INTERNATIONAL JOURNAL IN PHARMACEUTICAL SCIENCES

Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Research Article

Formulation and In-vitro Evaluation of Controlled Release Matrix Tablets of Anti-Hypertensive Drug: Verapamil Hydrochloride

Sunil Firangi*[1], Ananth Rao Kulkarni[2], R. B. Sangoligi[3], Dr. S. N. Hiremath[4], Dr Syed Sanaullah[5]

[1,2,3]*Luqman College of Pharmacy, Gulbarga, Karnataka*
[2]*K.C.T College of Pharmacy, Gulbarga, Karnataka*
[4]*Pravara Rural College of Pharmacy, Loni, Maharashtra*

ARTICLE INFO

Received: 29 Sept 2023
Accepted: 30 Sept 2023
Published: 01 Oct 2023
Keywords:
Verapamil hydrochloride, Hydroxypropyl methyl cellulose, FTIR, Higuchi's model, Korsmeyer's model
DOI:
10.5281/zenodo.8396256

ABSTRACT

The aim of the present study was to develop model controlled release (CR) matrix tablet formulations for Verapamil hydrochloride and to study the influence of hydroxy propyl methyl cellulose (HPMC) ratio on drug release and also to assess the potential value of HPMC mixtures as gelling agents in matrix tablets. The release of verapamil hydrochloride CR matrix tablets based on hydrophilic matrices of hydroxy propyl methyl cellulose of different viscosity grades of HPMC 50cps, HPMC K4M and HPMC K100M was studied. The compressed matrix tablets were evaluated for various parameters like hardness, friability, uniformity of weight, uniformity of drug content, FTIR drug-polymer interaction, invitro drug release and short term stability studies. A faster drug release rate was observed for the tablets prepared with low viscosity grades of HPMC and slower drug release rate was observed for the tablets prepared with high viscosity grades of HPMC. Analysis of drug dissolution profiles on the basis of Higuchi's model indicated that the drug release was in all cases diffusion limited.

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 a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose[1]. In the case of injectable dosage forms, this period may vary from days to months. In the case of orally administered dosage forms, this period is measured in hours and critically depends on the residence time of the dosage form in the gastrointestinal tract. The term controlled release has become associated with those systems from which therapeutic agents may be

***Corresponding Author:** Sunil Firangi
Address: *Luqman College of Pharmacy, Gulbarga, Karnataka*
Email ✉: sunil_eyz@rediffmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

automatically delivered at predetermined rates over a long period of time. Controlled release also denotes systems which can provide some control whether this be of a temporal or spatial nature or both for drug release in the body[2]. The system attempts to control drug concentrations in the target tissues or cells. Prolonged or sustained release systems only prolong therapeutic blood or tissue levels of the drug for an extended period of time.

Advantages of controlled release dosage forms[3]:

1. The frequency of drug administration is reduced.
2. Patient compliance can be improved.
3. Drug administration can be made more convenient as well.
4. The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced.
5. Better control of drug absorption can be attained, since the high blood level peaks that may be observed after administration of a dose of a high availability drug can be reduced.
6. The characteristic blood level variations due to multiple dosing of conventional dosage forms can be reduced.
7. The total amount of drug administered can be reduced, thus:
   - Maximizing availability with minimum dose;
   - Minimize or eliminate local side effects;
   - Minimize or eliminate systemic side effects;
   - Minimize drug accumulation with chronic dosing.
8. Safety margin of high potency drugs can be increased and the incidence of both local and systemic adverse side effects can be reduced in sensitive patients.
9. Improve efficiency in treatment.
   - Cure or control condition more promptly;
   - Improve control of condition i.e., reduce fluctuation in drug level;
   - Improve bioavailability of some drugs;
   - Make use of special effects; e.g. sustained release aspirin for morning relief of arthritis by dosing before bed-time.
10. Economy.

Disadvantages of controlled release formulations:

1. Administration of controlled release medication does not permit the prompt termination of therapy.
2. Flexibility in adjustment of dosage regimen is limited.
3. Controlled release forms are designed for normal population i.e. on the basis of average drug biologic half-lives.
4. Economic factors must also be assessed, since more costly process and equipment are involved in manufacturing of many controlled release dosage forms.

