International Journal of Pharmacy and Industrial Research (IJPIR)

ISSN: 2231-3656
Print: 2231-3648

IJPIR |Vol.13 | Issue 1 | Jan - Mar -2024
www.ijpir.com
DOI : https://doi.org/10.61096/ijpir.v13.iss1.2024.20-31

Research

Formulation And *In-Vitro* Evaluation Of Extended Release Tablets Of Metoclopromide Hcl Using Natural And Synthetic Polymers.

Mubashir Ahmed Awais[1*], D. Venkata Ramana[1], K. Sai Kiran[1], J. Pravalika[1]

[1]*Department of Pharmaceutics, Holy Mary Institute of Technology & Science (College of Pharmacy), Bogaram Village, Keesara Mandal, Hyderabad, Telangana, India*
*Author for Correspondence: Mubashir Ahmed Awais
Email: mubashirpharmacist786.com

Published on:14 Feb 2024

Published by:
DrSriram Publications

Abstract

The aim of the present study was to develop Metoclopramide HCl Controlled release tablets to maintain constant therapeutic levels of the drug for over 12 hrs. Xanthan gum, Guar gum, Carbopol 934 were used as polymers. All the formulations were passed various physicochemical evaluation parameters such as bulk density, tapped density, carrs index, hausners ratio, angle of repose, weight variation, hardness, thickness, friability and drug content. From the dissolution studies it was evident that the formulation F6 showed better and desired drug release pattern i.e., 98.10 % in 12 hours. It contains the Carbopol 934 as polymer. It followed zero order release kinetics mechanism.

Keywords: Metoclopramide, Xanthan gum, Guar gum, Carbopol 934 and Controlled release tablets.

INTRODUCTION

Historically, oral drug administration has been the predominant route for drug delivery. It is known to be the most popular route of drug administration due to the fact the gastrointestinal physiology offers more flexibility in dosage form design than most other routes. A major challenge for the pharmaceutical industry in drug development is to produce safe and efficient drugs, therefore properties of drugs and the way in which they are delivered must be optimized.(1)

A controlled release drug delivery system delivers the drug locally or systemically at a predetermined rate for a specified period of time. The goal of such systems is to provide desirable delivery profiles that can achieve therapeutic plasma levels. Drug release is dependent on polymer properties, thus the application of these properties can produce well characterised and reproducible dosage forms.(1)

Oral route still remains the most popular for drug administration by virtue of its convenience to the patient. A sizable portion of orally administered dosage forms, so called conventional, are designed to achieve maximal drug bioavailability by maximizing the rate and extent of absorption. While such dosage forms have been useful, frequent daily administration is necessary, particularly when the drug has a short biological half

life. This may result in wide fluctuation in peak and trough steady-state drug levels, which is undesirable for drugs with marginal therapeutic indices. Moreover, patient compliance is likely to be poor when patients need to take their medication three to four times daily on chronic basis. Fortunately, these short comings have been circumvented with the introduction of controlled release dosage forms. These dosage forms are capable of controlling the rate of drug delivery, leading to more sustained drug levels and hence therapeutic action.

Hydrophillic matrix systems are among the most commonly used means for oral controlled drug delivery as they can reproduce a desirable drug profile and are cost effective. The primary mechanism of drug release from hydrophilic matrices occurs when the polymer swells on contact with the aqueous medium to form a gel layer on the surface of the system. The drug then releases by dissolution, diffusion and/or erosion.[(1)]

TERMINOLOGY

A list of important terms that describe different modified release dosage forms are defined below.

Modified release dosage forms (MRDF): Defined as those dosage forms whose drug release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms.

Controlled release (CR): The drug is released at a constant (zero order) rate and the drug concentration obtained after administration is invariant with time.

Delayed release: The drug is released at a time other than immediately after administration.

Extended release (ER): Slow release of the drug so that plasma concentrations are maintained at a therapeutic level for a prolonged period of time (usually between 8 and 12 hours).

Prolonged release: The drug is provided for absorption over a longer period of time than from a conventional dosage form. However, there is an implication that onset is delayed because of an overall slower release rate from the dosage form.

Repeat action: Indicates that an individual dose is released fairly soon after administration, and second or third doses are subsequently released at intermittent intervals.

Sustained release (SR): The drug is released slowly at a rate governed by the delivery system.

