IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
July 2024 Vol.:30, Issue:7

Design, Preparation and In Vitro Evaluation of Loratadine Controlled Release Tablets

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

M. Mamatha[1], D. Avinash[2], A.Yasodha[3]

[1]*Department of Pharmaceutics, Dhanvanthri College of Pharmaceutical Sciences, Thirumala Hills, Centre City, Appannapally, Mahabubnagar, Telangana 509001 India.*

[2] *Professor, Department of Pharmaceutics, Dhanvanthri College of Pharmaceutical Sciences, Thirumala Hills, Centre City, Appannapally, Mahabubnagar, Telangana 509001 India.*

[3]*Professor & Principal, Department of Pharmaceutical Analysis, Dhanvanthri College of Pharmaceutical Sciences, Thirumala Hills, Centre City, Appannapally, Mahabubnagar, Telangana 509001 India.*

Submitted: 24 June 2024
Accepted: 30 June 2024
Published: 30 July 2024

HUMAN JOURNALS
ijppr.humanjournals.com

Keywords: Loratadine, Polymers, FTIR studies, direct compression technique, in vitro drug release studies, zero order kinetics.

ABSTRACT

The aim of the present work is to Formulate and Evaluate controlled release of Loratadine matrix tablets used for treatment of allergies. In the present work, attempts were made to formulate and evaluate controlled release of matrix tablets of Loratadine. Loratadine was subjected to preformulation studies; based on the results obtained Loratadine controlled release tablets were successfully formulated. Formulations prepared by direct compression technique. Set of trials were formulated for which Loratadine evaluated parameters (bulk density, tapped density, compressibility index, Hausner's ratio, weight, thickness, and hardness) were found to lie within the specifications. Dissolution study was performed in USP type II apparatus at 100 RPM in pH 6.8 phosphate buffer. From the results of the in vitro study, it appears that the release of the Loratadine was significantly influenced by the characteristics of the polymer used.

INTRODUCTION

Oral administration of drugs is the most common and preferred route for delivery of therapeutic agents. Oral route of drug administration is the ideal, convenient and preferred route.[1] Conventional oral drug administration does not generally offer target specificity or rate-controlled release. In controlled release drug delivery systems (CRDDSs), an active therapeutic is incorporated in the network structure of the polymer in such a way that the drug is released in a predefined controlled manner.[2] Loratadine is a long-acting tricyclic second generation antihistamine. It is an antagonist at peripheral histamine (H1) receptors. Desloratadine (decarboethoxy Loratadine) is the active metabolite of Loratadine and produces the same pharmacological effect as the parent compound.[3] In this regard, Loratadine controlled release tablets were prepared by using polymers such as HPMC and sodium CMC in different combinations and concentrations using direct compression technology to increase its bioavailability.

MATERIALS

Loratadine was obtained from Alkem Pvt Mumbai, Sodium CMC and HPMC were procured from SD fine chemicals Mumbai. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy Loratadine discs were created by compressing the Loratadine with KBr and the spectra was scanned in the range between 4000 to 400 cm-1. Perfect operational conditions were maintained. The absorption maxima which is denoted as lambda max in spectrum obtained with the drug substance is compared with the intensity to those of reference spectrum. [4]

Table-1: Formulation Table of Loratadine Controlled Release Tablets

S.No.	INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8
1	Loratadine	10	10	10	10	10	10	10	10
2	HPMC	25	50	75	100	-	-	-	-
3	Sodium CMC	-	-	-	-	25	50	75	100
4	Microcrystalline Cellulose	160	135	110	85	160	135	110	85
5	Magnesium stearate	3	3	3	3	3	3	3	3
6	Talc	2	2	2	2	2	2	2	2
7	Total Wt	200	200	200	200	200	200	200	200

Preparation Method:

Tablets of Loratadine were prepared by direct compression method as per the formulae given in Table. All the materials required as per the formulae were blended in a closed polyethylene bag. The blends were compressed into tablets on a tablet punching machine to a hardness of 6 kg/cm^2 using 8 mm concave punches.[5]