Physico-chemical factors influencing controlled release dosage form[4]:

- **Dose size:** In general a single dose of 0.5 to 1 gm is considered maximal.
- **Ionization, pKa and aqueous solubility:** The unchanged form of a drug species will be preferentially absorbed through many body tissues therefore it is important to note the relationship between pKa of the compound and its absorptive environment. For conventional dosage forms the drug can generally fully dissolve in the stomach and then be absorbed in the alkaline pH of the intestine.
- **Partition coefficient:** The compounds with a relatively high partition coefficient are predominantly lipid soluble and easily

penetrate membranes resulting high bioavailability. Compounds with very low partition coefficient will have difficulty in penetrating membranes resulting poor bioavailability. Further more partitioning effects apply equally to diffusion through polymer membranes.

- **Drug Stability:** Drugs that are unstable in the stomach can be placed in a slowly soluble form or have their release delayed until they reach the small intestine However, such a strategy would be detrimental for drugs that either are unstable in the small intestine or undergo extensive gut wall metabolism, as pointed out in the decreased bioavailability of some anticholinergic drugs from controlled /sustained release formulations.
- **Protein Binding:** It is well known that many drugs bind to plasma proteins with a concomitant influence on the duration of drug action. Since blood proteins are for the most part recirculated and not eliminated, drug protein binding can serve as a depot for drug producing a prolonged release profile, especially if a high degree of drug binding occurs.

In the recent years extensive efforts have been made in various pharmaceutical research laboratories for the development of controlled release drug delivery systems, with an aim of improved patient compliance, better therapeutic efficacy, less side effects and reduced dosage regimen with less toxicity for treatment of many chronic diseases[5]. The drug candidate selected under the study is Verapamil hydrochloride, a calcium channel blocking agent used in the treatment of angina pectoris, hypertension and cardiac arrhythmia. Its biological half life is 4 to 6 hours and its usual dose is 120 to 240mg three times a day[6].

Qiu. Y et al reported the formulation developments of sustained release hydrophilic matrix tablets of zileuton[7]. They used low and medium viscosity grades of hydroxyprppyl methyl cellulose and tablets were prepared by wet granulation. It was observed that the release rate decreased with higher polymer concentration or higher viscosity grades.

Xu.G and Sunada.H reported the influence of formulation change on drug release kinetics from hydroxypropyl methyl cellulose matrix tablets[8]. The polymer content was predominant controlling factor for the release of indomethacin from the HPMC matrix tablets. As the content increased, the release rate decreased and the mechanism of drug release gradually changed from Higuchis diffusion to Non-Fickian transport.

Hence the main objective of this research work was to study the relationship and influence of HPMC ratio on release of Verapamil hydrochloride and also to assess the potential value of HPMC mixtures as gelling agents in matrix tablets. The prepared matrix tablets were evaluated for various physical parameters, weight variation, uniformity of drug content, drug-excipient compatibility studies (IR) and invitro dissolution studies.

MATERIALS AND METHOD

Verapamil hydrochloride was obtained as gift sample from Micro Labs, Bangalore., HPMC 50cps, HPMC K4M and K100M were obtained as gift samples from Colorcon Asia Pvt.Ltd, Goa. Other excipients used in preparing matrix tablets were of IP grades, all other chemicals were of analytical grade and were provided by the college.

Preparation of matrix tablets of Verapamil hydrochloride:

Verapamil hydrochloride matrix tablets were prepared by wet granulation method using different viscosity grades of HPMC 50cps, HPMC K4M and HPMC K100M to give a drug to

polymer ratio of 1:1 and 1:2 as per the formula given in table 1.

Table 1. Different Formulations of Verapamil HCl

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Verapamil HCl	120mg	120mg	120mg	120mg	120mg	120mg	120mg	120mg	120mg
HPMC K50	240mg	-	-	120mg	-	-	60mg	30mg	90mg
HPMC K4M	-	240mg	-	-	120mg	-	-	-	-
HPMC K100M	-	-	240mg	-	-	120mg	60mg	90mg	30mg
Lactose	20mg	20mg	20mg	20mg	20mg	20mg	20mg	20mg	20mg
PVP K-30	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg	10mg
Talc	2mg	2mg	2mg	2mg	2mg	2mg	2mg	2mg	2mg
Magnesium Stearate	4mg	4mg	4mg	4mg	4mg	4mg	4mg	4mg	4mg
Total weight	**396mg**	**396mg**	**396 mg**	**276 mg**	**276 mg**	**276 mg**	**276 mg**	**276 mg**	**276 mg**

RESULTS AND DISCUSSION:

Pre-Compressional Parameters:

The properties/characteristics of powder blend plays an important in formulations. Table 2 shows the powder blend properties of prepared granules. Bulk density depends on particle size, shape and tendency of particles to adhere together, may influence compressibility, porosity, dissolution and other properties.

