IJPSR (2012), Vol. 3, Issue 09 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 16 May, 2012; received in revised form 13 June, 2012; accepted 25 August, 2012

DEVELOPMENT AND EVALUATION OF VERAPAMIL HYDROCHLORIDE XANTHAN GUM MICROCAPSULES AS CONTROLLED DRUG DELIVERY SYSTEM

B.E. Wanjari*[1] and N.J. Gaikwad [2]

Manoharbhai Patel Institute of Pharmacy [1], Kudwa, Gondia- 441 614, Maharashtra, India
Department of Pharmaceutical Sciences [2], Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, Maharashtra, India

Keywords:
Verapamil hydrochloride,
Xanthan gum complex,
Microcapsules

Correspondence to Author:

B.E. Wanjari

Manoharbhai Patel Institute of Pharmacy, Kudwa, Gondia- 441 614, Maharashtra, India

E-mail:
bhumeshwanjari_11@rediffmail.com

QUICK RESPONSE CODE

IJPSR:
ICV- 4.57

Website:
www.ijpsr.com

ABSTRACT

In the present study, the microspheres containing Verapamil hydrochloride xanthan complexes encoated with ethyl cellulose by emulsion solvent evaporation method. DSC shown absence of any new endothermic peak, disappearance of no shift of endothermic peak confirmed that there is no any interaction between drug, excipients and the drug was thermally stable. Drug polymer ratio was altered while the other formulation parameters were kept constant and percentage yield, incorporation efficiency, particle size and distribution of the microcapsules were analyzed. The microcapsules studied for effects of the increase polymer ratio in formulation. The dispersed phase viscosities were evaluated by comparing with variations in particle size and distribution of the microcapsules and the effect of the variation in polymer ratio on drug dissolution was evaluated. The percentage drug released at the end of 12th h (VXM2) was found be 95.95%. respectively. The mechanism of drug release may also be dissolution and diffusion mechanism controlled released formulation. The stability of Verapamil hydrochloride loaded microcapsules (VXM2) formulation was stored at 40^{o}C±2^{o}C/75% RH ±5% RH for three months.

Microcapsules offer greater versatility for encapsulation and more triggered release applications than microcapsules. Recent advances in the development of controlled drug release system from natural, semi synthetic and synthetic polymeric carrier systems; it is possible to increase absorption rate and oral bioavailability.

Natural polysaccharides and their semi-synthetic derivatives represent a group of polymers that are widely used in pharmaceutical dosage forms and obtained usually as plant exudates containing various sugars moieties other than glucose and having significant quantities of oxidized groups in adjunct to their normal polyhydroxy group. These materials result from normal metabolic processes, and many times, they represent the reserve carbohydrate in that system [1]. Natural polymers such as gaur gum, chitosan, gellan gum, alginic acid, konjac gum, etc. were commonly used for the retarded release of drugs but they have fairly low adhesive properties [2].

Now, a day more emphasis is diverted towards the use of vegetable and nontoxic products which by replacing of synthetic additives with natural one for controlled drug delivery system [3]. In the present work, the controlled drug delivery system using natural, semi-synthetics polymers were developed.

Verapamil hydrochloride (VH) is calcium antagonists are being used effectively in the treatment of several cardiovascular disorders, particularly angina pectoris, supraventricular tachycardia and hypertension. It is established that, as a result of oral usage, 90% of VH is absorbed and then it reaches maximum plasma concentration within 1–2 h.

However, due to the extensive first pass hepatic excretion, it has such low bioavailability 10–20% of oral dose. VH has nonlinear pharmacokinetic because of its saturation of pre-systemic metabolism leads to first pass effect which resulting in nonlinear absorption.

It is clear from the investigations that there is no difference between the controlled release dosage form administered once daily and conventional dosage form administered several times daily with the same doses in respect to their bioavailability and antihypertensive effect.

MATERIAL AND METHODS:

Material: Verapamil hydrochloride was a kind gift from Glenmark Ltd., Mumbai**.,** Ethyl cellulose was obtained from SD Fine Chemicals Ltd., Mumbai, Xanthan gum and TIC Gums Inc., USA., Acetone, SD Fine Chemicals Ltd., Mumbai, Petroleum ether, Methanol and Magnesium stearate were obtained from Loba Chemicals Ltd., Mumbai. All other solvents and reagents used were of analytical grade.

