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TO FORMULATE AND EVALUATE SUSTAINED RELEASE MATRIX TABLETS OF MOSAPRIDE CITRATE DIHYDRATE

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Abstract:

The present study was carried out to develop sustained release matrix tablets of mosapride citrate dihydrate. Matrix tablets of mosapride citrate dihydrate with two different viscosity grades of hydroxypropyl methylcellulose were prepared by dry granulation and direct compression method and evaluated.

The study demonstrated that combination of HPMC K4M and HPMC mosapride citrate dihydrate. This can be expected to reduce the frequency of administration and decrease the dose – dependent side effects associated with repeated administration of conventional mosapride citrate dihydrate tablets. The cumulative drug release of innovators brand (MOZA SR, Intas Pharmaceuticals) of sustained release tablet of mosapride citrate dihydrate were compaired for in vitro dissolution study.

Hence it can be concluded that once daily sustain release matrix tablet of mosapride citrate dihydrate having short half life, was found to exert a satisfactory sustained release profile which may provide an improved bioavailability, increased therapeutic efficacy and patient compliance.

Key words: Matrix Tablet, Sustained release

1. INTRODUCTION

Sustained release, sustained action, prolonged action, controlled release, extended action, timed release, depot and repository dosage forms are terms used to identify drug delivery systems that are designed to achieve prolonged therapeutic effects by continuously releasing medication over an extended period of time after administration of single dose. In general, the goal of a sustained release dosage form is to maintain therapeutic blood level or tissue level of the drug for extended period. This is usually accomplished by attempting to obtain zero order release from the dosage form. Zero order release constitutes of the amount of drug in the delivery system (i.e. a constant release rate). Sustained release systems generally don not attain this type of release and usually try to minis zero order release by providing drug in a slow first order fashion (i.e. concentration-dependent).

One of the least complicated approaches to the manufacture of sustained release dosage forms involves the direct compression of blends of drug, retardant material, and additives to form a tablet in which drug is embedded in a matrix core of retardant.

Compression granulation involves the compaction of components tablet formulation by means of a tablet press or specially designed machinery, followed by milling screening, prior to final compression into tablet. When the initial blend of powder is forced into the dies of large capacity tablet press and is compacted by means of flat punches, the compacted masses are called ***slugs,*** and process is referred to as ***slugging*****.** The slugs are then screened or milled to produce a granular form of a tabletting material, which now flows more uniformly than the original powder mixture. When a single slugging process is insufficient to confer the desired granular properties to the material, the slugs are some times screened, slugged again, and screened once more.

2.0 MATERIALS

	Material	Company Name
1.	Mosapride Citrate dihydrate	DR. Reddy's Holdings limited, Hyderabad
2.	HPMC K15M	Colourcon Asia Pvt. limited, Mumbai
3.	HPMC K4M	Colourcon Asia Pvt. limited, Mumbai
4.	Lactose	Concept pharmaceuticals limited, Aurangabad.
5.	Magnesium stearate	Concept pharmaceuticals limited, Aurangabad
6.	Aerosil 200	Concept pharmaceuticals limited, Aurangabad
7.	Talcum	Concept pharmaceuticals limited, Aurangabad
8.	PEG 200 & PEG 6000	Concept pharmaceuticals limited, Aurangabad
9.	Methylenechloride	Concept pharmaceuticals limited, Aurangabad
10.	IPA	Concept pharmaceuticals limited, Aurangabad
11.	Iron oxide Red	Concept pharmaceuticals limited, Aurangabad
12.	TiO_2	Concept pharmaceuticals limited, Aurangabad

EQUIPMENTS

13. Single punch tablet rotary machine	Cadmach
14. Dissolution apparatus	Electro lab
15. UV Visible spectrophotometer	Shimadzu (UV 1700)
16. Hardness tester	Monsanto
17. Friabilator	Electro lab
18. Vernier caliper	Baker
19. pH meter	Control Dynamic
FTIR	Shimadzu

3.0 METHODOLOGY

3.1 Potency Calculation

Quantity of Mosapride citrate dihydrate calculated for dose of 15.00 mg of Mosapride citrate anhydrate.

$$= \frac{\text{Dose x Mol. Wt. of Mosapride citrate dihydrate x 100 x 100}}{\text{Mol. Wt. of Mosapride citrate anhydrous x Assay x (100 – LOD)}}$$

$$= \frac{15 \text{ x } 650.50 \text{ x } 100 \text{ x } 100}{614.50 \text{ x } 99.95 \text{ x } (100 - 5.6)}$$

= 16.83 mg

i.e. 15 mg of Mosapride citrate anhydrate ≡ 16.83 mg of Mosapride citrate dihydrate.

3.2 Analytical data by FTIR spectroscopy

The FTIR spectra of pure mosapride citrate dihydrate, mosapride citrate dihydrate with HPMC K4M, HPMC K15M and mosapride citrate dihydrate with HPMC K4M, HPMC K15M, Lactose, Magnesium stearate, Talc, Aerosil were analyzed for compatibility study.