Table 2: Precompressional parameters of all the Formulations

Formulations	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index	Hausner Ratio	Angle of repose (θ)
F1	0.440 ± 0.01	0.380 ± 0.02	21.11 ± 0.10	1.08 ± 0.01	20.12 ± 0.06
F2	0.430 ± 0.02	0.430 ± 0.03	25.96 ± 0.04	1.07 ± 0.02	22.16 ± 0.09
F3	0.450 ± 0.03	0.445 ± 0.04	20.14 ± 0.06	1.05 ± 0.01	23.98 ± 0.10
F4	0.390 ± 0.02	0.420 ± 0.03	24.63 ± 0.07	1.04 ± 0.04	22.02 ± 0.07
F5	0.446 ± 0.01	0.390 ± 0.02	23.19 ± 0.08	1.10 ± 0.01	20.11 ± 0.08
F6	0.424 ± 0.02	0.370 ± 0.02	26.50 ± 0.05	1.06 ± 0.04	22.16 ± 0.10
F7	0.380 ± 0.01	0.381 ± 0.04	24.10 ± 0.10	1.08 ± 0.01	20.09 ± 0.08
F8	0.395 ± 0.08	0.443 ± 0.01	28.22 ± 0.05	1.09 ± 0.03	20.19 ± 0.07
F9	0.430 ± 0.01	0.400 ± 0.05	26.16 ± 0.12	1.07 ± 0.02	21.14 ± 0.06

Post-compressional parameters:

Tablet Weight, Hardness & Friability:

All the formulations were evaluated for various parameters like Weight variation, Hardness and Friability[9,10]. All the prepared tablets formulations F1 to F9 shown in Table 3, it was found that there was no much variation in thickness of tablets; it showed that powder blends was consistent in particle size and uniform behavior during tablet compression. The hardness of tablets was measured by Pfizer hardness tester. The hardness was in range of 5.6 ± 0.01 to 6.0 ± 0.02 Kg/cm^2. Tablet hardness reflects differences in tablet density and porosity, which showed results in difference release patterns of the drug by affecting the rate of penetration in the dissolution medium at the surface of the tablet.

Weight Variation: The weight (mg) of each of 20 individual tablets was determined by dusting each tablet off and placing it in an electronic balance. The weight data from the tablets were analyzed for sample mean and percent deviation. The results are showed in table 3.

Friability: The present study of tablets is within the limit and the slight variation in seen in friability because of the variation in compression force applied and its total weight. The friability of tablets also depends on type of filler and moisture contents present in it. The friability was found to be in the range of 0.55 ± 0.025 to 0.74 ± 0.020 shown in Table 3.

Drug Content: Drug content was in range of 97.37 ± 0.08 to 100.85 ± 0.98, which reflects good drug content uniformity in all the prepared formulations. The reading complies as per I P. which indicates drug was uniformly distributed throughout the tablet compressed shown in Table 3.

Table 3: Post-Compressional properties of Verapamil HCl tablets

Formulations	Average weight (mg)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	393.35 ± 0.01	5.6 ± 0.01	0.68 ± 0.041	97.62 ± 0.36
F2	393.05 ± 0.03	6.0 ± 0.02	0.62 ± 0.056	98.87 ± 0.65
F3	393.25 ± 0.04	5.7 ± 0.04	0.72 ± 0.047	99.37 ± 1.22
F4	273.40 ± 0.01	5.8 ± 0.06	0.58 ± 0.080	97.37 ± 0.08
F5	273.20 ± 0.03	5.7 ± 0.02	0.65 ± 0.054	99.40 ± 0.62
F6	273.25 ± 0.04	5.8 ± 0.04	0.67 ± 0.010	99.62 ± 1.10
F7	273.05 ± 0.02	6.0 ± 0.02	0.63 ± 0.016	100.85 ± 0.98
F8	273.00 ± 0.01	5.8 ± 0.05	0.74 ± 0.020	99.07 ± 0.46
F9	273.30 ± 0.04	5.7 ± 0.04	0.55 ± 0.025	97.45 ± 0.45

In-Vitro Release Study:

Table 4: *In vitro* release data of Verapamil Hydrochloride matrix tablets of formulations F1, F2 and F3.

