ISSN: 0975-766X
CODEN: IJPTFI
Available Online through *Research Article*
www.ijptonline.com

DESIGN AND EVALUATION OF SUSTAINED RELEASE TABLETS OF LAMIVUDINE

J.Rajkumar*, P.Ramesh
Department of Pharmaceutics, Vaageswari College of Pharmacy, Karimnagar, T.S, India.
Email: jampalarajkumar@gmail.com

Received on: 12-08-2017 *Accepted on: 28-09-2017*

Abstract

Lamivudine sustained-release matrix tablets were formulated using natural hydrophilic polymers like Guar gum,Xanthan gum, gum acacia, Pectin and Gum Tragacanth. The formulated tablets were evaluated for physical characteristics like weight variation, thickness, hardness, friability and drug content. The results of the physical characteristics of all formulations were within the acceptable limits. *In vitro* drug release study was performed using pH 6.8 phosphate buffer for a period of 24 hours. a better controlled drug release was obtained with the matrix tablet made up of the xanthan gum than that of tablets with other natural polymers used. The *in vitro* release data was well fit into first order release kinetics. Better controlled drug release was obtained with matrix tablets made of Xanthan gum than that of tablets with other polymers

Key words: Sustained release, lamivudine, Guargum, Xanthan gum, gum acacia, Pectin and gum Tragacanth.

Introduction

Matrix tablets composed of drug and polymer as release retarding material offer the simplest approach in developing a sustained-release drug delivery system. Recent trend in development of sustained-release drug delivery systems was the use of gums of plant origin to fulfill the aim of retarding the drug release. Natural gums are biodegradable, non-toxic and have capability to swell on contact with aqueous media. The natural polymers used do hold advantages over the synthetic polymers generally because they are non toxic, less expensive and freely available. Most common examples of natural gums are Guar gum,Xanthan gum, gum acacia, Pectin and Gum Tragacanth. Guar gum is a polysaccharide derivative having glycosidic linkage which is intended to be used as a matrix former for controlled release of drugs. gumtragacanth obtained for *A.gummifer* and is odour less, taste less and viscous water soluble mixture of polysaccharide. Pectin, a natural hydrophilic polymer is rich in galacturonic acid is used as a gelling agentand thickening agent. Pectin gum as

been shown to be usefull for the construction of drug delivery systems for targeted drug delivery. Lamivudine is a drug which is used in treatment of chronic hepatitis B and also for treatment of aids patients. sustained release tablets of lamivudine provide content plasma concentration with less frequent administration and also decrease the side effects to some extent this could extend its safe administration and improve patient compliance. The present study aims to develop a sustained release matrix tablets using hydrophilic polymers and to evaluate the effect of the same.

Material and Methods

Lamivudine was obtained as a gift sample from Macleod's pharmaceuticals, India. The Pharmacopoeial grade of Guar gum (GM), Pectin (P),Gum acacia, Gum Tragacanth (T) and Xanthan gum (XG) was obtained from Premcem gums pvt.ltd. Other materials & reagents used were of analytical grade, and procured from commercial sources.

Methods

Preformulation testing is the first step in the rationale development of dosage forms of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulation in developing stable and bioavailable dosage forms, which can be mass-produced.

Standard plot of lamivudine

100 mg of lamivudine was dissolved in small amount of water and volume wasmade up to 100ml using the same. From the stock solution serial dilutions were done to obtain solutions in the conc ranging from 1 to 10µg/ml. The absorbance of the solution was measured at 271nm using UV-visible spectrophotometer. A graph of concv/s absorbance was plotted. Similarly, standard calibration curve of lamivudine were prepared in pH 1.2 and pH 6.8, by using above said method.

FTIR spectroscopy

Samples of lamivudine, Xanthan gum, combination of lamivudine and Xanthan gum(optimized formula) was subjected for FTIR spectroscopic study.