Fig No.1 FTIR Spectra of mosapride citrate dihydrate

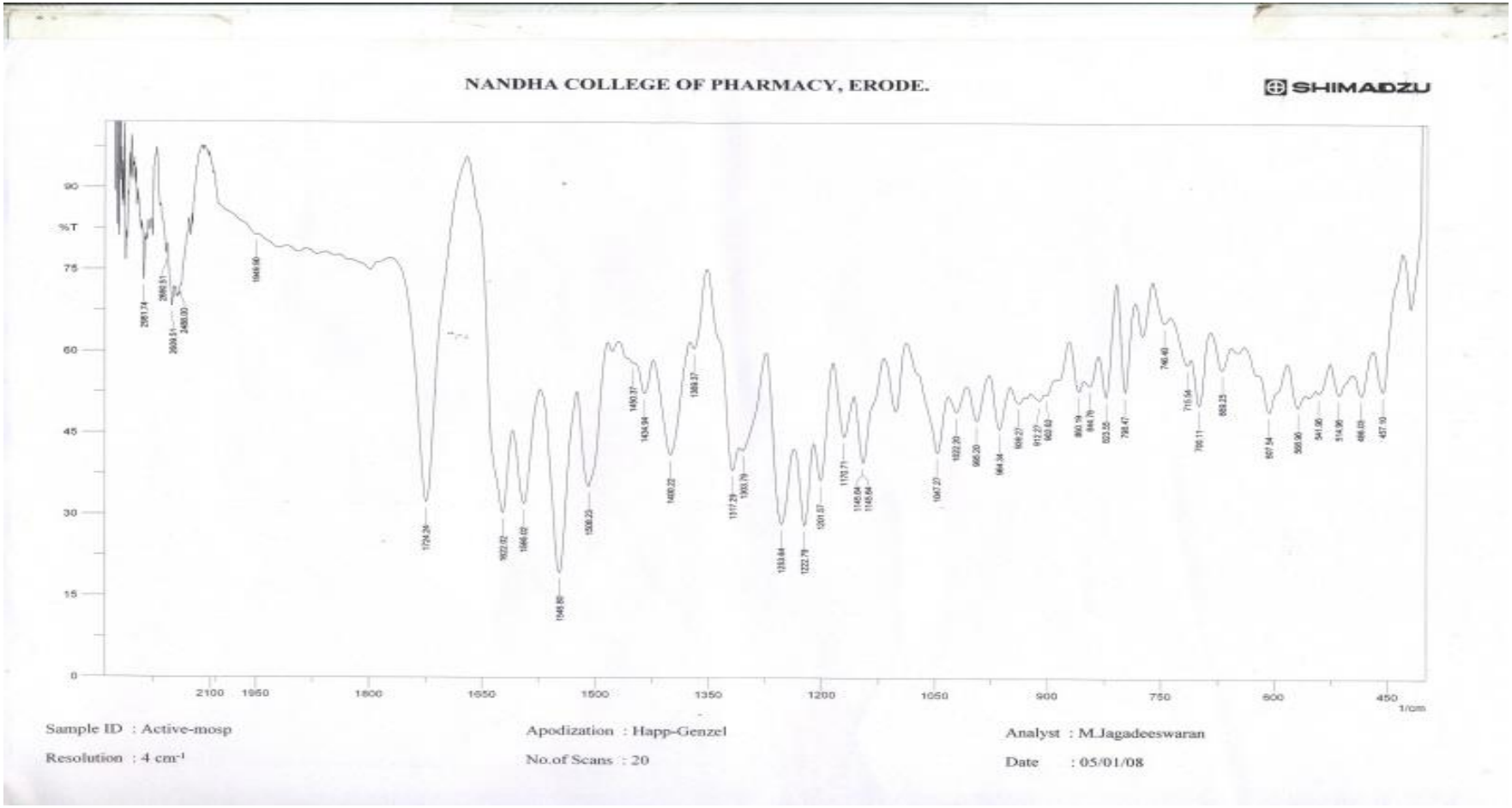


Fig.No.2 FTIR Spectra of mosapride citrate dihydrate with HPMC K4M and HPMC K15M

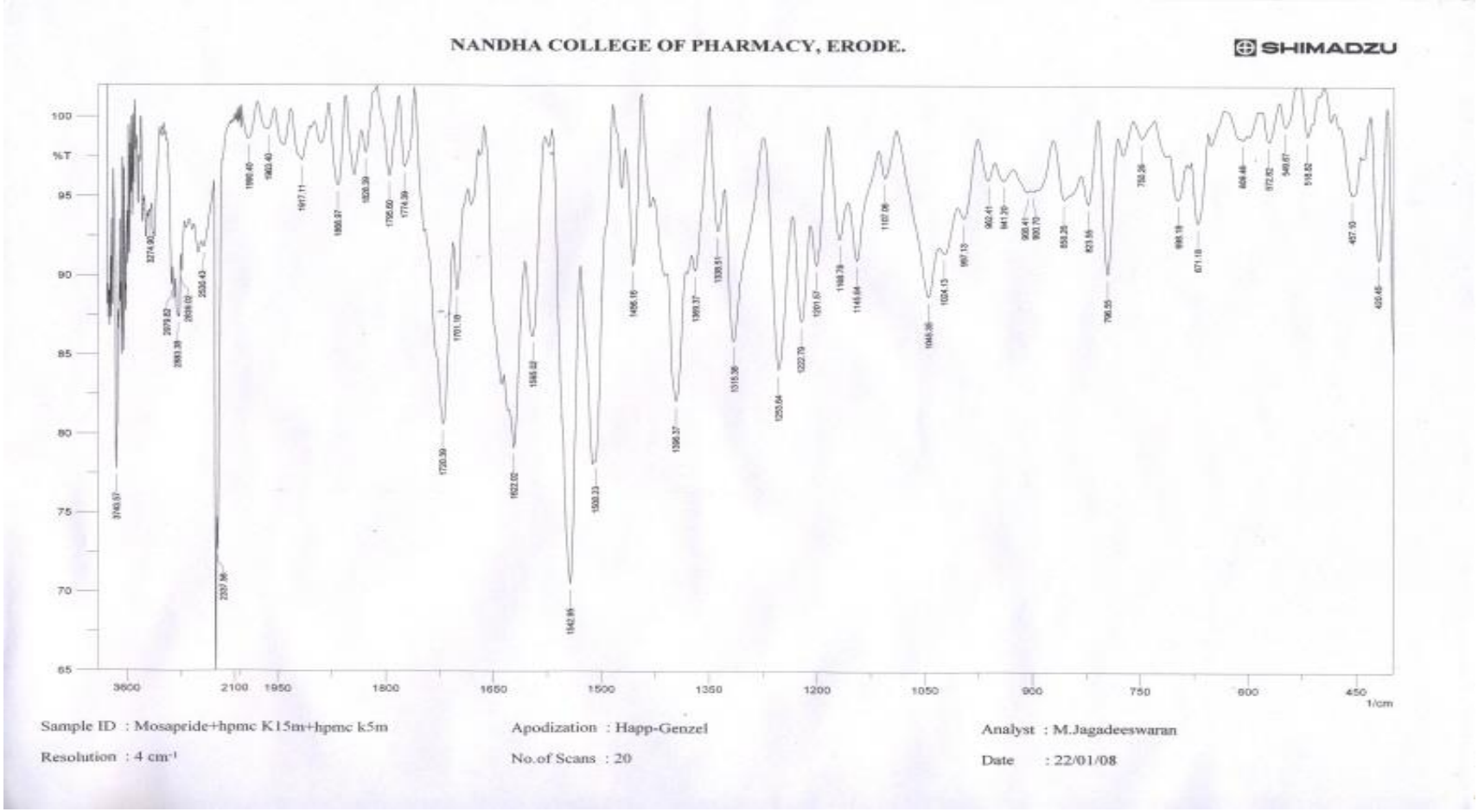


Fig No.3 FTIR Spectra of mosapride citrate dihydrate with HPMC (K4M/K15M) and other excipients of formulations

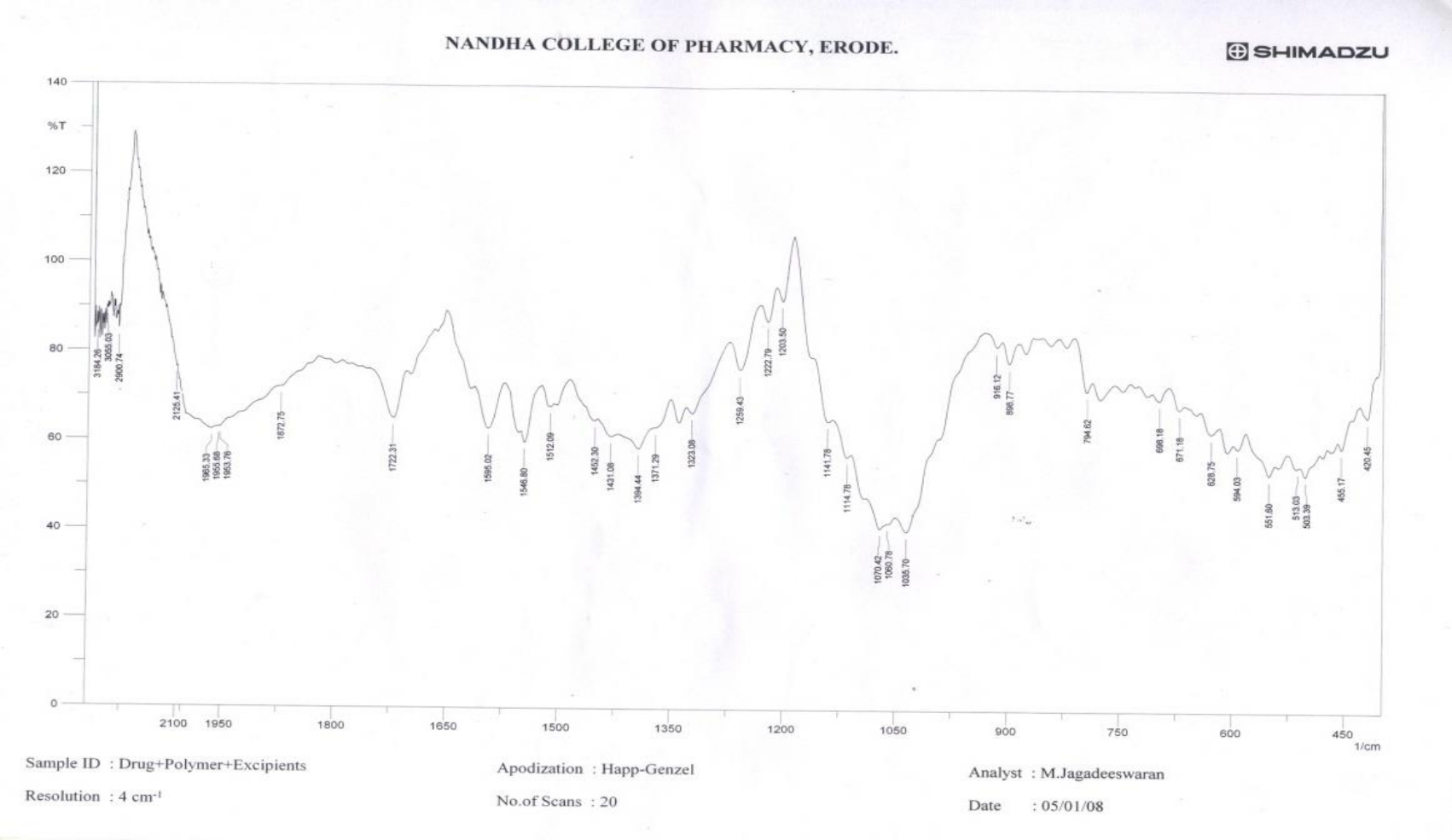


Table No.1 Interpretation of FTIR Spectra[33, 34]

Sr. No.	Functional groups presents in mosapride citrate dihydrate.	Standard FTIR range	Observed Peak
1	C=O (in ketone)	1705-1725	1724.24
2	C-N (vibrations)	1000-1400	1400.22,1434.94,1450.37
3	C-H	700-850	607,669,700,715,746,798
4	C-Cl	800-600	700.11
5	C-F	1000-1400	1201.57

The above study confirms that the identity and compatibility among the mosapride citrate dihydrate and other excipients of the formulation.