Sl. No.	Time (Hrs)	F1	F2	F3
		Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD
1.	01	23.01±0.17	15.98±0.49	12.85±0.42
2.	02	39.31±1.22	18.18±0.70	20.26±0.58
3.	03	48.07±0.69	23.81±0.60	25.90±0.41
4.	04	59.13±0.19	29.24±0.78	32.51±0.41
5.	05	68.72±0.49	32.58±0.42	39.51±1.61
6.	06	76.12±0.37	39.13±1.61	45.45±0.71
7.	07	87.63±0.29	46.39±0.38	52.76±0.92
8.	08	93.16±0.53	57.63±0.81	59.92±0.10
9.	09	96.23±1.23	63.39±0.19	64.76±0.92
10.	10		74.12±0.46	76.23±0.10
11.	11		79.85±0.67	80.91±0.42
12.	12		85.23±1.02	89.77±0.38
13.	13		92.68±0.25	93.57±0.84
14.	14			96.34±1.02

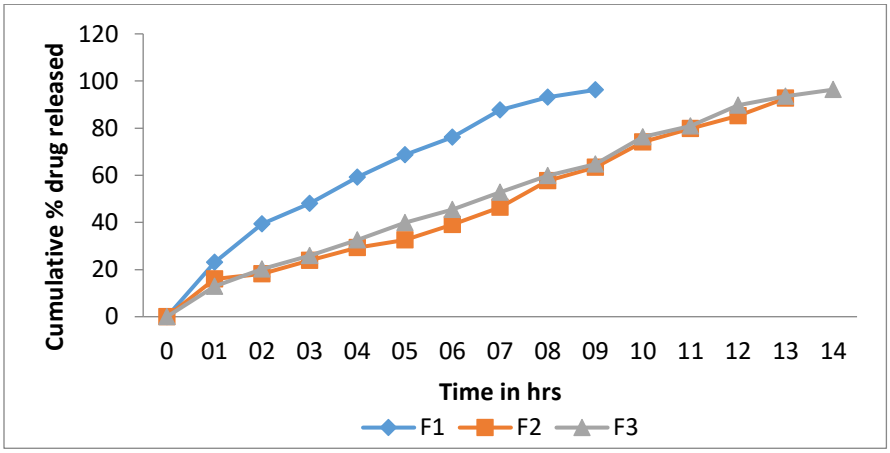

Fig 1: *In vitro* release data of Verapamil Hydrochloride matrix tablets of formulations F1, F2 and F3.

Table 5: *In vitro* release data of Verapamil Hydrochloride matrix tablets of formulations F4, F5 and F6.

Sl. No.	Time (Hrs)	F4	F5	F6
		Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD
1.	01	30.66±1.04	20.74±0.59	15.43±1.04
2.	02	52.74±0.63	32.21±1.04	24.83±0.56
3.	03	67.88±1.30	38.74±1.08	30.57±0.72
4.	04	82.85±0.31	45.21±0.16	35.89±0.33
5.	05	88.16±2.02	50.13±0.94	41.33±0.96
6.	06	90.59±1.29	56.12±0.74	46.72±0.55
7.	07	97.84±0.62	61.57±0.77	54.21±0.59
8.	08	100.20±0.78	66.24±0.60	61.24±0.35
9.	09		72.07±1.20	68.36±0.99
10.	10		76.29±0.70	72.31±0.77
11.	11		79.15±0.09	77.86±1.07
12.	12		88.99±0.34	84.15±0.77
13.	13		93.49±0.62	86.29±1.47
14.	14		98.64±0.11	89.39±0.58
15.	15			94.32±0.67
16.	16			97.86±0.32

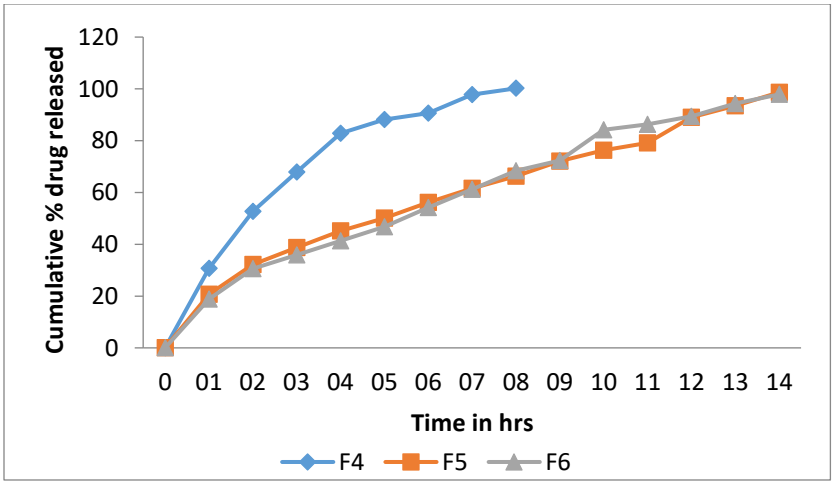

Fig 2: *In vitro* release data of Verapamil Hydrochloride matrix tablets of formulations F4, F5 and F6.

