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Fabrication and Assessment of Doxazosin Mesylate Nanosponges

Arpitha G.*[1], Brunda S.[2], Rajani B. K.[3], Shubha D. B.[4], Chinthana H. B.[5]
[1,2,3,4,5] Shridevi Institute of Pharmaceutical Sciences, Tumkur

ABSTRACT: Novel drug delivery system is a new approach to deliver the active molecules in a safe and effective manner to produce desired pharmacological actions. Nano technology has played a major role in overcoming some drawbacks of conventional drug delivery system. Nanosponges are tiny bodies filled with drug, they circulate throughout the body until they encounter specific target site and releases drug in a controlled and predictable manner. The major goal of the study was to create doxazosin mesylate nanosponges and to evaluate them. Nanosponges are prepared by emulsion solvent diffusion approach, using Ethyl cellulose, β-CD and HP-β-CD.The FTIR test is used as a preliminary test, and it shows that the active ingredient and polymers have no interaction. The particle size, PDI, zeta potential, SEM, entrapment efficiency of nanosponges were assessed. The particle size ranged from 443.46 to 683.93 nm, PDI ranged from 0.255 to 0.510, zeta potential from - 19.8 to -22.9 mV and entrapment efficiency was ranged from 51.62 to 92.82%. The cumulative percentage release from all nanosponges varied from 52.76 to 91.84 % after 12 hours depending upon the drug and polymers ratio and F5 formulation showed highest drug release i.e., 91.84%.

KEYWORDS: Cumulative drug release, Doxazosin mesylate, Nanosponges, Zeta potential.

INTRODUCTION

The modern approach of nanotechnology is focused drug delivery system. Nanosponges performs a key role in targeting a molecule to reach target site, it has grow to be an extensive step in accomplishing better consequences by minimizing the toxicity (1).

Nanosponges are microscopic particles with a few nm length cavities which can encapsulate an extensive range of compounds. These debris can convey each lipophilic and hydrophilic substances. The nanosponge is set the size of an epidemic and has an obviously degradable polyester backbone. They 'pass link' polyester segments to construct a spherical form with numerous pockets or cavities in which drug may be contained. Because the polyester is biodegradable, the medicine may be released on a predetermined time while it breaks down within the frame (2).

Hypertension is the pressure of blood towards the artery walls because it circulates via the body. Excess blood pressure or hypertension is the constant pumping of blood through blood vessels with immoderate pressure. Blood pressue is measured in millimeters of mercury (mmHg). When blood pressure is greater than both one hundred forty mmHg systolic strain or 90MmHg diastolic strain, that condition can be called as hypertension. Blood pressure is taken into consideration very excessive while it is more than one hundred eighty mmHg systolic or 110 mmHg diastolic (3).

Doxazosin mesylate (DM), a quinazoline spinoff, can be utilized in the treatment of moderate to slight high blood pressure and additionally inside the control of symptomatic benign prostatic hyperplasia (BPH). In hypertensive patients, DM reduces the blood strain by using selectively antagonizing the postsynaptic α1-adrenergic receptors. DM is a BCS magnificence II drug with negative aqueous solubility and high permeability and undergo hepatic first bypass metabolism resulting in reduced bioavailability(4).

The nanosponges are have some advantages, nanosponges can deliver each hydrophobic and hydrophilic molecules. The superior residences of nanosponges had been attributed to 'tunability', this is the potential to control the shape of particles and manage the character and size of aperture. Nanosponges have the capability to produce predictable/managed drug release. Nanosponges may be tagged with precise linkers to goal diseased cells subsequently reaching more efficacy while lowering aspect-effects, reducing dose and dosing frequency and in turn increasing affected person compliance.Nanosponges can considerably lessen the infection of medicine without lowering their efficacy. Biodegradable in nature and easy scale up for business manufacturing (5)

MATERIALS AND METHODS

Doxazosin mesylate (DM) was purchased from Balaji Chemicals, Bangalore. Ethyl cellulose from Research lab fine chem industries. β-CD and HP-β-CD from Gattefose Hyderabad, and all the reagents were analytical grade.

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λ max of Doxazosin mesylate:

DM is a white amorphous powder which is soluble in simulated saliva buffer of pH 6.8. UV spectrophotometric method was used in this study, DM shows absorbance at 246nm.