Preparation of SR matrix tablets

SR matrix tablets of lamivudine were prepared by using different drug:polymer ratios wiz 1:0.6,1:0.8,1:1 for F1, F2, F3, 1:0.6, 1:0.8, 1:1 for F4, F5, F6,1:0.6, 1:0.8, 1:1 for F7, F8, F9, 1:0.6, 1:0.8, 1:1 for F10, F11, F12, 1:0.6, 1:0.8, 1:1 for F13, F14, F15 respectively. Guar gum, Xanthan gum, gum acacia, Pectin and Gum Tragacanth were used as matrix

forming materials, while lactose was used as diluents magnesium stearate was in corporate as lubricant. all ingredient were passed through a #100 sieve, weighed and blended. the lubricated formulation were compressed by a direct compression technique, using 10mm punches.

Table.no.1 Composition of formulations containing natural polymers.

Sl. No	**Ingredients (mg)**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**
1	Lamivudine	240	240	240	240	240	240	240	240	240	240	240	240	240	240	240
2	Guar gum	160	200	240	-	-	-	-	-		-	-	-	-	-	-
3	Xanthangum	-	-	-	160	200	240	-	-	-		-	-	-	-	-
4	Gum acacia	-	-	-	-	-	-	160	200	240	-	-	-	-	-	-
5	Gumtragacanth	-	-	-	-	-	-	-	-	-	160	200	240	-	-	-
6	Pectin	-	-	-	-	-	-	-	-	-	-	-	-	160	200	240
7	Lactose	93	53	3	93	53	3	93	53	3	93	53	3	93	53	3
9	Mg sterate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
10	Talc	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5

Evaluation of Matrix Tablets

All prepared matrix tablets were evaluated for uniformity of weight as per I.P. method. Friability was determined using Roche Friabilator. Hardness was measured by using Rollex hardness tester, thickness was measured by Vernier caliper.

In vitro drug release study

Dissolution studies were conducted in USP I apparatus with 900ml of dissolution medium maintained at 37±1ºC for 24hrs, at stirring speed of 100 rpm.0.1N HCL was used as a dissolution medium for the first 2hrs, followed by pH 6.8 phosphate buffer further 22hrs. At predermined time intervals 0, 1, 2, 4, 6, 8,10,12,18 and 24 hr. 5 ml of the sample was withdrawn and was replaced by an equal volume of fresh dissolution medium of same pH. Collected samples were analyzed spectrophotometrically at 271 nm, and cumulative percent drug release was calculated.

Results and Discussion

Preformulation studies

In Preformulation studies, as the BP standards thus indicating purity of obtained drug sample and plot graph of absorbance V/s conc between 1-10 µg/ml ranges. The lamivudine calibration curve areshown in fig no.1 and 2 respectively. These concentrations obey the Beer-Lambert's law at 271nm, with a linearity of 0.999, 0.998 in respective media.

