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FORMULATION AND EVALUATION OF ATORVASTATIN CALCIUM LOADED NANOSPONGES BY EMULSION SOLVENT DIFFUSION METHOD

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ABSTRACT

Objective**:** The objective of the present study was to formulate Atorvastatin calcium loaded Nanosponges by emulsion solvent diffusion method and aimed to increase its bioavailability of the drug. **Methods:** The Atorvastatin calcium loaded Nanosponges was prepared by emulsion solvent diffusion method using different drug-polymer ratios (1:0.5 to 1:3) ethyl cellulose is used as a polymer. Fourier transform infrared spectroscopy (FT-IR) estimated the compatibility of Atorvastatin calcium with polymer. All formulations evaluated for percentage yield, drug entrapment efficiency, in-vitro drug release, scanning electron microscopy (SEM).

Results: The FT-IR studies revealed that no interaction between drug and polymer. The percentage yield of all batches in the range of 66.66% to 89.33%, the entrapment efficiency of all batches in the range of 67.33% to 87.16%. The average particle size ranges from 213 to 512 nm. By the end of 12th hour F II formulation shows highest drug release was found to be 94.9 %. The release kinetics of the prepared Nanosponges shows zero-order drug release. **Conclusion:** The results of various evaluation parameters, revealed that Atorvastatin calcium Nanosponges would be possible delivery systems to conventional formulation to improve its bioavailability, the emulsion solvent diffusion method was simple and best method for preparation of Nanosponges.

Keywords: Nanosponges, Atorvastatin calcium, Emulsion solvent diffusion method.

INTRODUCTION

Nanosponges are a new type of microscopic sponge that is roughly the size of a virus. They are filled with drug and attached with specific chemical "linkers" that tie preferentially to a characteristic present only on the surface of tumor cells before being injected into the body. These small sponges circulate throughout the body until they reach the surface of a tumor cell, where they adhere and begin releasing their strong medicine in a controlled and predictable manner [1].

Nanosponges resemble a three-dimensional scaffold or network, with long-length polyester serving as its backbone. It is combined with tiny molecules known as cross-linkers in solution, which serve as tiny grappling hooks to hold the various polymer components together. The end result is the formation of spherically shaped particles with cavities that can hold medicinal molecules. Because the polyester is biodegradable, the body breaks it down gradually. The proportion of cross-linkers to polymer can also be changed to regulate the size of the Nanosponge particles, making them larger or smaller [2].

Nanosponges, which resemble microscopic meshes, have the potential to transform the way numerous diseases are treated. This technique is five times more successful than traditional ways at delivering drugs for breast cancer [2].

Nanosponges are composed of tiny particles having chambers that are only a few nanometers across and can contain a wide range of materials. In addition to transporting hydrophilic and lipophilic compounds, these particles can increase the solubility of molecules that are not very soluble in water [3]. Drug molecules are encapsulated within the core of Nanosponges, a form of nanoparticle. In contrast to other nanoparticles, Nanosponges are porous, non-toxic, stable at temperatures as high as 300°C, and insoluble in organic solvents and water [4].

One of the main benefits of this method over other nanoparticle delivery systems currently in development is its predictable release. Numerous additional nanoparticle delivery techniques rapidly and uncontrollably release the majority of their medicine once they have reached their target. When nanosponges reach their target site, this phenomenon, known as the burst effect, makes it challenging to identify the

appropriate dosage levels. An enhanced delivery technique for anticancer treatments, such as direct injection into the tumor site, may be the controlled release nanoparticle drug delivery system. These nanoparticles travel throughout the body until they come into contact with a tumor cell's surface, where they attach and begin to release the medication in a regulated and predictable way [5].

The Nanosponges are solid in nature and can be formulated as oral, parenteral, topical or inhalational dosage forms. For oral administration, these may be dispersed in a matrix of excipients, diluents, lubricants and anticaking agents which is suitable for the preparation of tablets and capsules. For parenteral administration, these can be simply mixed with sterile water, saline or other aqueous solutions [6]. For topical administration, they can be effectively incorporated into topical hydrogel [7, 8].