Evaluation of Tablet

Weight Variation

Weight variation is one of the official quality control tests for tablets. This is important because it directly relates with drug content. To do this test, minimum 20 tablets were weighed separately and average weight was calculated and compared with the individual weight. The deviation gives the report of the weight variation. Usually it is expressed in percentage. Weight variation should be done in process checking and for finished products.[6]

Thickness

The dimensions like thickness and diameter of the tablets may have important effect in the drug content and other parameters. Hence it is required to maintain the thickness and diameter in the optimum acceptable range. This can be done by means of Vernier Caliperse. 10 tablets prepared from each trial were used. The average values were noted.[7]

Tablet Hardness

Monsanto hardness tester was utilized to find the tablet hardness. In each formulation, 10 tablets were taken and the hardness was measured. The tablet was kept in the perfect position in the axis in the two jaws of instrument. The measurement should be zero kg/cm2 at this stage. The knob is rotated to apply force to the tablet; the force is continued until there is fracture in the tablet. The point at which tablet breaks are break point and it was noted in kg/cm^2. [8]

Friability

Tablet strength can be measured by using friabilator. This is performed to know the impact of shock abrasion on tablets when on travelling and handling. The test involves keeping the tablets in a plastic chamber and allowing it to revolve at 25rpm for 4 minutes that is equivalent to 100 rotations. In this test the tablets are subjected to drop at heights of 6 inches in each revolution. The initial weight and final weight of the tablets after dedusting were noted. The limit acceptable is less than 1% weight variation. It was calculated as follows. The percentage friability was measured using the formula,[9]

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

Where,

% F = friability in percentage

Wo = Initial weight of tablet

W = weight of tablets after revolution

Drug Content

The drug content directly relates to the pharmacological efficacy, so it is mandatory to do the drug content test. It is an official quality control test. The drug content in all formulations were analysed by triturating 20 tablets in mortar and pestle, then from the powder 75 mg equivalent of Loratadine was taken and transferred to 100ml standard volumetric flask. Then the volume was prepared to 50ml with pH 6.8 phosphate buffer. This was shaken for 15 min to mix. Then the volume was prepared to 100ml with phosphate buffer. The solution was

strained by using Whatman filter paper and then it is diluted and absorbance was determined by using UV-Visible spectrophotometer at 285 nm using pH 6.8 phosphate buffer as blank.[10]

In Vitro Release Studies

This in vitro release can be done by using USP dissolution apparatus I. The test is performed at 50 rpm. The media used were pH 1.2 buffer for initial 2 h, followed by 8 h in pH 6.8 phosphate buffer. The temperature was maintained at 37 ± 0.5°C. The samples were taken at predetermined time and the dissolution basket is replenished with the buffer. The taken samples were filtered through filtered through a 0.45ʒ membrane filter. The absorbance was measured at 285 nm. For every trial, the experiments were done in triplicate. The release data of all the trials were analyzed to observe the release kinetics using zero order, first order and matrix, Korsmeyer- Peppas equations.[11]

Release Kinetics [12]

The release kinetics can be understand basically by applying the obtained data to the release kinetics models.

Zero order

$$C = K0t$$

K0 - rate constant for Zero-order (concentration/time) t - Time (h).

First order

$$LogC = LogC0 – Kt / 2.303$$

Where C0 - Initial Conc of drug K = constant first order and t = Time (h)

Higuchi

$$Qt = Kt1/2$$

Where Qt - Amount of the drug release drug in time t K- Kinetic constant and t- is time in hrs Korsmeyer Peppas

$$Mt / M = Kt\ n$$

Where, Mt - amount of the released drug at time t, M- Overall drug amount released after 8 hrs K- Diffusion constant n- Diffusion exponent mechanism of release of drug.

