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Research Article

FORMULATION OF SUSTAIN RELEASE SOLID DISPERSIONS OF VERAPAMIL HYDROCHLORIDE USING ETHYL CELLULOSE AND EUDRAGIT-RSPO

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ABSTRACT

A simple technique of sustained release solid dispersion (S.D) was used in the present investigation to control the release of verapamil hydrochloride (VPH) from tablets with ethyl cellulose (EC) and eudragit RSPO. In the present study the SD's containing EC and eudragit RSPO at different drug-polymer ratios of 1:0.5, 1:1, 1:2, 1:3, 1:5, 1:7, 1:7:0.25, 1:7:0.5, 1:7:0.75 as F1 –VPH:EC, F2 – VPH:EC, F3 – VPH:EC, F4 – VPH:RSPO, F5 – VPH:RSPO, F6 – VCH:RSPO, F7 – VPH:EC:RSPO, F8 – VPH:EC:RSPO, F9 – VPH:EC:RSPO respectively by solvent evaporation technique. The physical mixtures were prepared by physical mixing technique at the same ratio as solid dispersion. FTIR spectroscopy suggested that there was no major interaction between drug and polymers. The solid dispersions or physical mixtures were compressed to tablets. All these formulations were evaluated by *in-vitro* dissolution studies using USP apparatus II (paddle method) over a period of two hours in 0.1N HCl and in pH 6.8 buffer for 3-18 hours. The in-vitro drug release study revealed that the S.D's containing EC and eudragit RSPO in combination has extended the release rate for 20 hours compared to the physical mixtures at the same ratio. The in-vitro release profile indicates that the release of VPH can be effectively controlled from a tablet containing S.D. The release data was analysed as per the peppas equation model indicating that the non-fickian diffusion was the release mechanism.

Keywords: Solid dispersion, Verapamil hydrochloride, Ethyl Cellulose, Eudragit- RSPO

INTRODUCTION

More recently, the concept of solid dispersion has been explored using insoluble carrier materials. These sustained release solid dispersion system may be useful for enhancing bioavailability and suitable for sustained release formulations[1]. The sustained solid dispersion offer various potential advantages for drugs having poor bioavailability and can be delivered efficiently there by maximizing their bioavailability and sustained action[2].

Verapamil Hydrochloride[3] is a Calcium channel-blocking drug having class IV anti arrhythmic activity. It is used in the treatment of supraventricular arrhythmias angina, and hypertension. It is soluble in water, sparingly soluble in Ethanol (95%), and freely soluble in chloroform. Sustained release products are needed for Verapamil Hydrochloride to prolong its duration of action and reduction of usage frequency.

Reduction of dissolution rate is achieved by incorporating the drug in an insoluble carrier such as Ethyl Cellulose, PEG , Eudragit RSPO etc. such formulation are considered as a matrix system helps in prolonging the duration of time over which the drug is released and hence are considered suitable for formulation as sustained release dosage forms.

It is found that different insoluble polymers like EC, Eudragit RSPO etc., were attempted in designing of sustained release solid dispersions by employing various solid dispersion techniques. Hence, in the present investigation, it is aimed to study the suitability of using EC, Eudragit RSPO, in the development of solid dispersion system for controlling the drug release.

MATERIALS AND METHODS

Preparation of solid dispersions and physical mixtures

Preparation of sustained release solid dispersion by common solvent method[4]

The sustained solid dispersions of Verapamil Hydrochloride were prepared by the solvent method. The weighed amount of drug and polymer (EC, RSPO,) was dispersed in a given volume of methanol. These were stirred for 15 minutes to ensure homogenous mixing. The dispersion was then evaporated to dryness by storing it in a desiccator under vacuum the mass was then pulverized and fractioned. Two size fractions were selected, the particles which passed through sieve # 40 and retained on # 60 i.e. # 40/60 and particles which pass through sieve # 60 but retained on # 80 i.e. # 60/80 were subjected for In-Vitro dissolution performance. In each case different ratios of the drug and carrier were used in the preparation of sustained solid dispersions.

Preparation physical mixtures by employing physical mixing[5]:

The weighed amount of drug was mixed with the corresponding amount of polymer in a glass mortar. This was done by geometric dilution technique to ensure homogeneous distribution.

Preparation and evaluation of tablets from solid dispersions and physical mixtures[6-10]:

The tablets containing solid dispersions and physical mixtures of Verapamil hydrochloride were prepared by taking accurately weight 200 mg SD and PM in hydraulic press machine using 8 mm punch die set at 25 kg/cm^2 pressure machines using talc and magnesium stearate.

Evaluation parameters

Flow property: Various parameters viz., angle of repose, bulk density, tapped density, carr's index and hausner's ratio were determined for flow property of solid dispersions and physical mixtures.

Drug content uniformity: All the solid dispersions and physical mixtures were tested for drug content uniformity .Accurately weighed amount of SD and PM was dissolved in 0.1 N HCl in 100 ml volumetric flask, filtered and the filtrate volume was made up to the mark with 0.1 N HCl .The solution was then suitably diluted with 0.1 N HCl and assayed for drug content by measuring the Verapamil HCl content at an absorbance of 278 nm.