The drawbacks of the traditional dose forms can be partially addressed by the atorvastatin calcium-loaded Nanosponges. Atorvastatin calcium is a member of the drug class known as statins. Atorvastatin calcium is the most efficacious of the currently available HMG-CoA Reductase inhibitors used in anti-lipidemic and also used in atherosclerosis, stroke and cardiac risk. As a synthetic lipid-lowering drug, Atorvastatin calcium inhibits 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase, which catalyzes the early rate-limiting step in cholesterol manufacture where HMG-CoA is converted to mevalonate. Currently, Atorvastatin calcium is used to treat hypercholesterolemia as a calcium salt. Atorvastatin calcium ([R-(R*,R*)])-2-(4-fluorophenyl)5-(1-methylethyl)-β,γ-dihydroxy3-phenyl-4-[carbonyl(phenyl amino)]-1Hpyrrol, hemi-calcium salt of 1-heptanoic acid.is an off-white to white crystalline powder that is insoluble in pH 4 and lower aqueous solutions; it is soluble in methanol and ethanol-based phosphate buffers at pH 7.4, although it is very marginally soluble in water and acetonitrile at pH 7.4 [9-11]. It is used for the treatment of hyperlipidemia. Atorvastatin calcium is classified under class II according to biopharmaceutical classification system [BCS]. The drugs shows low pH dependent solubility. In acidic and neutral aqueous media, Atorvastatin calcium exhibits very poor solubility. Poor solubility can lead to unpredictable bioavailability and poor dissolution. Preparation of Nanosponges of Atorvastatin calcium to improve the dissolution rate of Atorvastatin calcium and subsequently its bioavailability. The study's primary goal was to raise the dissolving rate in order to increase the quantity of dissolved drug molecules at the absorption site, as class II drugs such as Atorvastatin calcium, in-vivo dissolution rate is rate-limiting step in drug absorption. Nanosponges were chosen as the preferred technique since they would be simpler to formulate later. The Nanosponges were prepared by Emulsion solvent diffusion method.

MATERIALS AND METHODS

MATERIALS

Drug: Atorvastatin calcium, **Polymer:** Ethyl cellulose, **Co-polymer:** PVA (Polyvinyl alcohol), **Solvent:** Dichloromethane and Distilled water.

METHODS

Atorvastatin Calcium Nanosponges were created using an emulsion solvent diffusion method. Nanosponges can be made using varying mixtures of ethyl cellulose (EC) and polyvinyl alcohol (PVA). The dispersed phase containing ethyl cellulose and drug was dissolved in 20ml of dichloromethane and gradually added to a specific amount of polyvinyl alcohol in 150ml of aqueous continuous phase. The reaction mixture was agitated at 1000 rpm for two hours. The Nanosponges were recovered using filtering and dried in an oven at 40°C for 24 hours. The dried Nanosponges were stored in vacuum desiccators to ensure that any leftover solvents were removed.

Table No.1 Formula for the preparation of Nanosponges

S.No	Ingredients	Quantity
1	**Atorvastatin calcium(mg)**	600mg
2	**Ethyl cellulose(mg)**	600mg
3	**PVA(mg)**	20mg

4	**Dichloromethane (ml)**	20ml
5	**Distilled Water (ml)**	150ml

Table No.2 Formula for the Preparation of various batches of Nanosponges

S.No	Materials	F I	F II	F III	F IV
1	**Drug: Polymer (mg)**	1:0.5	1:1	1:2	1:3
2	**PVA(mg)**	20	20	20	20
3	**Dichloromethane (ml)**	20	20	20	20
4	**Distilled Water (ml)**	150	150	150	150

PREFORMULATION STUDIES OF PURE DRUG

PHYSICAL CHARACTERISTICS

By visual examination, Physical characteristics such as color and texture were used to identify the drug.

SOLUBILITY ANALYSIS

Preformulation solubility studies must be performed, which involves choosing an appropriate solvent to dissolve the drug in concern as well as different excipients that have been employed since the development of nanoparticles.

PHYSICAL COMPATIBILITY

Physical compatibility of the drug and excipients were carried out at Room temperature and at 40°C±2°C/75±5% RH 9in days with the physical add mixture of drug and excipients.

COMPATIBILITY STUDIES FOR DRUG AND EXCIPIENTS

The drug and excipients compatibility studies were carried out by Fourier transform-infrared spectroscopy (FT-IR). The solid powder sample was pulverized using 100 times the amount of KBr in a mortar to create the potassium bromide pellets on a KBr press. The spectra recorded over the wave number of 4000 to 400 cm-1.

CONSTRUCTION OF THE CALIBRATION CURVE

Stock I

Accurately weighed 10 mg of Atorvastatin calcium was dissolved the insufficient amount of phosphate buffer 6.8 and volume was made to 10 ml with it. (Concentration1000 µg/ml).

Stock II

From stock-I 1ml sample is withdrawn by pipette and diluted to 10 ml of by using phosphate buffer 6.8 (100µg/ml).

Stock III

Form stock II working standard solution of strengths 5, 10, 15, 20, 25 (µg/ml) were made from the stock solution by appropriate dilution.