ADVANTAGES OF CONTROLLED DRUG DELIVERY SYSTEM[(2,3,1,5,4)]

1) Reduction in frequency of drug administration.
2) Improved patient compliance.
3) Reduction in total drug usage when compared with the conventional therapy.
    i. Reduction in drug accumulation with chronic therapy.
    ii. Reduction in drug toxicity (local/systemic).
    iii. Obtain less potentiating or reduction in drug activity in chronic use.
4) Stabilization of medical condition (because of more uniform drug levels).
5) Improvement in bioavailability of some drugs because of spatial control.
6) Economical to the health care providers and the patient.
7) Improve efficiency in treatment.
    i. Cures or controls condition more promptly.
    ii. Improves control of condition i.e., reduced fluctuation in drug level.
    iii. Improves bioavailability of some drugs.
    iv. Make use of special effects, E.g. Sustained –release aspirin for morning relief of arthritis.
8) Economy i.e. reduction in health care costs. The average cost of treatment over an extended time period may be less, with less frequency of dosing, enhanced therapeutic benefits and reduced side effects. The time required for health care personnel to dispense and administer the drug and monitor patient is also reduced.

DISADVANTAGES OF THE DRUG DELIVERY SYSTEMS[(2,3,1,5,4)]

1. Decreased systemic availability in comparison to immediate release conventional dosage forms, which may be due to incomplete release, increased first-pass metabolism, increased instability, insufficient residence time for complete release, site specific absorption, pH dependent stability etc.
2. Possibility of dose dumping due to food, physiologic or formulation variables or chewing or grinding of oral formulations by the patient and thus, increased risk of toxicity.
3. Retrieval of drug is difficult in case of toxicity, poisoning or hypersensitivity reactions.
4. Reduced potential for dosage adjustment of drugs normally administered in varying strengths.
5. Stability problems.
6. Increased cost & Poor *in vitro – in vivo* correlation.
7. More rapid development of tolerance and counseling.
8. Need for additional patient education and counseling.
9. Release rate: The drug release rate can be altered by food and gastric transit time; as a result differences may arise in the release rate between doses.

10. Cannot crush or chew products: Controlled release products should not be crushed or chewed as it can lead to loss of the 'slow release' characteristics as well as toxicity.

MATERIALS AND METHODS

Metoclopromide HCl,SURA LABS,Xanthan gum,Merck Specialities Pvt Ltd, Mumbai, India, Guar gum,Merck Specialities Pvt Ltd, Mumbai, India, Carbopol 934,Merck Specialities Pvt Ltd, Mumbai, India, MCC pH 102 , Merck Specialities Pvt Ltd, Mumbai, India, Magnesium stearate ,Merck Specialities Pvt Ltd, Mumbai, India, Talc, Merck Specialities Pvt Ltd, Mumbai, India.

METHODOLOGY

Analytical method development

Determination of Wavelength

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution again 1ml was taken it in to another volumetric flask and made it up to 10 ml with media (working solution - 10µg/ml). The working solution was taken for determining the wavelength.

Determination of Calibration Curve

10mg of pure drug was dissolved in 10ml methanol (primary stock solution - 1000 µg/ml). From this primary stock solution 1 ml was pipette out into 10 ml volumetric flask and made it up to 10ml with the media (Secondary stock solution – 100µg/ml). From secondary stock solution required concentrations were prepared (shown in Table 8.1 and 8.2) and those concentrations absorbance were found out at required wavelength.

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany(Alpha T).The solid powder sample directly place on yellow crystal which was made up of ZnSe. The spectra were recorded over the wave number of 4000 cm^{-1} to 400cm^{-1}.

Preformulation parameters

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose

The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend was carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

$\tan \theta = h / r$ $\tan \theta$ = Angle of repose

h = Height of the cone, r = Radius of the cone base

Table 1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density

Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size

distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume, Vo, was read.

The bulk density was calculated using the formula:

$$\text{Bulk Density} = M / V_o$$

Where, M = weight of sample

V_o = apparent volume of powder

Tapped density

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2 % and then tapped volume, V measured, to the nearest graduated unit. The tapped density was calculated, in gm per L, using the formula:

$$Tap = M / V$$

Where, Tap = Tapped Density

M = Weight of sample

V = Tapped volume of powder

Measures of powder compressibility

The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of interparticulate interactions. In a free- flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:

$$\text{Carr's Index} = [(tap - b) / tap] \times 100$$

Where, b = Bulk Density

Tap = Tapped Density

Formulation development of Tablets

All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 7.3.The tablets were prepared as per the procedure given below and aim is to prolong the release of Metoclopramide. Total weight of the tablet was considered as 100mg.

Procedure

1) Metoclopramide and all other ingredients were individually passed through sieve no ≠ 60.
2) All the ingredients were mixed thoroughly by triturating up to 15 min.
3) The powder mixture was lubricated with talc.
4) The tablets were prepared by using direct compression method.