Drug and polymer interaction study (FT-IR study): While studying the new formulation it is necessary to check the compatibility with the carrier or excipients used and have not undergone degradation. When it passed through various crosses evidential experiments are conducted to justify and prove the interaction of drug in the formulations.

Drug content

Twenty tablets from each formulation batch were powdered and quantity of 200 mg of powder was added to 100 ml of methanol and

the mixture was sonicated to dissolve the drug from EC & Eudragit RSPO. The filtrate was suitably diluted with methanol and analyzed against blank solution for the drug content at 278 nm spectrophotometrically.

***In-vitro* dissolution studies[11-16]**

In-vitro dissolution studies of all formulations (F1 – F18) were evaluated.

Following conditions were followed to study *In-vitro* dissolution of formulations (F1-F18)

USP dissolution apparatus : Type-II (Paddle method)

Dissolution medium: 0.1N HCl for 2 hours and pH 6.8 buffer for 3 to 18 hours.

Volume of dissolution fluid: 900 ml

Temperature : 37 ± 0.5 °C

Sample size : Equivalent to 30 mg of Verapamil hydrochloride

Sample of 5 ml, was withdrawn at regular intervals .The volume withdrawn was replaced by fresh volume of dissolution medium to maintain constant volume of dissolution medium. The filtered samples were analyzed spectrophotometrically at 278 nm. The amount of drug released was determined using respective calibration curves. Dissolution studies for each formulation were performed in triplicates.

Drug release kinetics study

To describe kinetics of drug release from the sustained release tablets of, mathematical models, such as zero order, first order and Higuchi square root of time model were used. The criteria for selecting most appropriate model were based on goodness of fit test. The zero order kinetics (equation 1) describes system in which drug release rate is independent of its concentration, the first order kinetics (equation 2) describes the systems in which drug release rate in concentration dependent, Higuchi (equation 3) described release of drug as a square root of time dependent process on basis of Fickian diffusion.

$$Q_t = K_0 t \quad \ldots\ldots (1)$$

$$Q_t = Q_0(1 - e^{-K_1 t}) \quad \ldots\ldots (2)$$

$$Q_t = K_H \sqrt{t} \quad \ldots\ldots (3)$$

Where,

Q_t = Amount of drug released in time t

Q_0 = Initial amount of drug

K_0, K_1, K_H are release rate constants for zero order, first order, Higuchi rate equations

Data analysis

To analyze the mechanism of the drug release rate kinetics of the formulations, the data obtained were plotted as:

1. Cumulative % Drug Released vs. Time (Zero order plot)
2. Cumulative % Drug Released vs. Square root of Time (Higuchi plot)
3. Log Cumulative % Drug Remaining vs. Time (First order plot)
4. Log % Drug Released vs. Log Time (Koresmayer plot)

RESULTS AND DISCUSSION

A simple technique of sustained release solid dispersion was used in the present investigation. Sustained release solid dispersions were prepared using polymers like (Eudragit RSPO, EC, and combination of both polymers).

Solid dispersions and physical mixtures

Sustained release solid dispersion and physical mixture formulations (F1 to F18) were prepared as described in the methodology. The ratios of drug: polymers were tabulated in Table 1 and 2. The products were uniform in appearance.

Table 1: Formulae of solid dispersions prepared by solvent evaluation technique (Total weight =200 mg)

Sl. No	Formulations	Drug: Polymer ratio	Drug (VPH)	EC	RSPO
1	F1	1:0.5	133.33	66.66	--
2	F2	1:1	100	100	--
3	F3	1:2	66.66	133.33	--
4	F4	1:3	50	--	150
5	F5	1:5	33.33	--	166.66
6	F6	1:7	25	--	175
7	F7	1:7:0.25	24.24	6.06	169.69
8	F8	1:7:0.5	23.52	11.76	164.70
9	F9	1:7:0.75	22.85	160	17.14

*F1-VPH: EC (1:0.5) SD, F2- VPH: EC (1:1) SD, F3- VPH: EC (1:2) SD
F4-VPH: RSPO (1:3) SD, F5- VPH: RSPO (1:5) SD, F6- VPH: RSPO (1:7) SD
F7-VPH: EC: RSPO (1:7:0.25) SD, F8- VPH: EC: RSPO (1:7:0.5) SD,
F9-VPH: EC: RSPO (1:7:0.75) SD

Table 2: Formulae of physical mixtures prepared by physical mixing technique (Total weight =200 mg)

Sl. NO	Formulations	Drug: Polymer ratio	Drug (VPH)	EC	RSPO
1	F1	1:0.5	133.33	66.66	--
2	F2	1:1	100	100	--
3	F3	1:2	66.66	133.33	--
4	F4	1:3	50	--	150
5	F5	1:5	33.33	--	166.66
6	F6	1:7	25	--	175
7	F7	1:7:0.25	24.24	6.06	169.69
8	F8	1:7:0.5	23.52	11.76	164.70
9	F9	1:7:0.75	22.85	160	17.14

*F10-VPH: EC (1:0.5) PM, F11- VPH: EC (1:1) PM, F12- VPH: EC (1:2) PM
F13-VPH: RSPO (1:3) PM, F14- VPH: RSPO (1:5) PM, F15- VPH: RSPO (1:7) PM
F16-VPH: EC: RSPO (1:7:0.25), F17- VPH: EC: RSPO (1:7:0.5),
F18-VPH: EC: RSPO (1:7:0.75) PM

Evaluation parameters

Flow property

Both physical mixture and solid dispersion showed improved flow-ability than the pure drug. From the data of Table 3 it is indicated that the flow property of solid dispersions was better than physical mixture and pure drug. Hence the flow properties of the prepared solid dispersions were within the theoretical limit for processing in to tablet dosage form.