3.3 PREFORMULATION STUDY

Angle of repose [7]

Angle of repose was determined using funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the heap of the blends. Accurately weighed blend is allowed to pass through the funnel freely on to the surface. The height and diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\Theta = \tan^{-1} (h/r)$$

Where,

h= Height of pile

r= Radius of pile

Θ= Angle of repose

Bulk Density and Tapped Density[49]

It is the ratio between a given mass of a powder and its bulk volume

$$\text{Bulk Density} = \frac{\text{Mass of powder}}{\text{Bulk Volume of the powder}}$$

A given quantity of powder (2 gm) is transferred to a measuring cylinder (10 ml) and is tapped mechanically till a constant volume is obtained. This volume is the bulk volume and it includes true volume of the powder and the void space among the powder particles.

Tapped density is calculated by using the formula

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped volume of the powder}}$$

Carr's Index[7]

A simple indication of the ease with which a material can be induced to flow is given by application of a compressibility index (I), is given by the equation

I= [1- Tapped density / Bulk density] x 100.

Values of I below 15% usually give rise to good flow characteristics, but readings above 25% indicate poor flow ability.

Hausner's Ratio[48]

A similar index has been defined by Hausner.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Poured Density}}$$

Values less than 1.25 (= 25% Carr's index) indicates good flow, while greater than 1.25 indicates poor flow (= 33% Carr's index). Between 1.25 and 1.5 added glidants normally improves flow.

Table No 2.Physical Parameters of granules before dry granulation (Slugging).

Physical Properties	F_1	F_2	F_3	F_4	F_5	F_6
Bulk Density**(gm/ml)	0.431 ±0.002	0.435 ±0.003	0.439 ±0.001	0.428 ±0.002	0.422 ±0.001	0.438 ±0.002
Tapped Density**(gm/ml)	0.628 ±0.002	0.630 ±0.0023	0.634 ±0.001	0.623 ±0.003	0.615 ±0.001	0.632 ±0.002
Compressibility Index**	31.36 ±1.55	30.95 ±1.78	30.75 ±1.91	31.30 ±1.65	31.38 ±1.25	30.69 ±1.68
Hausner's Ratio**(H.R.)	1.45 ±0.015	1.448 ±0.018	1.444 ±0.014	1.46 ±0.011	1.467 ±0.017	1.452 ±0.015
Angle of Repose**	33°75' ±1.08	32°42' ±1.55	32°05 ±1.48	31°47 ±1.65	32°55 ±1.49	33°32 ±1.46
Observation	Poor flow	Poor flow	Poor flow	Poor flow	Poor flow	Poor flow

(=Average of three determinations)**

3.4 EXPERIMENTAL WORK

STEP 1: **Weigh the raw material as per ORML & check control no. and record them**.

STEP 2: Sifting

Check the integrity of the sieves being used for sifter as per SOP & first sift the material dry mixing and then shift material required for dry lubrication as per the specified sieve for each material.

Table No 3: Materials used for Dry granulation:

Materials	Theoretical Quantity (grams/1000 tablets)	Actual Quantity (grams/1000 tablets)	Sieve no
Materials for dry mixing			
Mosapride Citrate Dihydrate	12.60	12.60	24#
Lactose IP/BP	33.05	33.05	24#
HPMC K4M	18.80	18.80	24#
HPMCK15M	23.22	23.22	24#
Talcum	0.48	0.48	40#
Magnesium Stearate IP/BP	0.48	0.48	40#
Aerosil IP/USP	0.09	0.09	40#
Materials for dry lubrication			
Mosapride Citrate Dihydrate	4.23	4.23	24#
Talcum	0.48	0.48	40#
Magnesium Stearate IP/BP	0.48	0.48	40#
Aerosil IP/USP	0.09	0.09	40#

STEP 3: **Dry Mixing**

. Blend of Mosapride Citrate Dihydrate with Polymer (HPMC) & lactose mix slowly in polybag for 15 minutes. Add half quantity of lubricants & reblend for 5-6 minutes. Now blend is ready for slug formation.

STEP 4: **Slugging**

Clean & operate the M/C as per S.C.P. & S.O.P for Slugging.

Parameters for Slugging

Punch size 16 mm

Average Weight 900 mg/slug

Hardness NLT 10 Kg/cm^2

STEP 5: **Deslugging**

Deslug the above slug, and screen it through 2 mm screen slowly. Pass l the final granules through #30.

STEP 6: **Dry Lubrication**

Mix final granules & remaining mosapride citrate dihydrate slowly in polybag for 15 minutes. Add remaining half quantity of lubricants slowly for 10 minutes. Record the total weight of granules. Now blend is ready for compression.

STEP 7: Compression

Clean & operate the machine as per S.C.P. ensure blend release before taking for compression. Check batch details on the label & total weight. of granules.

Parameters for compression

I.	Punch	UP: Plain SC, LP: Plain SC.
II.	Dimensions	6.00 mm
III.	Diameter	6.00 mm (± 0.05)
IV.	Theoretical Weight to Tablet	94mg / Tab
V.	Weight of two Tablets	188mg (±2%)
VI.	Weight variation (of actual average weight)	± 7.5%
VII.	Hardness of Tablet	NLT 4.0 Kg/cm^2
VIII.	Friability	NMT 1.0%
IX.	Thickness	3.0 (± 0.2) mm
X.	Appearance of tablet.	White to off-white, biconvex.

STEP 8: Initial batch sample was tested for sustained release action.

Table No 4. Initial sustained release profile.

Hours	% Drug Release
After first hour	NMT 30 %
After seventh hour	50 to 65%
After twelve hour	NLT 70%

STEP 9: Film Coating

Weight the coating material & check.

Note average weight of uncoated tablet.

Coating Solution Preparation:

A. Take

Hydroxy Propyl Methyl Cellulose IP 15 cps	6.5gm
Suspend it in Iso Propyl Alcohol IP	39 gm
Methylene chloride IP	26gm

Stir well with mechanical stirrer to get clear solution.

B. Take

Titanium Dioxide IP	0.36gm
Talc IP	0.100gm
Suspend it in Iso Propyl Alcohol IP	37gm

Pass the above suspension of step (B) through Nylon cloth.

C. Take

PEG 200 USP	0.034 gm
PEG 6000 USP	0.010 gm
Methylene chloride IP	5gm.

Transfer to the suspension of step (A). Stir properly to get uniform suspension, filter the above suspension through double Nylon cloth & store in closed container. Spray this coating suspension.

STEP 11: Coating Parameters

Clean & operate the coating pan .Switch on the blower so as to start hot air supply (30-35°C) on tablet bed for about 10 minutes. Tablet bed should be heated to 25 – 30°C.

I. Start compressed air & exhaust.
II. Start the Spray of the solution and maintain the following parameters,

III.	Pan speed	25-30 rpm
IV.	Tablet bed temperature	25 – 30°C
V.	Distance of gun from bed	about 12 – 15 cm.
VI.	Atomizing pressure	1.5 Kg/cm^2
VII.	Exhaust	On
VIII.	Inlet air temperature	25 – 30°C
IX.	Direction of spray pattern	90° to tablet bed

X. Observe the spray gun for chocking, if any chocking observed during the coating process, immediately stop the coating process. After spraying the total volume of solution stop the compressed air. Roll the tablets for another 15 – 20 minutes for complete drying.
XI. After completion of coating, note the following,
XII. Average weight of coated tablet. Weight gain should be 4-6%.