Table 2: Formulation composition for tablets

Formulation No.	Metaclopromide	Xanthan gum	Carbopol 934	Guar gum	Mag. Stearate	Talc	MCC pH 102
F1	10	10	-	-	2	2	QS
F2	10	20	-	-	2	2	QS
F3	10	30	-	-	2	2	QS
F4	10	-	10	-	2	2	QS
F5	10	-	20	-	2	2	QS
F6	10	-	30	-	2	2	QS
F7	10	-	-	10	2	2	QS
F8	10	-	-	20	2	2	QS
F9	10	-	-	30	2	2	QS

All the quantities were in mg

RESULTS & DISCUSSION

The present study was aimed to developing Controlled release tablets of Metoclopramide HCl using various polymers. All the formulations were evaluated for physicochemical properties and *in-vitro* drug release studies.

Analytical Method

Graphs of Metoclopramide HCl were taken in 0.1N HCl and in pH 6.8 phosphate buffer at 302 nm and 307 nm respectively.

Table 3: Observations for graph of Metoclopramide HCl in 0.1N HCl (302 nm)

Conc [µg/ml]	Absorbance
0	0
5	0.114
10	0.225
15	0.312
20	0.411
25	0.513

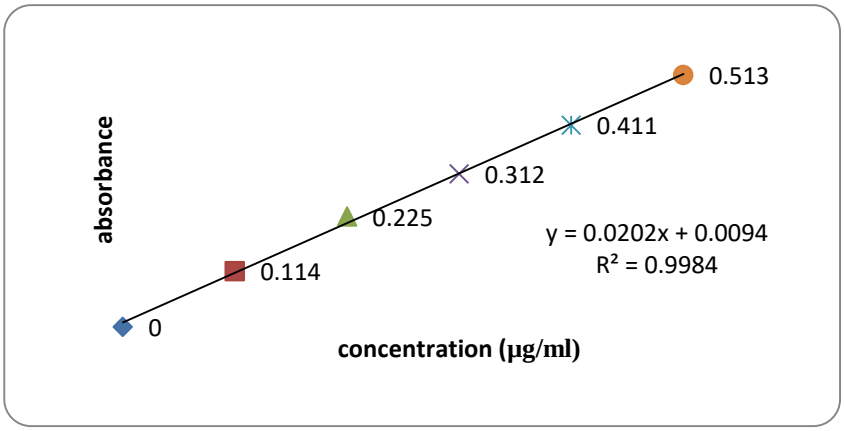

Fig 1: Standard graph of Metoclopramide HCl in 0.1N HCl

Table 4: Observations for graph of Metoclopramide HCl in pH 6.8 phosphate buffer (307nm)

Concentration [µg/ml]	Absorbance
0	0
5	0.148
10	0.275
15	0.425
20	0.576
25	0.712

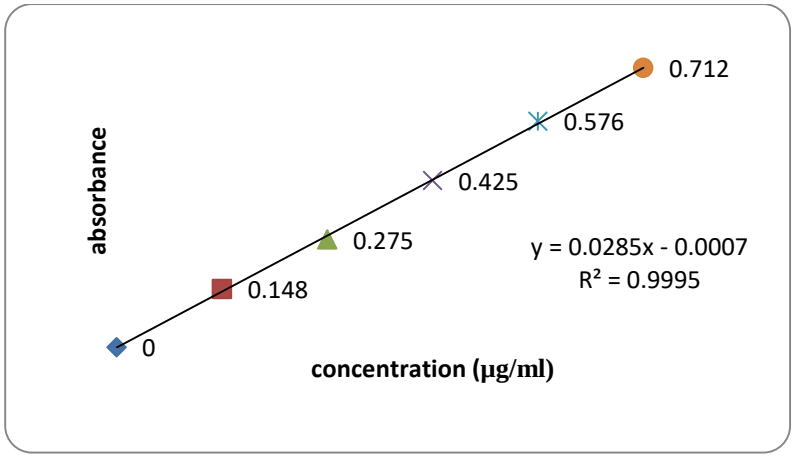

Fig 2 : Standard graph of Metoclopramide HCl pH 6.8 phosphate buffer (307nm)