Methods of Microcapsule preparation:

A. **Preparation of Verapamil hydrochloride-Xanthan complex:** The drug Verapamil hydrochloride was dissolved in an adequate amount of ethanol xanthan gum was suspended in the drug solution and various complexes were shown in **Table 1**. The solvent was removed under vacuum at 70^{o}C and the residue was kept in a desiccator for 24 h. The samples were screened through 125 μm sieve. The difference ratio's of drug to xanthan 1:0.2, 1:0.4 and 1:0.6 were used to prepare the microcapsules with various ratios of ethyl cellulose as a coating polymer [4].

B. **Preparation of Microcapsules by Solvent Evaporation:** Microcapsules were prepared using solvent evaporation technique[5] in an acetone/ heavy-liquid paraffin system. Different quantities of polymer (1, 2 and 3 g of ethylcellulose) and 1.0 g of VH complex (solid dispersion) was dispersed in 15 ml of acetone by using sonicator (PCI Services, Mumbai, India) for 15 min. Resulting solution was poured slowly in 500 ml vessel containing mixture of 250 ml heavy liquid paraffin and 30 ml light liquid paraffin added with variations of stirring rate and stirring continued for next 5 h, until acetone evaporated completely. After evaporation of acetone, the microcapsules formed were collected by vacuum filtration, washed 4-5 times with 50 ml n-hexane and was dried at room temperature for 24 h and various formulations were shown in **Table 2**.

TABLE 1: VERAPAMIL HYDROCHLORIDE - XANTHAN COMPLEXES PREPARED BY SOLVENT DEPOSITION.

Sr. No.	Formulation ID	VH (g)	Natural Gum Polymer (g)	Polymer Concentration Ratio
1	VX1	1	0.2	1:0.2
2	VX2	1	0.4	1:0.4
3	VX3	1	0.6	1:0.6

TABLE 2: VERAPAMIL HYDROCHLORIDE MICROCAPSULES PREPARED BY SOLVENT EVAPORATION

Sr. No.	Formulation ID	Core (Drug: Gum) (g)	Coating Polymer (g)	Coating Polymer Ratio	Stirring Speed (rpm)
1	VXM1	1:0.4	1	1:0.4:1	1100
2	VXM2	1:0.4	2	1:0.4:2	1100
3	VXM3	1:0.4	3	1:0.4:3	1100
4	VXM4	1:0.4	2	1:0.4:2	700
5	VXM5	1:0.4	2	1:0.4:2	1400

Microcapsule characterization:

Determination of Percentage Yield: Prepared microcapsules were accurately weighed and the percentage yield[6] was calculated using Equation- 1.

$$\% \ yield = \frac{Weight \ of \ Microcapsules}{Weight \ of \ Gum + Weight \ of \ drug} \times 100$$

---------- Equation -1

Drug content estimation: Determination of Verapamil hydrochloride the microcapsules were performed for three randomly picked up samples from each formulation. Each, 50 mg of sample was pulverized and dissolved in 50 ml of methanol, the resulting solution was filtered and further diluted with methanol and concentration of the Verapamil hydrochloride was determined spectrophotometrically at 278 nm using UV-2401 (Shimaduz 2401, Japan).

Determination of entrapment efficiency: The entrapment efficiency (%) of drug[7] was calculated using equation-2.

$$Drug \ entrapment \ efficiency = \frac{Experimental \ drug \ content}{Theoretical \ drug \ content} \times 100$$

-------Equation- 2

Particle size measurement and Surface Topology Evaluation: The average particle size distributed of was determined by using Motic digital biological microscope with inbuilt camera and the mean particle diameter was determined by measuring 100 particles using 1 mm stage micrometer [8] scanning electron microscopy examined the surface topography of the microcapsules. SEM carried out using scanning electron microscope (Steroscan 250-MK-III, Cambridge, UK). Before evaluation, samples were gold sputter-coated to render them electrically conductive.

