Journal of Pharmacreations

PharmaCreations

ISSN: 2348-6295

Pharmacreations | Vol.6 | Issue 1 | Jan - Mar - 2019

Journal Home page: www.pharmacreations.com

Research article *Open Access*

Preparation and evaluation of nanosponges of glipizide

Nellutla Jhancy Laxmi[*1], N.Sandeepthi [2], N.Sriram[3]

[1]Holy Mary Institute Of Science and Technology (College of Pharmacy) Bogaram(V),Keesara (M) Dist-501301

[2]Vignan Institute of Pharmaceutical Sciences, Deshmukhi Village,Yadadri Bhuvanagiri Dist

[3]Holy Mary Institute of Science and Technology (College of Pharmacy) Bogaram(V),Keesara (M) Dist-501301

Corresponding author: Nellutla Jhancy Laxmi

E-mail Id: nellutla.jhancy@gmail.com

ABSTRACT

Nanosponges are nano sized particles designed to look like red blood cell and protect the body. Nanoparticles have been used for unknown preventative measures, such as silverware and wound care products. Silverware contains small silver nanoparticles which contain an antimicrobial agent. The recent advance in nanotechnology has lead to the development of targeted drug delivery system. However, targeting a molecule to a particular site using a drug delivery system effectively requires a specialized drug delivery system. The discovery of nanosponge has become a significant step in overcoming certain problems such as drug toxicity, poor bioavailability and release of drug in a predictable fashion as they can accommodate both hydrophilic and hydrophobic drug. Nanosponges exhibit a porous structure in nature which has the unique ability to entrap the drug moieties and offers a merit of desire release. Nanosponges are tiny sponges that can circulate in the body to reach the specific site and binds on the surface to release the drug in a controlled and predictable manner. Nanosponges can be formulated by crosslinking of cyclodextrine [1] with carbonyl or di-carboxylate (Crosslinkers). Nano sponge's technology [8] has been explored widely for the delivery of drugs for oral administration, topical administration [6], and parental administration. Nanosponges can also serve as an effective carrier for enzyme, proteins, vaccine and antibodies. The Nanosponge was prepared by solvent evaporation method using polymethyl methacrylate, Ethyl cellulose, and pluronic F127 as rate retarding polymers and PVA as co polymer using ethanol as a solvent

Keywords: Targeted drug delivery system, Nanosponges, Hydrophilic and Hydrophobic drug, β-Cyclodextrine

INTRODUCTION

Glipizide is an oral rapid- and short-acting anti-diabetic medication from the sulfonylurea class. It is classified as a second-generation sulfonylurea, which means that it undergoes entero-hepatic circulation. Second-generation sulfonylurea are both more potent and have shorter half-lives than the first-generation sulfonylurea's. Originally available in 1984, it is marketed by Pfizer under the brand name

Glucotrol in the USA, where Pfizer sells Glucotrol in doses of 5 and 10 milligrams and Glucotrol XL (an extended release form of glipizide) in doses of 2.5, 5, and 10 milligrams. Other companies also market glipizide, most commonly extended release tablets of 5 and 10 milligrams.

METHOD OF LOADING OF DRUG INTO NANOSPONGES

Solvent method

The solvent required will be mix with the polymer mainly in a polar aprotic solvent for example- dimethylforamide, dimethylsulfoxide then add this mixture to cross linker in a exceed quantity, the ratio for cross linker/ molar ratio is preferred as 4 to 16. The reaction is proceed with a solvent reflux temperature and time ranging from 1 to 48 hr.The reaction is completed and solution is allow to cool at room temperature then product is added to excess of bi-distilled water and product is recovered by filtration under vaccum and simultaneously purify by prolonged soxhlet extraction with ethanol.The reaction is completed and solution is allow to cool at room temperature then product is added to excess of bi-distilled water and product is recovered by filtration under vaccum and simultaneously purify by prolonged soxhlet extraction with ethanol.

Ultrasound assisted synthesis

Nano-sponges are obtained by reacting polymer with cross linkers without adding or without using solvent and sonification is maintained. The polymer is mix with a cross linkers in a balanced ratio in a flask. The flask is placed in a molar ratio in an ultrasound bath field with water and temperature maintained at 90ºc.The mixture is sonicated for 5hr. Then the mixture is kept to cool and product is break roughly then the product is washed with water to remove non-reacted polymer and subsequently purified by soxhlet extraction with ethanol.The product is dried under vaccum at 25ºc until its further use is utilized.

