World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Check for updates

Formulation and evaluation of extended-release tablets of trimetazidine HCL

Penabaka Venugopalaiah, KP Benidicts Prem Prakash *, Yerikala Ramesh and M Alagusundaram

Department of Pharmaceutics, Ratnam Institute of Pharmacy, Pidathapolur (V), Muthukur (M), SPSR Nellore -524 346, Andhra Pradesh, India.

World Journal of Advanced Research and Reviews, 2023, 18(03), 993–1002

Publication history: Received on 16 April 2023; revised on 26 May 2023; accepted on 28 May 2023

Article DOI: https://doi.org/10.30574/wjarr.2023.18.3.1003

Abstract

The present study was undertaken with an aim to formulate develop and evaluate Trimetazidine HCL extended release matrix tablets using different polymers as release retarding agent. Pre formulation study was done initially and results directed for the further course of formulation. Based on Pre formulation studies different batches of Trimetazidine HCL were prepared using selected excipients. Powders were evaluated for tests Angle of repose, Bulk density, tapped density, compressibility index, and Hausner ratio before being punched as tablets. It was concluded that the tablets of batch F9 had considerable swelling behaviors and in vitro drug release. Percentage drug release in 8 hr is 80.77. It was observed that tablets of batch F9 followed the Huguchi release profiles. From the results and discussion it is concluded that formulation of Extended release matrix tablet of HCL containing HPMC K-15 (19.44%) and Hyper mellose (19.44%), Ethyl cellulose (19.44%) batch F9 can be taken as an ideal or optimized formulation Extended release matrix tablet for 8 hour release as it fulfills the requirements for extended release matrix tablet.

Keywords: Trimetazidine HCL; HPMC K-15; Hypermellose; Ethyl cellulose

1. Introduction

Oral route of drug administration is oldest and safest mode of drug administration. It does not possess the sterility problem and minimal risk of damage at the site of administration. It provides accurate dosing without assistantship of administration. In conventional oral drug delivery system, there is little or no control over release of drug, and effective concentration at the target site can be achieved by administration of grossly excessive dosage form [1]. This kind of dosing pattern result in constantly changing, unpredictable and often sub or supra therapeutic plasma concentration, leading to marked side effects in some cases. Moreover, the rate and extent of absorption from conventional formulation may vary greatly, depending on factor such as physiochemical properties of drug, presence of excipients, various physiological factors such as presence or absence of food, pH of gastrointestinal tract, G.I. motility etc. Diffusion systems are characterized by the release rate of a drug being dependent on its diffusion through an inert membrane barrier, which is usually a water-insoluble polymer. In general, two types or subclasses of diffusion systems are recognized: reservoir devices and matrix devices [2].

Since a controlled-release system is designed to alleviate repetitive dosing, it is naturally contained greater amount of drug that a corresponding conventional dosage form. For lose drugs requiring large conventional doses, the volume of sustained dose may be so large so to be impractical or unacceptable, depending on the route of administration. The same may be true for drugs that require a large release rate from the controlled-release system, e.g., drugs with shorter half-life. For oral route, the volume of the product is limited by patient acceptance [3].

*Corresponding author: KP Benidicts Prem Prakash

2. Material and methods

Trimetazidine HCL, Ethyl Cellulose, Metalose, Hydroxy propyl methyl cellulose K-15CR, Lactose, M.C.C, P.V.P.K.30, Magnesium stearate, Talc, Pre gelatinised Starch, HCL, and Iso propyl alcohol.

2.1. Formulation of Trimetazidine HCL Matrix Tablets

Each quantity mentioned will be taken in mgs, total weight of the tablet = 180mg, Each tablet contains = 35mg of the Trimetazidine HCL [Table 1]

Table 1 Formulation of Trimetazidine HCL Matrix Tablets

Ingredients	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Trimetazidine Hcl	35	35	35	35	35	35	35	35	35
Metalose	35	52.5	70	-----	-----	-----	35	35	35
HPMC K15CR	-----	-----	-----	35	52.5	70	8.75	17.5	35
Ethyl Cellulose	7	7	7	7	7	7	7	7	7
Pre gelatinised Starch	27	27	27	27	27	27	27	27	27
Micro crystalline Cellulose	18	18	18	18	18	18	18	18	18
Lactose	44	26.5	9	44	26.5	9	35.25	26.5	9
P.V.P.K.30	7	7	7	7	7	7	7	7	7
I.P.A.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Aerosil	1	1	1	1	1	1	1	1	1
Talc	3	3	3	3	3	3	3	3	3
Mg. Stearate	3	3	3	3	3	3	3	3	3

2.2. Identification of drug (Trimetazidine HCL) sample

2.2.1. FTIR Spectra

IR spectra of drug in KBr pellets at moderate scanning speed between 4000-400 cm^{-1} was carried out using FTIR (Jasco FTIR 6100 type A). The peak values (Wave number) and the possibility of functional group shown in spectra which compare with standard value [4]. The comparison of these results with Trimetazidine [4]. HCL chemical structure shows that the sample was pure Trimetazidine HCL.