Stability Studies: [13]

The stability studies are performed to analyze the quality of drug and drug product with exposure to different temperature and humidity conditions on estimated time. General conditions like light, environment and other general parameters are maintained and the general evaluation tests were performed at different time interval periods. It is undesirable and time consuming to do full shelf life period study. To avoid this accelerated stability studies has been adopted.

RESULTS AND DISCUSSION

FTIR Studies:

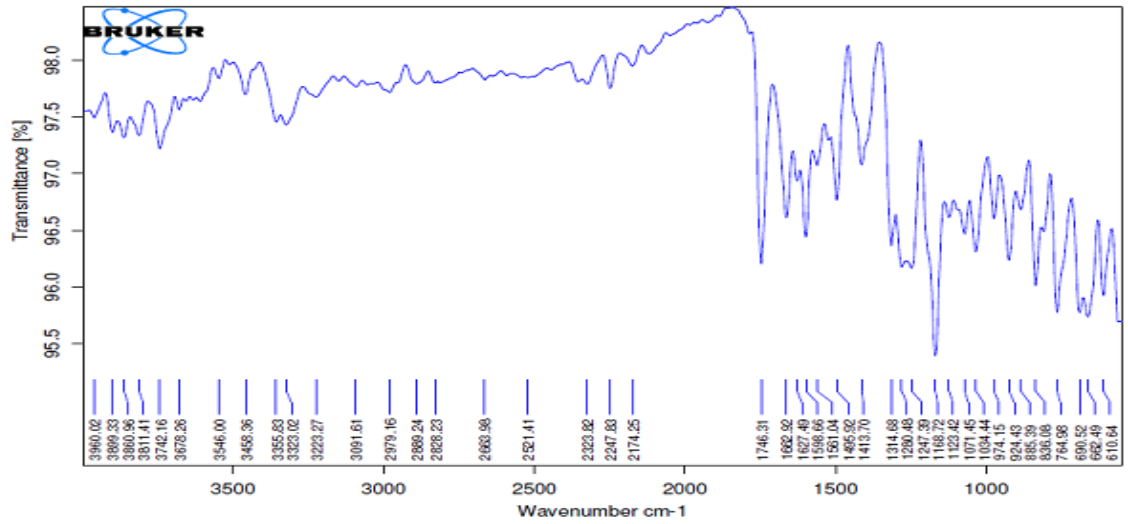

Fig-1: FTIR Spectra of Pure Drug

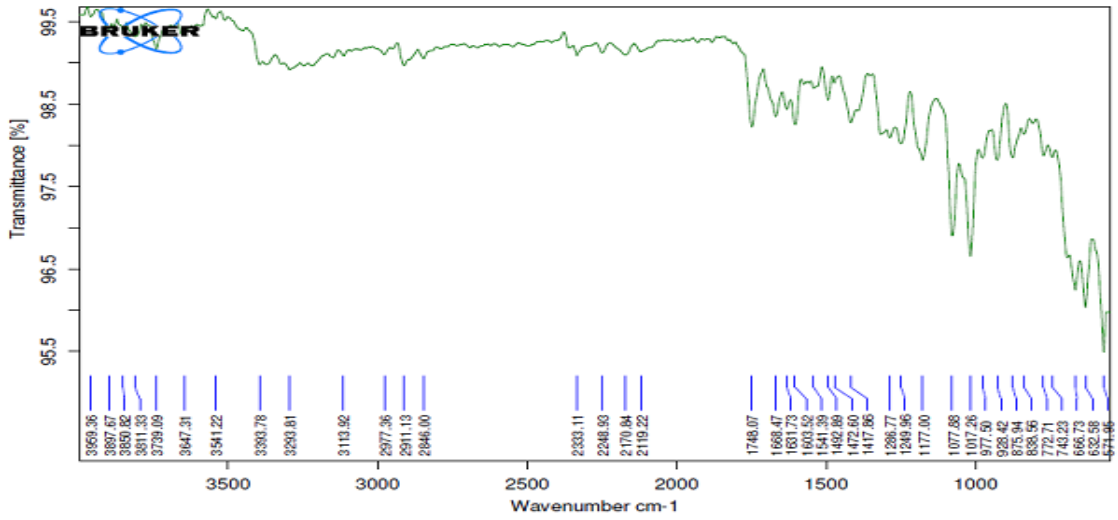

Fig-2: FTIR Spectra of Optimized Formulation

Evaluation of Tablet

Weight Variation:

