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Practical Approach for the Estimation of Alcohol Drug Release from fhe Sustained Release Dosage Forms of Verapamil Hydrochloride

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ABSTRACT

The aim of the present study was to develop sustained release formulation of Verapamil Hydrochloride to maintain constant therapeutic levels of the drug for over 12 hrs. Various grades of HPMC polymers, Guar gum and Xanthan gum were employed as polymers. Verapamil Hydrochloride dose was fixed as 120 mg. Total weight of the tablet was considered as 400 mg. Polymers were used in the concentration of 60, 120 and 180 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e., 96.10 % in 12 hours containing Guar gum polymer in the concentration of 180mg . It followed zero order release kinetics. For the optimized formulation alcohol effect has been studied by using various concentrations of alcohol in dissolution medium. As the concentration of alcohol increases the sustained action of polymer was decreased. Hence it was concluded that alcohol has significant effect on drug release pattern.

Keywords: Verapamil Hydrochloride, HPMC, Guar gum,Xanthum gum.

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INTRODUCTION

Oral Drug Delivery

Most conventional oral drug products, such as tablets and capsules, are formulated to release the active drug immediately after oral administration, to obtain rapid and complete systemic drug absorption. Such immediate-release products result in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects. However, after absorption of the drug from the dosage form is complete, plasma drug concentrations decline according to the drug's pharmacokinetic profile. Eventually, plasma drug concentrations fall below the minimum effective plasma concentration (MEC), resulting in loss of therapeutic activity. Before this point is reached, another dose is usually given if a sustained therapeutic effect is desired. An alternative to administering another dose is to use a dosage form that will provide sustained drug release, and therefore maintain plasma drug concentrations, beyond what is typically seen using immediate-release dosage forms.

The term modified-release drug product is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms as presently recognized" . Several types of modified-release drug products are recognized:

1. *Extended-release drug products*. A dosage form that allows at least a twofold reduction in dosage frequency as compared to that drug presented as an immediate-release (conventional) dosage form. Examples of extended-release dosage forms include controlled-release, sustained-release and long-acting drug products.

2. *Delayed-release drug products*. A dosage form that releases a discrete portion or portions of drug, at a time or at times other than promptly after administration, although one portion may be released promptly after administration. Enteric-coated dosage forms are the most common delayed-release products.

3. *Targeted-release drug products*. A dosage form that releases drug at or near the intended physiologic site of action. Targeted-release dosage forms may have either immediate- or extended-release characteristics.

SELECTION OF DRUG CANDIDATE FOR SUSTAINED RELEASE DOSAGE FORM

The physico - chemical properties of the drug such as pKa, partition coefficient, biological half

life, molecular weight, dose of the drug etc., have to be considered before selection.

Characteristics of drugs suitable for formulation as Sustained Release Products

1. Exhibit moderate rates of absorption and excretion.
2. Uniform absorption throughout the gastrointestinal tract.
3. Administered in relatively small doses.
4. Possess good margin of safety.
5. Used for treatment of chronic therapy.

Characteristics of drugs unsuitable for formulation as Sustained Release Products

1. Not effectively absorbed in the lower intestine (Riboflavin).
2. Absorbed and excreted rapidly i.e. short biological half lives, less than one hour (Penicillin G, Furosemide).
3. Long biological half lives greater than 12 hours (Diazepam, Phenytoin).
4. Large doses required, 1gm (Sulphonamides)
5. Drugs with low therapeutic index (Phenobarbital, Digoxin).
6. Precise dosage titrated to individuals required (anticoagulants)
7. No clear advantage for sustained release formulation (griseofulvin)

Calcium channel blocker:

Organic calcium-channel blockers (OCCBs) like verapamil (a phenylalkylamine) and diltiazem, (a benzothiazepine) have long been used in the treatment of cardiac arrhythmias and another class of OCCBs, which are dihydropyridines (e.g. nifedipine, amlodipine) are used in the treatment of hypertension. The only known mechanism of action of OCCBs is blockade of sarcolemmal L-type calcium channels. In the cardiac muscle, these drugs predictably produce a negative inotropism, but in the skeletal muscle, the OCCB diltiazem has been shown to have a paradoxical action–it increases twitch tension up to 80% over control. This action has not been well explained. The skeletal muscle does not depend on influx of calcium *via*sarcolemmal channels for contraction; Armstrong and therefore it is understandable if diltiazem does not reduce force; but the enhancement of force is intriguing.