2.3. Evaluation of Powder and Granules

2.3.1. Angle of repose

Flow ability of different batch of granules was determined by calculating angle of repose by fixed height method. A funnel with 10 mm inner diameter of stem was fixed at a height of 2 cm. over the platform. About 10 gm of sample was slowly passed along the wall of the funnel till the tip of the pile formed and touches the steam of the funnel. A rough circle was drawn around the pile base and the radius of the powder cone was measured [5].

Angle of repose was calculated from the average radius using the following

formula.

$$\tan\theta = (h/r)$$

Where, θ = Angle of repose, h = Height of the pile, r = Average radius of the powder cone.

2.3.2. Bulk density and Tapped density

An accurately weighed quantity of the powder (W) was carefully poured into the graduated cylinder and the volume (v_o) was measured then the graduated cylinder was closed with lid, set into the density determination apparatus (bulk density apparatus, electro lab, Mumbai). The density apparatus was set for 500 taps and after that, the volume (V_f) was measured and continued operation till the two consecutive readings were equal [6]. The bulk density, and tapped density were calculated using the following formulas.

$$\text{Bulk density} = W/V_o$$

$$\text{Tapped density} = W/V_f$$

Where,

V_o = initial volume

V_f = final volume.

2.3.3. Compressibility index

The Compressibility index and Hausner ratio are measures of the propensity of a powder to be compressed. As such, they are measures of the relative importance of inter particulate 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 inter particle interactions, and a greater difference between the bulk and tapped densities will be observed [7]. These differences are reflected in the Compressibility Index and the Hausner Ratio.

2.3.4. Hausner Ratio

It provides an indication of the degree of densification which could result from vibration of the feed hopper [8].

2.4. Coating procedure

Weigh accurately H.P.M.C 6 CP and Ethyl Cellulose and mixed in half portion of I.P.A. Dissolve titanium oxide, yellow iron oxide, talc in half portion of I.P.A. mix well half portion of Methylene chloride was added in above solution [9]. Dissolve PEG 6000 in half portion of methylene chloride and added to above solution and stirred well [Table 2].

Table 2 Coating Formula

Ingredients	**Quantity**
H.P.M.C. 6 cp	5 mg
Ethyl Cellulose	0.5 mg
Polyethylene Glycol	1 mg
Titanium Dioxide	1 mg
Yellow Iron Oxide	0.5 mg
Talcum	1 mg
I.P.A.	0.15 ml
Methylene Chloride	0.2 ml

2.5. Evaluation of Tablets

2.5.1. Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weights deviate from the average weight [10].

2.5.2. Thickness

Twenty tablets were randomly selected from each batch and there thickness and diameter was measured by using digital vernier caliper [11].

2.5.3. Tablet Hardness

The crushing strength Kg/cm^2 of prepared tablets was determined for 10 tablets of each batch by using Monsanto tablet hardness tester. The average hardness and standard deviation was determined [12].

2.5.4. Friability

Twenty tablets were weighed and placed in the Electro lab friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were dedusted and weighed again [13]. The percentage friability was measured using the formula,

$$\% F = \{1-(W_t/W)\} \times 100$$

Where,

$\% F$ = friability in percentage

W = Initial weight of tablet

W_t = weight of tablets after revolution

2.6. *In Vitro* Dissolution Studies

In Vitro dissolution study was carried out using USP II apparatus (paddle apparatus) in 900ml of phosphate buffer pH 6.8 for 8 hours. The temperature of the dissolution medium was kept at 37± 0.5°C and the paddle was set at 100 rpm. 10 ml of sample solution was withdrawn at specified interval of time. The absorbance of the withdrawn samples was measured at λ_{max} 269nm using UV visible spectrophotometer. The concentration was determined from the standard curve of Trimetazidine HCL prepared in phosphate buffer pH 6.8 at λ max 269nm. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve [14].