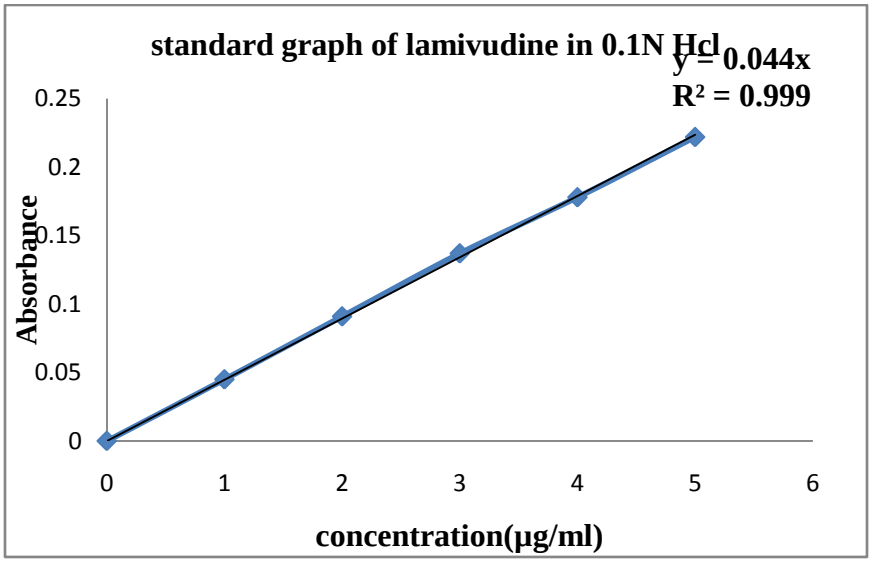

Figure.1.Standard graph of lamivudine in 0.1N Hcl

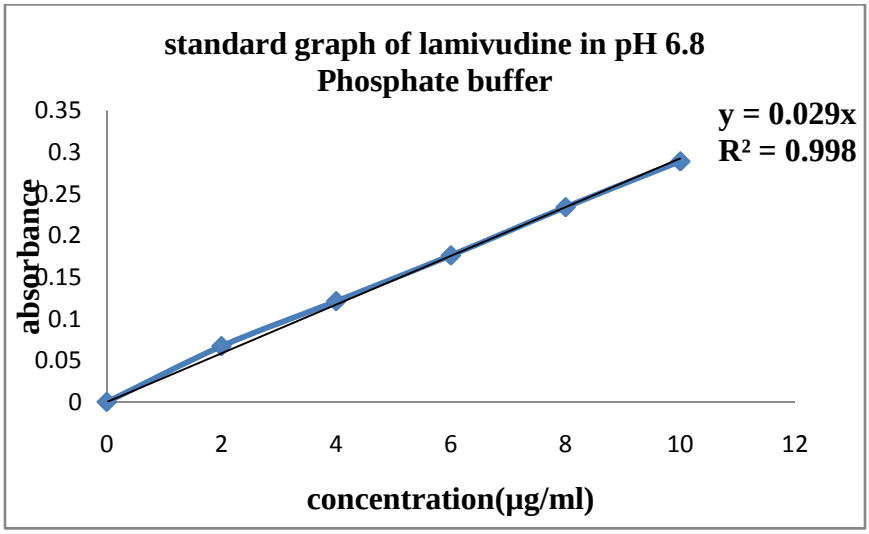

Figure.2. Standard graph of lamivudine in pH 6.8 buffer

Drug polymer interaction(FTIR) study

FTIR studies revealed that there was no significant drug-excipient interactions occurred. All the characteristic peaks exhibited by the lamivudine alone were present in the physical mixture of the drug-polymer, this indicates that the polymer in this are compatible with drug are shown in figure no.3,4 and 5.