While working with strips of frog ventricle, we found that the preparation showed a rest-induced decay (RID) of force of contraction like the mammalian cardiac muscle. The RID was significant for rest-periods more than 40 s. Verapamil and diltiazem prevented such RID and in fact enhanced the force of contraction of the post-rest beat as compared to the pre-test beat (rest-induced potentiation, RIP). Based on our observations, we propose that, in addition to sarcolemmal

calcium-channel blockade, verapamil and diltiazem either prevent a diastolic SR calcium-leak or augment a diastolic SR calcium-uptake.

MATERIALS AND METHOD

Verapamil hydrochloride, HPMC K100M, Guargum, Xanthan gum, PVP K30, Talc, Magnesium stearate, MCC PH 102.

ANALYTICAL METHOD DEVELOPMENT:

Determination of absorption maxima:

A solution containing the concentration 10 µg/ ml drug was prepared in 0.1N HCl and pH 4.8 Phosphate buffer UV spectrums was taken using Double beam UV/VIS spectrophotometer. The solution was scanned in the range of 200 – 400.

Preparation calibration curve:

100mg of Verapamil hydrochloride pure drug was dissolved in 100ml of 0.1 N HCl (stock solution)10ml of solution was taken and make up with100ml of 0.1 N HCl (100µg/ml).from this 10ml was taken and make up with 100 ml of 0.1 N HCl (10µg/ml). The above solution was subsequently diluted with 0.1N HCl to obtain series of dilutions Containing 5,10,15,20,25,30,35 and 40µg/ml of Verapamil hydrochloride per ml of solution. The absorbance of the above dilutions was measured at 229 nm by using UV-Spectrophotometer taking 0.1N HCl as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The above procedure was repeated by using pH 6.8 phosphate buffer solutions.

Drug – Excipient compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy:

The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 31200 cm to 1200 cm. The resultant spectrum was compared for any spectrum changes.

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:

$$\tan \theta = h / r \quad \tan \theta = \text{Angle of repose}$$

Where,

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 inter particle 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 4.3.The tablets were prepared as per the procedure given below and aim is to prolong the release of Verapamil hydrochloride. Total weight of the tablet was considered as 400mg.

Procedure:

1) Verapamil hydrochloride and all other ingredients were individually passed through sieve no ≠ 40.

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.	Verapamil hydrochloride	HPMC K 100	Guar Gum	Xanthan gum	PVP K 30	Mag. Stearate	Talc	MCC pH 102
F1	120	60	-	-	20	4	4	QS
F2	120	120	-	-	20	4	4	QS
F3	120	180	-	-	20	4	4	QS
F4	120	-	60	-	20	4	4	QS
F5	120	-	120	-	20	4	4	QS
F4	120	-	180	-	20	4	4	QS
F7	120	-	-	60	20	4	4	QS
F8	120	-	-	120	20	4	4	QS
F9	120	-	-	180	20	4	4	QS

All the quantities were in mg

Evaluation of post compression parameters for prepared Tablets

The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test:

To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Table 3: Pharmacopoeial specifications for tablet weight variation

Average weight of tablet (mg) (I.P)	Average weight of tablet (mg) (U.S.P)	Maximum percentage difference allowed
Less than 80	Less than 130	10
80-2120	130-324	7.5
More than	More than 324	5

Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage

transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calculated and presented with deviation.

Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

$$\% \text{ Friability} = [\ (W1-W2) / W] \times 100$$

Where,

W1 = Initial weight of three tablets

W2 = Weight of the three tablets after testing

Determination of drug content:

Tablets were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of Verapamil hydrochloride were accurately weighed, transferred to a 100 ml volumetric flask containing 120 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with water. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In vitro* drug release studies**

Dissolution parameters:

Apparatus	--	USP-II, Paddle Method
Dissolution Medium	--	0.1 N HCl , p H 4.8 Phosphate buffer
RPM	--	50
Sampling intervals (hrs)	--	0.5,1,2,3,4,5,4,7,8,9,10,11,12
Temperature	--	37°c $\pm$ 0.5°c

As the preparation was for floating drug release given through oral route of administration, different receptors fluids are used for evaluation the dissolution profile.