Calibration curve of Doxazosin mesylate in simulated Saliva Buffer pH 6.8

Accurately weighed Doxazosin mesylate was dissolved in 100 ml containing simulated saliva buffer of pH 6.8 in a volumetric flask & make up to the volume (stock I). Pipetted 5ml to 50ml volumetric flask (stock II). Prepared aliquots from stock II, i.e, 0.1, 0.2, 0.3, 0.4, 0.5, & 0.6ml.

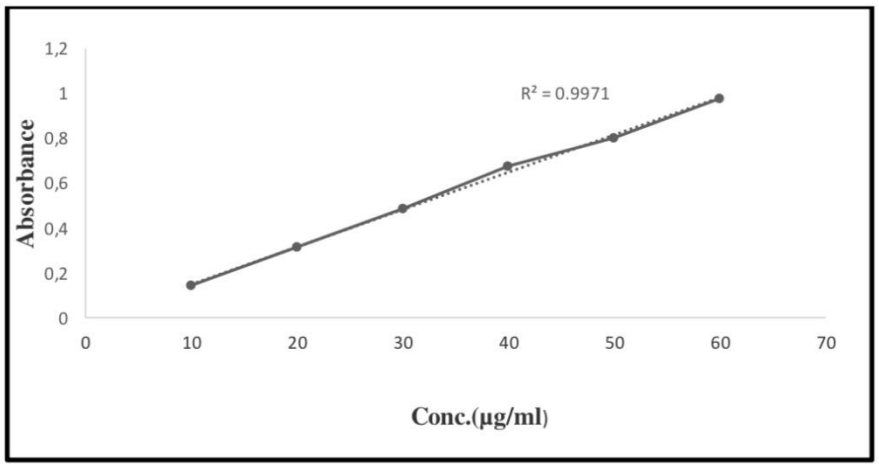

Figure 1. Calibration curve of Doxazosin mesylate

FORMULATION DESIGN

Preparation of Doxazosin mesylate nanosponges using Ethycellulose, β-Cyclodextrin, and HP-β-Cyclodextrin.

Nanosponges are prepared by emulsion solvent diffusion approach, using distinct percentage of Ethyl cellulose, β-CD and HP-β-CD. Disperse phase includes 100mg of DM and added ethyl cellulose dissolved in 5ml of solvent Ethanol changed into slowly brought to an aqueous phase containing exact quantity of polymer. The mixture stirred at 1000 rpm for 3 hours on a magnetic stirrer. The fashioned nanosponges were accumulated by filtration through whatmann filter paper and dried at room temperature.(6)

Table No 1: Composition of different formulation of Doxazosin mesylate nanosponges.

Formulations	Drug (mg)	EC (mg)	β-CD (mg)	HP-β-CD (mg)	DM (ml)
F1	100	100	100	---	30
F2	100	100	200	---	30
F3	100	100	300	---	30
F4	100	100	---	100	30
F5	100	100	---	200	30
F6	100	100	---	300	30

EVALUATION OF NANOSPONGES

Particle size analysis

The particle size was determined by using a Malvern system, with vertically polarized light supplied by an argon-ion laser (Cyonics) operated at 40 mW. The technique of laser diffraction is based around the principle that particles passing through a laser beam will scatter light at an angle that is directly related to their size. As the particle size decreases, the observed scattering angle increases logarithmically The observed scattering intensity is also dependent on particle sizes and diminishes, to a good approximation, in

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relation to the particle's cross-sectional area. Large particles therefore scatter light at narrow angles with high intensity, whereas small particles scatter at wider angles but with low intensity. (7)

Zeta potential

The stability of a nanosponge can be determined by the result of zeta potential. It is a measure of effect of electrostatic charges. A basic force that causes the repulsion between adjacent particles. Net results are attraction or repulsion depends upon the magnitude of both forces. The thumb rule describes the relation between zeta potential determination responses of the Nano-particles.