Table 6: *In vitro* release data of Verapamil Hydrochloride matrix tablets of formulations F7, F8 and F9.

Sl. No.	Time (Hrs)	F7	F8	F9
		Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD	Cumulative* percent drug released ± SD
1.	01	19.02±0.61	17.58±0.90	20.79±0.91
2.	02	27.44±0.82	25.48±2.18	27.03±1.56
3.	03	35.56±2.42	33.02±0.70	33.01±2.17
4.	04	44.26±0.64	42.04±0.66	46.12±0.86
5.	05	47.82±1.30	46.21±1.51	59.10±1.86
6.	06	57.50±0.37	48.69±2.00	65.54±2.28
7.	07	64.37±0.64	54.17±2.57	71.45±0.63
8.	08	71.51±1.88	57.94±1.32	87.17±1.44
9.	09	76.91±0.58	67.15±2.07	92.13±2.20
10.	10	84.56±0.31	72.68±1.54	95.62±0.71

11.	11	89.63±1.27	75.63±2.05	99.95±1.62
12.	12	96.86±0.93	86.20±0.52	
13.	13	100.36±0.21	92.20±0.87	
14.	14		99.39±1.11	

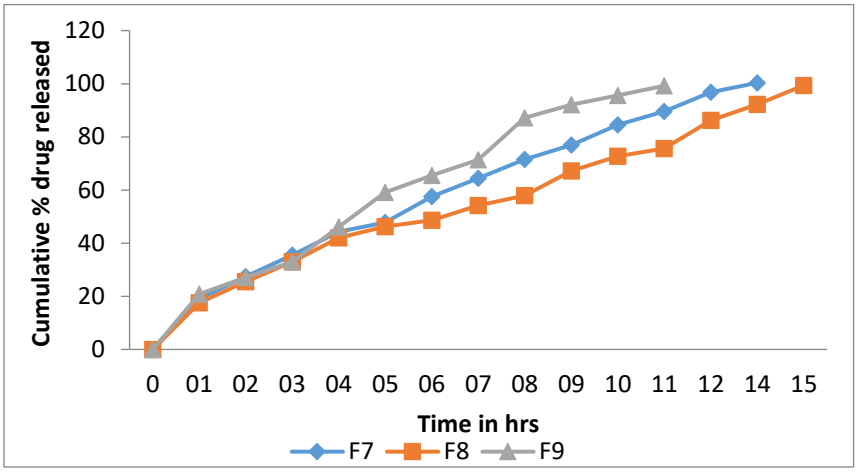

Fig 3: *In vitro* release data of Verapamil Hydrochloride matrix tablets of formulations F7, F8 and F9.

Linear regression analysis: The invitro drug release data was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equations. Higuchi's and Korsmeyer model in order to determine the mechanism of the drug release. The results of linear regression analysis data including regression coefficient are summarized in table 7.

When the regration coefficient 'r' value of zero order and first order plots were compared, it was observed that the 'r' values of zero order plots were in the range of 0.90 to 0.99 whereas the 'r' values of first order plots were in the range of -0.86 to -0.97 indicating drug release from all the formulation was found to follow zero order kinetics except for formulation F4. It was observed that the 'r' values for the Higuchi's plots were found to be in the range of 0.97 to 0.99 for the formulation studied indicated the release of drug from these formulations was governed by diffusion controlled process[11]. When Korsmeyer et al equation was fitted to dissolution data values, the exponent 'n' was found to be in the range of 0.57 to 0.76 indicating the drug release was by non-Fickian diffusion[12].

Table 7: Linear regression analysis data of Verapamil Hydrochloride Matrix Tablets