Table No. 5 Physical parameters of granules after dry granulation (slugging)

Physical Properties	F_1	F_2	F_3	F_4	F_5	F_6
Bulk Density(gm/ml)**	0.438 ±0.0021	0.435 ±0.0012	0.440 ±0.0019	0.426 ±0.0022	0.429 ±0.0011	0.443 ±0.0014
Tapped Density(gm/ml)**	0.5102 ±0.0023	0.516 ±0.0011	0.521 ±0.0017	0.511 ±0.0019	0.523 ±0.0010	0.512 ±0.0012
Compressibility Index**	14.15 ±1.45	15.69 ±1.68	15.54 ±1.51	16.63 ±1.69	17.01 ±1.28	15.10 ±1.33
Hausner's Ratio(H.R.)**	1.16 ±0.016	1.18 ±0.012	1.18 ±0.009	1.19 ±0.014	1.21 ±0.021	1.18 ±0.010
Angle of Repose**	24 ±1.47	24.5 ±1.65	25 ±1.48	23 ±1.55	26 ±1.43	25 ±1.43
Observation	good flow	good flow	good flow	good flow	good flow	good flow

(** Average of three determinations)

Formulation variables for mosapride citrate dihydrate tablets.

Table No-6 Formulation ingredients in percentage.

Ingredients (percentage/ tablet)	Specifications	F_1 (%)	F_2 (%)	F_3 (%)	F_4 (%)	F_5 (%)	F_6 (%)
Mosapride citrate dihydrate	In-House	17.9	17.9	17.9	17.9	17.9	17.9
Lactose	IP/BP	60.3	53.5	51.79	47.87	39.85	35.15
HPMC K15 M	IP/BP	10.00	10.00	10.00	15.00	20.00	24.70
HPMCK4M	IP/BP	10.00	15.93	18.06	16.98	20.00	20.00
Talcum	IP	1.021	1.021	1.021	1.021	1.021	1.021
Magnesium Stearate	IP/BP	1.021	1.021	1.021	1.021	1.021	1.021
Colloidal silicon dioxide(Aerosil)	IP/USP	0.191	0.191	0.191	0.191	0.191	0.191

3.5 EVALUATION OF TABLETS

3.5.1 Uniformity of weight [44]

The USP weight variation test was carried out by weighing 20 tablets individually, calculating the average weight, comparing the individual tablet weight to average weight. The tablet meet USP test if no tablet differs by more than two times of percentage deviation.

3.5.2 Thickness variation test[7]

Thickness of 5 tablets is measured by using Vernier caliper.

3.5.3 Tablet Hardness[7]

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under the condition of storage, transportation and handling before usage depends in its hardness. Hardness of tablets of each formulation was determined using Monsanto hardness tester.

3.5.4 Friability Test[7]

It is a measure of mechanical strength of tablets. The test was performed by using Electro lab friabilator test apparatus.

The preweighed tablets were placed in the friabilator. Friabilator consists of a plastic chamber that revolves at 25 rpm, dropping the tables at a distance of 6 inches in each revolution. The tablets were rotated in friabilator for 4 minutes. At the end of test, tablets were reweighed. The % weight loss in weight of tablet is the measure of friability and is expressed in percentage as,

$$\text{Percentage friability} = \frac{\text{Final weight}}{\text{Initial weight}} \times 100$$

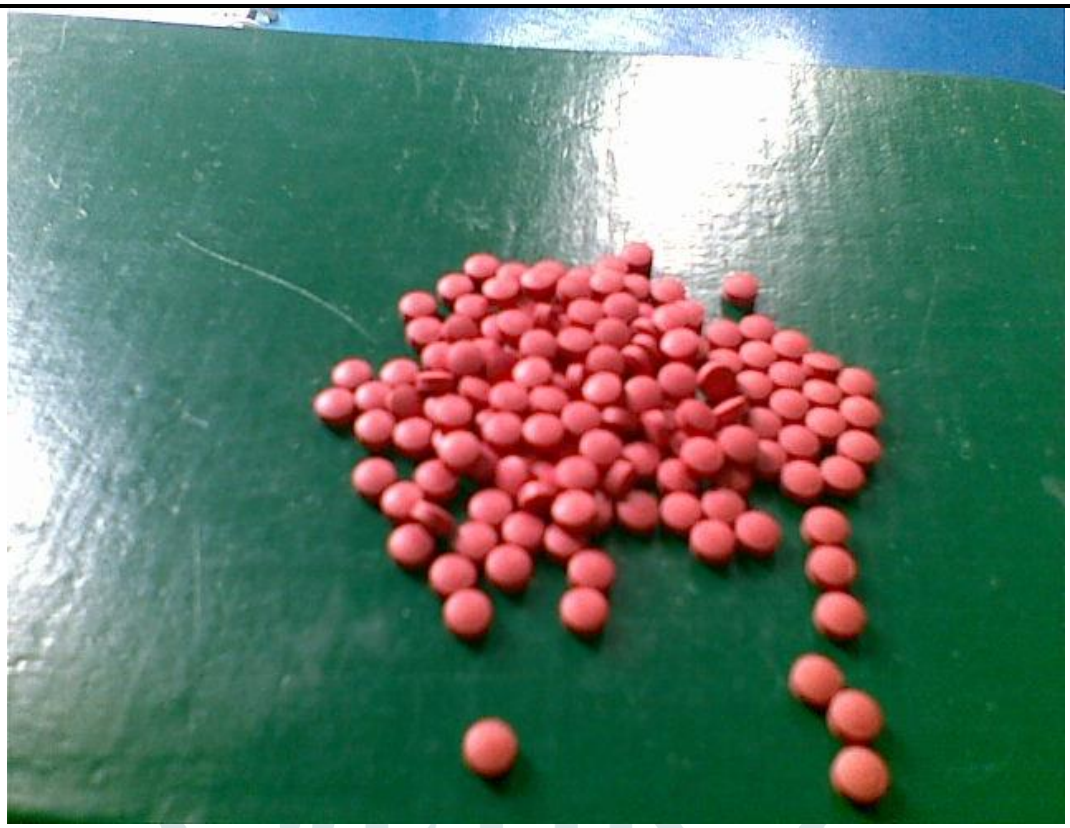


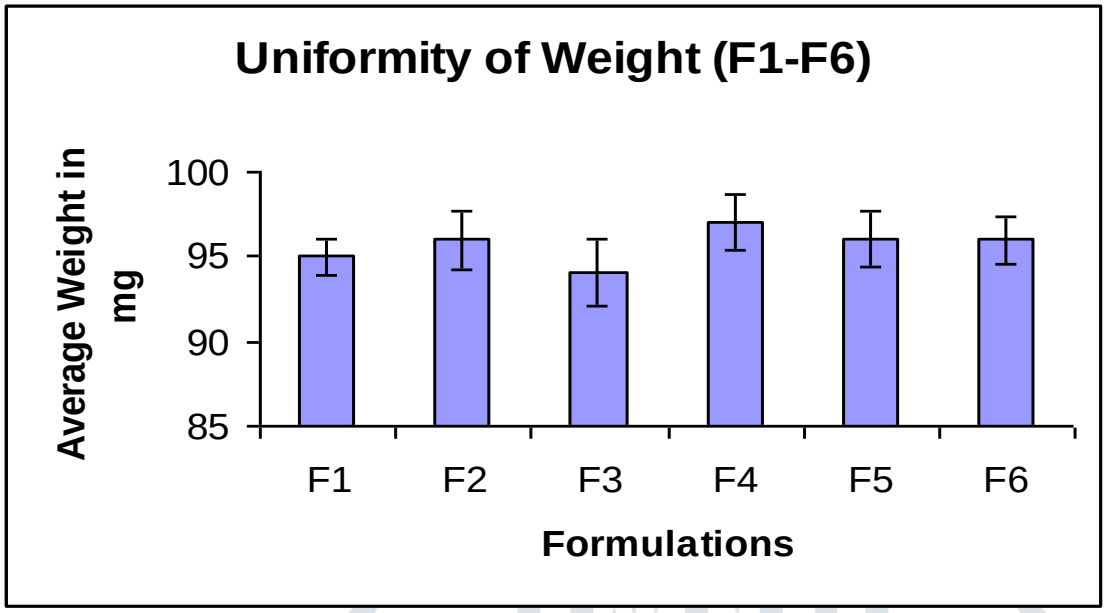
Fig.No.2 Compressed coated tablets of Mosapride citrate dihydrate .