Differential Scanning Calorimetric Analysis: The thermal analysis of pure drug and formulation was carried out using DSC instrument (Mettler Toledo DSC 822e, Mettler Toledo AG, Switzerland) to evaluate possible drug polymer interaction. Approximately 3 mg of sample accurately weighed into a 40 µl aluminum pan and sealed with a punched lid. Temperature range of 10 to 200^{o}C scanned using a heating rate of 10^{o}C/min. A nitrogen purge of 50 ml/min was used in the oven [9].

Infra-red Spectrophotometry: There is always possibility of drug excipients interaction in any formulation due to their intimate contact. IR spectroscopy is one of the most powerful analytical techniques, which offers possibility of chemical identification. The IR-spectra of Verapamil hydrochloride xanthan microcapsules were obtained by KBr pellet method.

***In-vitro* drug release studies of complexes and microcapsules:** *In-vitro* drug release studies of prepare microcapsules [10] were carried out using *USP XXIII* Type-II (paddle-type) dissolution test apparatus. A quantity of prepared microcapsules 100 mg were placed in a muslin bag (2µm) and tied to the paddle. The 10 ml samples were withdrawn at regular intervals. The volume withdrawn at each time interval was replaced with fresh quantity of phosphate buffer of pH 6.8 buffer as dissolution fluid. The samples were filtered and analyzed by *UV*-spectrophotometer at 278 nm. All the formulations, the dissolution was carried out in triplicates. The percentage of drug release at different time intervals (0-12 h) was calculated using the *PCP-Diss-V3 software* and plotted as the cumulative percent release versus time.

Drug Release Kinetics Study: To describe kinetics of drug release from the 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.

Zero Order Kinetics: A zero order release would be predicted by the equation -4 [11]

$A_t = A_0 - K_0 t$ ---------- Equation -4

Where, A_t = Drug released at time 't'; A_0 = Initial drug concentration; K_0 = Zero order rate constant (h^{-1})

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero order release kinetics with a slope equal to K_0.

Higuchi's Model: Drug released from the matrix devices by diffusion has been described by Higuchi's classical diffusion equation [12] -5.

$Q = KT^{½}$ ---------- Equation-5

When the data is plotted, according to Higuchi's equation ($Q=Kt^{½}$), cumulative drug release versus square root of time yields a straight line, indicating that the drug was released by diffusion mechanism. The slope is equal to 'K'.

Peppa's Model: In order to understand the mode of release of drug from swellable matrices, the data were fitted to power law equation [13]- 6.

$$\text{Log } \frac{M_t}{M_\infty} = \log K + n \log t \quad \text{---------- Equation -6}$$

When the data is plotted as log of drug released versus log time, it yields a straight line with a slope equal to 'n' and the 'K' can be obtained from y-intercept.

Stability Studies: The stability refers to the time frame from initial preparation and packaging during which the dosages continue to comply with quality and purity requirements. As a result of the marginal storage stability of many drugs, long term storage of drug dosages forms often goes along with conformational changes of the drugs incorporated and consequently, purity requirements cannot be fulfilled any longer. In order to evaluate storage stability of prepared microcapsules, samples were stored at 40 ± 2°C/75±5% RH for three months. Samples were withdrawn at intervals of 30, 60 and 90 days as per ICH guidelines. Prepared formulations evaluated for drug content and dissolution [14].

RESULT AND DISCUSSION: The physical properties of different formulations of microcapsules were shown in **Table 3**. The DSC curve of pure Verapamil hydrochloride exhibited a single endothermic response corresponding to the melting of drug. Onset of melting was observed at 142.1°C as shown in **Figure 1**. Xanthan showed an endothermic peak at 203 °C where as DSC thermogram of ethyl cellulose showed a peak at higher.

In Dispersion systems, the drug endothermic peak was observed at 148.3°C with Xanthan and Ethyl cellulose. DSC showed absence of any new endothermic peak, disappearance of no shift of endothermic peak confirmed that there is no any interaction between drug and excipients and the drug is thermally stable.