EVALUATION STUDIES OF PREPARED NANOSPONGES

From the results obtained by solubility and dissolution studies, The Nanosponges that performed better were chosen. Nanosponges were used for additional characterisation in order to determine whether there was any interaction between the drug and the polymer and what characteristics of the polymer made it a useful material for improving solubility and bioavailability. In present study, the Nanosponges of Atorvastatin calcium with ethyl cellulose were characterized by FT-IR, SEM, in vitro drug release study, percentage yield, entrapment efficiency etc.

PERCENTAGE YIELD

The percentage yield [PY] can be determined by weighing the raw ingredients at the initial and the Nanosponges at the final.

$$\textbf{Percentage yield} = \frac{\textit{Practical mass of nanosponges}}{\textit{Theoretical mass}\ (\textit{Polymer+Drug})} \times 100$$

The percentage yield of different batches was calculated by weighing the Nanosponges after drying [12].

DRUG ENTRAPMENT EFFICIENCY

The entrapment efficiency was measured by measuring the drug concentration in the supernatant following centrifugation. The

unentrapped Atorvastatin calcium were determined by adding 10 mg Atorvastatin calcium loaded Nanosponge in 10 ml of methanol and then the dispersion were centrifuged at 9,000rpm for 30minutes at 4ºC using a cooling centrifuge in order to separate entrapped from the unentrapped drug. The free drug concentration in supernatant layer after centrifugation is determined at λmax (246 nm) using UV Spectrophotometer The percentage entrapment efficiency (%EE) is calculated by following formula: [12].

$$\%\text{Entrapment efficiency} = \frac{weight\ of\ initial\ drug - weight\ of\ free\ drug}{weight\ of\ initial\ drug} \times 100$$

DETERMINATION OF PARTICLE SIZE

The size of particles is maintained during polymerization to produce free-following powders with fine aesthetic properties. Laser light diffractometry or the Malvern zeta sizer is used to analyze the particle sizes of loaded and unloaded Nanosponges. The cumulative graph is kept or shown as particle size against time to investigate the effect of particle size on drug release [13].

IN VITRO DRUG RELEASE STUDIES

In vitro drug release investigations were conducted in triplicate using the USP paddle method at 50 rpm and 37 ± 0.2 ℃ in 900 mL of phosphate buffer (PH 6.8) [15]. Each experiment uses 100mg of the specially prepared Nanosponges. Samples were collected at appropriate time intervals of one hour each for ten hours. The samples were analyzed spectrophotometrically at 246 nm. Each time a sample was extracted, fresh dissolving media was replenished to correct for volume.

KINETIC MODEL AND DRUG RELEASE MECHANISM

The design for Atorvastatin Calcium loaded; it was based primarily on its release profile using several mathematical models in the current investigation.

- Zero order model
- First order model
- Higuchi model
- Korsmeyer - Peppas model
- Hixson – Crowell model

ZERO ORDER MODEL

Zero order models are unreliable models in which the likelihood of an event of a random outcome at a challenging moment does not depend on any process outcome. According to the pharmacokinetics standard, the equation below can be used to model how much medication is released from a dose form.

$$C_0 - C_t = K_0 t \quad C_t = C_0 + K_0 t$$

- Where
- **Ct** the proportion of drugs released at one occasion t,
- **C0** is the drug's initial concentration at time. t=0,
- **K0** is the zero-order rate constant.

Zero order kinetics, which maintains a constant drug level in the blood throughout the delivery, is what gives a drug delivery system its anticipated drug release. The data from the in-vitro dissolution investigation is displayed between cumulative drug release (percent) and time to take release kinetics into account. The zero order rate constant and correlation coefficient can be calculated using the slope chart, which shows the order of kinetics. If the correlation coefficient value is larger than 0.9, the system adopts zero order of kinetics, which presents the best fit model [16].

FIRST ORDER MODEL

A process whose rate is directly related to the concentration of the drug undergoing response is referred to as a "first order model," meaning that a higher concentration of the medication results in a faster reaction. It uses linear kinetics. The drug release that follows first order kinetics is shown in the equation below.

$$DC/dt = -K_1 C$$

The first order rate constant, or K1, is measured in time-1 or in units of an hour. Tweaking and integrating the previous equation

$$\log C = \log C_0 - K_1 t/2.303$$

The evidence from the in-vitro dissolution experiment is plotted between the time to analyse release kinetics and the log percent of drug left.

The graph using the slope, which depicts the order of kinetics, can be used to calculate the correlation coefficient and zero order rate constant. If the correlation coefficient value is larger than 0.9, the system exhibits the best fit model and follows zero order of kinetics [12].