Loading of drug into nanosponges

- Nanosponges obtained should be pre-treated to maintain mean particle size blow 500nm. Nanosponges are suspended in water and were sonicated to avoid presence of aggregates and particles and got centrifuged to obtain colloidal fraction [2], then supernatant is separated and dried sample by freezing by drying.
- Drug is dispensed for maintaining suspension under constant stirring for specific time period for complexation is over the undissolved drug (uncomplexed condition) is separated from complexed drug with the process of centrifugation.
- Nanosponges obtained should be pre-treated to maintain mean particle size blow 500nm. Nanosponges are suspended in water and were sonicated to avoid presence of aggregates and particles and got centrifuged to obtain colloidal fraction, then supernatant is separated and dried sample by freezing by drying.

PREPARATION OF NANOSPONGES

- Nanosponges prepared from hyper-cross linked β-cyclodextrins [9]
- Emulsion solvent diffusion method
- Quasi-emulsion solvent diffusion

Emulsion solvent diffusion method

- ✓ In dessicators and ensurity of removal of residual solvents is done. In this metod 2 phases are used
- ✓ Organic phase
- ✓ Aqueous phase
- ✓ The dispersed phase having ethyl cellulose and drug get dissolved in dichloromethane (20 ml) and a definite amount of polyvinyl alcohol added to 150 ml of aqueous continuous phase.
- ✓ Then, the mixture is stirred properly at 1000 rpm for 2hr.
- ✓ The required nanosponges were collected by the process of filtration and kept for drying in oven at 40ºc for 24hr. Nanosponges which are dried were strored

Quasi-emulsion solvent diffusion

- ➢ The nano-sponges prepared using the polymer in different amounts.
- ➢ The inner phase is prepared using eudragitrs 100 [3] and added to a suitable solvent.
- ➢ Drug used provided with a solution and dissolved under ultrasonication at 35ºc.
- ➢ This inner phase added into external phase containing pva act as emulsifying agent.
- ➢ The mixture is stirred at 1000-2000 rpm for 3hr at room temperature and dried in an air-heated oven at 40ºc for 12hr.

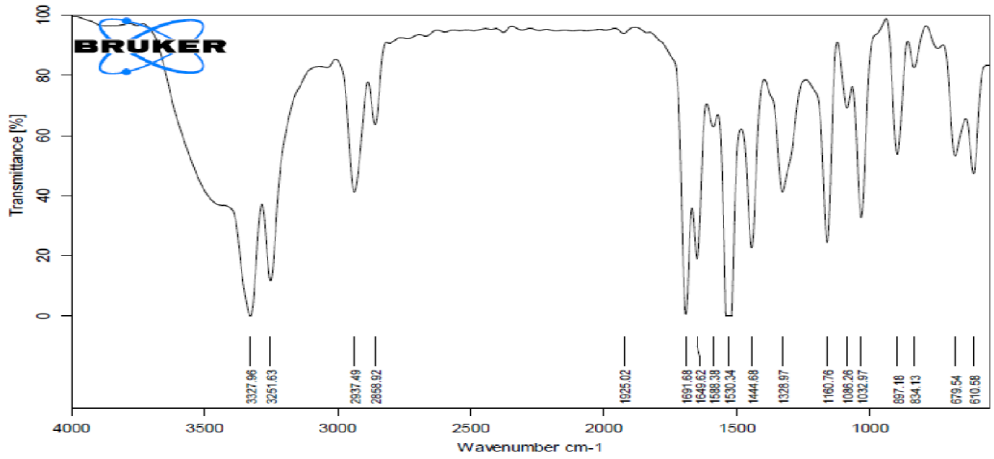
Procedure

For the oral dosage forms the in vitro dissolution study must be conducted in the dissolution medium which simulate the in-vivo conditions (actual physiological conditions)i.e., first 2hours in 0.1N HCL and remaining dissolution was carried out in 6.8pH buffer. The in vitro drug release studies for the prepared formulation were conducted for a period of 12 hrs using an Lab India DS8000 dissolution tester USP Type-1 apparatus (rotating basket) set at 50 rpm and a temperature of 37± 0.5°C weight equivalent to 40mg of glipizide nanosponge [4] was taken in basket apparatus and placed in the 900ml of the medium. At specified intervals 5ml samples were withdrawn from the dissolution medium and replaced with fresh medium to keep the volume constant. The absorbance of the sample solution was analyzed at 230nm for the presence of model drug, using a UV-visible spectrophotometer.