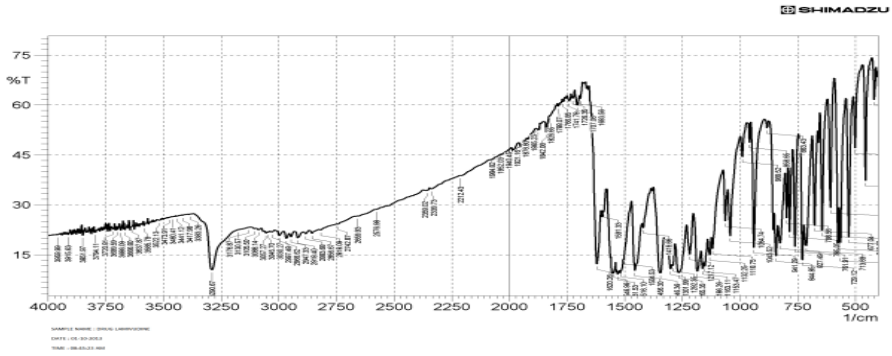

Figure.3. FTIR spectrum of Lamivudine

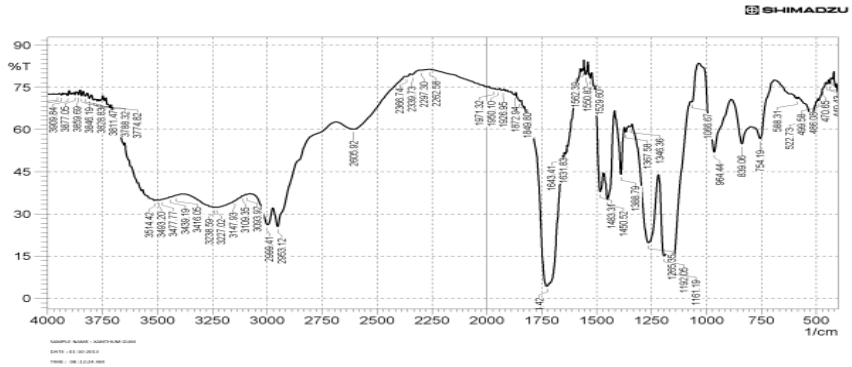

Figure.4. FTIR spectrum of Xanthan gum

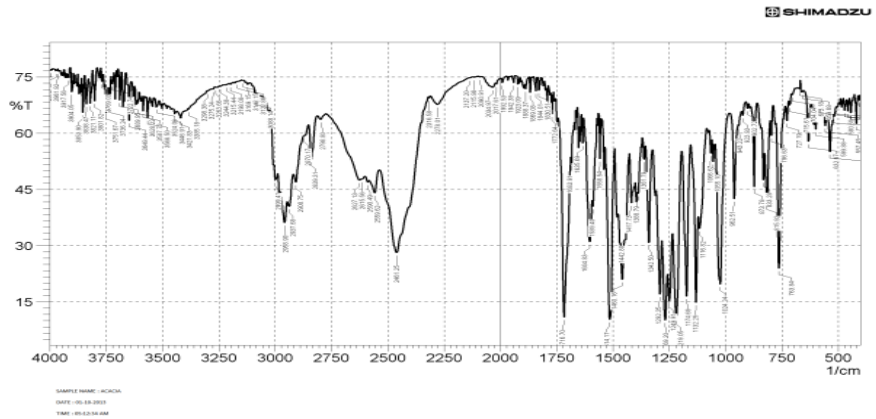

Figure.5. FTIR spectrum of Optimized formula

EVALUATION OF MATRIX TABLETS

The formulated matrix tablets met thepharmacopoeial requirement of uniformity of weight. All the tabletsconformed to the requirement of assay, as per I.P.Hardness, percentage friability and thickness was allwithin acceptable limits were shown in table no.2.

In vitro drug release studies

In-vitro dissolution data of formulation (F1 to F15) reported in Figure no: 1,2,3&4. When matrices containing swellable polymers are exposed to dissolution medium, tabletsurface becomes wet and hydrated to form a gel layer. The initial release of drug from these matrices occurs by the drug dissolution in the water penetrated into the matrix. The overall drug release from these matrices is governed by hydration, gel layer formation and drug diffusion into the gel layer and to the dissolution media. Polymer erosion also plays a major role in releasing drug from these matrices. These considerations indicate that hydrophilic natural polymers have the potential to sustain the drug release from matrix tablets.

Table.2. Physical characteristics sustained release tablets of lamivudine(F1-F15).

BATCH	Parameters				
	Thickness (mm)	Hardness (kP)	Friability (%)	Tablet Wt. (mg)	Assay (%)
Fl	3.84	6.5	0.165	499.1	98.1
F2	3.84	6.7	0.178	503.12	96.5
F3	3.84	6.8	0.058	500.2	96.43
F4	3.56	5.9	0.121	494.6	100.11
F5	3.55	6.6	0.104	497.4	98.73
F6	3.85	7.1	0.06	506.4	98.46
F7	3.85	7.6	0.088	502.6	97.91
F8	3.84	6.9	0.304	495.4	100.43
F9	3.82	7.4	0.198	498.6	96.86
F11	4.18	7.6	0.216	503.4	100.17
F12	4.08	7.3	0.185	501.6	99.46
F13	4.19	6.8	0.316	500.4	100.28
F14	4.09	6.7	0.239	50306	99.17
F15	4.19	7.4	0.201	497.6	96.86

The formulation f5 containing drug and Xanthan gum ratio (1:0.8) were able to sustain the drug release up to 24hrs with percentage drug release as (98.75)respectively. Because of Xanthan gum having high viscous in nature **so** it forms a viscous gel layer of surrounding tablet matrix, its resisting to erosion and the diffusion of the drug is controlled primarily by the gel viscosity.