All the formulated (F1 to F8) tablets passed weight variation test as the % weight variation was within the Pharmacopeial limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

Thickness:

Tablets mean thickness were uniform in F1 to F8 formulations and were found to be in the range of 2.74 mm to 3.24 mm.

Hardness:

The measured hardness of tablets of each batch ranged between 4.28 to 5.64 kg/cm^2. This ensures good handling characteristics of all batches.

Friability:

The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

Content Uniformity:

The percentage of drug content for F1 to F8 was found to be between 86.98% and 93.15 % of Loratadine it complies with official specifications.

Table-2: Results of Evaluation Parameters of Tablets

F. No.	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	200	2.98	5.64	0.35	86.98
F2	199	3.12	4.98	0.43	92.14
F3	200	2.89	5.55	0.38	89.68
F4	200	3.14	4.65	0.41	93.15
F5	201	2.48	4.28	0.39	90.28
F6	200	3.24	5.51	0.45	91.69
F7	200	2.74	4.66	0.46	88.39
F8	199	2.99	4.82	0.37	93.02

***In-Vitro* Dissolution Study**

Table-3: In-Vitro Dissolution Study

Time (hrs.)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
0	0	0	0	0	0	0	0	0
1	25.64	19.86	24.52	26.58	24.10	23.96	22.28	20.25
2	35.63	31.15	32.81	32.42	29.72	35.20	33.72	30.85
3	40.92	38.65	39.90	41.18	32.70	41.28	42.70	40.28
4	52.65	48.23	53.41	50.90	49.65	52.62	56.65	51.27
5	61.25	59.95	65.50	63.82	52.38	60.74	65.38	62.32
6	73.12	72.82	74.84	73.86	68.72	78.56	73.72	71.63
7	80.19	81.84	83.90	84.82	80.09	81.68	85.09	82.75
8	92.59	91.59	93.89	95.24	94.69	92.95	91.25	94.90