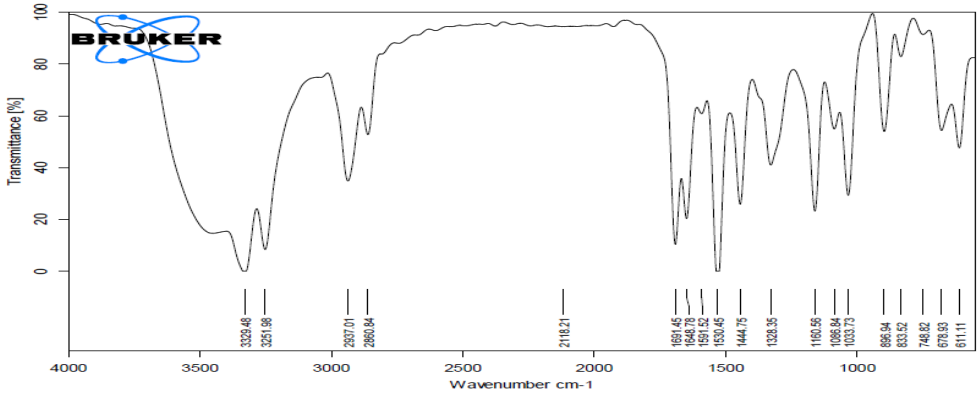
RESULTS AND DISCUSSION

Drug excipient compatibility

Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of Pure drug with that of various excipients used in the formulation



FTIR Spectra of Pure Drug



DISCUSSION

Compatibility studies were performed using IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and excipients were studied. The characteristic absorption peaks of drug and excipients were obtained as shown above and as they were in official limits (±100 cm^{-1}) the drug is compatible with excipients.

Particle size analysis of Nanosponges

S.NO	FORMULATION CODE	PARTICLE SIZE(NM)
1	F1	321.6
2	F2	398.2
3	F3	318.2
4	F4	332.4
5	F5	407.2
6	F6	329.6
7	F7	396.4
8	F8	454.8
9	F9	

Drug content

The drug content of the formulated Nanosponges (F1-F9) was found in the range of 82.8to 97.2% respectively.

FORMULATION CODE	MEAN % DRUG CONTENT
F1	88.22
F2	94.69
F3	90.82
F4	85.28
F5	89.56
F6	80.24
F7	92.16
F8	97.02
F9	90.28

Entrapment efficiency

- It is calculated to know about the efficiency of any method, thus it helps in selection of appropriate method of production. After the preparation of formulations the Practical yield was calculated as Nanosponges recovered from each preparation in relation to the sum of starting material (Theoretical yield). It can be calculated using following formula.

$$\textbf{Entrapment efficiency} = \frac{\text{Practical yield}}{\text{Theoretical yield (drug + polymer)}} \times 100$$