2.7. Swelling Index

The swelling index of tablets was determined in phosphate buffer pH 6.8 at room temperature [15]. The swollen weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation:

$$\text{Swelling index WU} = \frac{(W_1 - W_0)}{W_0} \times 10$$

Where,

W_t = Weight of tablet at time t.

W_0 = Initial weight of tablet

2.8. Modeling of Dissolution Profiles

In vitro dissolution has been recognized as an important element in drug development under certain assessment of Bioequivalence. Several theories/kinetics models describe drug dissolution from immediate and modified release dosage forms. There are several models to represent the drug dissolution profiles where f_t is a function of 't' (time) related to the amount of drug dissolved form the pharmaceutical dosage system. Whenever a new solid dosage form is developed or produced, the drug release/dissolution from solid pharmaceutical dosage form is necessary to ensure that the drug dissolution occurs in an appropriate manner. The quantitative interpretation of the value obtained from the dissolution assay is facilitated by mathematical equation which translates the dissolution curve in function of some parameters related with the pharmaceutical dosage forms [16].

In the present study, data of the *in vitro* release were fitted to different equations and kinetic models to explain the release kinetics of Trimetazidine HCL from the matrix tablets. The kinetic models used were a Zero order equation, Higuchi release.

2.9. Drug release models

To describe the kinetics of the drug release from the matrix tablet batches, mathematical models such as zero-order, first order, Higuchi, Hixon crowell models were used. The criterion for selecting the most appropriate model was chosen on the basis of the goodness-or fit test [17].

The zero-order kinetic describes the systems in which the drug release rate is independent of its concentration. The first order kinetic describes the systems in which the drug release rate is concentration dependent. Higuchi described the release of drug from an insoluble matrix as square root of time dependent process.

In case of the Higuchi square root model gives the drug release from a planer surface of an insoluble heterogeneous matrix by diffusion through the intragranular openings created by porosity of the matrix tablet.

2.10. Stability Studies

Selected formulations were subjected to stability studies as per I.C.H. Guidelines.

Following conditions were used for stability studies [18]

$30^{o}C/65$ % RH analyzed till a period of 30 days

$40^{o}C/75$ % RH analyzed till a period of 30 days

Following parameters were check for stability studies Hardness, friability, drug content and in vitro release.

3. Results and discussion

3.1. FTIR Spectra

IR spectra of drug in KBr pellets at moderate scanning speed between 4000-400 cm^{-1} was carried out using FTIR (Jasco FTIR 6100 type A). The peak values (Wave number) and the possibility of functional group shown in spectra which compare with standard value.

3.2. Drug Excipients Compatibility study

Compatibility of the drug with recipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients [Figure 1 - 4].