Drug – Excipient compatability studies
Fourier Transform-Infrared Spectroscopy

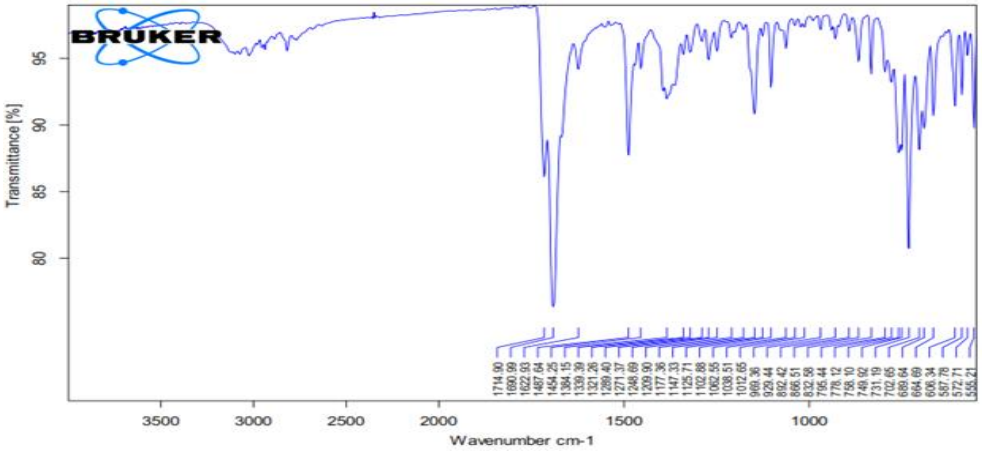

Fig 3: FT-TR Spectrum of Metoclopramide HCl pure drug.

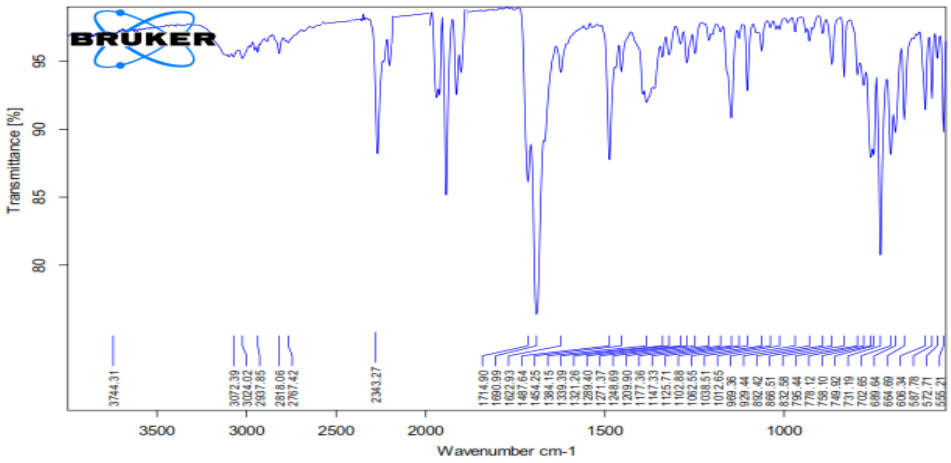

Fig 4: FT-IR Spectrum of Optimised Formulation

Preformulation parameters of powder blend

Table 5: 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	25.11±0.91	0.53±0.04	0.56±0.06	17.65±0.09	1.06±0.09
F2	25.67±1.02	0.58±0.06	0.67±0.02	17.97±0.02	1.15±0.09
F3	25.54±0.84	0.49±0.04	0.54±0.04	16.21±0.06	1.10±0.06
F4	25.43±0.93	0.42±0.09	0.52±0.04	16.87±0.05	1.23±0.05
F5	25.34±1.09	0.47±0.03	0.57±0.03	16.92±0.04	1.2±0.08
F6	24.22±1.31	0.50±0.05	0.58±0.05	17.11±0.01	1.16±0.03
F7	25.18±0.94	0.49±0.06	0.59±0.04	16.43±0.05	1.2±0.03
F8	24.22±0.74	0.51±0.06	0.59±0.07	17.67±0.08	1.15±0.04
F9	25.05±0.81	0.45±0.08	0.52±0.03	17.54±0.09	1.15±0.02

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.42±0.07 to 0.58±0.06 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.52±0.04 to 0.67±0.02 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 18 which show that the powder has good flow properties. All the formulations has shown the hausner ratio below 1.25 indicating the powder has good flow properties.

Quality Control Parameters For 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.

Table 6: *In-vitro* quality control parameters

Formulation codes	Weight variation(mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	102.6±1.13	2.5±0.02	0.57±0.05	2.48±0.07	98.69±0.15
F2	98.6±1.53	2.5±0.04	0.61±0.05	2.39±0.02	99.45±0.24
F3	101.6±1.15	2.4±0.05	0.67±0.04	2.62±0.02	98.34±0.042
F4	100.6±0.85	2.5±0.02	0.75±0.06	2.42±0.04	99.87±0.25
F5	99.4±1.52	2.4±0.05	0.66±0.07	2.65±0.05	99.74±0.31
F6	96.7±1.31	2.5±0.021	0.55±0.08	2.47±0.01	101.56±0.41
F7	98.3±1.24	2.5±0.36	0.61±0.02	2.34±0.06	99.42±0.52
F8	101.2±2.03	2.4±0.04	0.59±0.08	2.67±0.08	99.89±0.36
F9	98.3±0.95	2.5±0.06	0.65±0.06	2.56±0.05	100.94±0.16

Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 8.4. The average weight of the tablet is approximately in range of 96.7±1.31 to 102.6±1.13 mg, so the permissible limit is ±7.5% (>250 mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit.