The behavior is attributable to the inter molecurintraction or entanglement, increasing the effect micro molecule dimensions and molecular weight. this results in a continuous viscous elastic matrix that fills the interstices', matining the integrity of the tablet, and retarding further penetration of the dissolution medium. the in vitro drug release profile with viscous behavior the formulation (f5) as optimized for further studies.

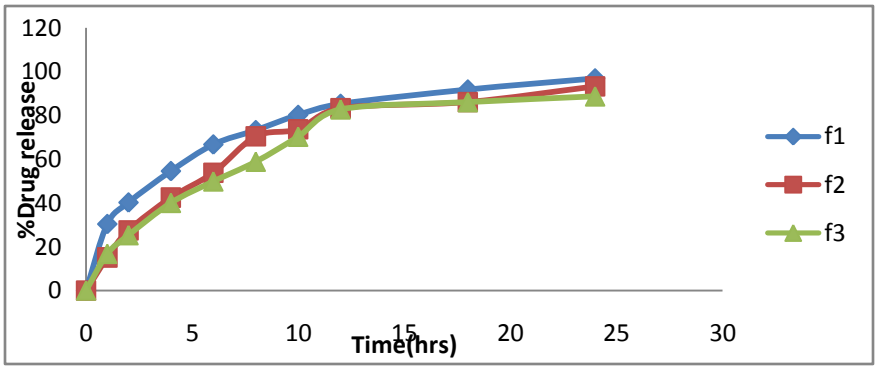

Figure.6. % Drug release of f1, f2&f3 formulations.