Procedure:

900ml 0f 0.1 HCl was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c ± 0.5°c. Tablet was placed in the vessel and the vessel was covered then the apparatus was operated for 2 hours and then the medium 0.1 N HCl was removed and pH 4.8 phosphate buffer was added process was continued for upto 12 hrs at 50 rpm. At definite time intervals 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at 229 nm using UV-spectrophotometer.

The optimized formulation is further being subjected to dissolution by using 5%,10%,15%,20%,25%,30%, alcohol in both the dissolution media for up to 12 hrs at 50 rpm. At definite time intervals 5 ml of the receptors fluid was withdrawn, filtered and again 5ml receptor fluid was replaced. Suitable dilutions were done with receptor fluid and analyzed by spectrophotometrically at 229 nm using UV-spectrophotometer.

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.

Zero order release rate kinetics:

To study the zero–order release kinetics the release rate data ar e fitted to the following equation.

$$F = K_o t$$

Where, 'F' is the drug release at time't', and 'K_o' is the zero order release rate constant. The plot of % drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

$$\text{Log } (100\text{-}F) = kt$$

A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

$F = k\ t1/2$ Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

Korsmeyer and Peppas release model:

The mechanism of drug release was evaluated by plotting the log percentage of drug released versus

log time according to Korsmeyer- Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$$M_t / M_\infty = K\, t^n$$

Where, M_t / M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M_t / M_∞) versus log (time) is linear.

Hixson-Crowell release model:

$(100-Q_t)^{1/3} = 100^{1/3} - K_{HC}.t$ Where, k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where there is a change in surface area and diameter of particles or tablets).

RESULTS AND DISCUSSION

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

Analytical Method

Graphs of Verapamil hydrochloride was taken in Simulated Gastric fluid (pH 1.2) and in p H 6.8 phosphate buffer at 298 nm and 294 nm respectively.

Table 4: Observations for graph of Verapamil hydrochloride in 0.1N HCl (298nm)

Conc [µg/l]	Abs
5	0.104
10	0.205
15	0.302
20	0.411
25	0.503
30	0.608
35	0.710
40	0.808

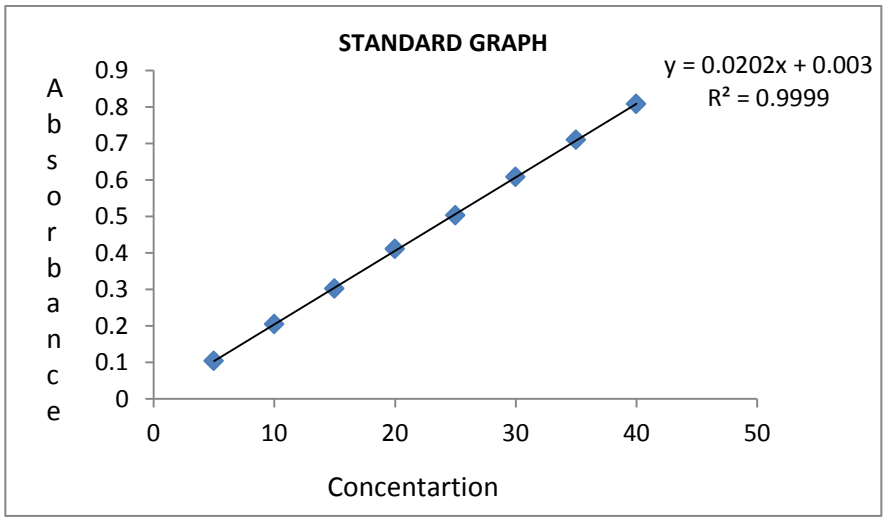

Figure 1: Standard graph of Verapamil hydrochloride in 0.1N HCl

Table 5: Observations for graph of Verapamil hydrochloride in pH 6.8 phosphate buffer (229nm)

Conc [µg/l]	Abs
5	0.098
10	0.195
15	0.298
20	0.392
25	0.490
30	0.595
35	0.690
40	0.776