Hardness test

Hardness of the three tablets of each batch was checked by using Pfizer hardness tester and the data's were shown in Table 8.4. The results showed that the hardness of the tablets is in range of 2 to 2.5 kg/cm^2, which was within IP limits.

Thickness

Thickness of three tablets of each batch was checked by using Micrometer and data shown in Table-8.4. The result showed that thickness of the tablet is raging from 2.34±0.06 to 2.67±0.08 mm.

Friability

Tablets of each batch were evaluated for percentage friability and the data were shown in the Table 8.4. The average friability of all the formulations was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Drug content

Drug content studies were performed for the prepared formulations. From the drug content studies it was concluded that all the formulations were showing the % drug content values within 98.34±0.042 - 101.56±0.41 %.

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

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

Table 7: Dissolution Data of Metoclopramide HCl Tablets Prepared with Xanthan gum

TIME	CUMULATIVE PERCENT DRUG DISSOLVED		
(hr)	F1	F2	F3
0	0	0	0
0.5	26.5	23.1	17.4
1	48.7	34.4	25.7
2	7645	48.3	33.6
3	99.4	55.3	42.4
4		67.3	51.4
5		80.4	58.4
6		98.34	66.4
7			72.5
8			83.3
9			90.45
10			100.21
11			
12			

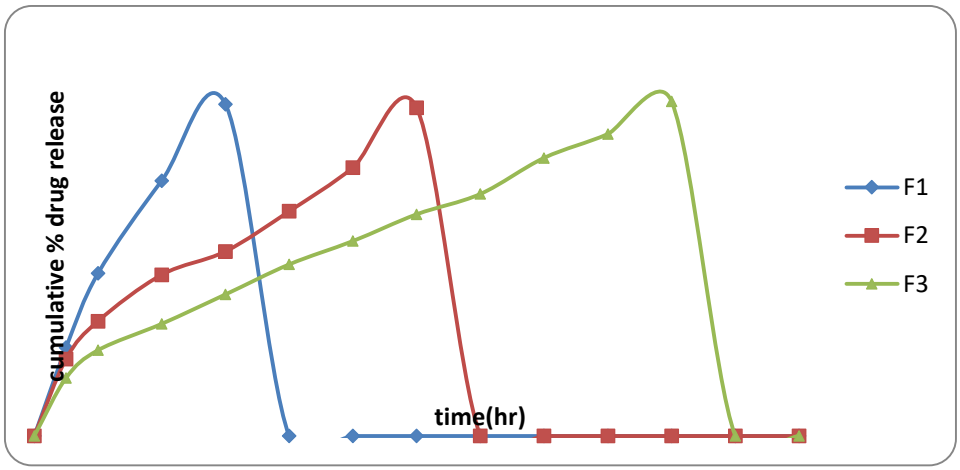

Fig 5: Dissolution profile of Metoclopramide HCl (F1, F2, F3 formulations).

Table 8: Dissolution Data of Metoclopramide HCl Tablets Prepared With Carbopol 934

TIME	CUMULATIVE PERCENT DRUG DISSOLVED		
(hr)	F4	F5	F6
0	0	0	0
0.5	20.25	15.42	14.62
1	37.26	24.73	19.86
2	52.16	39.63	25.35
3	68.01	48.04	30.45
4	88.26	57.25	39.8
5	97.1	66.33	47.25
6		70.41	58.24
7		85.84	65.73
8		99.8	71.34
9			77.52

10	80.17
11	89.1
12	98.1

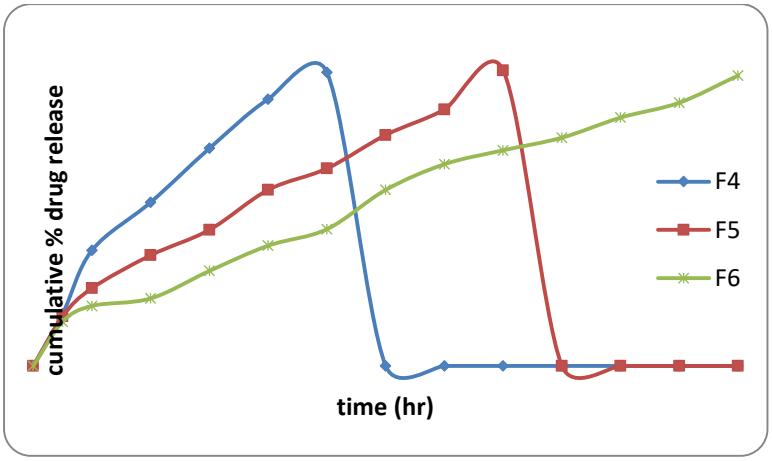

Fig 6: Dissolution profile of Metoclopramide HCl (F4, F5, F6 formulations)