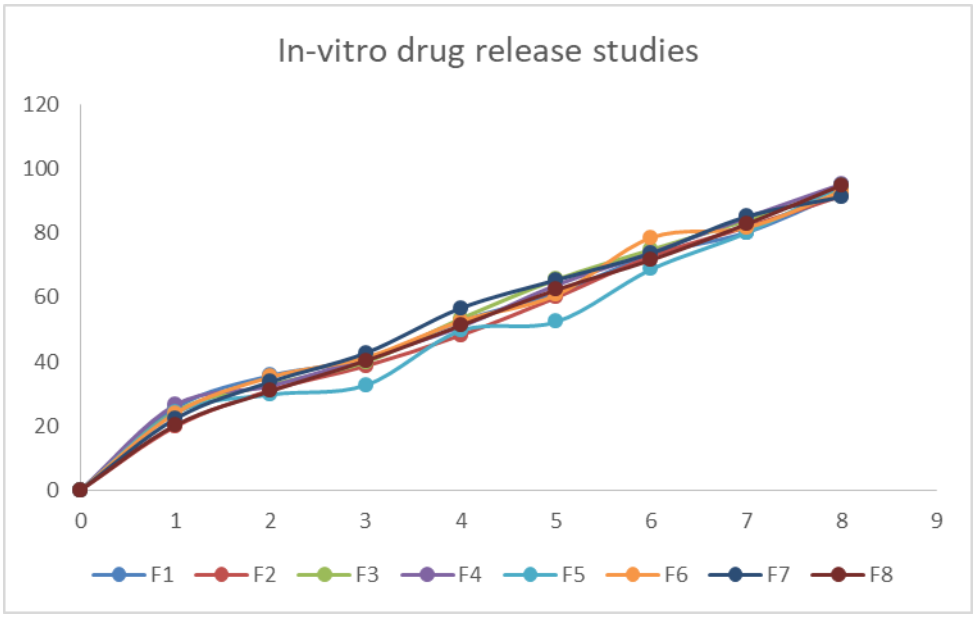

Fig-3: In Vitro Drug Release of F1-F8 Formulations

Kinetic Modelling of Drug Release

All the 8 formulation of prepared matrix tablets of Loratadine were subjected to in vitro release studies these studies were carried out using dissolution apparatus.

The dissolution medium consisted of 900 ml of Standard buffer pH 1.2 for the first 2 hrs, followed by pH 6.8 for remaining period of time.

The results obtaining in vitro release studies were plotted in different model of data treatment as follows:

1. Cumulative percent drug released vs. time (zero order rate kinetics)

2. Log cumulative percent drug retained vs. time (First Order rate Kinetics)

3. Cumulative percent drug released vs. square root of time (Higuchi's Classical Diffusion Equation)

4. Log of cumulative % release Vs log time (Peppas Exponential Equation)

Table-4: Drug Release Kinetics of Formulation F4

TIME	%CDR	SQARE T	LOG T	LOG%CDR	ARA	LOG%ARA
0	0	0	0	0	0	0
1	26.58	1	0	1.42455498	73.42	1.86581438
2	32.42	1.41421356	0.30103	1.51081301	67.58	1.82981819
3	41.18	1.73205081	0.47712	1.61468634	58.82	1.76952502
4	50.9	2	0.60206	1.70671778	49.1	1.69108149
5	63.82	2.23606798	0.69897	1.8049568	36.18	1.55846856
6	73.86	2.44948974	0.77815	1.8684093	26.14	1.41730558
7	84.82	2.64575131	0.8451	1.92849827	15.18	1.18127177
8	95.24	2.82842712	0.90309	1.97881939	4.76	0.67760695