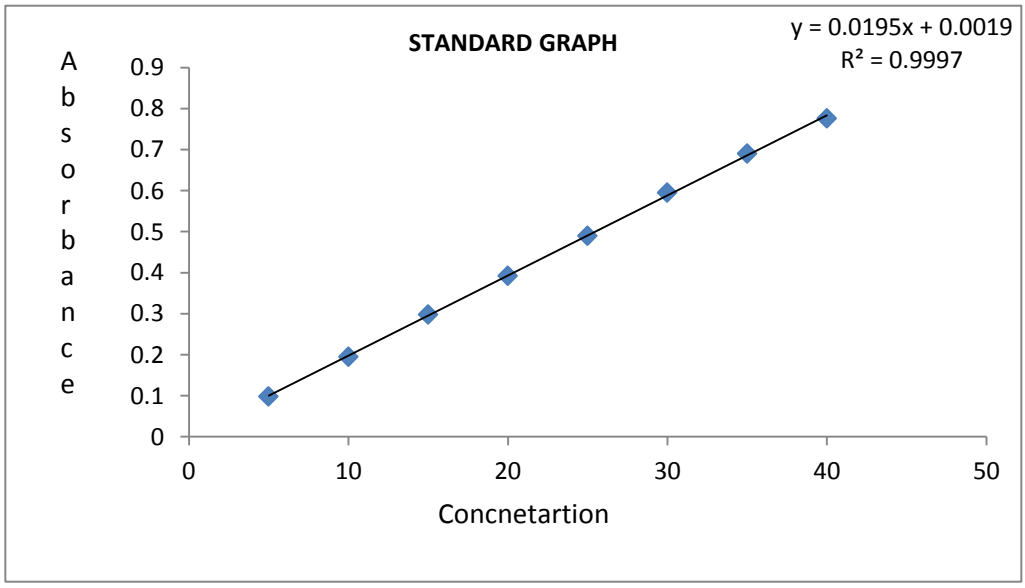

Figure 2: Standard graph of Verapamil hydrochloride pH 6.8 phosphate buffer (294nm)

Table 6: Preformulation parameters of powder blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	24.11	0.49±0.04	0.54±0.04	16.21±0.06	0.86±0.06
F2	25.67	0.52±0.09	0.52±0.04	16.87±0.05	0.98±0.05
F3	25.54	0.50±0.05	0.58±0.05	17.11±0.01	0.64±0.03
F4	25.43	0.51±0.06	0.54±0.07	17.67±0.08	1.12±0.04
F5	25.34	0.52±0.03	0.57±0.03	16.92±0.04	1.2±0.08
F6	25.22	0.53±0.04	0.56±0.06	17.65±0.09	1.06±0.09
F7	25.18	0.54±0.06	0.59±0.04	16.43±0.05	0.76±0.03
F8	24.22	0.58±0.04	0.67±0.02	17.97±0.02	1.15±0.09
F9	25.05	0.55±0.08	0.5 2±0.03	17.54±0.09	1.17±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 0.43±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 0.57 to 0.69 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 16 to 18 which show that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 0 to 1.2 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 7: In-vitro quality control parameters for tablets

Formulation codes	Weight variation(mg)	Hardness (kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	412.5	4.5	0.50	6.8	99.76
F2	405.4	4.5	0.51	6.9	99.45
F3	398.6	4.4	0.51	4.9	99.34
F4	405.6	4.5	0.55	6.9	99.87
F5	403.4	4.4	0.56	6.7	99.14
F6	400.7	4.5	0.45	6.5	98.56
F7	402.3	4.1	0.51	6.4	98.42
F8	401.2	4.3	0.49	6.7	99.65
F9	398.3	4.5	0.55	6.6	99.12

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 8:Dissolution Data of Verapamil hydrochloride Tablets Prepared With HPMC K100M,Guar gum and Xanthan gum in Different Concentrations

TIME (hr)	CUMULATIVE PERCENT DRUG DISSOLVED								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
0.5	25.5	20.1	16.4	17.25	16.42	14.62	10.4	9.4	8.5
1	46.7	39.4	26.7	38.26	25.73	19.86	16.5	15.6	14.5
2	76.5	55.3	34.6	54.16	36.63	22.35	28.6	21.4	18.4
3	98.4	75.3	42.4	72.01	45.04	31.45	39.5	36.7	23.4
4		87.3	55.4	88.26	58.25	39.80	48.5	42.4	28.2
5		99.4	67.4	97.10	65.33	45.25	59.4	49.6	34.8
6			85.4		76.41	58.24	69.2	55.3	40.2
7			91.5		84.84	66.73	74.5	60.3	44.8
8			97.3		97.80	71.34	82.3	72.8	50.4
9						75.52	87.78	83.52	63.34
10						82.17	98.78	88.65	69.27
11						87.10		96.56	74.86
12						96.10			79.97