Scanning electron microscopy

For the evaluation of the surface morphology of nanosponges, the sample was analyzed in a scanning electron microscope after preparing the sample by lightly sprinkling on a double adhesive tape stuck to an aluminum stub. The stubs were then coated with platinum. The stub containing the coated sample was placed in a scanning electron microscope. The samples were then randomly scanned and photomicrographs were taken at the acceleration voltage of 20 kV. From the resulting image, average particle size was determined. (8)

Drug Content

An accurately weighed amount of 20mg of nanosponges were added to 20ml of ethanol and placed in a thermo-shaker, operated at 100rpm at 25^0 C for 45minutes followed by vortexing for 10min. the solution was filtered through a 45µm membrane filter. Filtrate is observed under UV spectrophotometry. (9)

$$\%\ \boldsymbol{Drugcontent} = \frac{\boldsymbol{Practicalamount\ of\ the\ drug\ obtained}}{\textbf{Theroretical amount of drug added}} \boldsymbol{X100}$$

***In vitro* Drug Release Study**

In vitro drug release studies were carried out in *Franz* diffusion cell. 20mg of nanosponges dispersed in 2ml of Simulated saliva buffer. The dispersion was used for diffusion study. Nanosponges containing drug were placed in donor compartment while the receiver compartment consists of 22 ml of diffusion medium Simulated saliva buffer pH 6.8 is maintained at room temperature in Franz diffusion cell. The rpm of the magnetic bead was maintained at 50 rpm. 1 ml of the aliquot was withdrawn at predetermined intervals. The samples were analysed for the drug content by UV spectrophotometer at 246 nm. Equal volume of the diffusion medium was replaced in the vessel after each withdrawal to maintain sink condition. Three trails were carried out for all formulation. From the data obtained the percentage drug release was calculated and plotted against function of time to study the pattern of drug release. (10,11)

RESULTS AND DISCUSSION

Drugs-polymer interaction study by FT-IR spectrophotometer

FTIR spectroscopy studies were performed separately to analyze the drug (doxazosin maleate), polymer (ethylcellulose), and copo lymers (β-cyclodextrin and HP-β) used to prepare the nanosponges. - cyclodextrin).

FT-IR was performed on physical mixtures of chemicals, polymers and copolymers.

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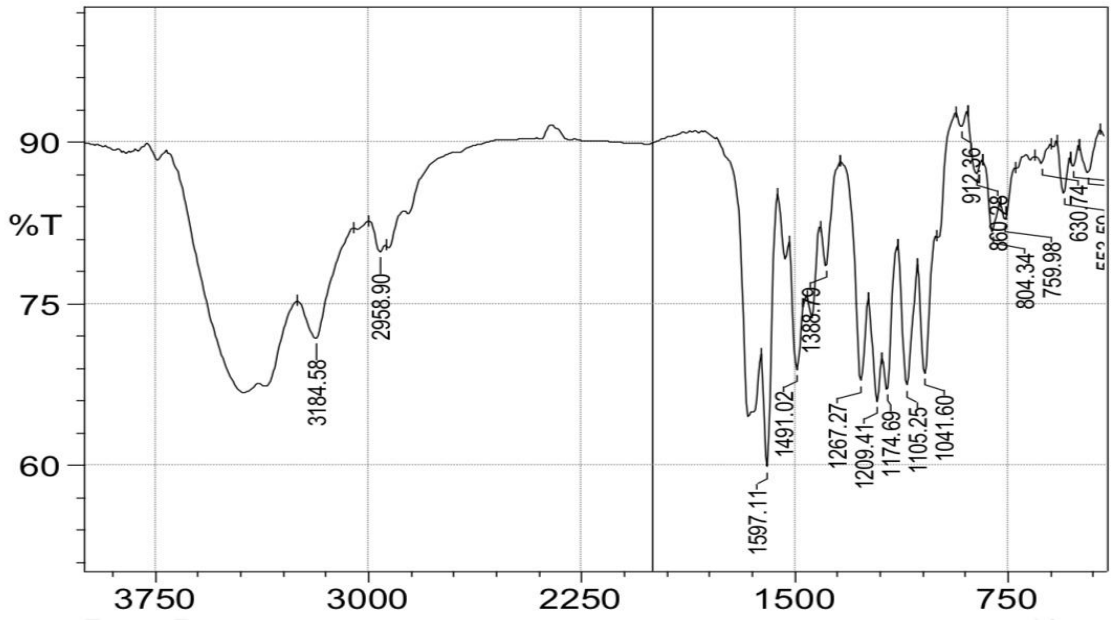

Figure 2.FTIR of Pure Doxazosin mesylate Drug.