3.3. Drug Excipients Compatibility study

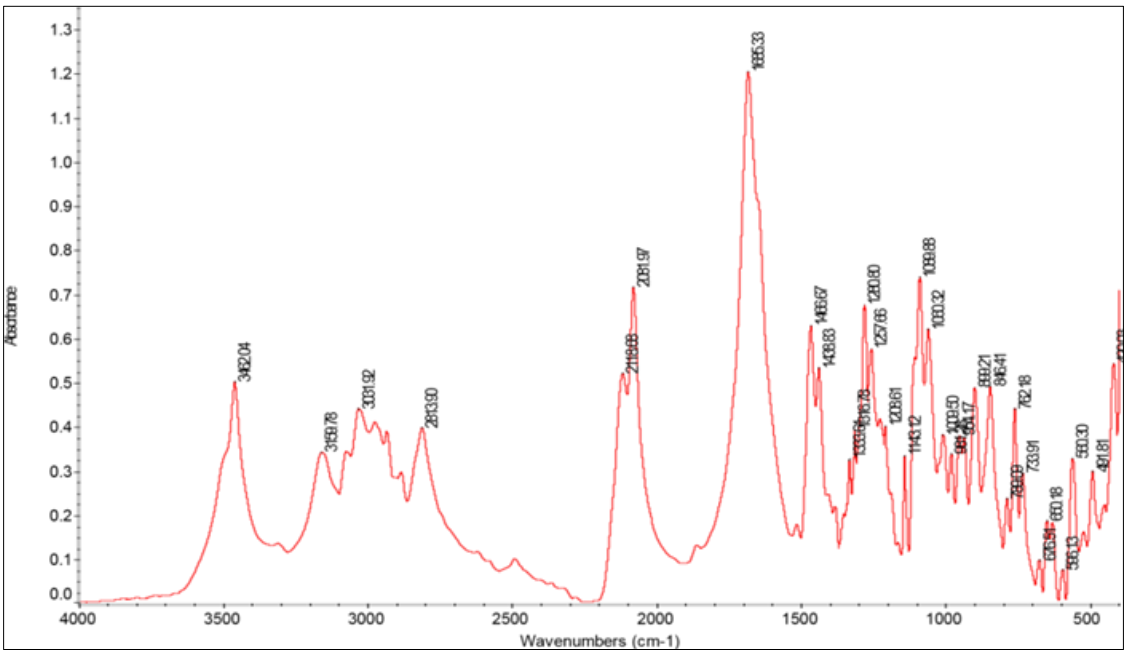

Figure 1 IR Spectrum of Pure Drug (Trimetazidine HCL)