Zero Order Kinetics

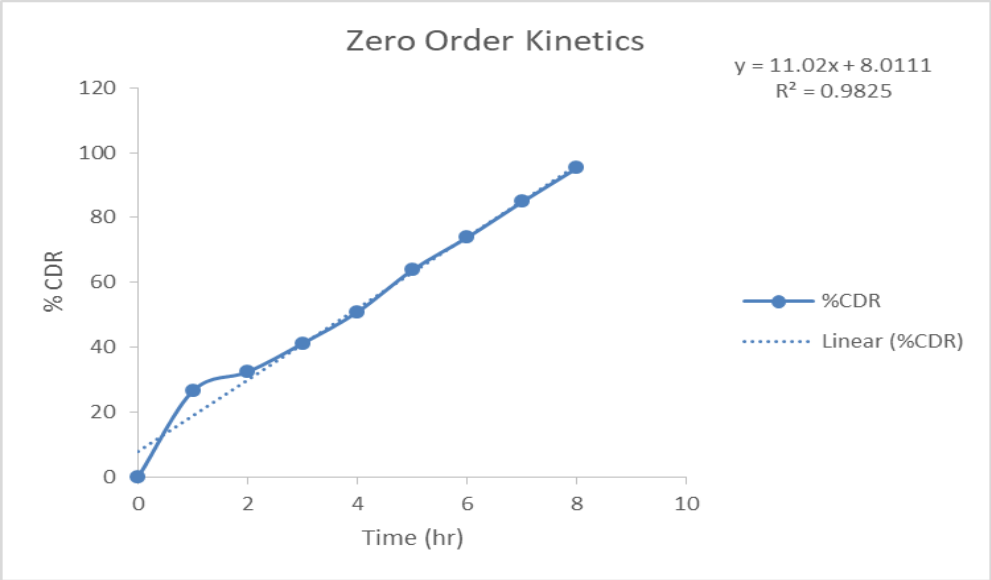

Fig-4: Zero Order Kinetics Optimized Formulation

First Order Kinetics

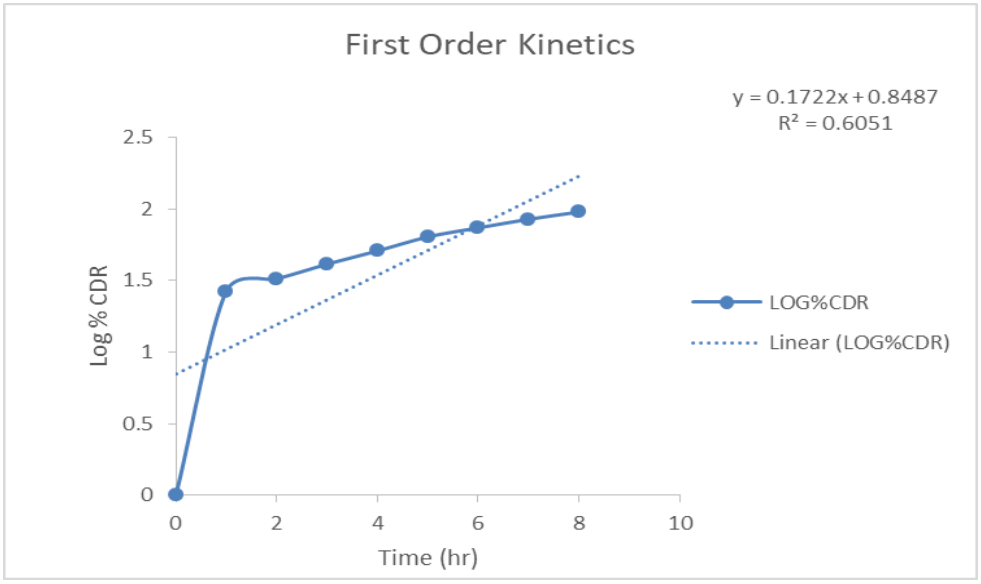

Fig-5: First Order Kinetics Optimized Formulation

Higuchi Model

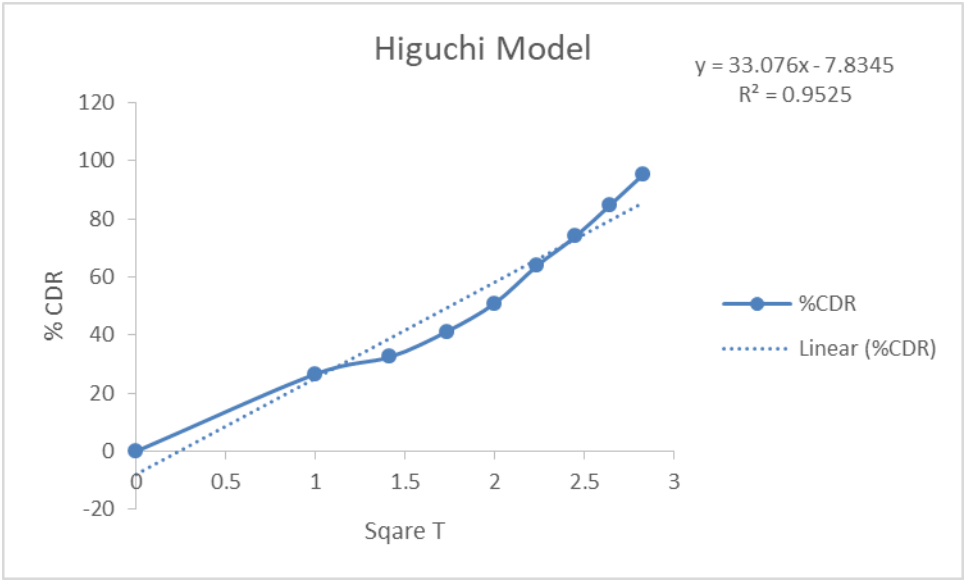

Fig-6: Higuchi Model of Optimized Formulation

Korsmeyer Peppas

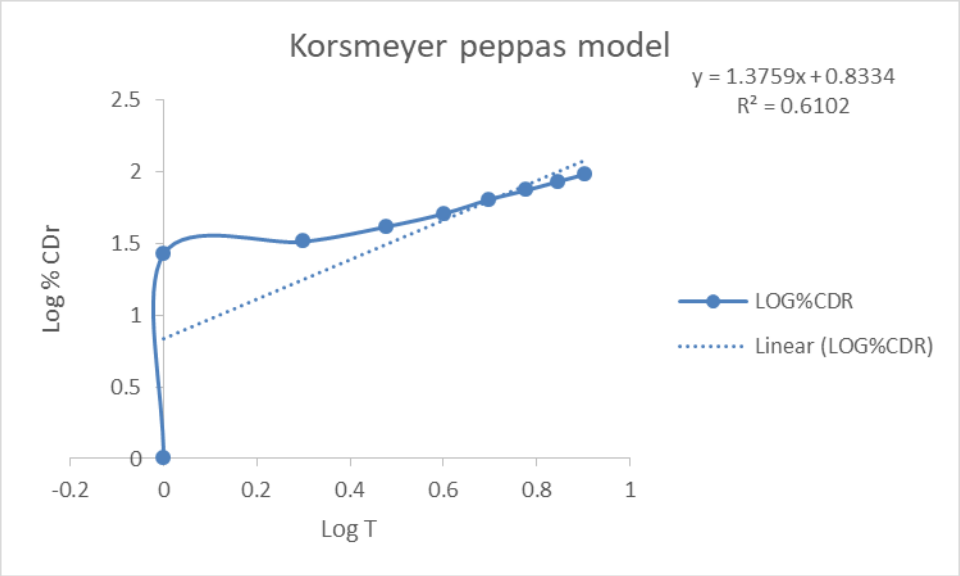

Fig-7: Korsmeyer Peppas Optimized Formulation

The kinetic values obtained for formulation F4 were shown. The values of in vitro release were attempted to fit into various mathematical models. Regression values are higher with Zero order release kinetics. Therefore all the Loratadine tablets Zero order release kinetics. Therefore all the Loratadine tablets follow first order release kinetics.

Table-5: Regression Equations of Loratadine Tablets F4

Film Code	In Vitro Release in Phosphate Buffer pH 7.4 Regression Values			
	Zero Order	First Order	Higuchi Plot	Korsmeyer Peppas
F_4	0.982	0.605	0.952	0.601

The table indicates that r^2 values are higher for Higuchi's model compared for all the tablets. Hence Loratadine release from all the tablets followed diffusion rate controlled mechanism.

Stability Studies

There was no significant change in physical and chemical properties of the tablets of formulation F-4 after 3 months. Parameters quantified at various time intervals were shown;

Table-6: Results of Stability Studies of Optimized Formulation F4