ENTRAPMENT EFFICIENCY OF NANOSPONGES

FORMULATION CODE	ENTRAPMENT EFFICACY %
F1	80.12
F2	83.48
F3	79.54
F4	79.16
F5	82.02
F6	76.24
F7	72.84
F8	76.88
F9	70.12

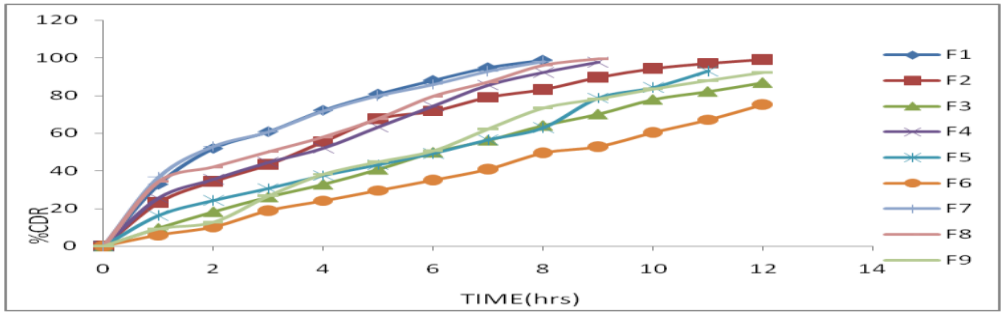
FORMULATION F1-F9 COMPOSITION

Percentage of drug release of Nanosponges formulations

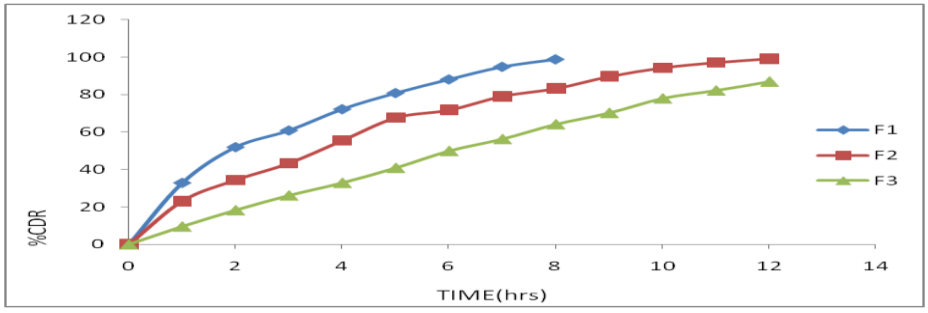
Time(hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	32.86	23.16	9.54	25.56	16.24	5.89	36.62	34.28	9.12
2	51.92	34.41	18.26	35.50	24.21	10.16	53.04	42.12	12.71
3	60.84	43.39	26.12	44.49	30.62	18.87	60.78	50.16	26.63
4	72.22	55.58	32.86	52.02	37.48	24.05	71.82	58.06	38.12
5	80.84	67.70	40.84	63.30	43.18	29.57	79.94	67.82	44.68
6	88.12	71.80	49.88	74.39	49.22	35.06	85.92	79.68	50.54
7	94.86	79.18	56.26	85.50	56.47	40.89	92.96	87.24	62.24
8	98.84	83.32	64.12	92.26	62.82	49.48	98.12	96.12	73.26
9		89.75	70.18	97.70	78.54	52.87		99.56	78.12
10		94.40	77.94		84.16	60.40			83.36
11		97.22	82.18		92.94	67.11			87.90
12		99.26	86.92			75.26			92.14

The entrapment efficiency of formulation F1 was found to be 90.86%,formulation F2 was found to be 95.12%, formulation F3 was found to be 89.54%, formulation F4 was found to be 89.16%, formulation F5 was found to be 92.02%, and formulation F6 was found to be 86.24%, formulation F7 was found to be 92.84%, formulation F8 was found to be 96.88%, and F9 was found to be90.12 %. Among all the formulation F8 shows high entrapment efficiency of 86.88%.

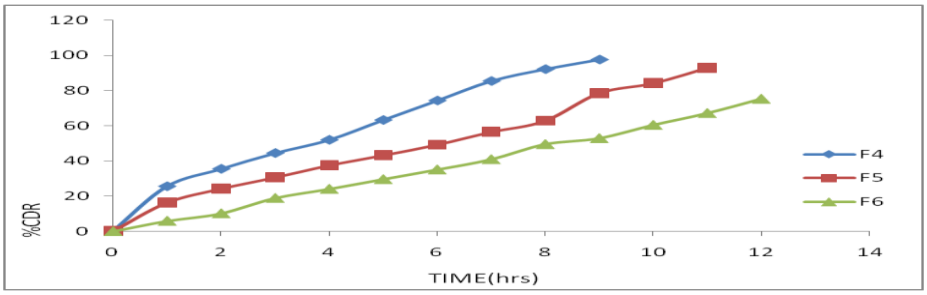
In vitro dissolution studies



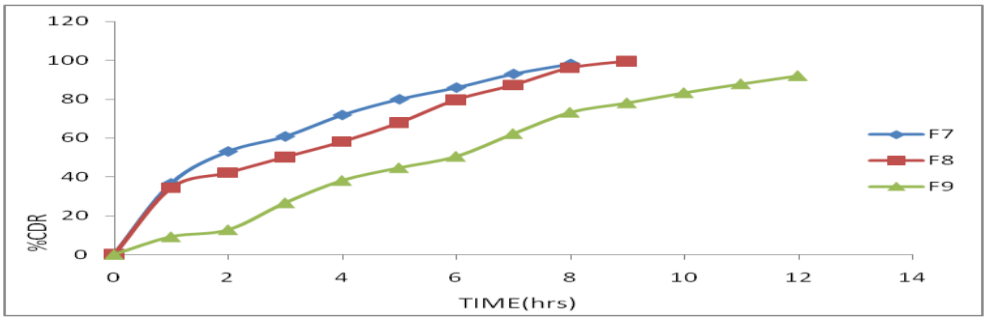
Percentage of drug release graph of formulations F1-F3