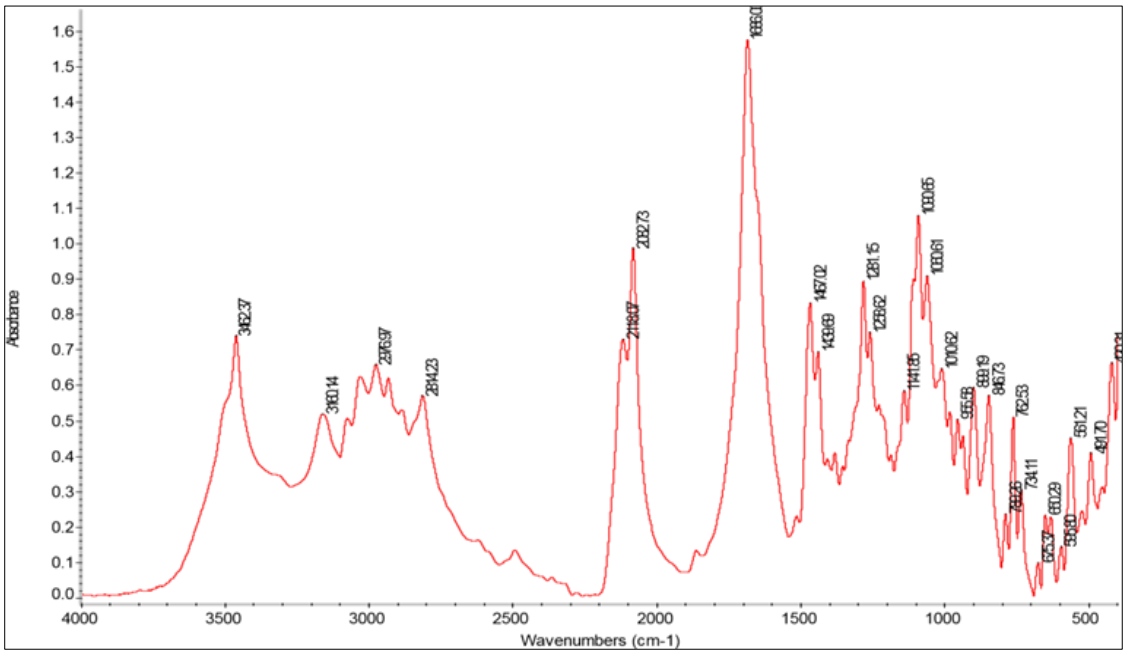

Figure 2 IR Spectrum of drug + HPMC K15 CR

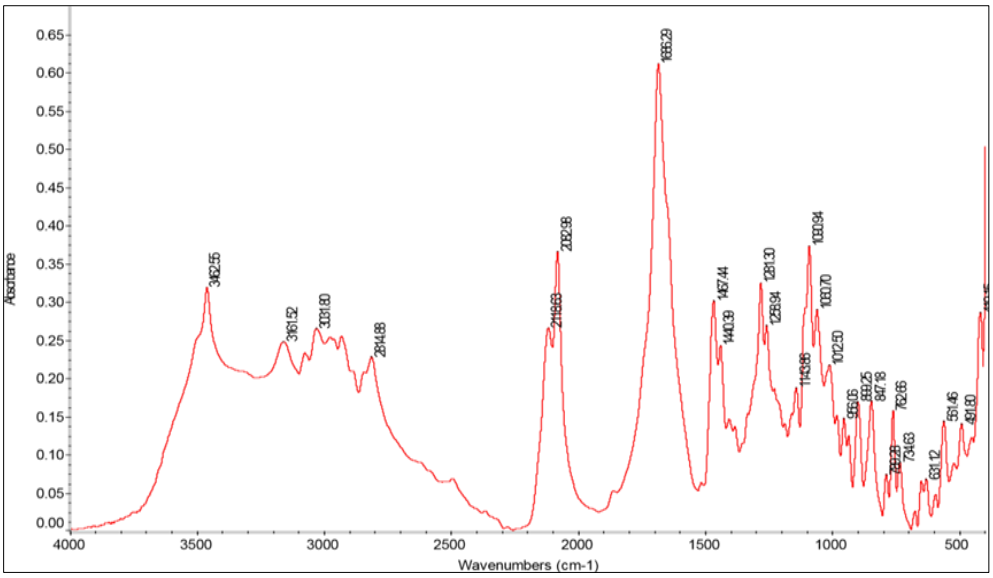

Figure 3 IR Spectrum of Drug + Metalose

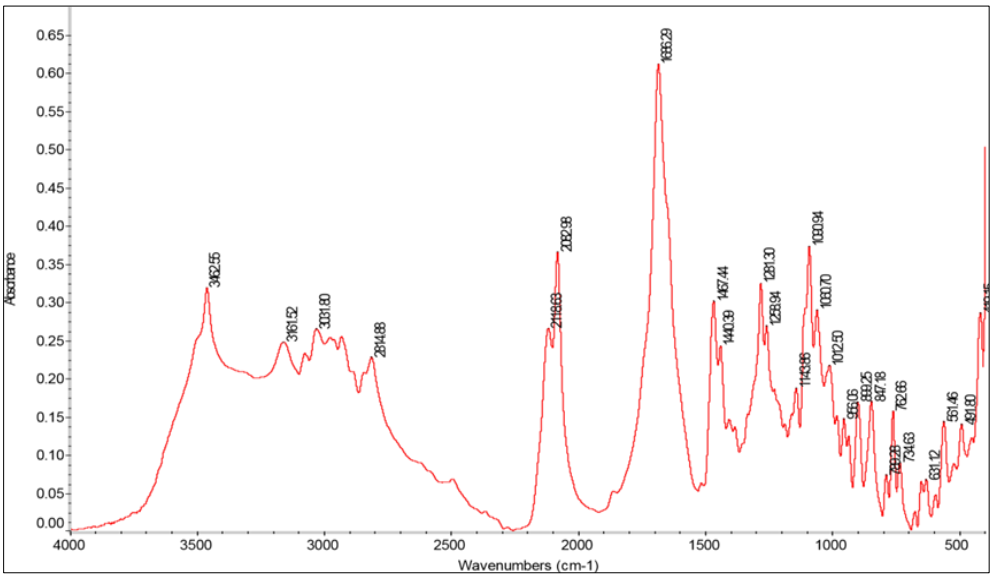

Figure 4 IR Spectrum of Drug + Ethyl cellulose

3.4. Evaluation of Powders

3.4.1. Preformulation Studies

Table 3 Preformulation studies of pure drug and polymers

Parameter	**Results**			
	Trimetazidine HCL	**HPMC-K-15 CR**	**Metalose**	**Ethyl Cellulose**
Angle of Repose	24	22	19	26
Bulk Density (gm/cm^3)	0.46	0.31	0.35	0.60
Tapped Density (gm/cm^3)	0.72	0.52	0.59	0.77
Compressibility Index	36.11	40.34	40.67	22.07
Hauser's Ratio	1.56	1.60	1.68	1.28

Table 4 Preformulation studies of blend

BATCH NO.	BULK DENSITY (g/ml)	TAPPED DENSITY (g/ml)	COMPRSI BILITY (%)	HOUSNER RATIO	ANGLE OF REPOSE (°)
F1	0.314	0.389	19.2	1.237624	25^0
F2	0.368	0.426	13.6	1.157407	18^0
F3	0.399	0.476	16.2	1.193317	20^0
F4	0.354	0.416	17.51	0.86	$29^011'$
F5	0.399	0.476	16.2	1.193317	$20^o12'$
F6	0.421	0.512	17.7	1.215067	23^0
F7	0.458	0.534	14.3	1.166861	20^0
F8	0.316	0.409	29.43	0.77	$31^016'$
F9	0.366	0.457	24.86	0.80	24^0

Preformulation study was done initially, and results directed for the further course of formulation. Based on Preformulation studies different batches of Trimetazidine HCL (F1 to F9) were prepared using selected excipients.

Powders were evaluated for tests Angle of repose, Bulk density, tapped density, compressibility index, Hausner ratio before being punched as tablets [Table 4].