HIGUCHI MODEL

Dissolution and diffusion are both a part of the drug discharge from the drug delivery system (DDS). Different numerical models that outline drug release from the DDS exist. In the ongoing period of controlled release formulation, the "Higuchi condition" is the most significant active condition. The Higuchi condition is one of the most often employed conditions for controlled-release formulation.

The Higuchi equation is represented by

$$Q = A\sqrt{D(2Co - Cs)Cst}$$

Where Q is the total amount of drug released per unit area over time t, and D is the drug's matrix diffusion coefficient. The initial drug concentration is C0, and the drug's matrix solubility is Cs.

When the above plot's correlation coefficient is high, we can infer that a diffusion-controlled delivery system is the key to a drug's release mechanism. In this Higuchi condition, certain important possibilities are made forth. They are i) a significantly higher initial drug solubility in the matrix Concentration in the framework, ii) perfect sink maintenance, iii) constant drug diffusivity, iv) little polymer growth are all factors. By ensuring that the concentration of the delivered medication in the delivery medium never exceeds 10% of its saturation solvency, the sink conditions are achieved. The delivery profile of the Atorvastatin calcium loaded Nanosponges benefited from this strategy. The estimation was performed via (Cumulative) in the graphical presentation [13].

KORSMEYER-PEPPAS MODEL

The drug release will then takes place and depend on the type of diffusion when it has been considered that diffusion controlled by the Higuchi plot is the crucial mechanism of drug release. In order to force the matrix's component to dissolve, the conveyance data were set using the outstanding appropriate condition explored by Korsmeyer and Peppas. Drug release from a polymeric system follows a particular kind of dissociation, according to a straightforward connection offered by Korsemayer and Peppas. Additionally, they addressed the issue as

$$M_t/M_\infty = Kkpt^n$$

Mt/M∞ is a fraction of drug released at time t,

$$\text{Log } (M_t/M_\infty) = \log Kkp + n\log t,$$

Where

- The amount of drug released at time t is called Mt, while the amount released at time is called M∞.
- N is the diffusional exponent or drug release exponent,
- Kkp is the Korsmeyer release rate constant.
- A graph between log cumulative percent drug release and log time is generated to investigate the release kinetics [15].

HIXSON-CROWELL MODEL

The surface area and diameter of the delivered particles may change, according to the Hixson-Crowell model. Particles in the standard area and their relation to the cube root of the volume. Based on the prior assumption, Hixson-Crowell created a relationship between the time and medicine release. Condition speaks to it since we can conclude that the cycle's change in surface area.

$$W_0^{1/3} - W_t^{1/3} = K_H Ct$$

Wt is the remaining amount of medication in the drug dose design at time t, where W0 is the underlying amount of medication in the drug dose structure (amount of medication present at time 0); The Hixson-Crowell consistent (KHC) is used to differentiate between surface volume relations. This condition is used to translate the dissolving information for dosage structures with conventional, dispersible, and rapid delivery. If the correlation coefficient for the preconceived ideas is higher, we can infer that the change in surface area during the disintegration cycle has a considerable impact on the delivery of the medication. The graphic is placed in the midst of the cube root of the drug rate remaining vs time to study the release kinetics

This scenario is used to interpret the dissolving information from the CAZ, the dispersible dosage structure, and the fast delivery dose structure. If the aforementioned condition has a greater connection coefficient, we might conclude that the cycle's fluctuation in surface area of disintegration has a substantial impact on the delivery of the medication. The diagram is plotted in the middle of a 3D square basis of medicine rate remaining vs time to take delivery activity into consideration [14].

RESULTS

PREFORMULATION STUDIES

PHYSICAL CHARACTERIZATION OF ATORVASTATIN CALCIUM.

Table No.3 Physical characterization of Atorvastatin Calcium

S.No	Properties	Observation
1	Description	White to off – white powder
2	Odour	Characteristic odour
3	Colour	White to off white

Solubility of Atorvastatin calcium pure drug in Water, Ethanol, Methanol, Acetone, Petroleum ether, Isopropyl alcohol, 0.1M NaOH. It was found to be freely soluble in Methanol, soluble in Acetone, slightly soluble in Ethanol, very slightly soluble in Distilled water, Isopropyl alcohol and insoluble in Pet ether and 0.1M NaOH.