Formulation code		Zero Order	First Order	Higuchi Model	Korsmeyer Equation
	r	0.9897	-0.9690	0.9977	0.9975
F1	A	19.831	2.168	-15.453	1.369
	B	9.176	-0.159	37.836	0.6557
	r	0.9931	-0.9550	0.9720	0.9730
F2	A	4.234	2.166	-29.396	1.066
	B	6.560	-0.8059	31.689	0.7614
	r	0.994	-0.9798	0.9888	0.9935
F3	A	11.206	2.168	-24.033	1.073
	B	5.742	-0.0827	29.977	0.7643
	r	0.952	-0.968	0.9831	0.984
F4	A	30.457	2.140	-5.048	1.522
	B	10.626	-0.227	40.517	0.593

	r	0.9960	-0.8841	0.9939	0.9977
F5	A	20.631	2.174	-9.623	1.313
	B	5.626	-0.1011	27.718	0.5749
	r	0.9945	-0.937	0.9942	0.9966
F6	A	14.381	2.183	-19.080	1.162
	B	5.512	-0.0880	28.921	0.6949
	r	0.9978	-0.9331	0.9937	0.9966
F7	A	14.888	2.222	-19.505	1.245
	B	6.838	-0.1173	32.549	0.6699
	r	0.9971	-0.8687	0.9838	0.9828
F8	A	13.935	2.200	-17.242	1.266
	B	6.450	-0.0962	28.955	0.5919
	r	0.9910	-0.9531	0.9877	0.9854
F9	A	12.066	2.208	-25.550	1.247
	B	8.563	-0.1372	37.967	0.7274

'r'=Regression co-efficient

'A'= Intercept

'B'= Slope

FTIR Studies: The drug Verapamil hydrochloride which is in the form of hydrochloride exhibits: Peak at 1461.84 cm^{-1} and 10.27.68 cm^{-1} are due to alkyl aryl ether linkage and Peak at 1608.46 cm^{-1} is due tertiary amine, confirms the drug structure. In case of HPMC a broad band is observed at 3473.6 cm^{-1} indicating the presence of polyhydroxyl group in the IR spectrum. The C-H absorption frequency was noticed at 2924.2 cm^{-1} in conformation of presence of alkyl moieties. The IR spectrum of formulation (F9) containing (1:1) K100M-30mg, 50 cps-90mg shows Peaks at 1461.85 cm^{-1} and 1019.4 cm^{-1} are due to alkyl aryl ether linkage and Peaks at 1608 cm^{-1} is due to tertiary amine, conforms the undisturbed drug in formulation. Shown in figure 4 & 5