3.4.2. Physico-Chemical Evaluation of Matrix Tablets:

The results of the thickness, Hardness, weight variation, drug content, friability, disintegration time [Table 5]

Table 5 Results of Thickness, weight variation, Hardness, Friability and Drug content

BATCH NO.	WEIGHT VARIATION	FRIABILITY (%)	HARDNESS (kg/cm^2)	THICKNESS (mm)	DRUG CONTENT (%)
F1	±4.0	0.12	4.5	3.9	96.20
F2	±2.0	0.19	5	4	97.26
F3	±3.0	0.39	5	4.1	98.93
F4	±2.55	0.14	5	4	97
F5	±2.0	0.24	5	3.9	99.89
F6	±3.44	0.11	5.5	3.8	98.53
F7	±2.0	0.43	4	4.1	97.11
F8	±5.66	0.16	5	3.9	97
F9	±5.22	0.18	5.5	3.8	96.00

3.5. In Vitro Dissolution Studies

Table No.11 shows the data for in vitro release of Trimetazidine HCL from matrix tablet of batches F1, F2, F3, F4, F5, F6, F7, F8 and F9 respectively [Table 6, Figure 5].

Table 6 Cumulative % Release of Drug of various Formulations

Time (Hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	40.5	41.1	42.31	38.25	45.04	36.83	33.78	37.47	34.61
2	54.44	59.07	58.14	48.75	54.14	51.01	45.73	55.06	50.36
4	80.51	84.25	81.38	81.18	78.1	73.38	67.16	77.81	68.95
6	88.23	90.08	89.99	89.99	85.31	84.43	72.93	85.52	72.98
8	91.19	92.86	92.95	92.95	86.84	89.96	85.02	87.75	80.77

As follows the dissolution profiles shows the comparative release profile of Trimetazidine HCL with different concentration of different polymer from batches F1, F2, F3, F4, F5, F6, F7, F8, F9 of matrix tablet. Percentage drug Release Profile of F1 to F9

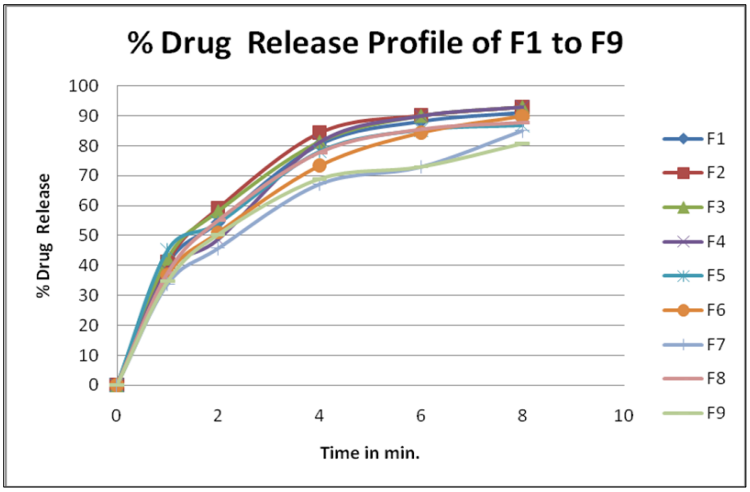

Figure 5 Graph of the Cum. % drug release versus Time (hrs) 7.5.4

Table 7 % Swelling Index of Tablets of Batch F1 to F9

Batch	TIME (HRS)						
	0	1	2	3	4	5	6
F1	0	32.23	41.38	54.32	63.78	74.12	81.2
F2	0	49.25	61.54	72.90	82.37	92.54	100.22
F3	0	29.09	39.45	51.32	61.12	71.97	80.35
F4	0	39.21	51.92	63.76	72.52	84.2	96.56
F5	0	45.65	53.35	64.32	75.45	80.09	94.58
F6	0	56.73	66.76	77.72	82.26	94.60	101.25
F7	0	39.06	47.96	55.32	65.34	76.09	87.11
F8	0	25.87	36.54	47.86	57.98	69.96	72.44
F9	0	26.76	40.98	49.54	59.06	69.78	75.99