Table No.4 Solubility studies of Atorvastatin calcium

S.No	Solvent	Description
1	Methanol	Freely soluble
2	Acetone	Soluble
3	Ethanol	Slightly soluble
4	Distilled Water	Very slightly soluble
5	Isopropyl alcohol	Very slightly soluble
6	Petroleum ether	Insoluble
7	0.1M NaOH	Insoluble

SOLUBILITY STUDIES

PHYSICAL COMPATIBILITY STUDIES

Table No.5 Physical compatibility Studies

S.No	Drug (D) and excipients	Description and condition initial	Room temperature (40^0 C±2^0 C/75±5% days)			Relative humidity(in days)		
			10	20	30	10	20	30
1	**Drug**	NCC	NCC	NCC	NCC	NCC	NCC	NCC
2	**D + EC**	NCC	NCC	NCC	NCC	NCC	NCC	NCC
3	**D+ PVA**	NCC	NCC	NCC	NCC	NCC	NCC	NCC

NCC – No Characteristic change.

INFERENCE

The drug and the formulation's excipients are physically compatible. They were evaluated for

10, 20, and 30 days at room temperature and at (400 C±20/75±5% days) Relative humidity.

CHEMICAL COMPATIBILITY

FT-IR spectroscopy provides information on the interaction of the drug and polymer.

DRUG-EXCIPIENT COMPATIBILITY STUDIES

FT-IR SPECTROSCOPIC STUDIES

Drug and excipient compatibility was established by comparing the FT-IR spectra of the pure drug to those of the various excipients employed in the formulation.

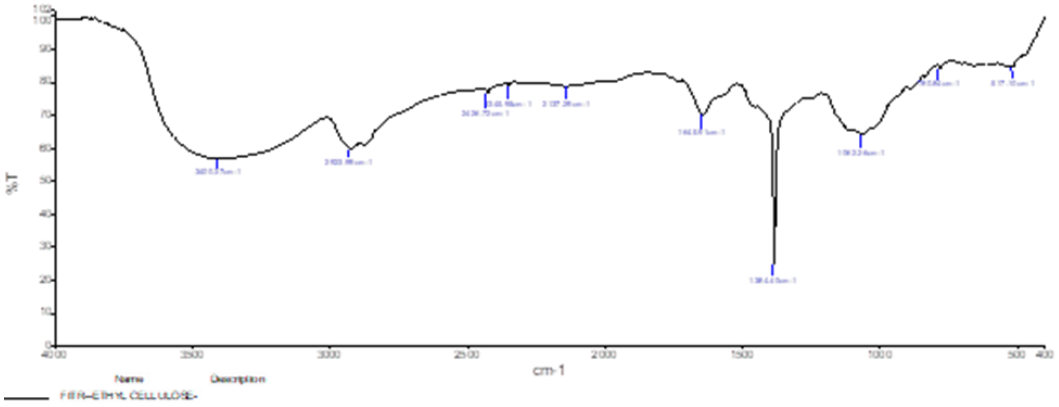

Figure No.1 FT-IR Spectra of Ethyl cellulose.

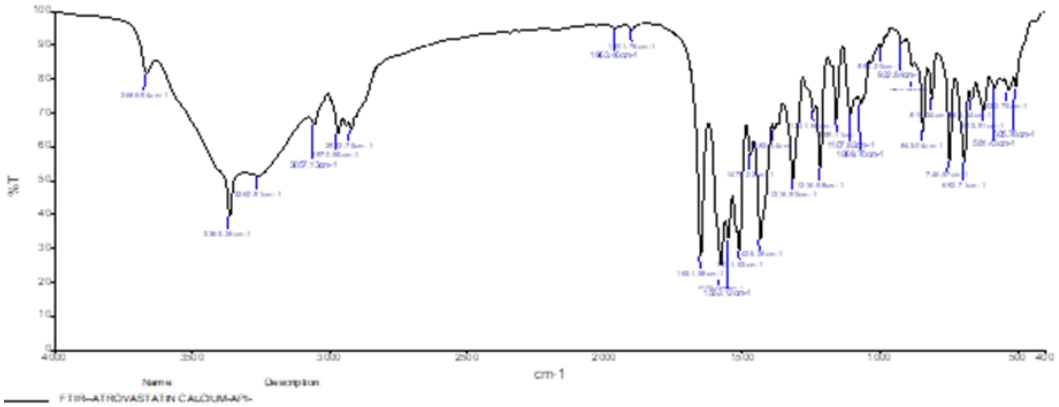

Figure No.2 FT-IR Spectra of Atorvastatin calcium (pure drug).