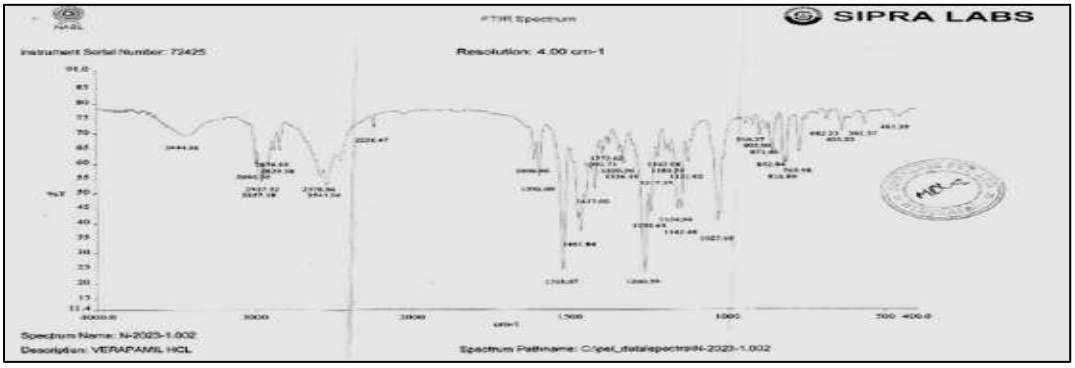

Fig 4: FTIR of Pure drug: Verapamil HCl

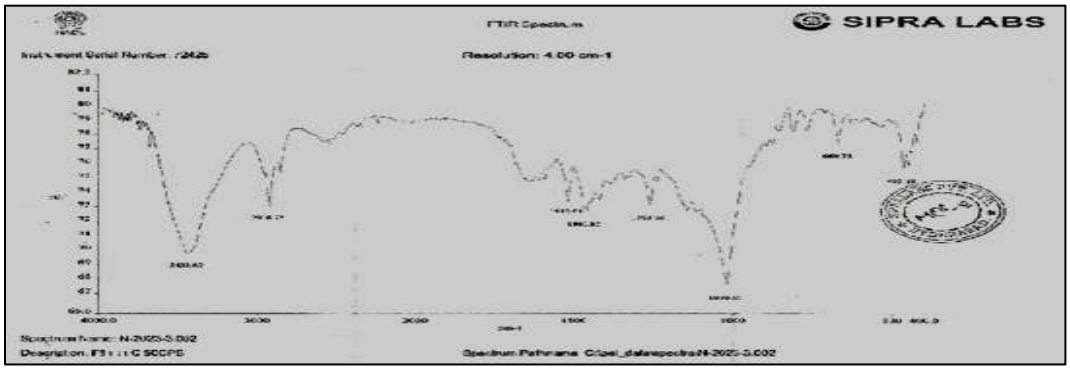

Fig 5: FTIR of Formulation F9

Dissolution t_{50} and t_{85} values: The dissolution t_{50} and t_{85} values for all the matrix tablets formulations of Verapamil hydrochloride given in table 8 & in figure 6. The comparative effect of different viscosity grades of HPMC on the release profiles of verapamil hydrochloride from the matrix tablets in terms of dissolution t_{50} and t_{85} values is shown in figure 6. It was observed that the formulations containing lower viscosity grades of HPMC i.e. HPMC 50cps exhibited shortest dissolution times followed by formulations containing higher viscosity grades viz. HPMC K4M and HPMC K100M.

Table 8: Dissolution T_{50} and T_{85} values of various formulations of Verapamil hydrochloride matrix tablets

Sl. No.	Formulations	t_{50} (hr)	t_{85} (hr)
1	F1	3.2	6.8
2	F2	7.3	11.9
3	F3	6.6	12
4	F4	1.85	4.4
5	F5	5	11.6
6	F6	5.4	11.5
7	F7	4.35	11.2
8	F8	5.2	10.5
9	F9	4.2	7.9

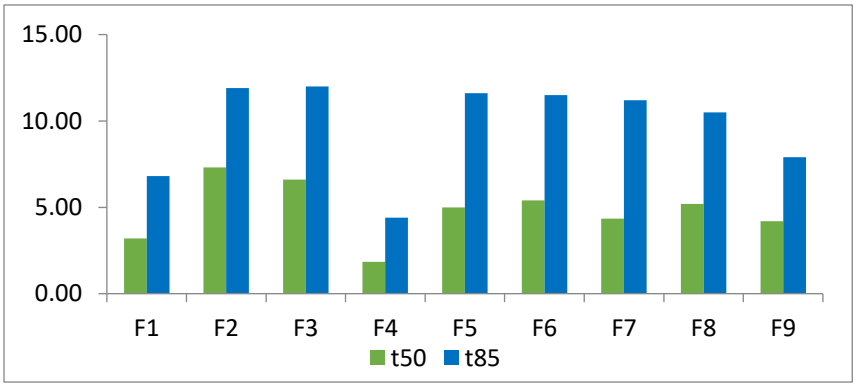

Fig 6: Dissolution T_{50} and T_{85} values of various formulations of Verapamil hydrochloride matrix tablets

Stability Studies: Short term stability studies were performed for formulation F9 at 45^0c ± 1^0c for 3 weeks (21 days). The sample were analyzed for percent drug content and invitro drug release studies. The results are given in table 9, no appreciable difference was observed for the above parameters.

Table 9: Stability studies of Formulation F9

Sl no	Time in days	Physical changes	Mean ± SD (45° C)
1.	01	--	99.63±0.74
2.	07	No Change	99.18±0.12
3.	14	No Change	98.05±0.28
4.	21	No Change	98.04±1.10

Table-10: In Vitro release data of formulation F9

Sl. No.	Time (Hrs)	Cumulative*percent drug released ± SD	
		$45±1^0$ C	$45±1^0$ C
		1st Day	21st Day
1.	01	18.79±0.91	17.09±0.07
2.	02	27.03±1.56	26.00±0.54
3.	03	33.01±2.17	32.74±1.20

4.	04	46.12±0.86	45.52±1.60
5.	05	59.10±1.86	57.08±0.99
6.	06	65.54±2.28	63.93±1.02
7.	07	71.45±0.63	70.10±0.84
8.	08	87.17±1.44	86.22±0.81
9.	09	92.13±2.20	91.67±0.74
10.	10	95.62±0.71	94.84±1.24
11.	11	97.86±1.62	96.31±1.12
12.	12	98.82±0.20	97.86±0.42