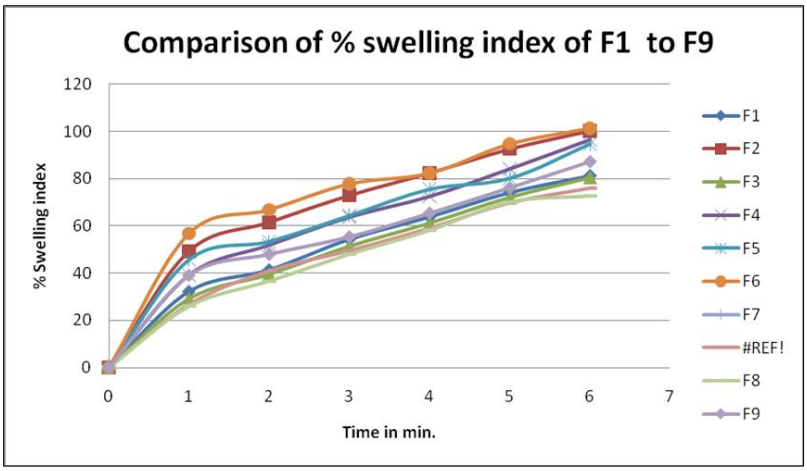

Figure 6 Comparison of % swelling index of various formulations

Kinetic assessment of Extended-release Matrix tablet containing

Trimetazidine HCL-

3.6. Huguchi Modeling

Table 8 Huguchi Modeling

BATCHES	r^2 VALUE (ZERO ORDER)	r^2 VALUE(HUGUCHI)
F1	0.809	0.971
F2	0.787	0.961
F3	o.798	0.969
F4	0.802	0.975
F5	0.768	0.955
F6	0.851	0.988
F7	0.865	0.991
F8	0.802	0.968
F9	0.807	0.973

3.7. Stability Study of Optimized Formulation

As per I.C.H. Guidelines

Table 9 Stability studies of formulation F-9 stored at 30oC/65% RH

Time (hr)	Cumulative % Drug Release	
	Initial	After 30 Days
0	0	0
1	34.61	34.01
2	50.36	50.98
4	68.95	67.33

6	72.98	71.61
8	80.77	80.11
Hardness	5.5	5.5
Friability	0.18	0.17
Drugcontent	96	95.92

Table 10 Stability studies of formulation F-9 stored at 40oC/75 % RH

Time (hr)	**Cumulative % Drug Release**	
	Initial	**After 30 Days**
0	0	0
1	34.61	33.53
2	50.36	50.12
4	68.95	66.65
6	72.98	72.53
8	80.77	79.78
Hardness	5.5	5.5
Friability	0.18	0.18
Drugcontent	96	94.99

4. Conclusion

The present study was undertaken with an aim to formulate develop and evaluate Trimetazidine HCL extended release matrix tablets using different polymers as release retarding agent. Pre formulation study was done initially and results directed for the further course of formulation. Based on Pre formulation studies different batches of Trimetazidine HCL were prepared using selected excipients. Powders were evaluated for tests Angle of repose, Bulk density, tapped density, compressibility index, and Hausner ratio before being punched as tablets. Results of *in vitro* release profile indicated that formulation F9 was the most promising formulation as the extent of drug release from this formulation was high as compared to other formulations. Results of in-vitro swelling study indicate that the formulation F9 was having considerable swelling index.It was concluded that the tablets of batch F9 had considerable swelling behaviors and *in vitro* drug release. Percentage drug release in 8 hr is 80.77. It was observed that tablets of batch F9 followed the Huguchi release profiles. From the above results and discussion it is concluded that formulation of Extended release matrix tablet of Trimetazidine HCL containing HPMC K-15 (19.44%) and Hyper mellose (19.44%), Ethyl cellulose (19.44%) batch F9 can be taken as an ideal or optimized formulation Extended release matrix tablet for 8 hour release as it fulfills the requirements for extended release matrix tablet.

Compliance with ethical standards

Acknowledgments

I would like to thank Principal Dr. Y Prapurna Chandra and Dr. Penabaka Venugopalaiah, Professor and HOD, Department of Pharmaceutics, Ratnam Institute of Pharmacy, Pidathapolur (V), Muthukur (M), SPSR Nellore carry out these research work.

Disclosure of conflict of interest

The authors attest that they have no conflict of interest in this study.

References

[1] Bathala Anitha, Praveen Kumar C H, Jampani Susmitha, & Poolla Ramya Krishna. Formulation and Evaluation of Prolonged-Release Tablets Containing Solid Dispersions of Rosuvastatin Calcium. Future Journal of Pharmaceuticals and Health Sciences, 2021, 1(4), 180–185.

[2] Naito, S.I., Osumi, S., and Hirose, M., Trimetazidine in blood, bile, organs and urine. Chemical and Pharmaceutical Bulletin, 1972. 20(4): p. 682–688.