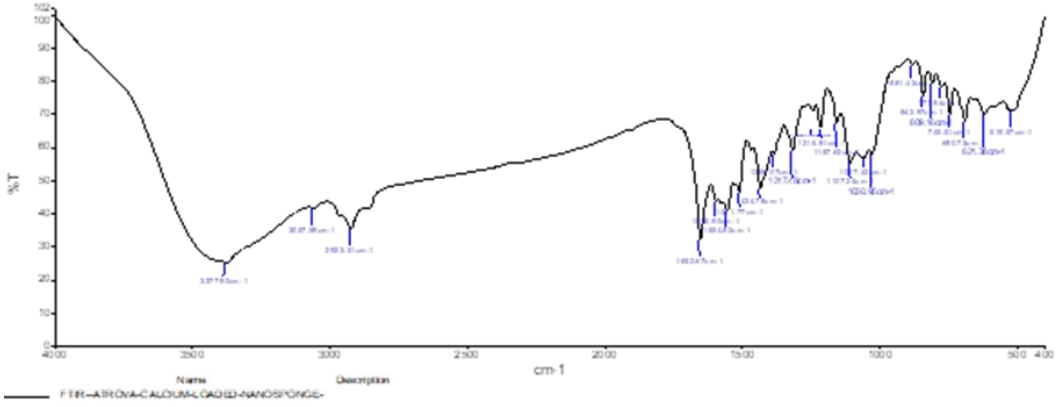

Figure No.3 FT-IR Spectra of Atorvastatin loaded Nanosponges.

FT-IR spectroscopy of Atorvastatin calcium, Ethyl cellulose and mixture of drug and polymer was done using KBr pellets, the spectrum indicating there is no chemical interaction between the drug molecule and polymers.

CALIBRATION CURVE FOR ATORVASTATIN CALCIUM

Table No.6 Linearity study of Atorvastatin at 246 nm

S.No	Concentration(µg/ml)	Absorbance at 246nm
1	1	0.089
2	2	0.202
3	3	0.347
4	4	0.462
5	5	0.508

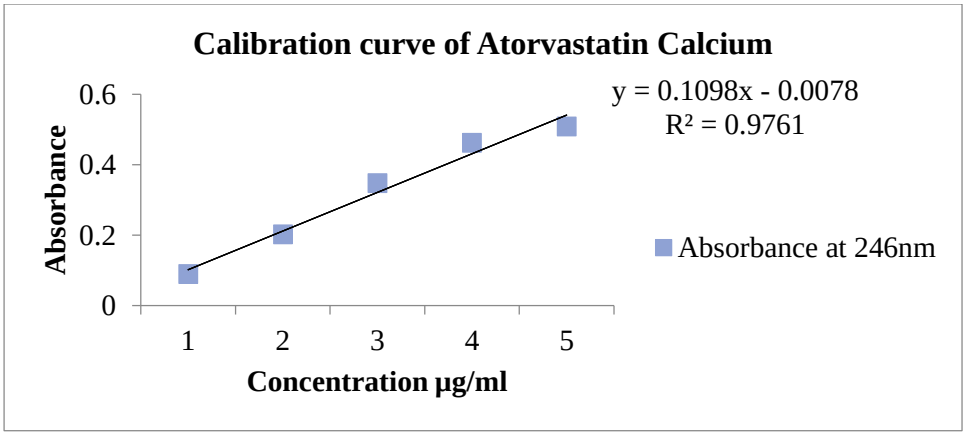

Figure No.4 Standard plot of Atorvastatin in 246 nm

EVALUATION STUDIES OF PREPARED NANOSPONGES

PERCENTAGE YIELD

For different formulation percentage yield was calculated by weighing the Atorvastatin calcium loaded Nanosponges after drying. The percentage yield of Atorvastatin calcium loaded Nanosponges were found to be in the range of 66.66% - 89.33%.The F II was found the percentage yield of 76.83%.

Table No.7 Percentage Yield

S.No	Batch	Percentage yield (%)
1	**F I**	66.66%
2	**F II**	76.83%
3	**F III**	83.53%
4	**F IV**	89.33%

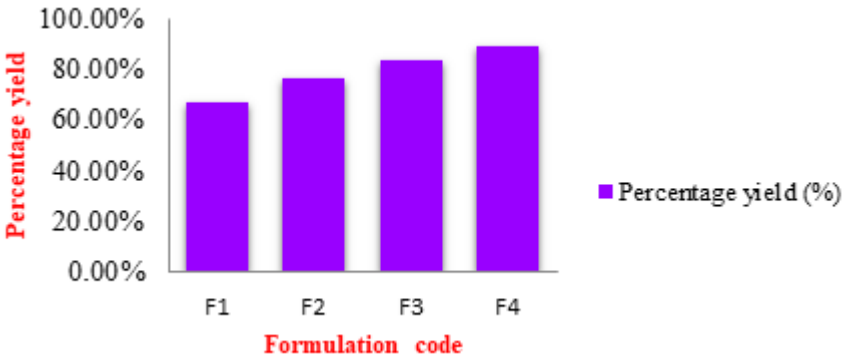

Figure No.5 Percentage yield

DRUG ENTRAPMENT EFFICIENCY

The drug entrapment efficiency of the prepared Atorvastatin calcium loaded Nanosponges were found to be in the range of 67.33% - 87.16%. The increase in the concentration of Ethyl cellulose had increased in the percentage drug entrapment of the drug and the results are shown in the figure no.6.