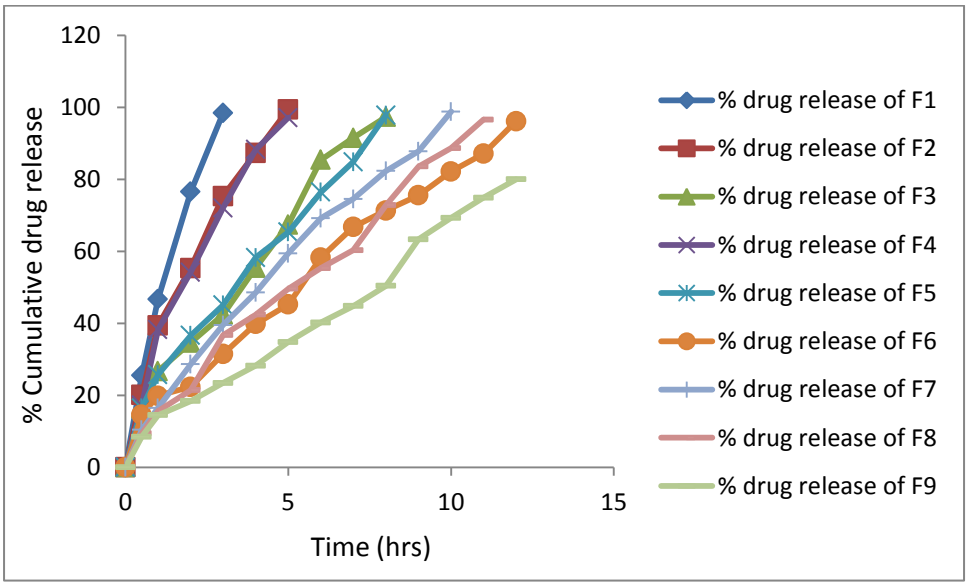

Figure 3: Dissolution profile of Verapamil hydrochloride Tablets Prepared With HPMC K100M,Guar gum and Xanthan gum in Different Concentrations.

From the dissolution data it was evident that the formulations prepared with HPMC K100M as polymer were unable to retard the drug release up to desired time period i.e., 12 hours.

Whereas the formulations prepared with Guar gum retarded the drug release in the concentration of 180 mg showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 96.10% in 12 hours with good retardation.

The formulations prepared with Xanthan gum showed more retardation even after 12 hours they were not shown total drug release. Hence they were not considered

Table 12: Dissolution Data of Verapamil hydrochloride Optimised Formulation in the 5%,10%,15% alcoholic media.

Time	5%	10%	15%	20%	25%	30%
0.5	7.03	8.09	3.00	5.72	3.85	4.76
1	11.77	10.05	5.01	14.23	5.10	16.78
2	17.02	15.06	9.89	26.89	8.99	28.43
3	28.89	22.05	11.08	36.78	12.30	38.12
4	39.21	29.08	15.07	49.32	18.06	44.64
5	41.21	32.07	21.98	58.12	26.83	59.76
6	52.35	40.12	32.77	72.45	33.45	69.14
7	65.07	53.04	40.02	82.44	42.16	98.65
8	78.92	60.29	48.06	90.13	75.86	
9	85.67	71.38	53.27	93.44	86.07	
10	93.45	80.70	68.55	97.77	95.03	
11	96.77	88.34	83.01	97.87		
12	98.88	95.45	97.20			