Table 3: Comparisons of bulk properties and tablet properties

Properties	Solid dispersion	Physical mixture	Pure drug
Angle of repose (θ)	22	34	50
Bulk density (gm/ml)	0.44	0.24	0.26
Tapped density (gm/ml)	0.56	0.35	0.55
Compressibility index (%)	14.55	26.89	46.79
Hausner's ratio	1.14	1.38	2.1

Drug content uniformity

The weighed quantities of SD & PM were evaluated for drug content uniformity. The percentage of drug content was found to be 91-96 %, which was within acceptable limits.

The results of the drug content uniformity in each of SD and PM are presented in Table 4 and 5. Higher drug content for both SD & PM indicated that uniform distribution of drug and polymer.

Table 4: Drug content uniformity of solid dispersion (SD) of Verapamil hydrochloride

Serial No	SD Formulations	% Drug Content
1	F1	94.2±0.34
2	F2	95.5±0.45
3	F3	96.6±0.67
4	F4	91.9±0.45
5	F5	92.7±0.62
6	F6	94.9±0.34
7	F7	93.4±0.50
8	F8	94.8±0.65
9	F9	96.3±0.43

Table 5: Drug content uniformity of physical mixture (PM) Verapamil hydrochloride

Serial No	PM Formulations	% Drug Content
1	F10	90.4±0.45
2	F11	91.9±0.35
3	F12	94.2±0.39
4	F13	89.2±0.33
5	F14	91.5±0.43
6	F15	94.3±0.37
7	F16	90.5±0.55
8	F17	93.3±0.39
9	F18	94.6±0.48

Drug and polymer interaction study (FT-IR study)

The IR spectra of pure drug and sustained release solid dispersions were shown in Fig. 1, 2, 3. The characteristic peak of solid dispersion in the spectra was found to be super imposable to that of pure drug and there were no extra peaks, which give the evidence that the drug is intact in the solid dispersions.