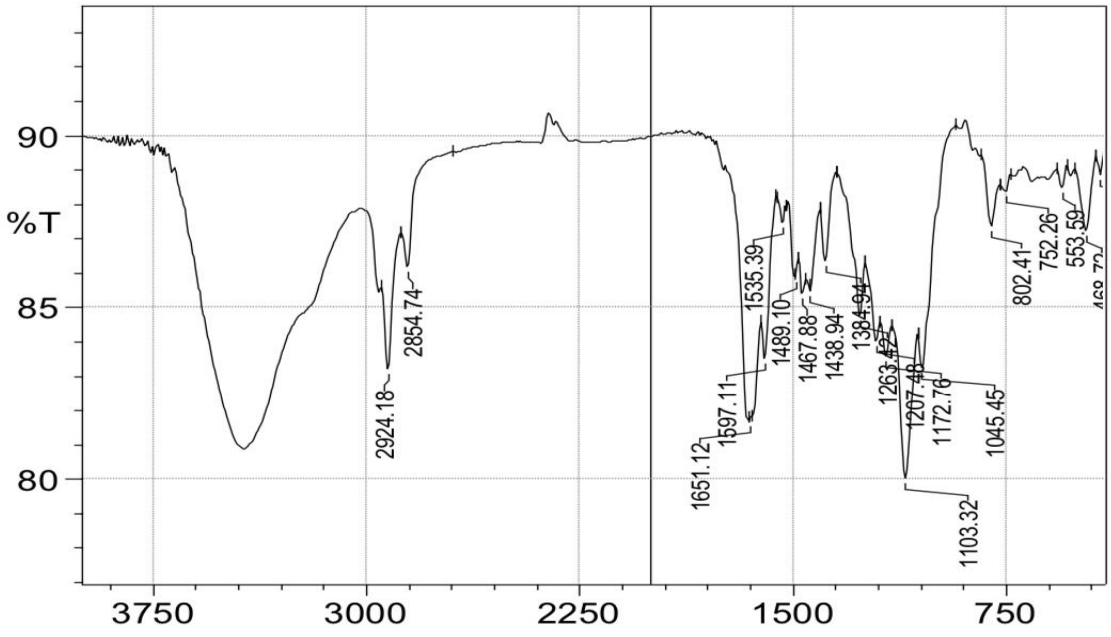

Figure 3. FTIR of Doxazosin mesylate, Ethyl Cellulose and β-CD

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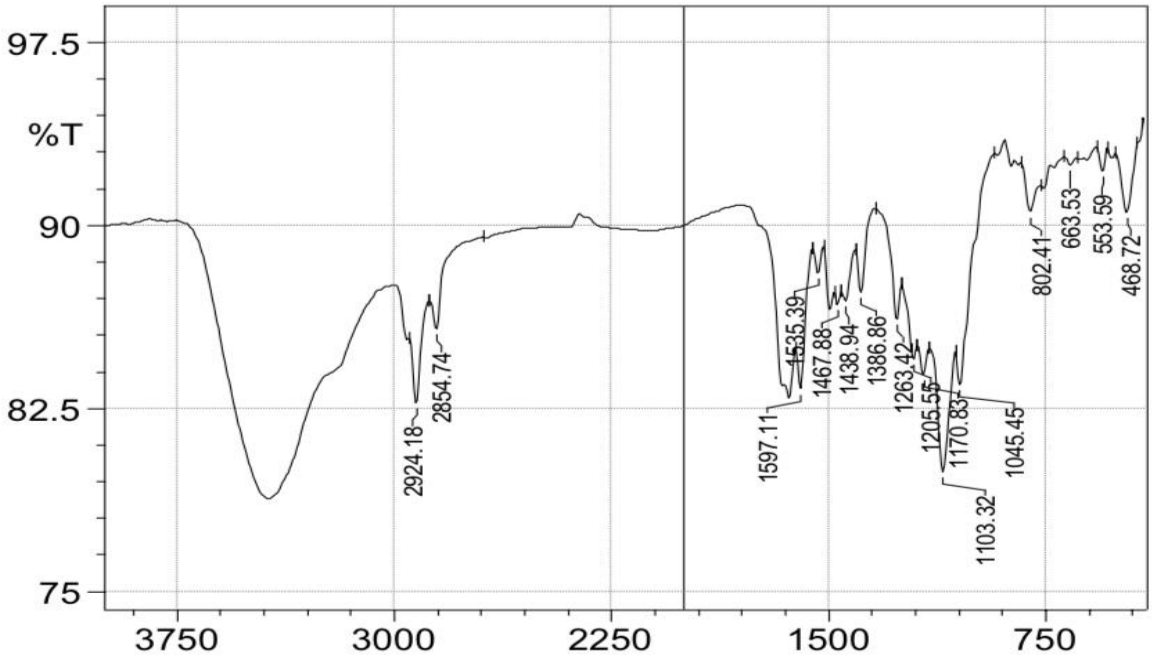

