: In-vitro % drug release profile of F1-F9

Time, h	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	18.34	16.38	14.28	18.39	15.23	10.38	9.29	12.19	15.32
1	22.82	19.37	18.18	26.55	17.39	16.18	15.29	25.38	21.83
2	36.12	29.81	24.19	37.39	28.82	26.29	27.28	29.39	37.19
3	45.18	49.34	34.19	49.28	39.27	32.83	37.18	45.29	49.29
4	63.28	62.81	55.38	55.29	58.28	48.28	45.81	63.92	61.91
5	74.18	68.28	68.29	73.28	68.29	63.83	59.17	73.28	76.18
6	79.28	74.84	75.93	89.82	77.27	78.29	84.28	83.82	82.82
7	82.46	81.12	89.47	90.12	89.76	86.27	91.28	89.23	87.19
8	86.28	84.31	82.21	93.52	94.72	92.28	94.28	91.37	90.83
9	94.37	96.38	94.38	95.28	96.27	97.38	95.01	93.28	92.65
10	97.27	96.82	95.39	96.28	97.72	99.82	96.91	94.28	92.87

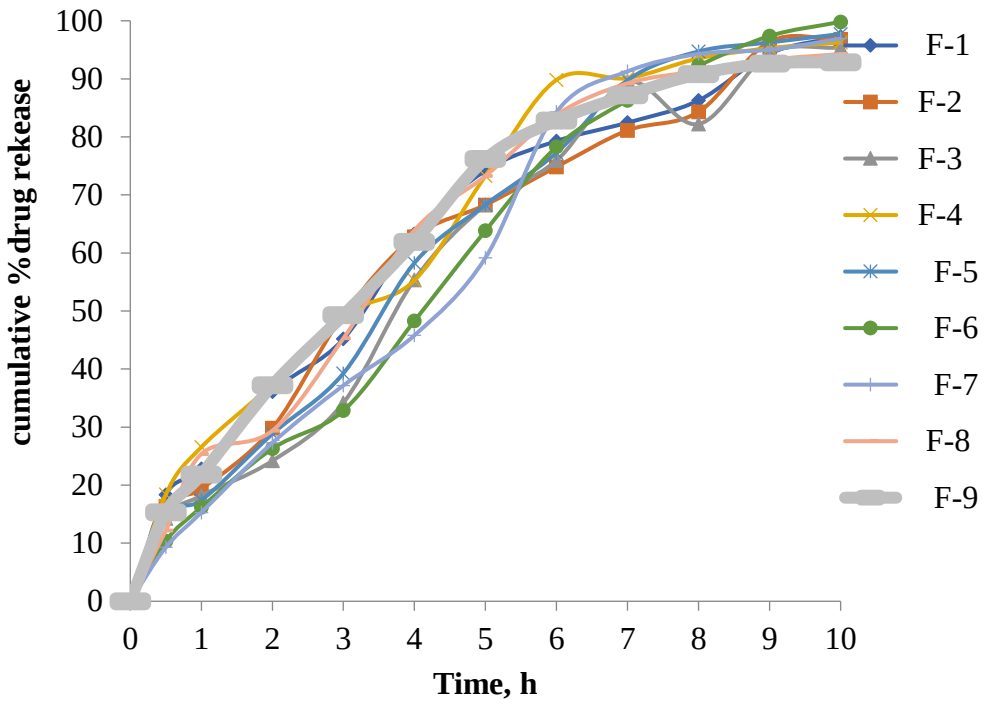

Fig 7: Graphical representation comparative drug release

Graphical representation of release rate kinetics:

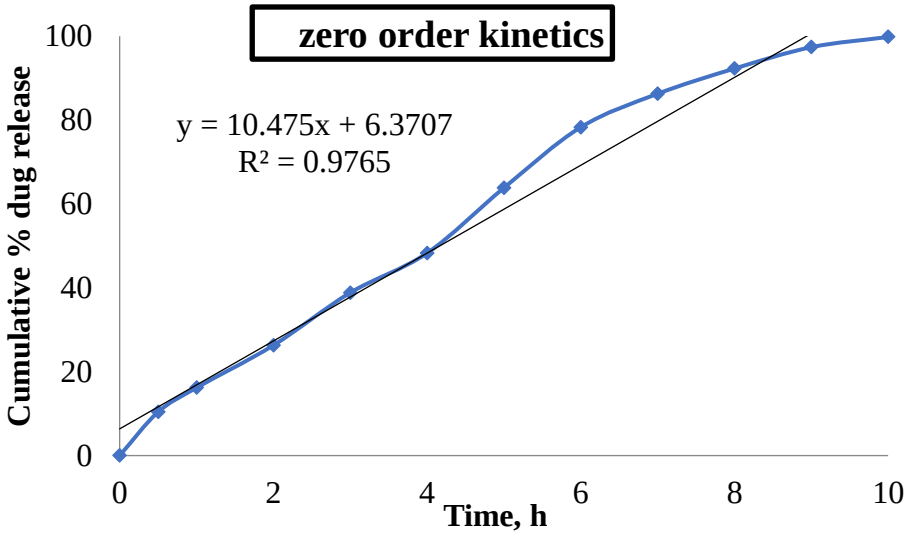

Fig 8: Graphical representation of zero order kinetic

CONCLUSION

A gastroretentive floating drug delivery system for isometheptene mucate was effectively developed and assessed in this work. The drug's eligibility for formulation development was established by preformulation tests, and compatibility between the drug and specific excipients was shown by FTIR analysis. Acceptable micromeritic properties showed that the powder mixes had good flow and compressibility characteristics.

Pharmacopoeial standards for postcompression properties, such as hardness, friability, thickness, weight variation, and homogeneity of drug content, were met by all tablet formulations. Additionally, the prepared pills demonstrated longer stomach retention and excellent floating behavior. Formulations F5 and F6 showed the maximum drug release of 97.72% and 99.82%, respectively, according to in vitro drug release experiments that showed sustained drug release over 10 hours.

Drug release kinetics suggested anomalous (non Fickian) diffusion and revealed a regulated release mechanism best explained by the Korsmeyer–Peppas model.

Overall, the isometheptene mucate gastro-retentive floating tablets showed favorable physicochemical characteristics, extended stomach residency, and regulated drug release, suggesting their potential to improve patient compliance, therapeutic efficacy, and bioavailability.

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