Table 9: Dissolution Data of Metoclopramide HCl Tablets Prepared With Guar gum

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED		
	F7	F8	F9
0	0	0	0
0.5	30.4	27.4	24.5
1	46.5	35.6	32.5
2	68.6	41.4	38.4
3	79.5	56.7	43.4
4	88.5	62.4	48.2
5		79.6	54.8
6		85.3	60.2
7		97.3	68.8
8			75.4
9			83.34
10			98.27
11			
12			

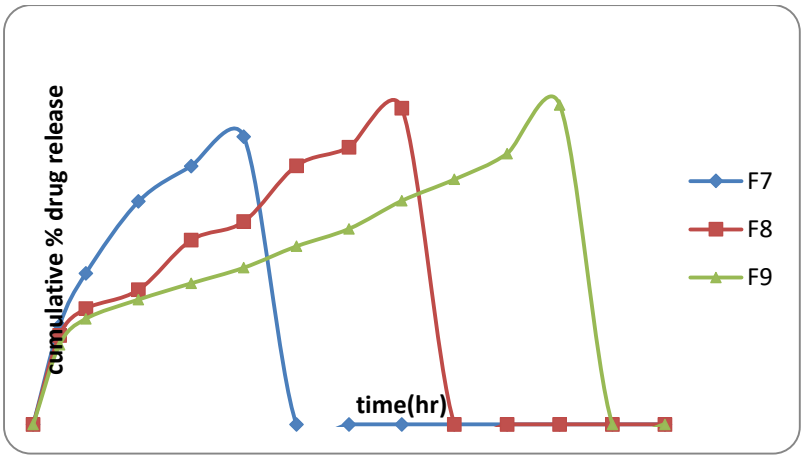

Fig 7: Dissolution profile of Metoclopramide HCl (F7, F8, F9 formulations)

From the dissolution data it was evident that the formulations prepared with Xanthan gum as polymer were unable to retard the drug release up to desired time period i.e., 12 hours.

Formulations prepared with Carbopol 934 retarded the drug release in the concentration of 30 mg (F6 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 98.10% in 12 hours with good retardation.

The formulations prepared with Guar gum were unable to retard up to 12 hours. Hence they were not considered.

Application of Release Rate Kinetics to Dissolution Data

Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Table 10: Release kinetics data for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE/t)	1/CUM% RELEASE
0	0	0			2.000		
14.62	0.5	0.707	1.165	-0.301	1.931	29.240	0.0684
19.86	1	1.000	1.298	0.000	1.904	19.860	0.0504
25.35	2	1.414	1.404	0.301	1.873	12.675	0.0394
30.45	3	1.732	1.484	0.477	1.842	10.150	0.0328
39.8	4	2.000	1.600	0.602	1.780	9.950	0.0251
47.25	5	2.236	1.674	0.699	1.722	9.450	0.0212
58.24	6	2.449	1.765	0.778	1.621	9.707	0.0172
65.73	7	2.646	1.818	0.845	1.535	9.390	0.0152
71.34	8	2.828	1.853	0.903	1.457	8.918	0.0140
77.52	9	3.000	1.889	0.954	1.352	8.613	0.0129
80.17	10	3.162	1.904	1.000	1.297	8.017	0.0125
89.1	11	3.317	1.950	1.041	1.037	8.100	0.0112
98.1	12	3.464	1.992	1.079	0.279	8.175	0.0102