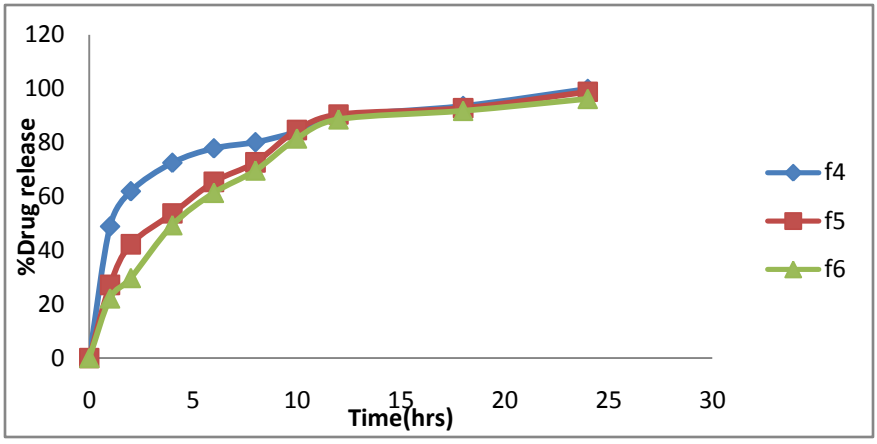

Figure.7. % Drug release of f4, f5&f6 formulations

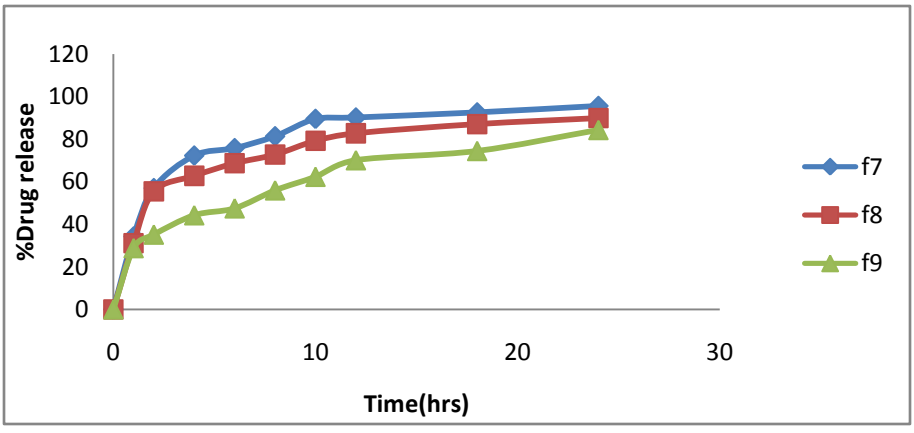

Figure.8. % Drug release of f7, f8&f9 formulations

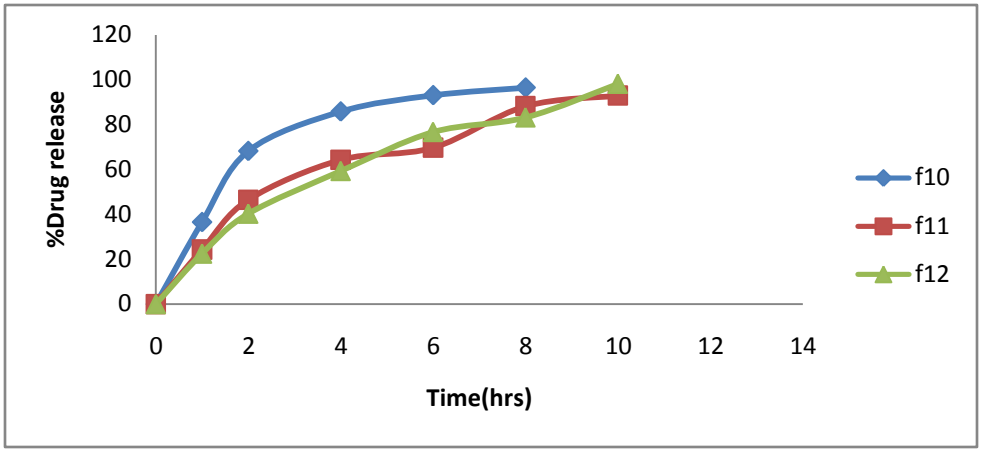

Figure.9. % Drug release of f10, f11&f12 formulations.

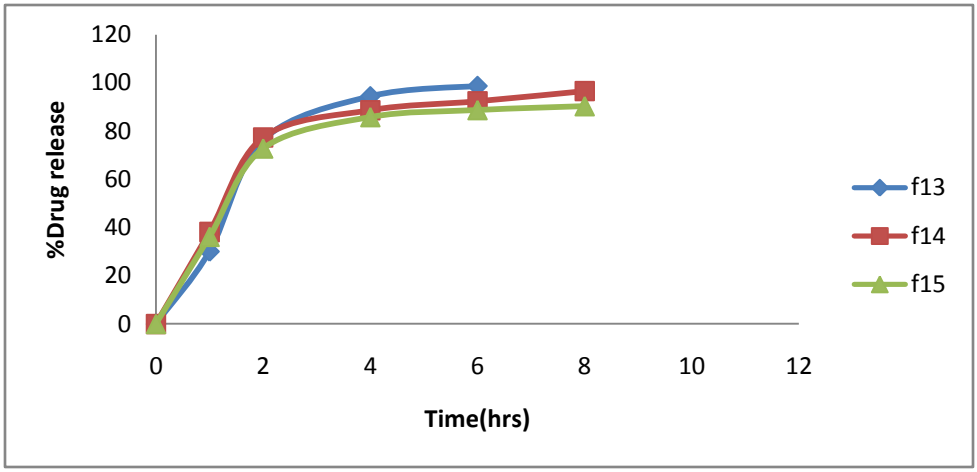

Figure.10. % Drug release of f13, f14&f15 formulations.