Table No.7: Physical Parameters of Prepared Tablets

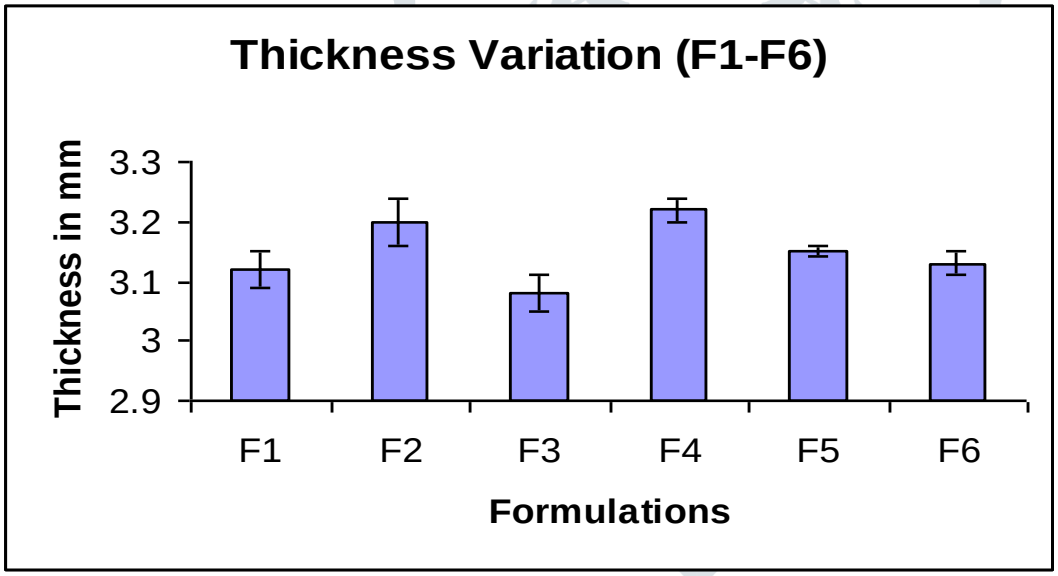
Physical Properties	F_1	F_2	F_3	F_4	F_5	F_6
Uniformity of weight in (mg)***	95.00 ±1.04	96.00±1.76	94.00±1.98	97.00±1.66	96.00±1.66	96.00±1.39
Thickness variation(mm)***	3.12 ±0.03	3.20 ±0.04	3.08 ±0.03	3.22 ±0.02	3.15 ±0.01	3.13 ±0.02
Hardness in (kg/cm^2)***	5.30 ±0.40	4.60 ±0.33	4.70 ±0.21	5.30 ±0.28	4.90 ±0.31	5.20 ±0.29
Friability (%) ***	0.158±0.025	0.21±0.017	0.265±0.032	0.106±0.019	0.150±0.026	0.160±0.021

(***Average of five determinations)

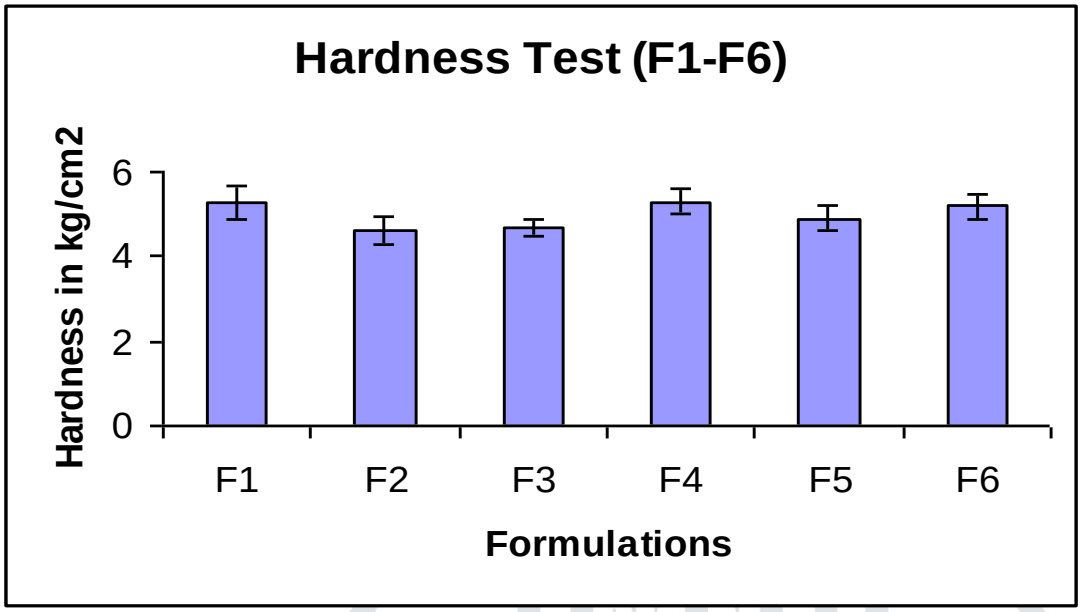
Graph No.1 Uniformity of weight of formulations F_1-F_6



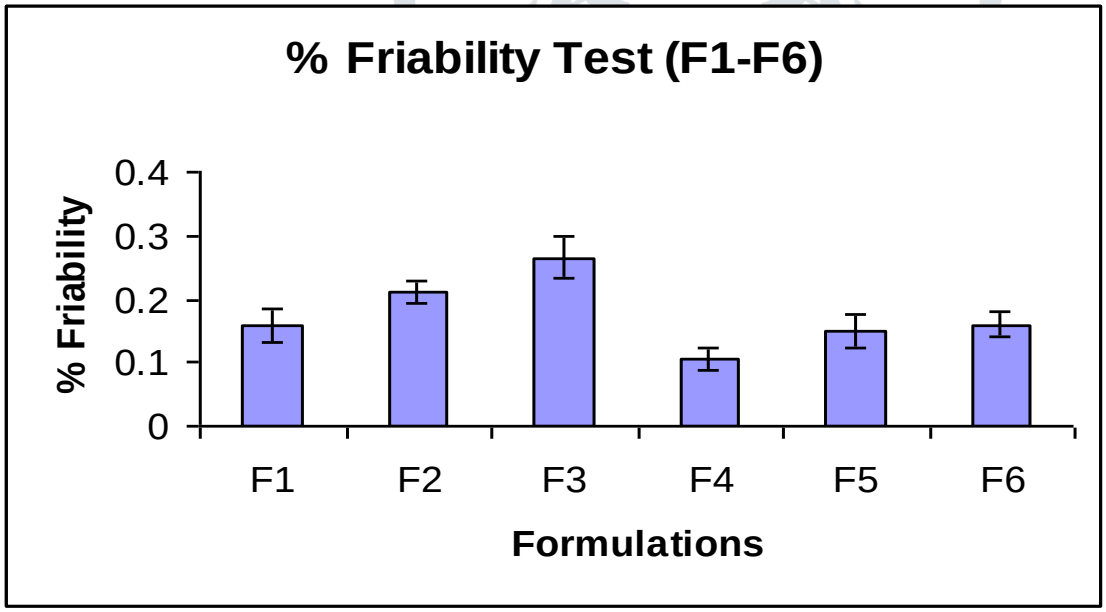
Graph No.2 Thickness variation of formulations F_1-F_6



Graph No.3 Hardness test of formulations F_1-F_6



Graph No.4 Percentage friability of formulations F_1-F_6



3.6 METHOD OF ANALYSIS

3.6.1 DISSOLUTION [19, 20]

Medium – Acetate buffer pH – 4.0

Apparatus – USP (Type II) paddle type.

Medium volume – 900.0 ml

Speed – 100 rpm

Temperature – 37°C [± 0.5°C]

Wavelength– 274 nm

Sample Withdrawal-At the end of 1st, 4th, 7th, 12th, 16th and 24th hours

Sample volume- 5 ml

Table No 08 Standard Dissolution Profile.