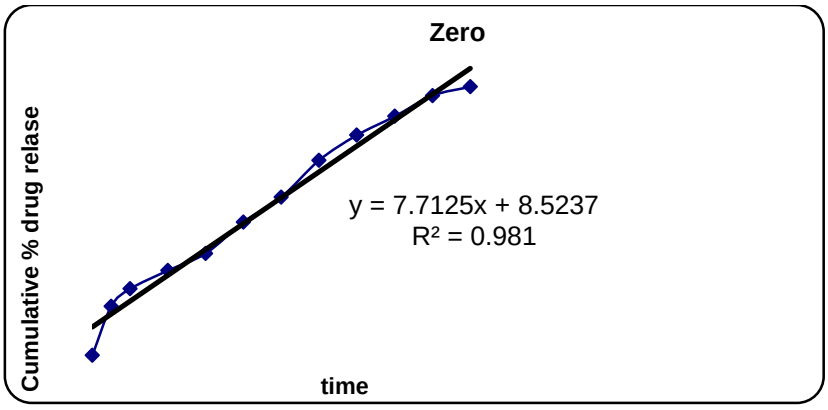

Fig 8: Zero order release kinetics graph

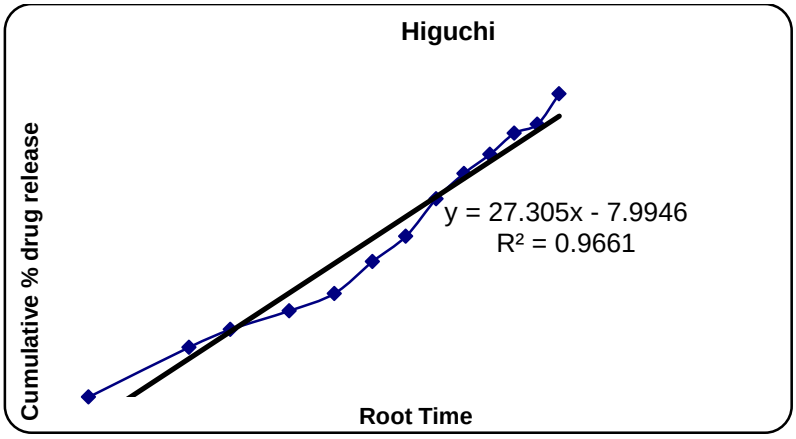

Fig 9: Higuchi release kinetics graph

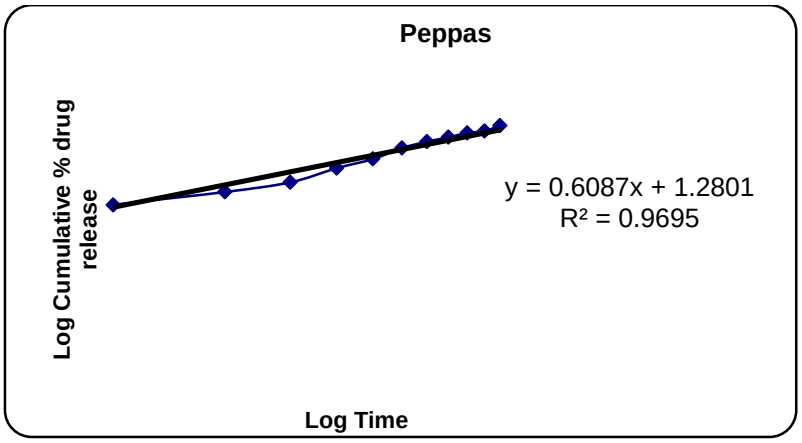

Fig 10: Kars mayer peppas graph

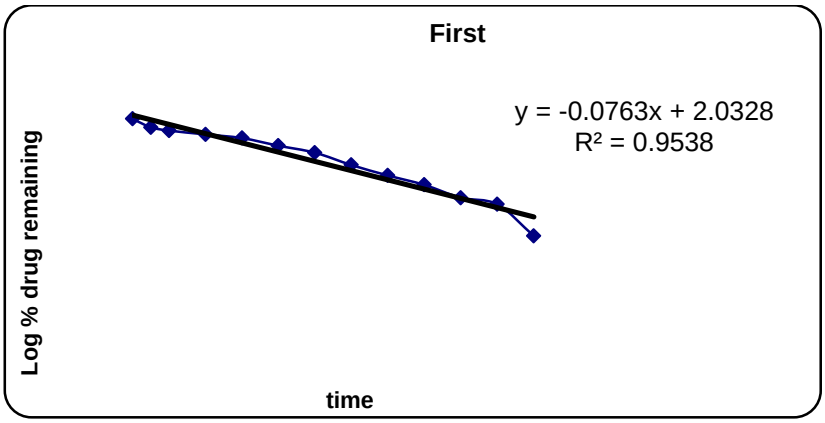

Fig 11: First order release kinetics graph

From the above graphs it was evident that the formulation F6 was followed Zero order release kinetics.

CONCLUSION

The present study was carried out on metoclopramide HCl. It has half life about 5-6 hrs. The main aim of this study is to extend the drug release up to 12 hrs. Drug wavelength and calibration curve was developed in 0.1N HCl and pH 6.8 Phosphate buffer. The drug and excipient compatability studies were shown good compatability between drug and excipients. Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk

density of all the formulations was found to be in the range of 0.42±0.07 to 0.58±0.06 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.52±0.04 to 0.67±0.02 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 18 which show that the powder has good flow properties. All the formulations has shown the hausner ratio below 1.25 indicating the powder has good flow properties.