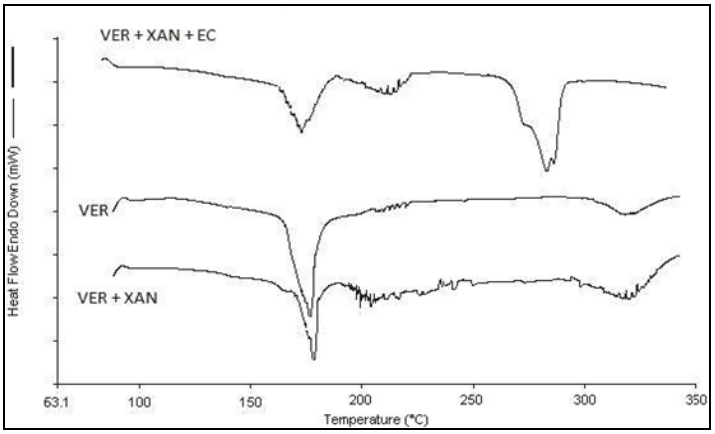

FIGURE-1 :DSC CURVES A) VERAPAMIL HYDROCHLORIDE-XG COMPLEX, B) VERAPAMIL HYDROCHLORIDE, C) VERAPAMIL HYDROCHLORIDE -XG- EC MICROCAPSULES

TABLE 3: THE COMPOSITION, PERCENT CONTENT AND PERCENT YIELD OF COMPLEXES

Formulations	Drug : Xanthan Gum	Mean % content SD (n=3)	Mean %Yield SD
VS1	1 : 0.2	96.78 ±0.09	96.03±0.72
VS2	1 : 0.4	97.27 ±0.02	97.24±0.27
VS3	1 : 0.6	97.45 ±0.68	88.93±0.62

It was observed that, the natural polymer concentration directly correlated with the content and yield of complexes. The content of Verapamil hydrochloride loaded VS1, VS2 and VS3 complexes were shows in the range of 96.78 ±0.09, 97.27 ±0.02 and 97.45 ±0.68 respectively shown in Table-3. The percentage yield of Verapamil hydrochloride loaded VS1, VS2 and VS3 complexes were shows in the range of 96.03 ±0.72, 97.24 ±0.27 and 88.93 ±0.62 respectively.

The drug entrapment efficacies of complexes increase with increase in concentration of hydrophilic gum. The dissolution rate profile of Verapamil hydrochloride-xanthan complexes in the different concentration ratios are shown in **Figure 2**. The ratio of xanthan gum was increase, the complexes show increased retardation of the drug release.

***In-vitro* drug release studies of prepared Complexes:** The release of drug from the complexes prepared by the solvent deposition i.e., VS1, VS2 and VS3 which has released 97.56%, 99.74% and 99.34% at the end of 1 h, 3 h and 5 h respectively. The release of pure drug was found to be 98.98% at the end of 0.5 h.

Determination of percentage yield of VH-XAN loaded Ethyl Cellulose Microcapsules: The percentage yield of Verapamil hydrochloride loaded microcapsules were determined by weight after drying and enumerated in **Table 4**. It was observed that, the polymer concentration and stirring speed directly correlated with the yield of microcapsules.

TABLE 4: THE RESULTS OF DRUG CONTENT, DRUG ENTRAPMENT EFFICIENCY AND MEAN PARTICLE SIZE OF PREPARED MICROCAPSULES

Formulation Code	Mean % Yield (±SD) of microcapsules	Mean drug content (mg)	% drug content (theoretical)	% Drug Content (Practical)	Entrapment efficiency (%)	Mean Diameter (μm)
VXM1	63.10 ±0.17	45.88 ±0.26	49.80	45.88	92.13	428.7
VXM2	65.60 ±0.37	32.01 ±0.18	33.20	32.01	96.43	456.4
VXM3	66.20 ±0.27	23.86 ±0.25	24.90	23.86	95.82	487.2
VXM4	66.36 ±0.82	25.08 ±0.18	33.20	25.08	75.54	678.6
VXM5	67.50 ±0.40	29.57 ±0.20	33.20	29.57	89.06	401.6

The microencapsulation efficiency of VXM1, VXM4 and VXM5 were low as compare to other formulations of microcapsules as shown in Table 4. The encapsulation efficiency was positively correlated with polymer concentration, stirring speed for microcapsule formulation. An increasing stirring rate causes a decrease in the average diameter size of microcapsules. At higher stirring rates a finer dispersion is obtained, since the shear force is greater.