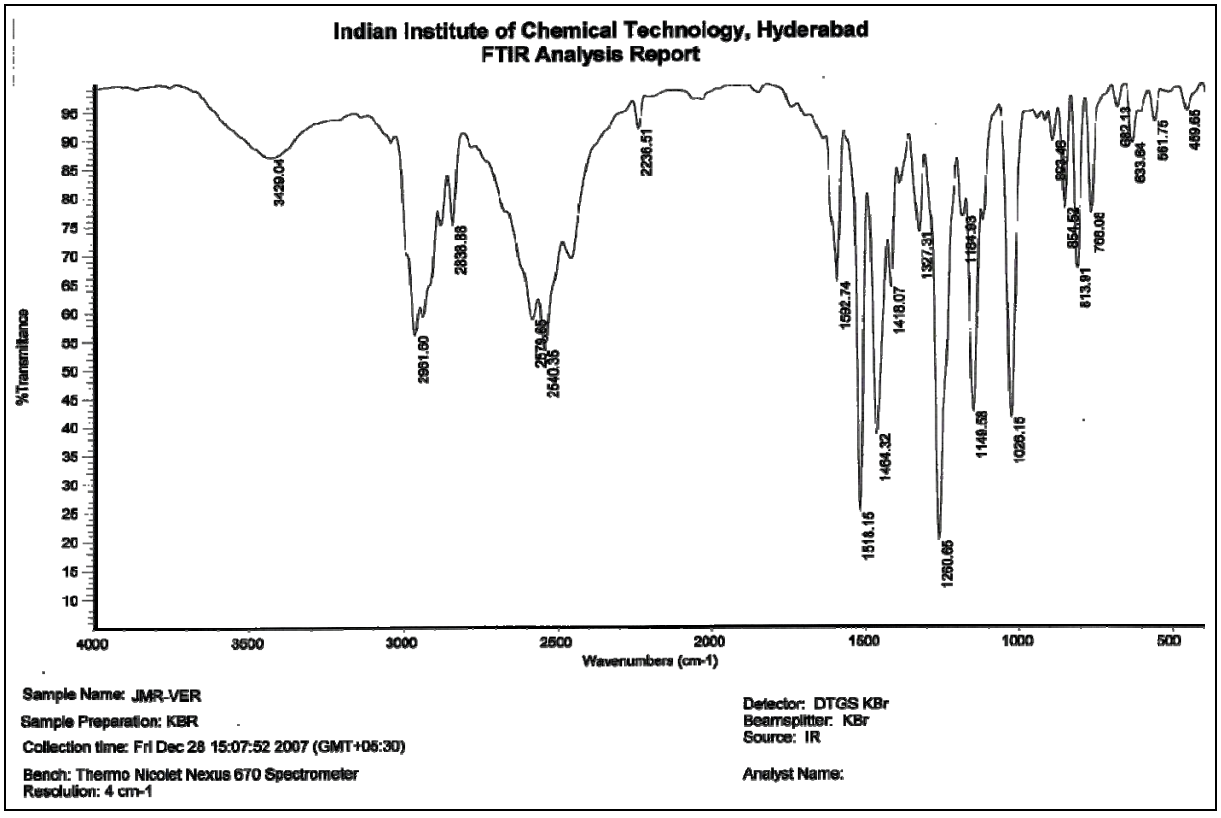

Fig. 1: FTIR Analysis report of Verapamil hydrochloride

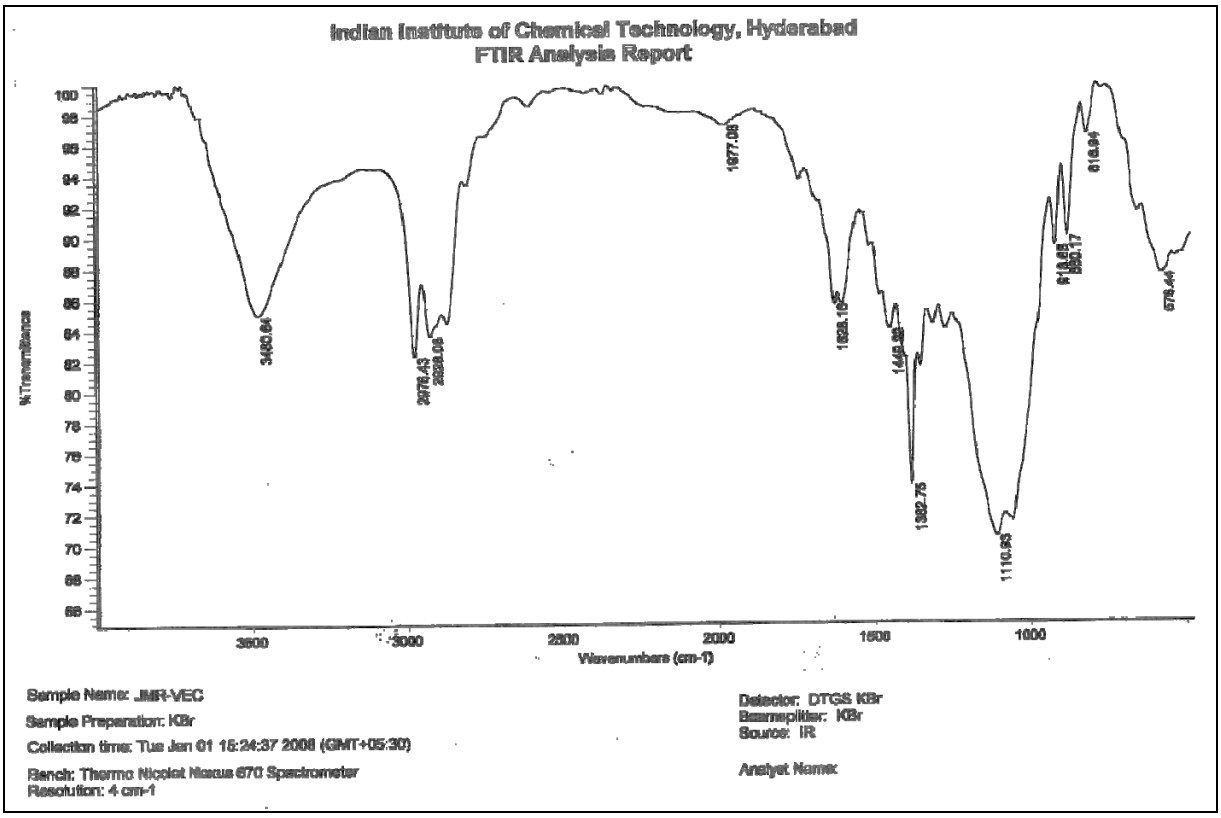

Fig. 2: FTIR Analysis report of Verapamil hydrochloride & EC

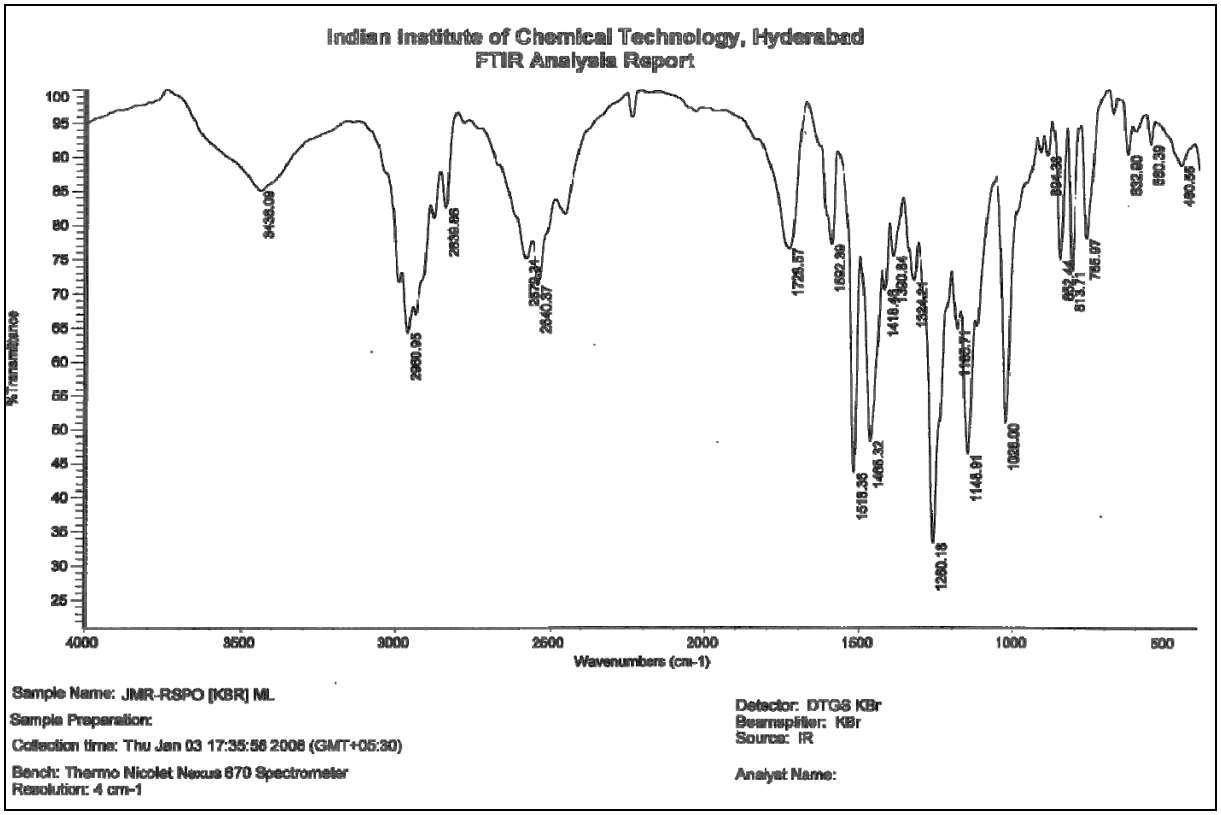

Fig. 3: FTIR Analysis report of Verapamil hydrochloride & Eudragit RSPO

In-vitro dissolution study

The dissolution rate studies were performed by using USP-XXXIII six stage dissolution apparatus employing rotating basket at a speed of 100 rpm in the dissolution medium of 0.1 N HCl for initial 2 hrs and followed by phosphate buffer pH 6.8 for the remaining hours. At suitable time intervals, samples of 5 ml were withdrawn by using pipette and it was immediately replaced with fresh dissolution medium .The withdrawn sample were analyzed for the drug content after appropriate dilution by measuring the absorbance at 278 nm with uv spectrophotometer. The drug release profiles were shown in Table 6, 7, 8 and Fig 4 to 9.