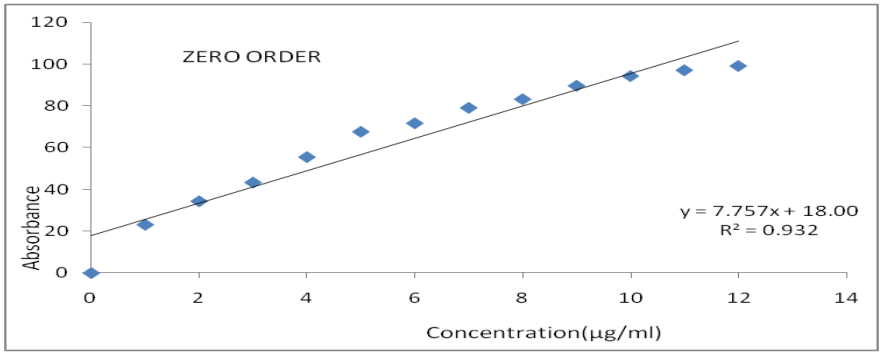
Percentage of drug release graph of formulations F-F6



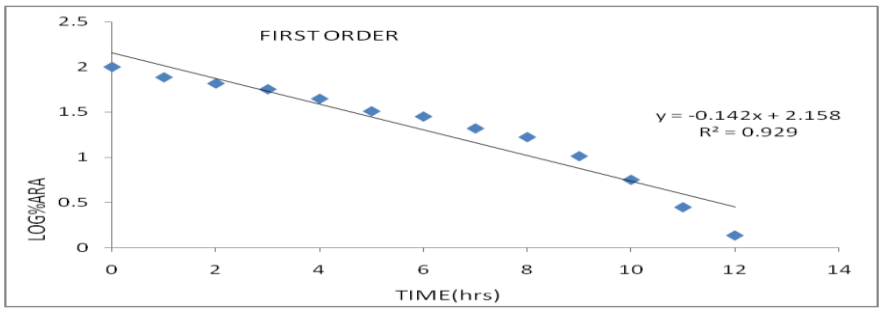
Percentage of drug release graph of formulations F7-F9



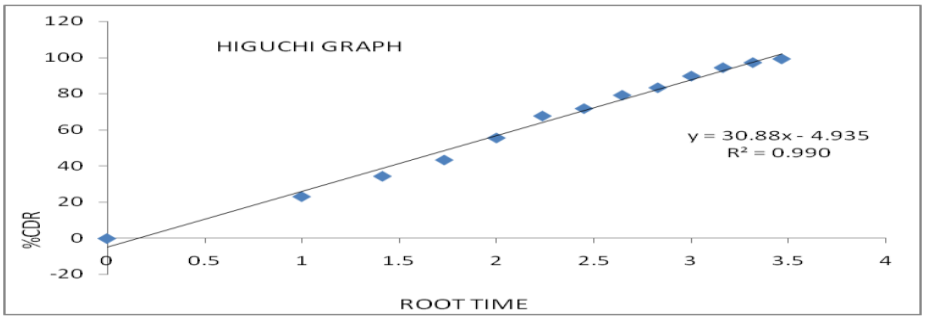
Kinetics Analysis for F2



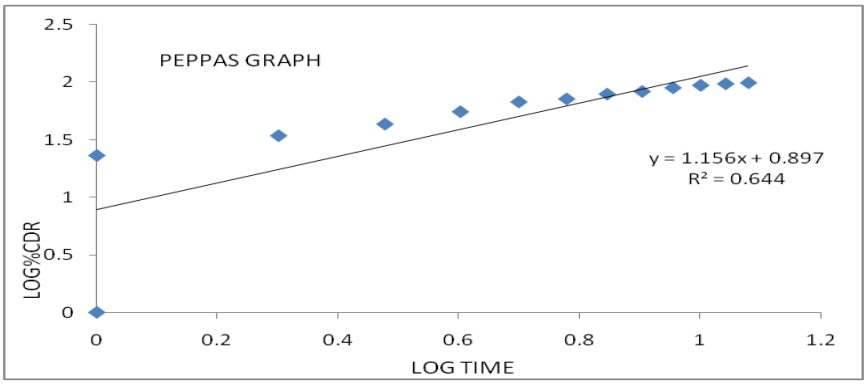
Zero Order Plot for F2



First order kinetics for F2



Higuchi graph for F2



Peppas graph for F2

Drug release kinetics of F2 formulation

S.NO	Zero order	First order	Higuchi	Peppas
Code	R^2	R^2	R^2	R^2
F2	0.932	0.929	0.990	0.664

DISCUSSION

The optimized formulation **F2** has coefficient of determination (R^2) values of 0.932, 0.929, 0.990 and 0.664 for Zero order, First order, Higuchi and KorsmeyerPeppas respectively. A good linearity was observed with the Zero order, the slope of the regression line from the Higuchi plot indicates the rate of drug release through the mode of diffusion and to further confirm the diffusion mechanism, data was fitted into the KorsmeyerPeppas equation which showed linearity with n value of 1.156 for optimized formulation. Thus n value indicates the Super case II transport mechanism. Thus, the release kinetics of the optimized formulation was best fitted into Higuchi model and showed zero order drug release with super case II transport mechanism.