Table No.8 Percentage Drug Entrapment efficiency

S.No	Batch	Entrapment efficiency (%)
1	F I	67.33%
2	F II	75.16%
3	F III	79.33%
4	F IV	87.16%

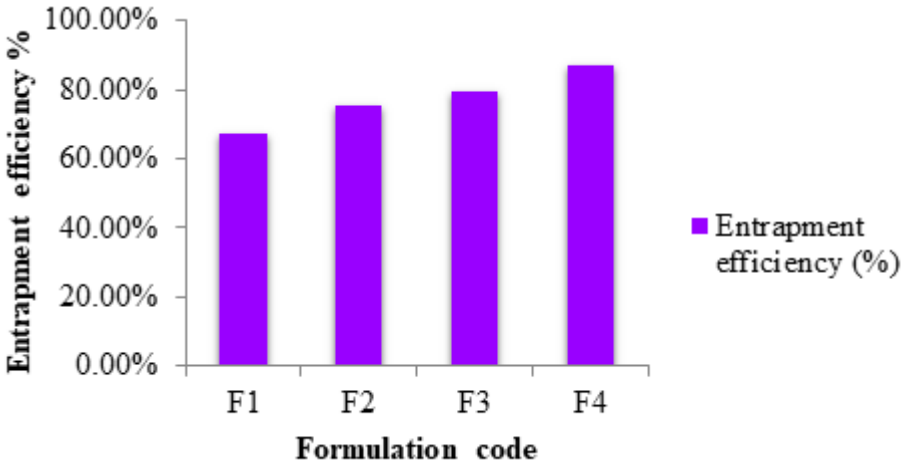

Figure No.6 Percentage Drug Entrapment efficiency

PARTICLE SIZE ANALYSIS

The Particle size analysis was done by the Malvern Zetasizer and the particle size was found to be better for all the formulation. The data for the Particle size was given below in the table no.9. It was found that the FII has the size of 107.5 nm**.**

Table No.9 Particle size Analysis

Formulation Code	Particle Size (nm)
F I	213
F II	107.5
F III	308
F IV	512

INVITRO DRUG RELEASE

In vitro drug release studies was performed in using USP paddle method at 50 rpm and 37 ± 0.2 ℃ in 900 ml of phosphate buffer (PH 6.8). 100mg of the formulated Nanosponges is used for each experiment. Samples were taken at appropriate time intervals for 2 hour interval for 12 hours. From the dissolution profile of formulations F I to F IV, it is concluded that formulation batch F II shows a better drug release profile than other formulations. Cumulative % drug release for all the formulations are depicted in the table.

Table No.10 *Invitro drug* release studies for all four formulations

Time (hrs)	FI	FII	FIII	FIV
0	0	0	0	0
2	10.9	19.9	18.5	13.2
4	20.8	28.6	28.2	26.31
6	29.9	39.1	36.5	37.2
8	48.9	58.7	56.6	55.9
10	56.9	78.7	69.8	68.3
12	68.8	94.9	80.7	73.02