Table 6: % Cumulative drug release profile of sustained release solid dispersions tablets (F1, F2, F3) and physical mixture tablets (F10, F11, F12) of Verapamil hydrochloride (VPH) using ethyl cellulose (EC) polymer

Time (hrs)	% Cum. Drug Release					
	F1	F2	F3	F10	F11	F12
0	0	0	0	0	0	0
0.5	38.13±0.45	22.27±0.44	13.96±0.35	40.65±0.46	32.75±0.64	18.65±0.44
1	51.46±0.56	38.13±0.67	21.211±0.37	58.54±0.44	39.75±0.57	24.88±0.45
1.5	61.34±0.53	49.98±0.55	29.85±0.54	68.24±0.75	48.86±0.53	36.22±0.56
2	66.61±0.65	60.25±0.66	34.00±0.36	82.65±0.64	59.67±0.55	49.99±0.58
3	78.99±0.87	68.35±0.78	42.41±0.32	93.65±0.84	72.55±0.68	56.65±0.77
4	85.43±0.34	74.70±0.85	51.64±0.57	98.67±0.36	83.68±0.57	68.68±0.55
5	93.56±0.22	79.2±0.45	55.32±0.62		92.88±0.35	79.67±0.54
6	98.63±0.53	85.25±0.76	62.54±0.68		98.56±0.88	89.44±0.68
7		90.25±0.0	74.97±0.56			94.78±0.84
8		94.25±0.43	76.63±0.12			97.89±0.58
10		98.88±0.54	78.65±0.22			
12			85.69±0.36			
18			99.14±0.86			

Table 7: % Cumulative drug release profile of sustained release solid dispersions tablets (F4, F5, F6) and physical mixture tablets (F13, F14, F15) of Verapamil hydrochloride (VPH) using Eudragit RSPO polymer