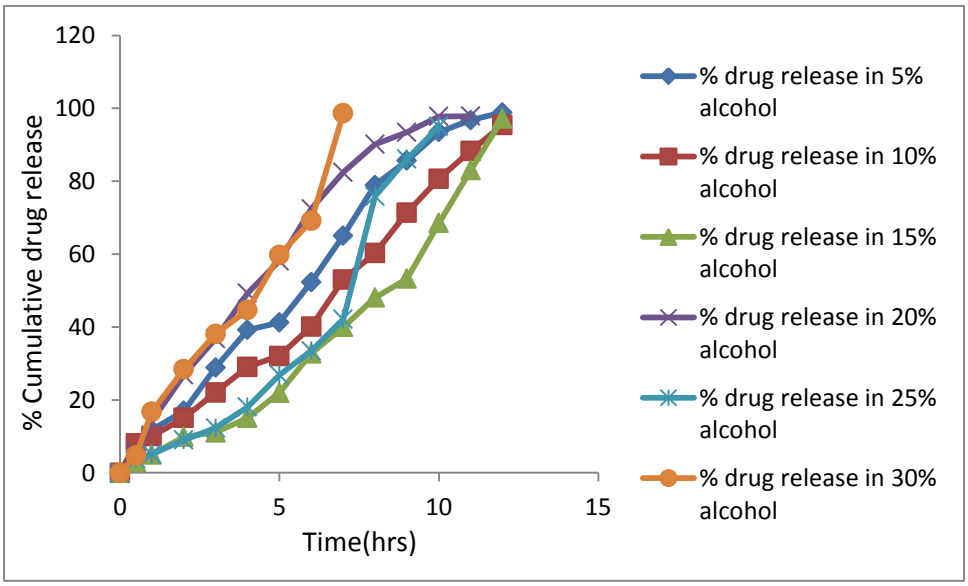

Figure 4: Dissolution profile of optimized formulation in the 5%,10%,15%,20%,25% and 30% alcoholic media

The optimized formulation shown the drug release of 98.88%,95.45%,97.20% upto 12 hours in the 5%,10%,15% alcoholic media respectively the formulation shown 97.87% drug release in the 11th hour in the 20% alcoholic medium, in the 25% alcoholic medium 95.03% drug release in the 10th hour and in the 30% alcoholic medium the the formulation showed max drug release by the 7th hour only.

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.