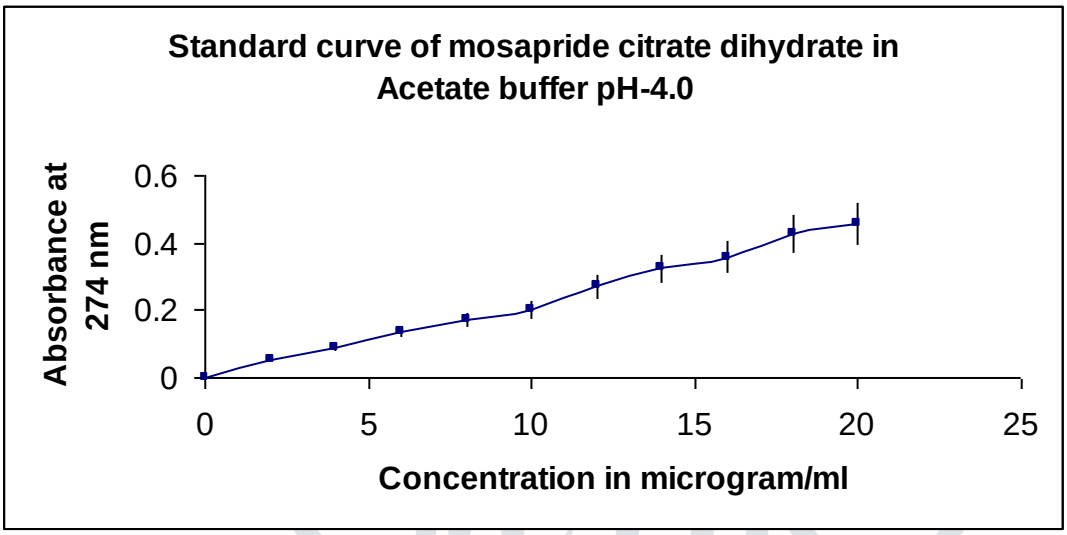
Dissolution	Sustained release profile
After 1st hour	NMT – 30%
After 4th hour	30 -50%
After 7th hour	50 – 65%
After 12th hour	70-75%
After 16th hour	75-85%
After 24th hour	NLT 90%

Table No-09 Standard Curve 0f Mosapride citrate dihydrate in Acetate Buffer pH-4.0

Concentration In mcg/ml	**Absorbance at 274 nm in Acetate buffer pH- 4.0**
0	**0 ± 0**
2	**0.055 ± 0.0019**
4	**0.09 ±0.0016**
6	**0.137 ± 0.0021**
8	**0.172 ± 0.0013**
10	**0.202 ±0.0018**
12	**0.271 ±0.0013**
14	**0.325 ±0.0011**
16	**0.358 ±0.0019**

18	**0.428 ±0.0011**
20	**0.457 ±0.0014**

Graph No.5 Standard Graph 0f Mosapride in Acetate Buffer pH-4.0

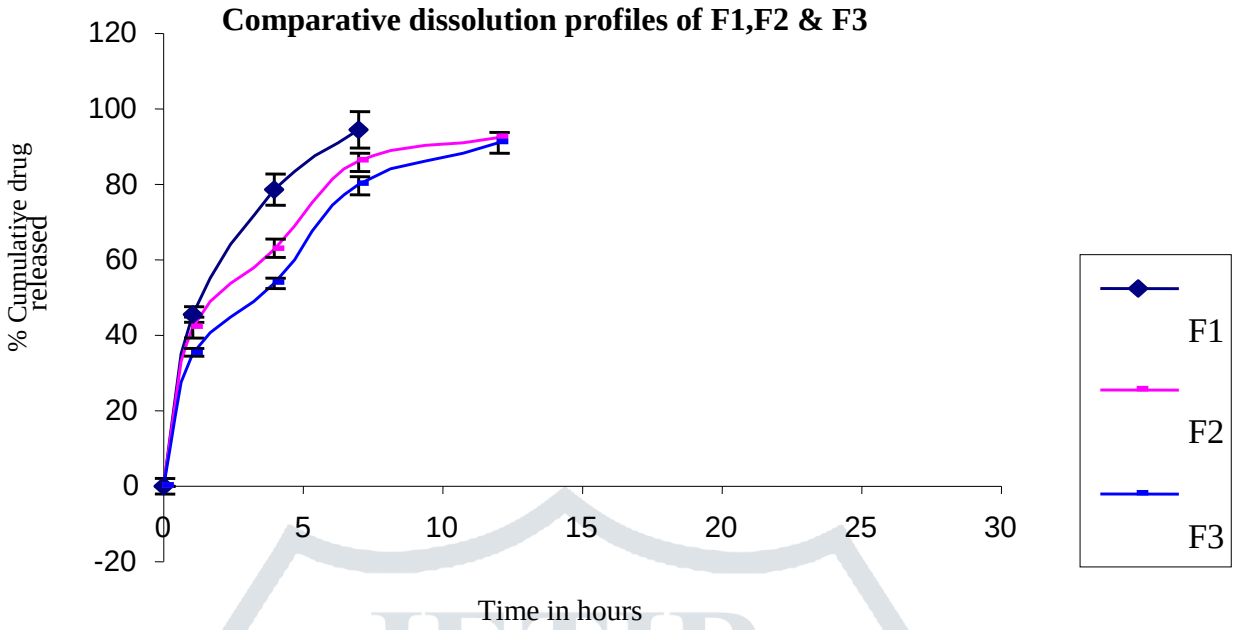


y= 0.0203x-0.003, (R^2=0.9944)

y = 0.0203x-0.003, (R^2= 0.9944)

Time (hrs)	*Average % drug release		
	F_1	F_2	F_3
	Mean % dissolution	Mean % dissolution	Mean % dissolution
0	00.00 ±0	00.00 ±0	00.00 ±0
1	45.60 ±2.97	42.20 ±2.39	35.30 ±2.65
4	78.70 ±2.37	63.00 ±2.88	53.70 ±1.90
7	94.60 ±2.39	86.10 ±2.46	79.70 ±0.76
12	--	92.40 ±2.38	91.20 ±3.43
16	--	--	--
24	--	--	--

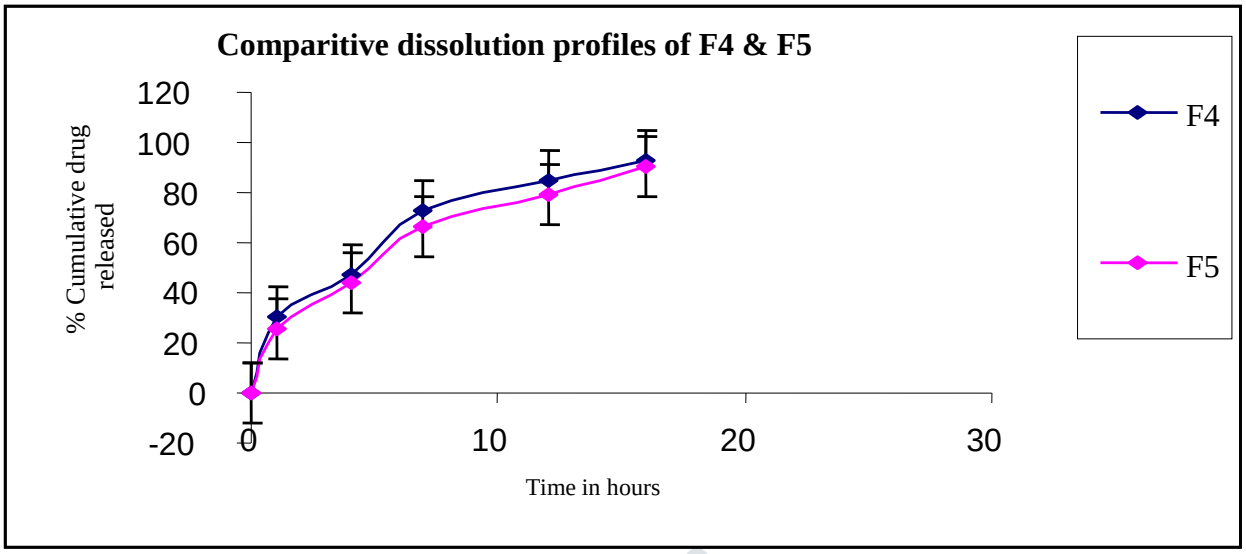
Table No -10 Dissolution Profiles of Formulation F_1, F_2 and F_3



Graph No.6

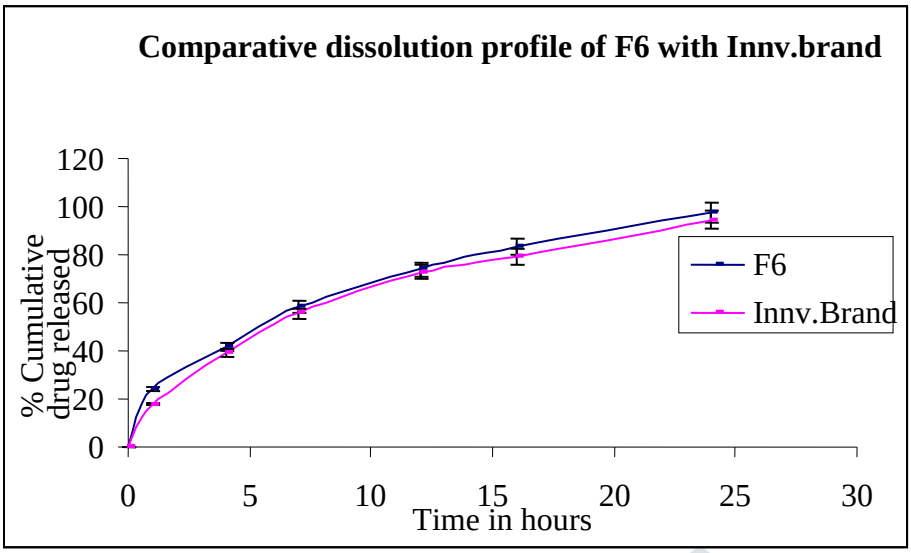
Table no.11 Dissolution Profiles of Formulation F_4 and F_5