SUMMARY AND COCLUSSION

The Nanosponge was prepared by solvent evaporation method using polymethyl methacrylate, Ethyl cellulose, and pluronic F127 as rate retarding polymers and PVA as co polymer using ethanol as a solvent.The prepared nanosponges were evaluated for its different parameters which revealed many interesting results for efficient preparation of the nanosponge. The formulation F2 has better results than other eight formulations. F2 have its particle size 398nm, entrapment efficiency 96.88%,Drug content 94.6**%** drug release release 99.26% in 12 hour, all these parameters are in optimized range for preparing a sustained release dosage form so showing itself as an optimized formulation in this project work..

FTIR spectroscopy analyses indicated the chemically stable, amorphous nature of the drug in these nanosponge. SEM photographs revealed the spherical nature of the nanosponge in all

variations.With the revealed results by different evaluation parameters, it is concluded that nanosponge drug delivery system has become highly competitive and rapidly evolving technology and more and more research are carrying out to optimize cost-effectiveness and efficacy of the therapy. The optimized formulation **F2** has coefficient of determination (R^2) values of 0.932, 0.929, 0.990 and 0.664 for Zero order, First order, Higuchi and KorsmeyerPeppas respectively. A good linearity was observed with the Zero order, the slope of the regression line from the Higuchi plot indicates the rate of drug release through the mode of diffusion and to further confirm the diffusion mechanism, data was fitted into the Korsmeyer Peppas equation which showed linearity with n value of 1.15 for optimized formulation. Thus n value indicates the super caseIItransport mechanism. Thus, the release kinetics of the optimized formulation was best fitted into Higuchi model and showed zero order drug release with super caseIItransport mechanism.

REFERENCES

[1]. Trotta F, Tumiatti W, Cavalli R, Rogero C, Mognetti B, Berta G. Cyclodextrin-based nanosponges as a vehicle for antitumoral drugs. WO. 8, 2009, 3656:A1.

[2]. Sharma R, Walker RB, Pathak K. Evaluation of the kinetics and mechanism of drug release from econazole nitrate nanosponge loaded carbapol hydrogel. Indian Journal of Pharmaceutical Education and Research. 1, 45(1), 2011, 25-31.

[3]. Ahmed RZ, Patil G, Zaheer Z. Nanosponges–a completely new nano-horizon: pharmaceutical applications and recent advances. Drug development and industrial pharmacy. 1, 2013, 39(9), 1263-72.

[4]. David F. Nanosponge drug delivery system more effective than direct injection. Pharm Dev Technol. 16(4), 2011, 367-76.

[5]. Zuruzi AS, MacDonald NC, Moskovits M, Kolmakov A. Metal oxide ―nanospongesǁ as chemical sensors: highly sensitive detection of hydrogen with nanosponge titania. Angewandte Chemie International Edition. 4, 2007, 46(23):4298-301.

[6]. Nacht S, Kantz M. The Microsponge: A Novel Topical Programmable Delivery System, In: Topical Drug Delivery Systemsǁ, David WO, Anfon H A editors. New York: Marcel Dekker, 42, 1992, 299-325.

[7]. Kılıçarslan M, Baykara T. The effect of the drug/polymer ratio on the properties of the verapamil HCl loaded microspheres. International journal of pharmaceutics. 18, 252(1), 2003, 99-109.

[8]. Maravajhala V., Papishetty S., Bandlapalli S. ―Nanotechnology in the development of drug delivery systemǁ, International journal of pharmaceutical sciences & research, 2(1), 2012.

[9]. Ansari KA, Vavia PR, Trotta F, Cavalli R. Cyclodextrin-based nanosponges for delivery of resveratrol: in vitro characterisation, stability, cytotoxicity and permeation study. Aaps Pharmscitech. 1, 12(1), 2011, 279, 86.

[10]. Kydonieus AF, Berner B. Transdermal delivery of drugs. CRC Press 1987.