Time (hrs)	% Cum. Drug Release					
	F4	F5	F6	F13	F14	F15
0	0	0	0	0	0	0
0.5	60.66±0.56	28.25±0.55	25.74±0.44	70.25±0.57	65.32±0.46	35.13±0.56
1	69.89±0.44	34.23±0.65	28.85±0.45	84.25±0.44	73.58±0.43	48.98±0.47
1.5	73.65±0.47	38.32±0.43	36.96±0.36	95.47±0.47	85.56±0.49	65.23±0.44
2	78.86±0.84	44.89±0.21	42.78±0.38	97.78±0.57	92.36±0.33	72.36±0.17
3	86.23±0.56	60.98±0.12	49.45±0.48		97.67±0.38	78.26±0.28
4	92.56±0.33	66.81±0.31	55.12±0.67			83.41±0.50
5	90.56±0.65	77.25±0.34	64.95±0.64			88.95±0.35
6	98.99±0.47	84.18±0.45	70.75±0.86			98.89±0.47
7		94.66±0.37	77.48±0.23			
8		98.33±0.35	83.68±0.36			
10			88.35±0.66			
12			94.48±0.49			
16			99.67±0.55			

Table 8: % Cumulative drug release profile of sustained release solid dispersions tablets (F7, F8, F9) and physical mixture tablets (F16, F17, F18) of Verapamil hydrochloride (VPH) using combination of Eudragit RSPO and EC Polymers

Time (hrs)	% Cum. Drug Release					
	F7	F8	F9	F16	F17	F18
0	0	0	0	0	0	0
0.5	24.52±0.47	22.63±0.44	16.52±0.48	34.78±0.22	32.74±0.46	30.84±0.47
1	26.45±0.48	24.56±0.32	22.65±0.47	46.45±0.35	44.44±0.57	43.58±0.56
1.5	34.56±0.57	32.56±0.94	30.54±0.47	62.85±0.46	60.54±0.52	58.12±0.28
2	40.85±0.46	38.45±0.93	34.21±0.38	70.95±0.36	68.95±0.46	64.98±0.83
3	47.98±0.38	45.68±0.30	42.48±0.39	75.46±0.38	73.25±0.55	72.12±0.76
4	52.15±0.49	50.56±0.49	48.69±0.96	80.73±0.30	75.91±0.46	74.85±0.57
5	63.15±0.16	62.54±0.43	60.58±0.13	85.62±0.35	84.95±0.56	80.96±0.47
6	68.62±0.20	65.98±0.33	64.25±0.17	94.56±0.49	90.58±0.47	88.98±0.48
7	75.12±0.34	74.69±0.23	72.96±0.28		94.58±0.33	93.85±0.46
8	80.45±0.48	78.25±0.30	75.96±0.45			97.32±0.24
10	87.47±0.59	85.69±0.40	82.96±0.36			
12	90.75±0.48	88.65±0.42	84.25±0.43			
16	97.98±0.33	94.58±0.38	88.95±0.39			
18		97.69±0.39	92.98±0.53			
20			96.25±0.33			