Formulation Code	Parameters	Initial	1st Month	2nd	3rd	Limits as per Specifications
F-4	**25^{0}C/60%RH**	96.38	95.89	94.98	93.47	**Not less than**
F-4	**30^{0}C/75% RH**	96.38	95.67	94.58	93.5	**Not less than**
F-4	**40^{0}C/75% RH**	96.38	95.6	9452	93.47	**Not less than**

CONCLUSION

All the prepared tablet trials showed acceptable Pharmaco technical properties and pass the official Pharmacopeial standards. The in vitro release profiles were applied on various kinetic models. The release studies revealed that the release rate was decreased with increase in polymer proportion. From the results of present study it appears that the release of Loratadine was significantly influenced by the characteristics of polymer and excipients used. In-vitro release from the formulation F4 with the hardness of 4.65 kg/cm^2. Higher hardness tablets contain a compact mass of polymer with relatively less pore, resulting in slower release. All other tested parameters of F4 formulation were in the acceptable limits. So formulation F4 was found to be better than other batch of formulations. In the current research work, matrix formulation F4 were perhaps show maximum delay of drug release and it shows super case-II transport, for these causes, it was reflected that the formulation F4 as optimum formulation among all formulations Stability study was carried out with F4 formulation and the marketed sample as per ICH guidelines and found to be stable both in accelerated and long term stability conditions.