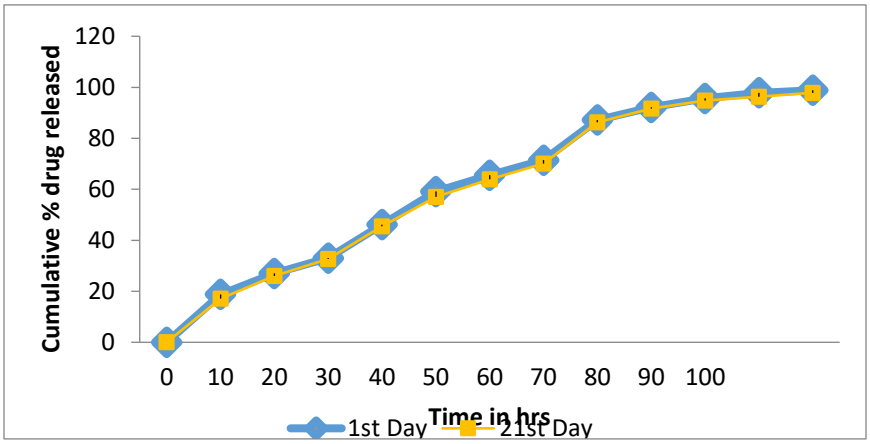

Fig 7: In Vitro release data of formulation F9

CONCLUSION

From the present study the following conclusions can be ruled.

1. Matrix tablets of Verapamil hydrochloride using hydrophilic swellable polymer HPMC by wet granulation method were found to be good without chipping, capping and sticking.
2. In the present study, an attempt was made to prepare matrix tablets of verapamil hydrochloride by wet granulation method.
3. Matrix tablets of Verapamil hydrochloride were prepared by using different viscosity grades of HPMC with lactose as channeling agent.
4. The drug polymer ratio, the viscosity grades of HPMC were found to influence the release of drug from the formulations. As the amount of polymer increased the drug release rate was found to be decreased. A faster drug release was observed for tablets with lower viscosity grades when compared to higher viscosity grades.
5. The drug release from the prepared HPMC formulation was found to follow zero order kinetics and governed by non-Fickian diffusion.
6. Formulation F9 containing drug polymer ratio 1:1 with polymer composition of HPMC K100M: HPMC 50 cps (1:3) exhibited promising results as that of commercial formulation.
7. Short term stability studies performed formulation F9 at 45^0c indicated no appreciable changes in the percent drug content and invitro drug release studies.

ACKNOWLEDGEMENTS

I would like to express my sincere thank to my guide Dr. S. N. Hiremath for his valuable guidance & support.

REFERENCES

1. Lachmann L, Lieberman HA, Kanig JL. The Theory & Practice of Industrial Pharmacy, 3rd Edition, Varghese Publishing House, Bombay 1991: 430.

2. Robinson JR, Lee HL (Ed). Controlled Drug Delivery: Fundamentals & Applications. 2nd Edition, Marcel Dekker Inc., New York, 1987; 373.
3. Gennaro AR (Ed.) Remington. The Science & Practice of Pharmacy. 19th Edition, Vol. II; 1995: 1662.
4. Shargel L and Andrew BC. Applied Biopharmaceutics and Pharmacokinetics (4th Edn.), 174.
5. Remingtons; The science & practice of pharmacy, 20th Edn., Lippan cott, Williams & Wilkins, Baltimore, Marryland, 1995; 721-752.
6. Martindale, The Complete Drug Reference, 33rd Edn, The Pharmaceutical Press, London, 2001: 332-33.
7. Qiu. Y et al., Formulation development of sustained release hydrophilic matrix tablets of zileuton, Pharmaceutical Development and Technology, 2 (3): 197-204, 1997.
8. Xu. G and Sunada. H., Influence of formulation change on drug release kinetics from hydroxypropyl methyl cellulose matrix tablets, Chem.Pharm.Bull., 43 (mar): 483-487, 1995.
9. USP; The United States Pharmacopial Convention Inc., CD-2004; USP 27-NF-22.
10. Lachmann L, Lieberman HA, Kanig JL. The Theory & Practice of Industrial Pharmacy, 3rd Edn, Varghese Publishing House, Bombay 1991: 430.
11. Higuchi.T., Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices, J. Pharm. Sci., 51: 1145-1149, 1963.
12. Korsmeyer, R. W., Gurny. R., Doelker. E., Buri. P., Peppas. N.A., Mechanism of solute release from porous hydrophilic polymer, Int. J. Pharm, 15: 25-35, 1983.

HOW TO CITE: Sunil Firangi*, Ananth Rao Kulkarni, R. B. Sangoligi, Dr. S. N. Hiremath, Dr Syed Sanaullah, Formulation and In-vitro Evaluation of Controlled Release Matrix Tablets of Anti-Hypertensive Drug: Verapamil Hydrochloride, Int. J. in Pharm. Sci., 2023, Vol 1, Issue 10, 1-12. https://doi.org/10.5281/zenodo.8396256