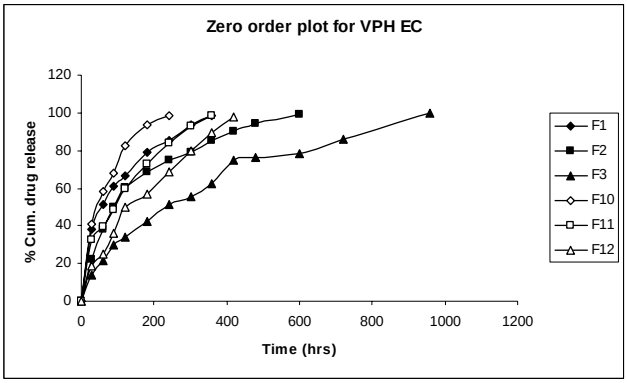

Fig.4: Zero order plot for VPH EC

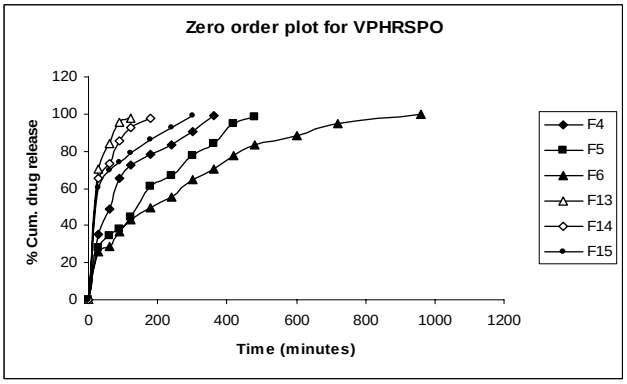

Fig. 5: Zero order plot for VPHRSPO

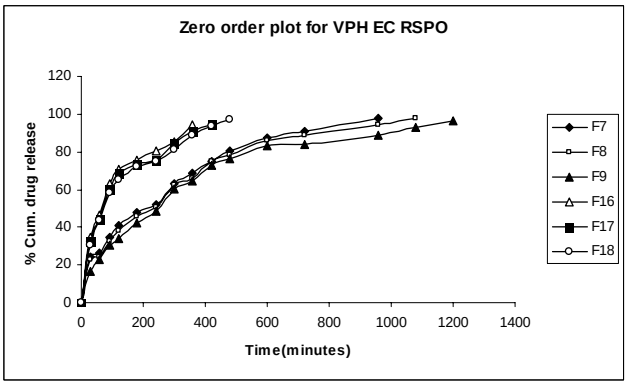

Fig. 6: Zero order plot for VPH EC RSPO

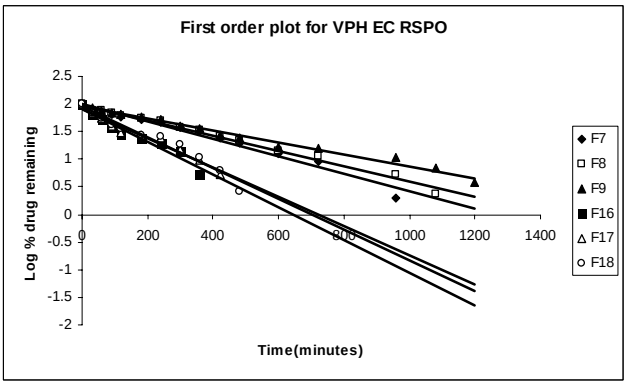

Fig. 7: First order plot for VPH EC RSPO

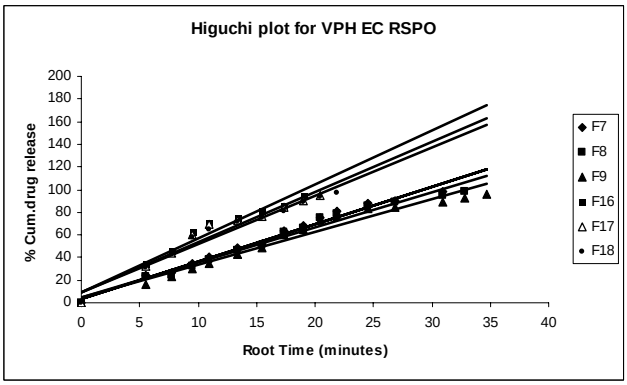

Fig. 8: Higuchi plot for VPH EC RSPO

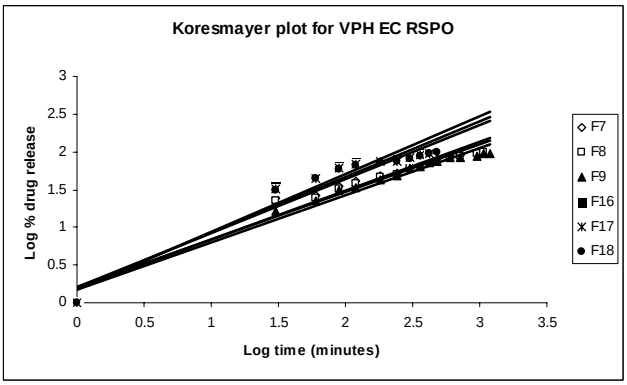

Fig. 9: Koresmayer plot for VPH EC RSPO

Drug release kinetics study

The release of Verapamil hydrochloride from the prepared formulations was analyzed by plotting the cumulative percent drug released *vs*. time as shown in Figs. 4, 5, 6.

The release mechanism of Verapamil hydrochloride from sustained release tablets studied by fitting the data into zero order, first order Higuchi square root model, and koresmayer equation. As the tablets prepared from PM could not sustain the release for more than 8 hrs, hence further discussions were made only for SD tablets.

Sustained release solid dispersion tablets of Verapamil hydrochloride using Ethyl cellulose (EC):

EC reduces the drug release due to a reduction in the penetration of the solvent molecules into the system because of the hydrophobic nature of Ethylcellulose. As the proportion of ethylcellulose increased, the release process of Verapamil hydrochloride decreased. The in vitro study revealed that with increased concentration of ethyl cellulose the release rate of verapamil HCl is controlled and it was extended upto 18hours compared to the physical mixtures prepared at the same ratio of ethyl cellulose where the release rate was extended upto 8hours.

Formulation	Drug release kinetics (R^2)			Release exponent (n)
	Zero-order	First-order	Higuchi type	
F1	0.8157	0.9145	0.9679	0.5721
F2	0.879	0.9369	0.9785	0.6078
F3	0.8946	0.9508	0.9878	0.5662

To further analyse the type of diffusion release mechanism, the value of release exponent (*n*) for the F1, F2, F3 formulation was 0.5721, 0.6078 0.5662 respectively, indicated that the release was governed by non-Fickian diffusion mechanism.

Sustained release solid dispersion tablets of Verapamil hydrochloride using Eudragit RSPO:

As the proportion of Eudrajit RSPO increased the permeability of water in the formulation decreased and hence better sustained release was observed with higher proportion of Eudragit RSPO. The in vitro study revealed that with increased concentration of Eudrajit RSPO the release rate of verapamil.HCl is controlled and it was extended upto 16hours compared to the physical mixtures prepared at the same ratio of Eudrajit RSPO where the release rate was extended upto 6hours. To further analyse the type of diffusion release mechanism, the value of release exponent (*n*) for F4, F5, and F6 formulation was 0.6154, 0.5280, .6454 respectively, indicated that release was governed by non-Fickian diffusion

Sustained release solid dispersion tablets of Verapamil hydrochloride using combination of Ethyl cellulose (EC) and Eudragit RSPO:

The solid dispersions in combination with ethyl cellulose and eudragit RSPO showed the release profile upto 20 hours compared to that of physical mixtures where the release rate was extended upto 8hours with constant ratio VPH:EC and with increased concentration of eudragit RSPO.