REFERENCES

1. Liberman HA, Lachman L, Schwartz JB. Pharmaceutical dosage forms: Tablets. 2nd edition (Volume-2), New York (USA); Marcel Dekker, 2005; 165-67.
2. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste masking and clinical studies. Crit Rev Ther Drug Carrier Syst, 2004; 21: 433-7
3. Eryol C, Demirturk E, Oner L, Preparation of Meloxicam Tablet Formulation and Evaluation of invitro Release Similarities, Journal of Pharmaceutical sciences, 29(2), 2004, 53-61.
4. Fukuda M, Peppas NA, McGinity JW, Properties of sustained release hot-melt extruded tablets containing chitosan and Xanthum gum, International Journal of Pharmaceutics, 310, 2006, 90-100.
5. Mahajan P, Mahajan SC, Mishra DK, Valsartan release from sustained release matrix tablet and effect of cellulose derivatives, International Journal of Pharmacy and Life Science, 2, 2011, 521
6. Lachman L, Liberman HA and Kanig JL. The Theory and Practice of Industries Pharmacy, 3rd edition. Varghese publishing house, 2008; 296-303,430-456.

7. Venkatesh DN, Jawahar N, Ganesh GNK, Kumar RS, Senthil V, Samanta MK, Sankar S and Elango K. Development and In Vitro evaluation of sustained release matrix tablet of theophylline using hydrophilic polymer as release retardant. Int J Pharm Sci Nano. 2009; 2(1): 34-38.
8. Mridanga RR, Bose SK and Sengupta K. Design, Development and in vitro evaluation of directly compressed sustained release matrix tablet of famotidine Research J Pharm and Tech. 2008;1(3):175-178.
9. Hingmire LP, Deshmukh VN and Sakarkar DM. Development and evaluation of sustained release matrix tablet using natural polymer as release modifier. Research J Pharm Tech. 2008; 1(3):123.
10. Debjit M, Chandira M, Chiranjib, Kumudhavalli and Jayakar B. Formulation, design and development of buccoadheshive tablets of verapamil hydrochloride. Int J Pharm Tech. Research. 2009;1(4):1663-1677
11. Arfat, Surya Prakash, A, Swarnalatha. D, Usha Sree, Formulation and Evaluation of Ethyl Cellulose Coated Microcapsules of Glibenclamide for Controlled Release, Asian Journal of Chemistry; Vol. 26, No. 3 (2014), 770-772
12. Deepthi, Veena S. Kasture, Sarita S. Pawar, Sanjay B. Kasture, Formulation and evaluation of Telmisartan microspheres by emulsion solvent evaporation technique, Journal of Applied Pharmaceutical Science Vol. 2 (10), pp. 113-116, October, 2012.

 **Author -1**	M. Mamatha – Corresponding Author Department of Pharmaceutics, Dhanvanthri College of Pharmaceutical Sciences, Thirumala Hills, Centre City, Appannapally, Mahabubnagar, Telangana 509001
Image **Author -2**	D. Avinash Professor, Department of Pharmaceutics, Dhanvanthri College of Pharmaceutical Sciences, Thirumala Hills, Centre City, Appannapally, Mahabubnagar, Telangana 509001
Image **Author -3**	A.Yasodha Professor & Principal, Department of Pharmaceutical Analysis, Dhanvanthri College of Pharmaceutical Sciences, Thirumala Hills, Centre City, Appannapally, Mahabubnagar, Telangana 509001