Additionally, more intense agitation prevents agglomeration of 'immature' microcapsules more successfully. It is shows from Table 4 that drug complex: coating polymer ratio appears to influence the mean diameter of microcapsules, when the drug complex: polymer ratio is high and the proportion of larger particles formed. The viscosity of the polymer solution at such high drug loading is very high and is responsible for the formulation of larger droplets that leads to increasing mean diameter of microcapsules.

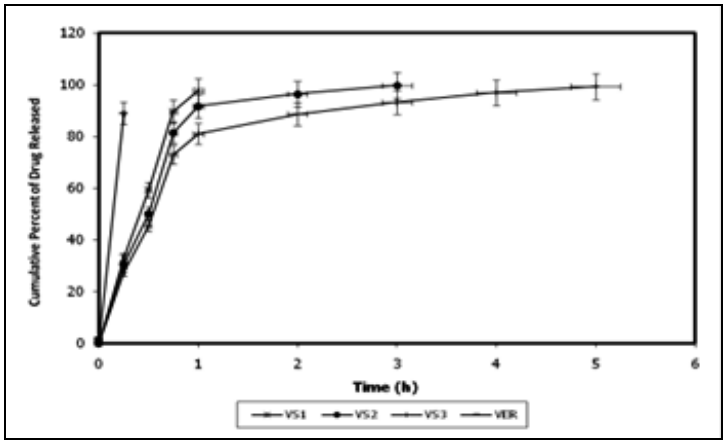

FIGURE 2: DISSOLUTION PROFILE PLOT OF CUMULATIVE PERCENT DRUG RELEASED VERSUS TIME FOR COMPLEXES

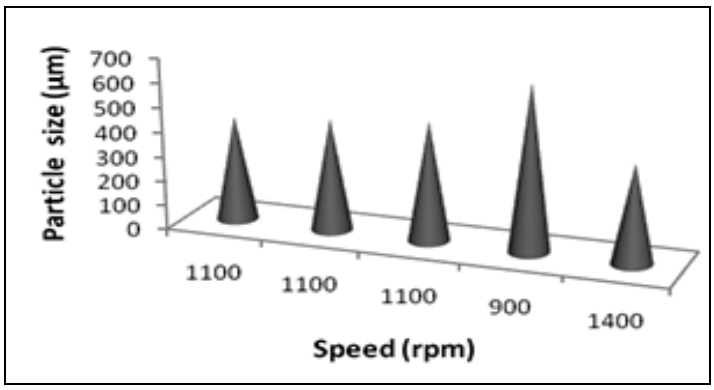

FIGURE 3: DETERMINATION OF PARTICLE SIZE ANALYSIS

Effect of drug loading in Microcapsule on Drug Release Rate: The effect of drug loading in microcapsule on drug release pattern compared to time required to achieve 40 % drug release of prepared microcapsules in phosphate buffer of pH 6.8 with 33.33 % and 50 % drug loadings (n=3). As shown in **Figure 4,** microcapsules of similar size with higher drug loading, the faster the drug release, the unencapsulated drug present on the surface of microcapsules with increase in the percentage of drug in polymer matrix the initial small burst release also increases. The size distribution of the microcapsules was influenced by viscosity of the polymer.

Effect of percentage of Polymer: As the drug complex: polymer ratio increases from 1:1 to 1:3 the yield of microcapsules as shown in Table 4. It shows that high amount of polymer is required to encapsulate the drug effectively, when polymer solution concentration was above 50 %w/w with respect to drug. The good entrapment efficiency was achieved by increasing drug: polymer ratio.

***In-vitro* drug release studies of prepared Microcapsules:** The percentage drug released at the end of 1st and 12th h from the microcapsules of drug xanthan complex (ratio 1:2) as core material to coat of ethyl cellulose of formulations VXM1, VXM2 and VXM3 were found to be 12.23% , 10.59%, 10.20%, and 98.47%, 95.95%, 93.65% respectively. Similarly, the drug released at the end of 1st and 12th h from the microcapsules at various stirring speed 700 and 1400 i.e., VXM4 and VXM5 were studied cumulative percentage drug released were found to be 12.23%, 10.20% at 98.47%, 93.67% respectively. The cumulative percentage released at 1st h and 12th h, the time interval were found to be 11.76% and 96.64% respectively shown in **Figure 4**.