[3] Thoppil, S.O., Cardoza, R.M., and Amin, P.D., Stability indicating HPTLC determination of trimetazidine as bulk drug and in pharmaceutical formulations. Journal of Pharmaceutical and Biomedical Analysis, 2001. 25(1): p. 15–20.

[4] Praveen Gujjula, Angala Parameswari S, & Varun Dasari. Formulation Design and Evaluation of Olmesartan Mucoadhesive Buccal Tablets. Future Journal of Pharmaceuticals and Health Sciences, 2021, 1(4), 186–192.

[5] Gupta, R., Sawhney, J.P., and Narain, V.S., Treatment of stable angina pectoris with trimetazidine modified release in Indian primary-care practice. American Journal of Cardiovascular Drugs, 2005. 5(5): p. 325-329.

[6] Javeer, S.D., Pandit, R., Jain, S.P., and Amin, P., Formulation and evaluation of trimetazidine dihydrochloride extended release tablets by melt congealing method.Indian Journal of Pharmaceutical Science, 2010. 72(6): p. 704-709.

[7] Balakrishnan M, Sudarsanam P, and Nethaji D U. Formulation and Evaluation of Controlled-release matrix Vildagliptin tablets. International Journal of Clinical Pharmacokinetics and Medical Sciences, 2021, 1(2), 35–41.

[8] Chowdary, K.P.R., Mohapatra, P., and Murali Krishna, M.N., Olibanum and its resin as rate controlling matrix for controlled release of diclofenac. Indian Journal Pharmaceutical sciences, 2006. 68(4): p. 497-500.

[9] Patil, S.A., Kuchekar, B.S., Chabukswar, A.R., and Jagdale, S.C., Formulation and evaluation of Extended-Release Solid Dispersion of Metformin Hydrochloride. Journal of Young Pharmacists, 2010. 2(2): p. 121–129.

[10] Yerikala Ramesh, Sri krishna.T, A.Datta Charan, P. Venugopalaiah. Formulation & In-Vitro Evaluation Of Sustained Release Tablets Of Frovatriptan For The Treatment Of Migraine. Journal of Xi'an Shiyou University, Natural Science Edition. 2022, 18(12), 53-70.

[11] Muppavarapu Anusha, & Vanitha K. Formulation and Evaluation of Immediate-Release Tablets of EdoxabanTosylate. International Journal of Experimental and Biomedical Research, 2022, 1(4), 177–190.

[12] Reddy, V. S., Ramesh, Y. and Parameshwar, K. Formulation and Evaluation of Mouth Dissolving Tablets of Metoprolol tartrate by new Co-processed Technique. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 2011, 2(3), 385-389

[13] Nagamani D, Ramesh Y, Saravanan kumar K, Gnanaprakash K, Gobinath M. Formulation And Evaluation Of Chlorpheniramine Maleate Extended Release Tablets By Using Direct Compression Technique. International Journal of Biopharmaceutics, 2015,6(2):81-92.

[14] Sankar Rao. K Madhavi C, Ramesh Y, Deepthi A, Gnana Prakash. K, Gobinath. M. Formulation and Evaluation of Sustained Release Matrix Tablets of Cefadroxil by Using Direct Compression Method. American Journal of Pharm Tech Research. 2015, 5(4), 1-13.

[15] B Nageswara Naik C. Sadak Vali, Abdullah Khan, M. Pratibha Bharati, M. Pradeep Kumar. Fabrication, Characterization And Optimization Of Gastro-Retentive Floating Tablets Of Moxifloxacin Using Natural And Semi Synthetic Polymers. European Journal Of Pharmaceutical And Medical Research. 2020, 7(10); 595-603.

[16] Hari Kumar C Shaik Nissar, Pradeep Kumar M, Chandrakala P. Preparation of colon-Targeted Avermectins Tablets and its release properties in-vitro studies. Future Journal of Pharmaceuticals and Health Sciences. 2022, 2(1):29-34.

[17] Satyabrata Jena M Pradeep Kumar, Uttam Prasad Panigrahy. Solubility Enhancement Of Orally Disintegrating Tablets Of Pranlukast By Solid Dispersion Technique. European Journal of Molecular & Clinical Medicine. 2022, 9(7); 3549-3564.

[18] Pradeep Kumar, M., Murthy, G. S., Poojitha, A. L., Sindhuri, P., Sreekanth, A., & Ramesh, Y. Formulation and Evaluation of Colchicine Sustained release tablet by using factorial designs. Journal of Drug Delivery and Therapeutics, 2021, 11(5-S), 100-107