Time (hrs)	*Average % drug release	
	F_4	F_5
	Mean % dissolution	Mean % dissolution
0	0.00 ±0	0.00 ±0
1	30.1 ±1.53	25.8 ±0.62
4	47.00 ±1.13	44.40 ±1.72
7	72.80 ±180	66.50 ±1.71
12	84.70 ±1.87	79.20 ±1.76
16	92.90 ±3.98	90.10 ±2.83
24	--	--



Graph No.7

Table no.12, Dissolution Profiles of Formulation F_6 and innov.brand

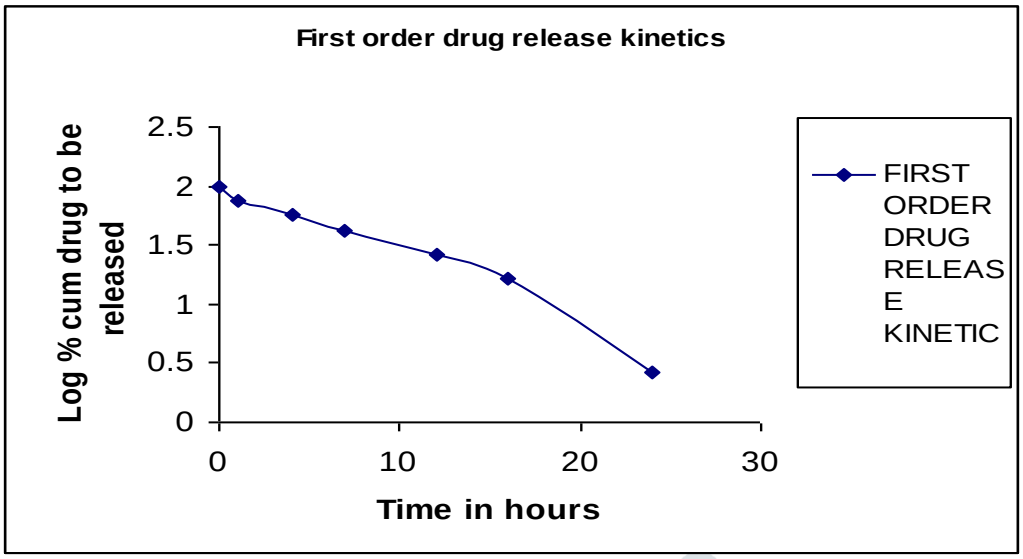


Graph No.8

- **Innovators brand.**

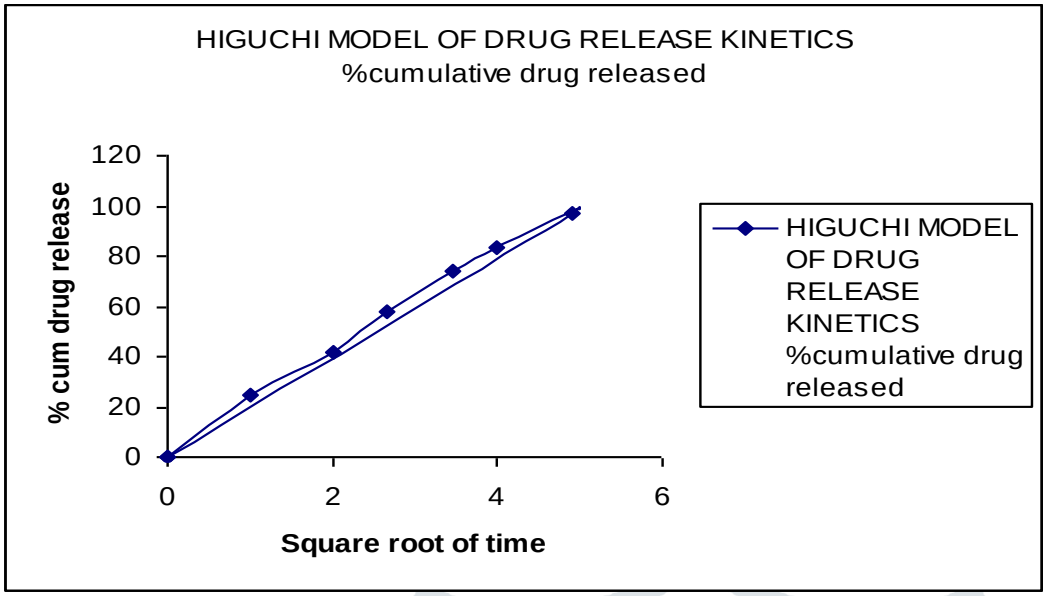
Table No.13 FIRST ORDER DRUG RELEASE KINETICS OF F_6

First Order Drug Release Kinetics	
Time(hrs)	log % cum drug remaining
0	2
1	1.87909588
4	1.764176132
7	1.621176282
12	1.413299764
16	1.217483944
24	0.414973348
corr. Co-efficient (R^2)	0.958313043



Graph No.9

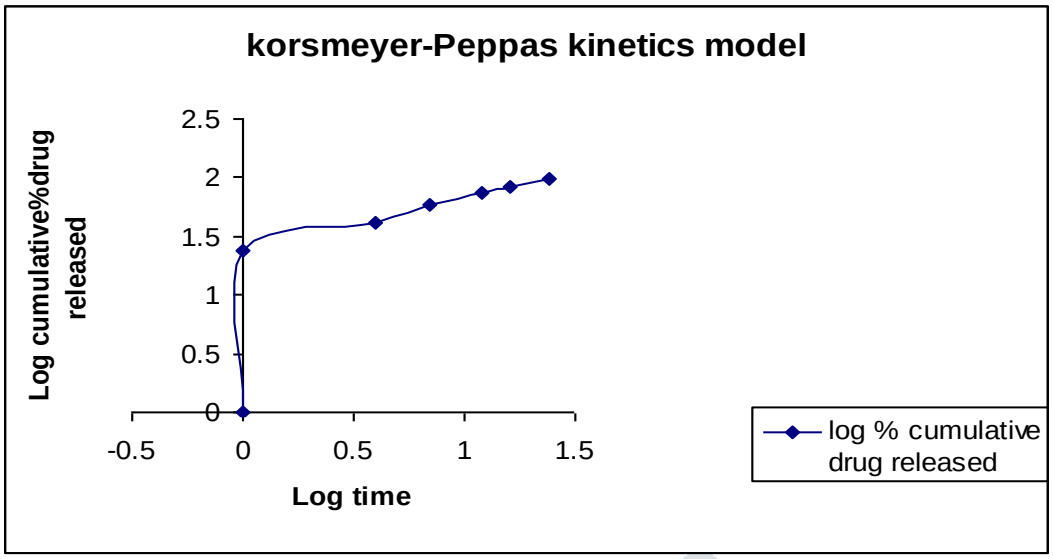
Table No.14 HIGUCHI MODEL OF DRUG RELEASE KINETICS FOR F_6