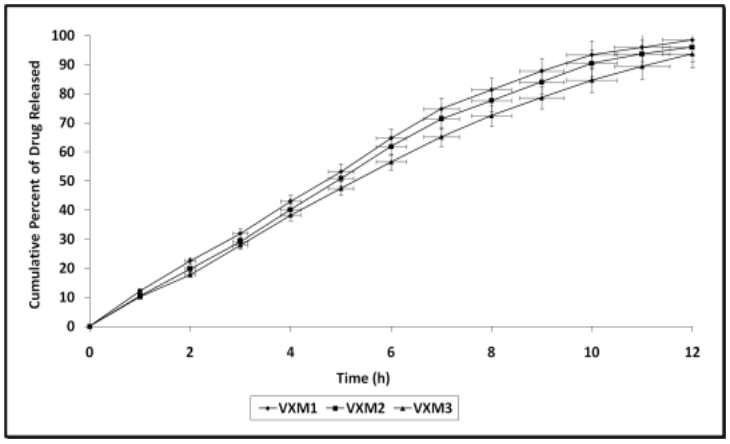

FIGURE 4: THE CUMULATIVE PERCENT DRUG RELEASE OF MICROCAPSULES. (mean ±SD, *n* =3)

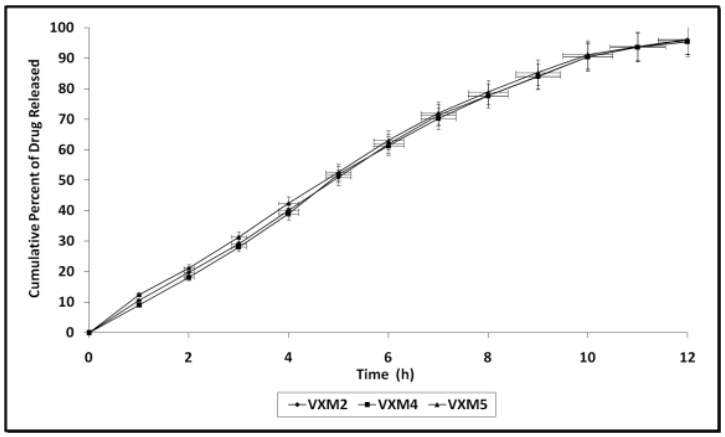

FIGURE 5: EFFECT OF STIRRING ON THE PERCENT DRUG RELEASE OF MICROCAPSULES. (mean ±SD, *n* =3).

Effect of natural gum on Drug Release: The prepared complex retarded drug release on some extended. The increase concentration of natural gum, retard the specific drug release. A natural gum is cost-effective, non-irritant, nontoxic, easily available, safe and biocompatible.

The drug release rate increased as the microsphere size decreased for both microsphere formulations. The lower entrapment efficiency at 700 rpm agitation speed may be due to inadequately stirring of droplets, which leads to increased chances of coalescing. At higher agitation speed i.e., 1400 rpm, the globules were forced towards the wall of the flask due to high rotation and it ultimately lowers the contact time between polymer and drug molecules. But at 1100 rpm, no sticking of polymeric material around the walls of flask was observed which may leads to improved drug entrapment efficiency.

An increasing stirring rate causes a decrease in the average diameter size of microcapsules. The percentage drug released at the end of 1st and 12th h shown in **Figure 6**, VXM2 and MP were found be 10.59%, 11.76%, and 95.95%, 96.64% respectively. The mechanism of drug release may also be dissolution and diffusion mechanism controlled released formulation.