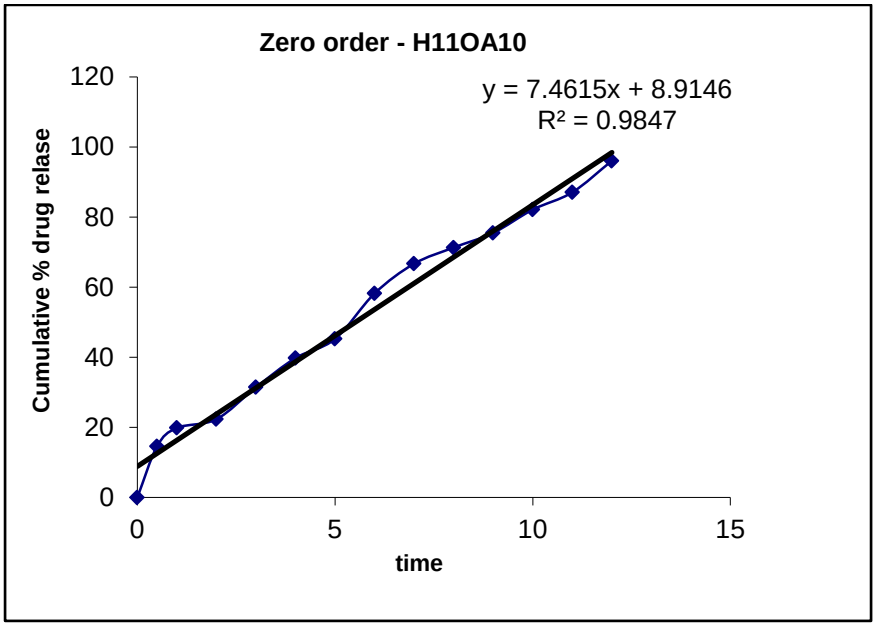

Figure 5 : Zero order release kinetics graph

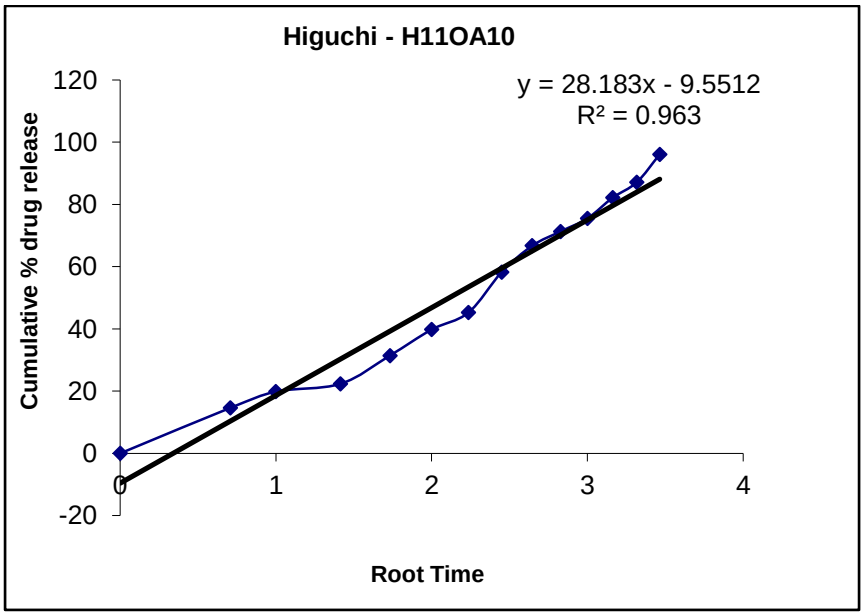

Figure 6 : Higuchi release kinetics graph

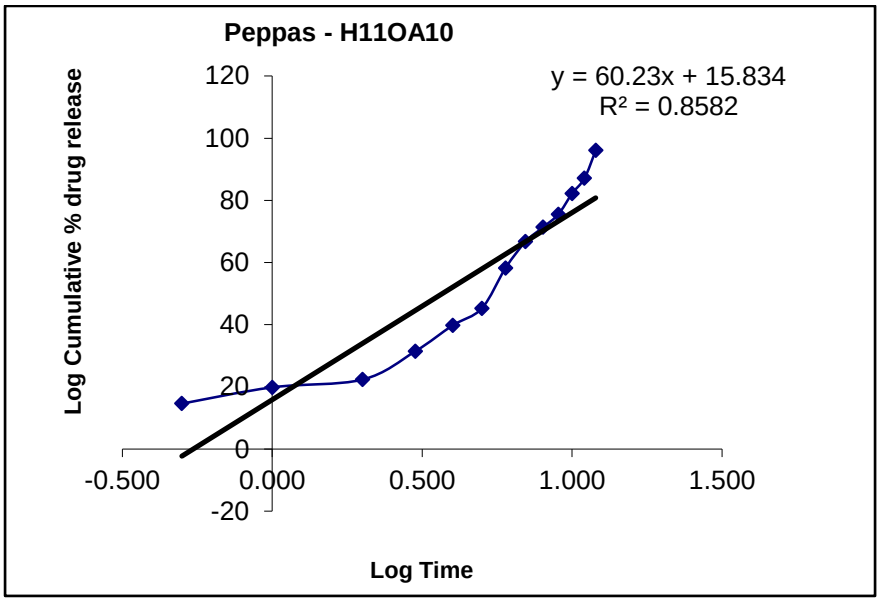

Figure 7: Kars mayer peppas graph

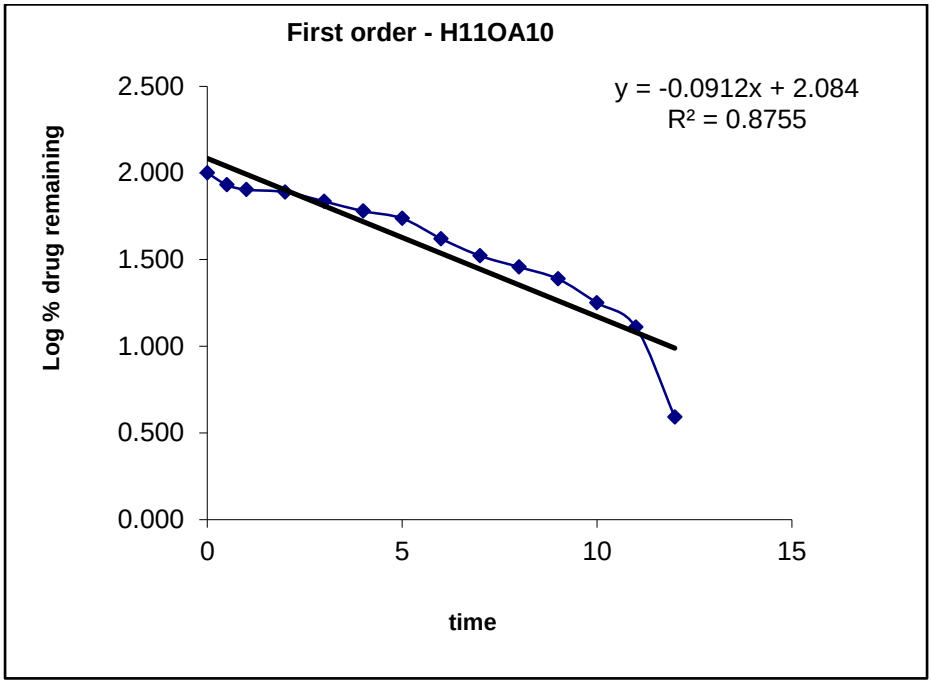

Figure 8: First order release kinetics graph

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

CONCLUSION

The aim of the present study was to develop sustained release formulation of Verapamil Hydrochloride to maintain constant therapeutic levels of the drug for over 12 hrs. Various grades of HPMC polymers, Guar gum and Xanthum gum were employed as polymers. Verapamil Hydrochloride dose was fixed as 120 mg. Total weight of the tablet was considered as 400 mg.

Polymers were used in the concentration of 60, 120 and 180 mg concentration. All the formulations were passed various physicochemical evaluation parameters and they were found to be within limits. Whereas from the dissolution studies it was evident that the formulation (F6) showed better and desired drug release pattern i.e., 96.10 % in 12 hours containing Guar gum polymer in the concentration of 180mg . It followed zero order release kinetics. For the optimized formulation alcohol effect has been studied by using various concentrations of alcohol in dissolution medium. As the concentration of alcohol increases the sustained action of polymer was decreased. Hence it was concluded that alcohol has significant effect on drug release pattern.

REFERENCES

1. Leon Shargel, Susanna Pong, Andrew B.C., Applied Biopharmaceutics and Pharmacokinetics, Modified-Release Drug Products, Pg 515 Fifth Edition, 2004