Graph No.10

Table no.15 KORSMEYER-PEPPAS RELEASE KINETICS OF F_6

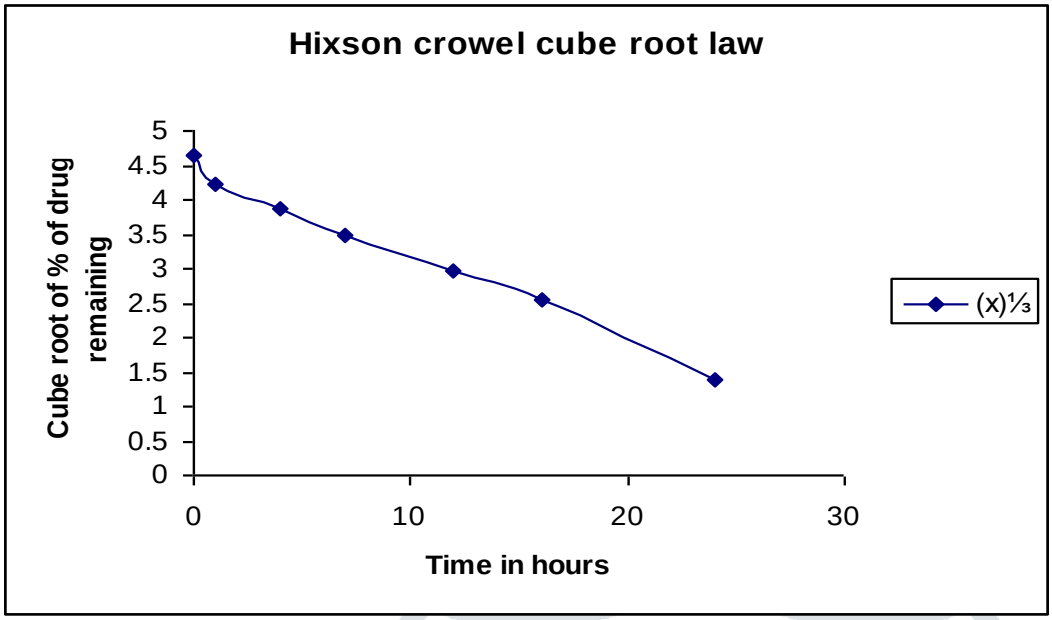
Korsmeyer-Peppas Drug Release Kinetics	
log T	log % cumulative drug released
0	1.385606274
0.602059991	1.622214023
0.84509804	1.764922985
1.079181246	1.869818208
1.204119983	1.921686475
1.380211242	1.988558957
corr. Co-efficient (R^2)	0.989525574
Release exponent(n)	0.447290872



Graph No.11

Table No.16 HIXON-CROWEL CUBE ROOT LAW OF F_6

Hixon-Crowel Cube Root Law	
Time(hrs)	$(x)^{1/3}$
0	4.641588834
1	4.230242783
4	3.873100005
7	3.470500361
12	2.958693117
16	2.545821685
24	1.375068867
corr. Co-efficient (R^2)	0.989804073



Graph No.12

4.0 RESULTS AND DISCUSSION

The FTIR study was carried out to know the compatibility of the excipients with mosapride citrate dihydrate, the active constituent of the formulation. The FTIR spectrum of pure mosapride citrate dihydrate, mixture of mosapride citrate dihydrate with HPMC K15M,HPMC K4M polymers and mixture of mosapride citrate dihydrate, HPMC K15M,HPMC K4M with. Lactose, talc, magnesium stearate, aerosil were analyzed for compatibility study. The study of FTIR spectrum confirms that the mosapride citrate dihydrate and excipients used in the formulation are compatible with each other.

The Sustained release Matrix tablets of mosapride citrate dihydrate were prepared by Dry granulation / roller compaction technique and Direct Compression Method. The angle of repose of the granules after slugging (dry granulation) was found to have 24° to 26°. The matrix tablets were compressed by applying optimum force of compression and the hardness of tablets was found to be in the range of 4.6 to 5.3kg/cm^2.

The flow property of the granules was good after slugging that was confirmed by the determination of angle of repose which indicates better uniformity of weight. Good hardness of the matrix tablets with less standard deviation indicated retardation in the release as observed in dissolution profile.

On performing the friability for all the formulations the % weight loss falls between the range 0.26% and 0.60% indicates that it falls within the limit showing good compressibility and non defective tabletting.

The Graph Numbers.2, 3, 4 showed the effect of different concentrations of HPMC K15M and HPMC K4M on release rate of Mosapride citrate dehydrates from matrix tablets of different formulations respectively.

By observing the dissolution data, it is clear that HPMC K4M retards the release of drug up to 12 hrs, so, to sustain the drug release for more than 12 hours concentration of HPMC with higher viscosity (HPMC K15M) was increased.

As observed in graph No. 4, the release of F_4 (HPMC K4M 16.98 % & HPMC K15M 15%.) sustained the release of the drug up to 16 hours(92.90 %) , which indicates that by increasing the concentration of HPMC K15M the drug release may be sustained more than 12 hours.

The formulation F_5 (20% w/w, HPMC K15M, 20% w/w HPMC K4M) showed the drug release 90.10% ± 0.25 for 16 hrs, so in order to increase the retardation of drug release the concentration HPMC K15M is increased. Formulation F_6 (24.70%HPMC K15M, 20 % HPMC K4M) 97.40% showed good dissolution profile compared to standard dissolution profile. The formulation F_6 best suited with first order release kinetics (corr. coefficient =0.958313043) than the zero order release kinetics (corr. Coefficient = 0.88082441). The formulation F_6 follows Higuchi model of drug release kinetics (corr. coefficient=0.99610457).The Hixon-crowel cube root law for F_6 (corr. coefficient=0.98980407).

The Koresmyer peppas drug release kinetics showed correlation coefficient (0.989525574) and release exponent (n) 0.449789453 which indicates that the drug release mechanism is fickanian diffusion.

5.0 SUMMARY AND CONCLUSION

The present study was carried out to develop sustained release matrix tablets of mosapride citrate dihydrate. Matrix tablets of mosapride citrate dihydrate with two different viscosity grades of hydroxypropyl methylcellulose were prepared by dry granulation and direct compression method and evaluated.

In first attempt of study, matrix tablets were prepared by using combination of hydroxypropyl methylcellulose (HPMC) of higher viscosity i.e. .HPMC K15M (10%) and lower viscosity grade HPMC K4M (10%). This formulation (i.e. F_1) failed to sustain the drug release for extended time and all most all the drug released in 7^{th} hours. For sustaining the drug release up to 24^{th} hours the percentage of HPMC K4M in F_2 increased but the formulation does not sustained the drug release more than 12^{th} hrs.

In formulation F_3 the percentage of HPMC K4M increased (i.e. 18.06%) and the tablets were evaluated for in vitro dissolution study. The formulation F_3 fails to sustain the release up to extended period of time. It clearly indicates that the lower viscosity grade of hydroxypropyl methylcellulose (HPMC K4M) is able to sustain the drug release up 12^{th} hours and for sustaining the drug release for extended period up to 24^{th} hours, percentage of higher viscosity grade of hydroxypropyl methylcellulose (HPMC K15M) must be increased. In Formulation F_4 (HPMC K4M 16.98%, HPMC K15M 15%) sustained the drug release up to 16^{th} hours so that in formulation F_5 the percentage of HPMC K15 increased along with HPMC K4M,formulation F_5 slowly released the drug, up to 16^{th} hours. The total drug release from formulation F_5 was (90.10%).

In formulation F_6, percentage of HPMC K15M was increased from 20% (in F_5) to 24.70% (in F_6) while the percentage of HPMC K4M was kept constant up to 20% and tablets of formulation F_6 were evaluated for in vitro dissolution study. The matrix tablets of formulation F_6 released the drug slowly as per standard dissolution profile up to 24^{th} hours and total drug release from matrix tablet of formulation F_6 at the end of 24^{th} hours was 97.40%.

Hence the above study demonstrated that combination of HPMC K4M and HPMC mosapride citrate dihydrate. This can be expected to reduce the frequency of administration and decrease the dose – dependent side effects associated with repeated administration of conventional mosapride citrate dihydrate tablets. The cumulative drug release of innovators brand (MOZA SR, Intas Pharmaceuticals) of sustained release tablet of mosapride citrate dihydrate were compaired for in vitro dissolution study.

The formulation F_6 matrix tablet releases the drug appropriately in comparison of innovators brand. The cumulative drug release at the end of 24th hours from formulation F_6 (97.40%) and the cumulative drug release at the end of 24th hours from innovators brand was (94.30%).

The in vitro drug release result indicates that formulation F_6 released more drug than innovators brand and hence more drug is available at the absorption site from formulation F_6 as compared to innovators brand, hence the formulation F_6 has better bioavailability than innovators brand of mosapride citrate dihydrate sustained release matrix tablet and also the sustained release matrix tablet was found to be beneficial in terms of reduction in frequency of administration.

Hence it can be concluded that once daily sustain release matrix tablet of mosapride citrate dihydrate having short half life, was found to exert a satisfactory sustained release profile which may provide an improved bioavailability, increased therapeutic efficacy and patient compliance.

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