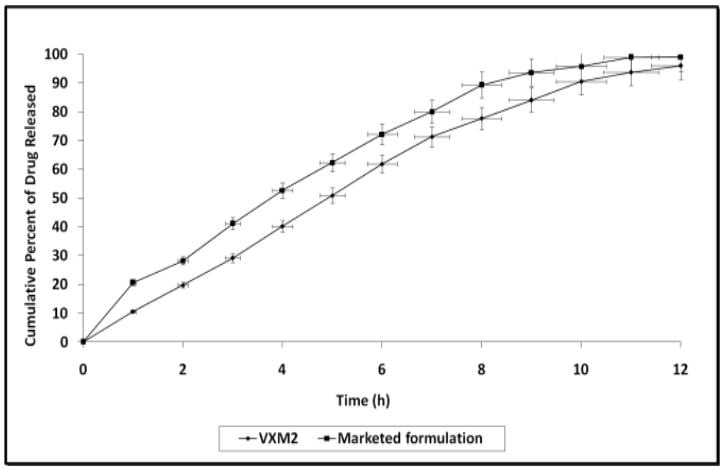

FIGURE 6: COMPARISON OF CUMULATIVE % DRUG RELEASE VERSUS TIME OF VXM2 AND MARKETED PRODUCT

The microcapsules were discrete, uniform and spherical in shape shown in **Figure 7 and 8**. The surface Verapamil hydrochloride complex coated ethyl cellulose of microcapsules was very smooth but having few small pores on the surface was observed. The stability of Verapamil hydrochloride loaded microcapsules (VXM2) formulation was stored at 40°C±2°C/75% RH ±5% RH for three months. Samples were withdrawn at intervals of 30, 60 and 90 days. The VXM2 formulation retained drug content and did not change to a grater degree from the initial values (**table 5**).

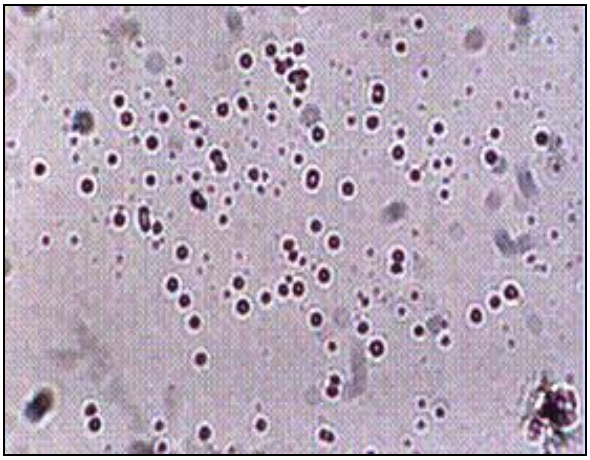

FIGURE 7: OPTIC MICROSCOPIC STUDIES OF MICROCAPSULES (100X)

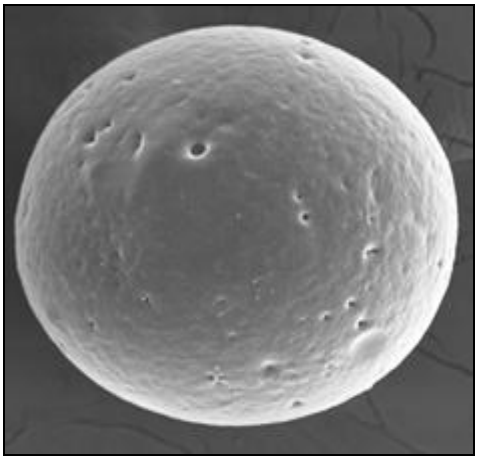

FIGURE 8: SCANNING ELECTRON MICROSCOPIC STUDIES OF MICROCAPSULES

TABLE 5: STABILITY STUDIES OF MICROCAPSULE VXM2 FORMULATION

Sr. no.	Time in days	Physical changes	Mean percent drug Content	Content ±SD
01	30	No change	31.81	31.81 ±0.38
02	60	No change	31.26	31.26 ±0.55
03	90	No change	31.01	30.01 ±0.64

(n=3), Average of three determinations

CONCLUSION: The microcapsule for controlled release formulation using Verapamil hydrochloride -xanthan complex prepared by solvent deposition technique varying with Xanthan gum ratio [1:0.2, 1:0.4 and 1:0.6] respectively. The effect of microcapsules formulation variables like drug and gum ratio, percent yield, drug content, and *in-vitro* drug release influenced by polymer concentration.

The natural polymer concentration directly correlated with the drug content and yield of complexes. Similarly, the drug entrapment efficacy of complexes increases with increase in concentration of hydrophilic gum.