Post compression studies like Weight variation, Hardness, thickness, friability, drug content was determined. The average weight of the tablet is approximately in range of 96.7±1.31 to 102.6±1.13 mg, so the permissible limit is ±7.5% (>250 mg). The results showed that the hardness of the tablets is in range of 2 to 2.5 kg/cm^2, which was within IP limits. The result showed that thickness of the tablet is raging from 2.34±0.06 to 2.67±0.08 mm. The average friability of all the formulations was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets. From the drug content studies it was concluded that all the formulations were showing the % drug content values within 98.34 - 101.56%.

From the dissolution data it was evident that the formulations prepared with Xanthan gum as polymer were unable to retard the drug release up to desired time period i.e., 12 hours. Formulations prepared with Carbopol 934 retarded the drug release in the concentration of 30 mg (F6 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 98.10% in 12 hours with good retardation. The formulations prepared with Guar gum were unable to retard up to 12 hours. Hence they were not considered.

BIBLIOGRAPHY

1. Nokhodchi, Shaista Raja, Priya Patel, Kofi Asare-Addo. The Role Of Oral Controlled Release Matrix Tablets In Drug Delivery Systems. Bioimpacts. 2012; 2(4):175-187.
2. Aravind Singh Rathore, Jat RC, Narendra Sharma, Rahul Tiwari. An Overview: Matrix Tablet As Controlled Drug Delivery System. International Journal Of Research And Develoment In Pharmacy And Life Sciences. 2013;2(4):482-492.
3. Bhalla Neetika, Deep Arsh, Goswami Manish. An Overview On Various Approaches To Oral Controlled Drug Delivery System Via Gastoretentive Drug Delivery System. Int. Res. J. Pharm. 2012; 3(4):128-133.
4. Maggi L, Bruni R, Conte U. High Molecular Weight Polyethylene Oxides As An Alternative To HPMC Controlled Release Dosage Forms. Int. J. Pharm. 2000:195(1-2);229-38.
5. Vyas SP, Khar RK. Controlled Drug Delivery Concepts and Advances. CBS Publishers, 2001;1st:1-53.
6. Ronald A Siegel, Michael J Rathbone. Departments Of Pharmaceutics And Biomedical Engineering: Chapter 2: Overview Of Controlled release mechanisms. Minnepolis. 2012:19-43.
7. Bramhanker DM, Jaiswal SB. Controlled Release Medications. Biopharmaceutics And Pharmacokinetics a Treatise. Vallabh Prakashan, 1995;2nd:335-375.
8. Harnish Patel, Dhrupesh R. Panchal, Upendra Patel, Tushar Brahmbhatt, Mayur suthar. Matrix Type Drug Delivery System: A Review. Journal of pharmaceutical science and bioscientific research. 2011: 1(3);143-151.
9. Jadhav AS, Tarkase KN. Formulation Aspects With An Comparative Influence Of Different Parameters Over Matrix Tablet. International Journal Of Pharmaceutical Review And Research. 2012: 3(2);33-42.
10. Mahesh Hemnani, Upendra Patel, Ghanshyam Patel, Dhiren Daslaniya, Amarish Shah. Matrix tablets: A Tool Of Controlled Drug Delivery. American Journal Of Pharmatech Research. 2011: 1(4);2249-3387..
11. Ranjith Kumar Mamidala, Vamshi Ramana, Sandeep G, Meka Lingam, Ramesh Gannu, Madhusudan Rao Yamsani. Factors Influencing The Design And Performance Of Oral Sustained/ Controlled Release Dosage Forms. International Journal Of Pharmaceutical Sciences And Nanotechnology. 3(2);583-594:2009.
12. Steve I shen, Bhaskara R. Jasti, Xiaoling Li. Standard Handbook Of Biomedical Engineering And Design: Chapter 22- Design Of Controlled- Release Drug Delivery Systems. Mc Graw-Hill. 2004;1-14.
13. Chien YW, Controlled Drug Delivery Systems. Novel Drug Delivery Systems, Marcel Dekker, 1992; 2nd: 139-196.
14. Robinson J R,Jantzen G M. Controlled-Release Drug Delivery Systems-Fundamentals And Applications. Marcell Dekker, 1995: 2nd; 575-609.
15. Sunilkamboj.Matrix Tablets- An Important Tool For Oral Controlled Release Dosage Forms. Pharma.Info. 2009: 23-25; 1-29.