Figure 4. FTIR of Doxazosin mesylate, Ethyl Cellulose and HP-β-CD

Characterization of Nanosponges

Particle size, zeta potential and PDI

Report of size, PDI and zeta potential obtained from the zeta sizer, shown in the Table no.2 The particle size ranged from 480.6 to 753.4 nm, PDI ranged from 0.284 to 0.437, zeta potential from -20.9 to -35.96 mV

Table No.2: The particle size, PDI and zeta potential of Doxazosin mesylate prepared with Ethyl cellulose, β-CD, HP-β-CD.

Formulation Code	Particle size (d. nm)	PDI	Zeta potential (mV)
F1	517.60	0.510	-20.8
F2	683.93	0.432	-20.9
F3	652.63	0.384	-21.9
F4	548.63	0.286	-22.9
F5	443.46	0.255	-20.5
F6	623.45	0.406	-19.8

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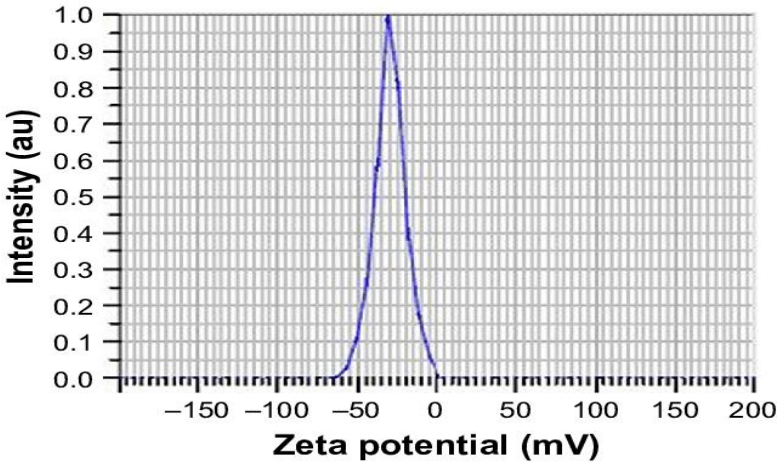

Figure 5. Zeta Potential of Optimized formulation.

Scanning Electron Microscopy

SEM analysis of the formulated Oxiconazole loaded nanosponges were performed to evaluate the surface morphology of Nanosponges. The SEM images of Optimised formulation is shown in below.

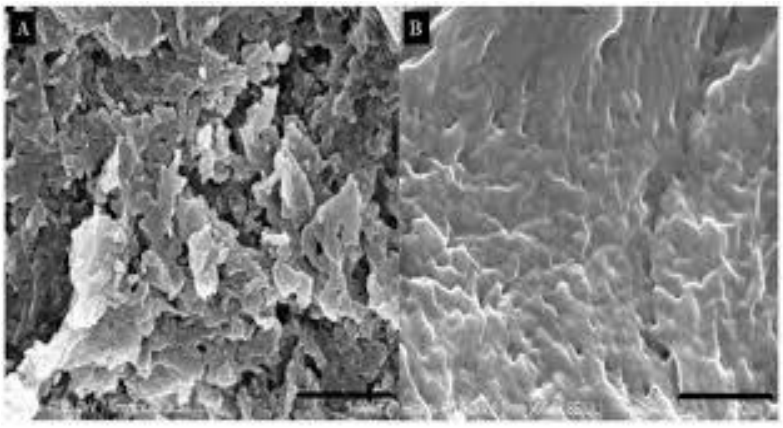

Figure 6. Drug content and Entrapment Efficiency

The drug content and the entrapment efficiency results are shown in the Table no.4 The drug content results of nanosponges were obtained in the range from 95.25 to 98.95%. Entrapment efficiency of nanosponges were obtained in the range from 51.62 to 92.82%.

Table No. 3: Data of drug content and Entrapment Efficiency of Doxazosin loaded nanosponges with Ethyl cellulose β-CD and HP- β-CD.