ACKNOWLEDGEMENTS: The authors acknowledge the facilities provided Head, Department of Pharmaceutical Sciences, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur (India) in carrying out the work. The authors would like to thank Glenmark Ltd., Mumbai and TIC Gums, USA, for providing gift sample of the drug and gums respectively.

REFERENCES:

1. Baveja, S.K., Ranga Rao, K.V. and Padmalatha, D.K., 'Zero-Order Release Hydrophilic Matrix Tablets of Adrenergic Blockers', Int. J. Pharm. Sci., 1987:; 4: 39-45.
2. Nakano, M., Nakamura, Y., Juni, K. and Tomitsuka, T., 'Evaluation of a New Sustained Release Theophylline Formulation by the Measurements of Salivary Levels of the Drug in Humans', Pharmacobiodyn., 1980; 3(12): 702-708.
3. Nakano, M., Kouketsu, M., Nakamura, Y., and Juni, K., 'A Therapeutic Composition in Unit Dosage form as a Non-Compressed Tablet', Chem. Pharm. Bull., 1980; 28: 2905
4. Nagar, V.F., El-Khawas M. and Ismail F.A., 'Pectin A Possible Matrix for Oral Sustained Release Preparations of Water-Soluble Drugs', STP-Pharm. Sci., 1992; 2(3): 227-234.
5. Müge, Kiliçarslan and Tamer Baykara, 'The Effect of the Drug/Polymer Ratio on the Properties of the Verapamil hydrochloride Loaded Microspheres', Int. J. Pharm., 2003; 252: 99–109.
6. Thompson, C.J., Hansford, D., Higgins, S., Rostron, C., Hutcheon, G.A. and Munday, D.L., 'Evaluation of Ibuprofen-Loaded Microspheres Prepared from Novel Copolyesters', Int. J. Pharm., 2007; 329: 53-61.
7. Das, M. and Rama rao, K., 'Evaluation of Zidovudine Encapsulated Ethylcellulose Microspheres Prepared by Water-in-Oil-in-Oil (W/O/O) Double Emulsion Solvent Diffusion Technique', Acta. Poloniae. Pharm. Drug Res., 2006; 63(2): 141-148.
8. Pandit, S.S. and Patil, A.T., 'Formulation and *In-vitro* Evaluation of Buoyant Controlled Release Lercanidipine Lipospheres', J. Microencap., 2009; 26(7): 635-641.
9. Tayade, P.T. and Kale, R.D., 'Encapsulation of Water-Insoluble Drug by a Cross-linking Technique: Effect of Process and Formulation Variables on Encapsulation Efficiency, Particle Size and *In-vitro* Dissolution Rate', AAPS Pharm. Sci., 2004; 6(1): 26-38.
10. Fulzele, S.V., Satturwar, P.M., Kasliwal, R.H. and Dorle, A.K., Preparation and Evaluation of Microcapsules using Polymerized Rosin as Novel Wall Forming Material., J. Microcap., 2004; 21: 83-89.
11. Donbrow, M. and Samuelov, Y., 'Zero Order Drug Delivery from Double-Layered Porous Films: Release Rate Profiles from

Ethylcellulose, Hydroxypropylcellulose and Polyethylene glycol Mixtures', J. Pharm. Pharmacol., 1980; 32 (7): 463–470.
12. Higuchi T., 'Mechanism of Sustained Action Medication: Theoretical Analysis of Rate of Release of Solid Drugs Dispersed in Solid Matrices', J. Pharm. Sci., 1963; 52: 1145-1149.
13. Peppas, N.A., 'Analysis of Fickian and Non-fickian Drug Release from Polymers', Pharm. Acta. Helv., 1985; 60: 110-111.
14. Mukherjee, B., Mahanti, B., Panda, P. and Mahapatra, S., 'Preparation and Evaluation of Verapamil hydrochloride Microcapsules', Am. J. Ther., 2005; 12: 417-424.

How to cite this article:
Wanjari BE and Gaikwad NJ: Development and Evaluation of Verapamil Hydrochloride Xanthan Gum Microcapsules as Controlled Drug Delivery System. *Int J Pharm Sci Res*, 2012; Vol. 3(9): 3296-3303.