Conclusion:

Results of the present study successfully formulated sustained release matrix tablets of lamivudine.

Lamivudine is soluble at all pH conditions and exhibits good solution state stability. Its solubility in highly acidic medium was almost twice as compared to other media.

The standard plot of lamivudine was linear for all the media. The drug was found to have good solution state solubility.

The tablets prepared were found to be within the official limits with respect to thickness, hardness, friability, weight variation and drug content.

Based on mathematical data revealed from models, it was concluded that the F6 formulation was selected as an optimized formulation.

Optimized formulation F5 (drug to polymer ratio 1:0.8) which includes 40% Xantham gum has successfully sustained the drug release for 18-24 hours and the drug release pattern was similar to theoretical release profile.

FTIR studies proved that there is no chemical interaction in drug and polymer of the developed matrix tablets. Thus, sustained release matrix tablets of Lamivudine using natural Biodegradable and biocompatible polymers were successfully formulated, evaluated and found to be suitable candidates in extending the release of the drug from the matrix tablets

Reference:

1. Gothi G.D., Parikh B.N., Patel T.D., Prajapati S.T., Patel D.M. and Patel C.N. (2010) Study on Design and Development of Sustained Release Tablets of Metoprolol Succinate. *Journal of Global Pharma Technology* 2, 69-74.
2. Jain S., Yadav S. and Patil U. (2008) Preparation and Evaluation of Sustained Release Matrix Tablet of Furosemide using Natural Polymers. *Research Journal for Pharmacy and Technology* 1, 374 - 376.
3. Modi S.A., Gaikwad P.D., Bankar V.H. and Pawar S.P. (2011) Sustained Release Drug Delivery System : A Review. *International Journal of Pharma. Research and Development* 2.
4. Reddy K.R., Mutalik S. and Reddy S. (2003) Once-daily sustained-release matrix tablets of nicorandil: formulation and in vitro evaluation. *AAPS PharmSciTech*4, E61.
5. Sayed A.-R.I., Gamal M.M. and El-Badry M. (2009) Preparation and comparative evaluation of sustained release metoclopramide hydrochloride matrix tablets. *Saudi Pharmaceutical Journal* 17, 283-288.
6. Varshosaz J., Tavakoli N. and Kheirolahi F. (2006) Use of hydrophilic natural gums in formulation of sustained-release matrix tablets of tramadol hydrochloride. *AAPS PharmSciTech*7, 168 - 174.
7. Kuksal A, Tiwary AK, Jain NK, Jain S. (2006). Formulation and in vitro, *in vivo* evaluation of extended- release matrix tablet of zidovudine: influence of combination of hydrophilic and hydrophobic matrix formers. AAPS PharmSciTech, 7:E1
8. Joint United Nations programme on HIV/AIDS(UNAIDS) and world health organization (WHO).AIDS Epidemic update 2007. Geneva, Switzerland: UNAIDS Available 2007.

9. V. P. Pandey, R. Manavalan, S. Rajan, and K. S. Ganesh.Formulation and release characteristics of sustained release diltiazemhydrochloride tablet. Indian J. Pharm. Sci 651:44–48 (2003).
10. P. M. Morkhade, S. V. Fulgel, P. M. Satturwar, and S. B. Joshi.Gum Copal and Gum Damar: Novel matrix forming material forsustained drug delivery. Indian J. Pharm. Sci 681:53–58 (2006).
11. The United States Pharmacopoeia (USP/NF).Physical tests/dissolution. The U. S. Pharmacopoeial Convention, Rackville,MD. 2002; 25/20:2011–2012.
12. Venkatarajua MP, Gowdaa DV, Rajeshb KS, Shivakumara HG.Xanthan and locust bean gum (from Ceratoniasiliqua) matrixtablets for oral controlled delivery of propranolol hydrochloride.Asian J Pharm Sci. 2007;2:239–48.

Corresponding Author:

J.Rajkumar*, P.Ramesh

Email: jampalarajkumar@gmail.com