To further analyse the type of diffusion release mechanism, the value of release exponent (*n*) for F7, F8, and F9 formulation was 0.5488, 0.5298, .6414 respectively, indicated that release was governed by non-Fickian diffusion

Formulation	Drug release kinetics (R^2)			Release exponent (n)
	Zero-order	First-order	Higuchi type	
F4	0.8257	0.9245	0.9732	0.6154
F5	0.8352	0.9358	0.9743	0.528
F6	0.8982	0.9621	0.9852	0.6454

Formulation	Drug release kinetics (R^2)			Release exponent (n)
	Zero-order	First-order	Higuchi type	
F7	0.8223	0.9741	0.9856	0.5488
F8	0.8439	0.9768	0.9868	0.5298
F9	0.8645	0.9822	0.9898	0.6414

CONCLUSION

A systematic study involving preparation and evaluation of sustained release solid dispersion of Verapamil Hydrochloride using release retarding polymers was made.

- Drug content uniformity was made for all prepared sustained release solid dispersion .They are found to be 91-96 and are within the acceptable limits.
- IR study was performed and confirmed absence of any possible solid state drug and polymer interactions.
- In-vitro release profile studies suggested that the drug release has been extended up to 20 hrs when combinations of polymers are used.
- Approximately, all the sustained release solid dispersions exhibit polymer concentration dependent release retardation effect.

REFERENCES

1. Chou WC, Riegelman S. J Pharma Sci 1971; 60:1281-1302.
2. Kala H, Dittgen M. Solid dispersion technique for controlling drug release and absorption. Eastern Pharmacist 1995;3:141.
3. Goodman and Gilman's "The pharmacological basis of therapeutics", 10th ed., Mc grew. 536.
4. Popli H, Murthy RS, Miglani BD. Solid Dispersions as Drug delivery system for Sulfamethoxazole and Nitrofurantoin. Ind J Hos Pharma1994; 31: 97-100.
5. Sjokviste E, Nystron C, Alden M, Caram Lelham N. Physicochemical aspects of drug release:XIV. The effects of some ionic and non-ionic surfactants on properties of a sparimgly soluble drug solid dispersion. Int J Pharma 1992; 79 (2-3): 123-134.
6. Tanabe K, Itoh S, Iwasaki T, Nakano Y, Yamazaki M. Rectal Absorption Enhancement of Oxaprozin using Solid Dispersions with Polyvinylpyrrolidone. Jpn J. Hosp. Pharm. Byoin. Yakugaku (Japanese Journal of Hospital Pharmacy) 1994; 20(6):509-514.
7. Rabasco AM, Ginesh JM, Fernandez, Arevalo M, Holgado MA. Dissolution rate of Diazepam from polyethylene glycol 6000 solid dispersions. Int J Pharma 1991; 67 (2): 201-206.
8. Craig DQM, Newton JM. The dissolution of Nortriptyline Hydrochloride from polyethylene glycol solid dispersion. Int J Pharma 1992; 78 (2-3): 175-182.
9. Ahmed SM, Abdul Rahman AA, Saleh SI, Ahmed MO. Comparitive dissolution characteristics of Bropirimine-beta-cyclodextrin inclusion complex and its solid dispersions with PEG -6000. Int J Pharma 1993; 96 (1-3): 5-11.
10. Kerc J, Mohar M, Srcic S, Kofler B, Smid Korbar J. Dissolution study of Felodipine solid dispersions. Acta Pharma Zagreb1993; 43 (2): 113-120.
11. Sanghavi NM, Kotwaney HN, Shah VJ. Solid State Dispersion System of Methaqualone and its Effect on the Dissolution Rate. Ind Drugs, 1981; 1-3.
12. Chowdary KPR, Radha Rani. Physical stability and dissolution rate of Nimesulide suspensions formulated employing its solid dispersions. The Eastern Pharmacist 1998; .41: 163-164.
13. Jayaswal SB, Subha P, Gupta VK. Studies on dissolution behavior of sustained release solid dispersion of Furosemide. Eastern Pharmacist Aug 1994; 159-161.
14. Nagarsenker M.S, Rane M.S. Design and Evaluation of Solid Dispersions of Weakly Basic Drugs for Controlled Release. Ind J Pharma; May-June 2002.
15. Haznedar S, Dortunc B, Hossein Faghihian. Preparation and in vitro evaluation of Eudragit microspheres containing acetozolamide. Int J Pharma. 2004; 269(1): 131-40.
16. Khanfar MS, Salem MS, Hiroshi Yuasa. Dissolution behaviour of sustained release formulations of indomethacin with Eudragit RS. Acta Pharm Hung 1997; 67 (6): 235-9.