Formulation Code	Drug Content %	Entrapment efficiency %
F1	96.22	66.04
F2	97.46	51.62
F3	98.50	81.38
F4	95.25	89.72
F5	98.95	92.82
F6	96.12	80.02

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Release studies

The drug release from the Nanosponges were studied by *Franz* diffusion method. The cumulative drug release percentage shown in Table No.4

Table No.4: Percentage drug released from different formulations (F1-F6) during 12 Hours.

Time (Hours)	F1	F2	F3	F4	F5	F6
0.5	7.18	10.79	11.64	9.58	9.56	7.75
1	18.24	20.77	17.10	14.04	18.73	12.05
2	25.43	24.13	19.15	18.11	28.09	15.14
3	30.52	23.83	23.04	20.02	36.16	18.55
4	39.06	30.51	30.35	17.08	46.14	25.55
5	46.09	34.26	44.76	30.04	55.36	32.85
6	51.07	40.99	50.28	40.15	64.67	40.84
8	63.76	48.28	69.72	55.02	76.53	63.39
12	70.16	52.76	78.31	78.77	91.84	74.75

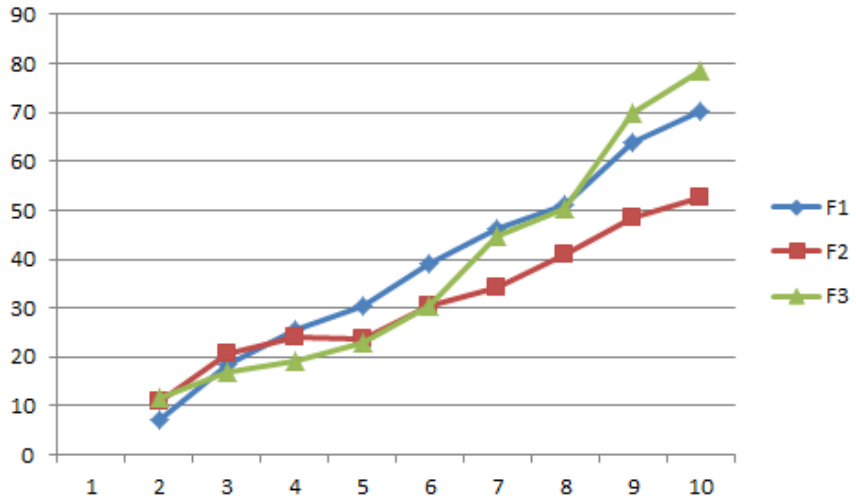

Figure 7. Cumulative drug release data of Doxazosin mesylate formulations F1-F3.

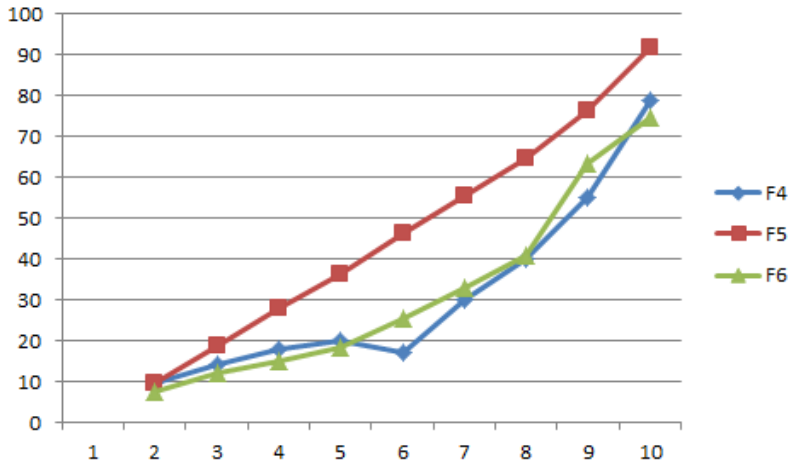

Figure 8. Cumulative drug release data of Doxazosin mesylate formulations F4-F6.

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CONCLUSION

The present study was to develop Nanosponge delivery system for Doxazosin mesylate using Ethyl cellulose, β-cyclodextrin and HP-β-cyclodextrin as polymers, which are used for better anti-hypertensive activity. FT-IR studies revealed that there was no interaction between the drug and polymers. nanosponges were prepared by emulsion solvent diffusion method, which was able to produce Nanosponges of acceptable range and stability. All the formulations showed good entrapment efficiencies. Among the all batches F5 was optimized after considering their particle size, SEM, zeta potential and *in vitro* drug release profile.

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