2. Chien Y.W., Controlled- and modulated-release drug-delivery systems. Encyclopedia of pharmaceutical technology. New York, Dekker, pgs 281-313, 1992.
3. J. R. Robinson, S. P. Eriksen, Theoretical formulation of sustained-release dosage forms. J Pharm Sci. 1966
4. Gilbert S. Banker, Christopher T. Rhodes, Modern Pharmaceutics, Sustained - and Controlled -release drug-delivery systems, Pg 505 Fourth Edition, 2002
5. Leon Lachman, The Theory and Practice of Industrial Pharmacy, Sustained Release Dosage Forms, pgs 430-431, Third Edition, 1987
6. Gilbert S. Banker, Christopher T. Rhodes, Modern Pharmaceutics, Sustained - and Controlled -release drug-delivery systems, Pgs 505-506 Fourth Edition, 2002
7. Gilbert S. Banker, Christopher T. Rhodes, Modern Pharmaceutics, Sustained - and Controlled -release drug-delivery systems, Pgs 507-508 Fourth Edition, 2002
8. Barzegar-Jalali M, Siahi Shadbad M.R, Azarmi Sh, Barzegar-Jalali A, Mohammadi Gh, Adibkia Kh., Study on the release of acetazolamide from matrices containing tragacanth and acacia gums, Journal of Faculty of Pharmacy, Tabriz University of Medical Sciences, 2007
9. V. Jannin, E.Pochard and O. Chambin, Influence of poloxamers on the dissolution performance and stability of controlled-release formulations containing Precirol ATO 5, PubMed, 2005

10. Celine Valeria Liew, Lai Wah Chan, Ai Ling Ching and Paul Wan Sia Heng., Evaluation of sodium alginate as drug release modifier in matrix tablets, International Journal of Pharmaceutics, Volume 309, Issues 1-2, 17 February 2006, Pages 25-37
11. Juan M. Aceves, R. Cruz and E. Hernandez, Preparation and characterization of Furosemide-Eudragit controlled release systems, International Journal of Pharmaceutics, Volume 195, Issues 1-2, 15 February 2000, Pages 45-53