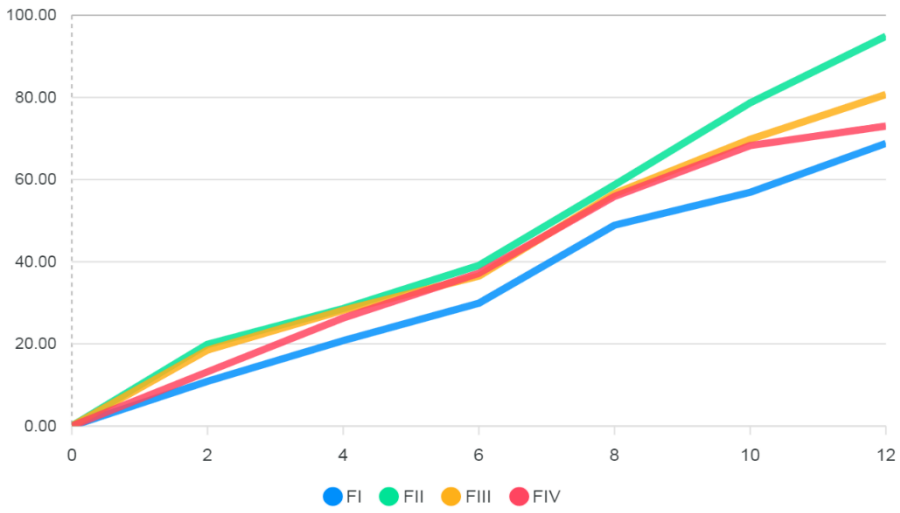

Figure No. 7 *Invitro drug* release studies for all four formulations

KINETIC MODEL AND DRUG RELEASE MECHANISM

In the present study, different release kinetic equations (zero order, first order, Higuchi equation, Korsmeyer-peppas equation and Hixson Crowell model) were applied to interpret the release rate of drug from Nanosponges. The data of invitro release were fitted to these models and equations to explain the release kinetics of Atorvastatin calcium from Nanosponges. The invitro release profile of the formulations indicates that the rate of drug release was higher for formulations, among all the formulations F II shows more amount of drug release with the medium amount of polymer ratio. The plot of time vs cumulative % drug release for the zero-order kinetics, Korsmeyer-peppas, Higuchi equation, first order kinetics and Hixson Crowell model the regression coefficient value shows linearity as shown in (figure no.16, 17, 18, 19 and 20) respectively. The slopes and regression coefficient values (R^2) of various mathematical models for zero order, first order, Higuchi and Korsemayer Peppas model and Hixson Crowell model was in the (table no.11). The good linearity observed with the zero-order and regression coefficient value is higher. Hence this formulation is best fitted into zero-order release model.

Table No.11 Result of different models in the terms of r^2 for all four formulation

Formulation Code	Zero order kinetics	Korsmeyer Peppas model	Higuchi Model	First order kinetics	Hixson Crowell model
F I	0.89	0.9614	0.968	0.9472	0.9806
F II	**0.9957**	**0.9912**	**0.9734**	**0.9575**	**0.9722**
F III	0.9788	0.8572	0.9588	0.7696	0.9029
F IV	0.9791	0.9964	0.932	0.9472	0.9736

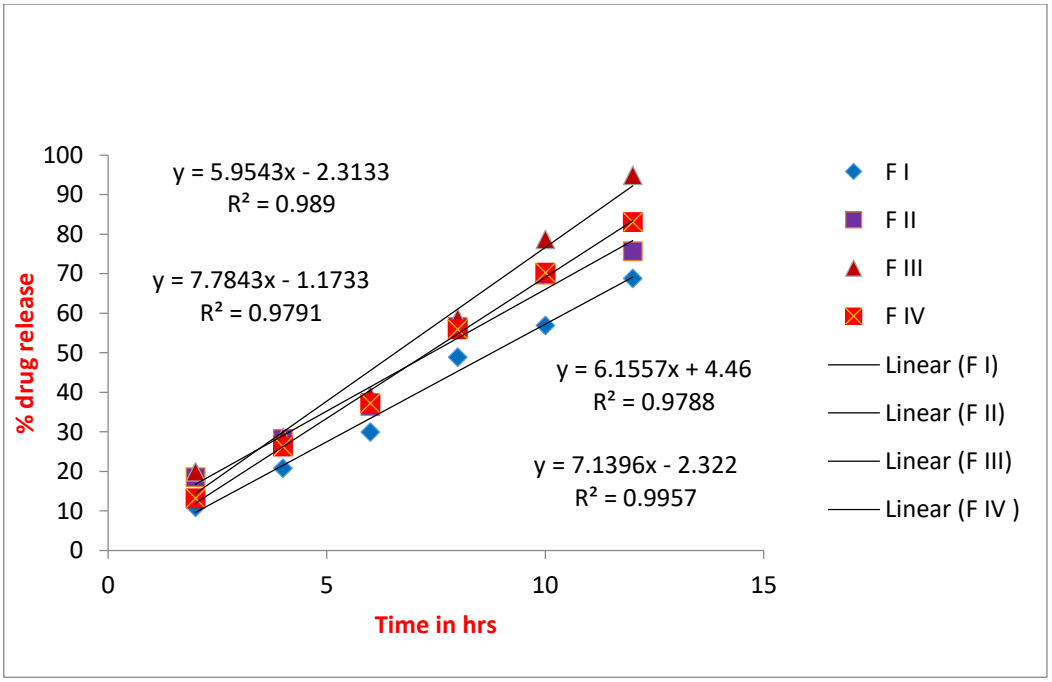

Figure No.8 Zero Order Kinetics for all four formulations

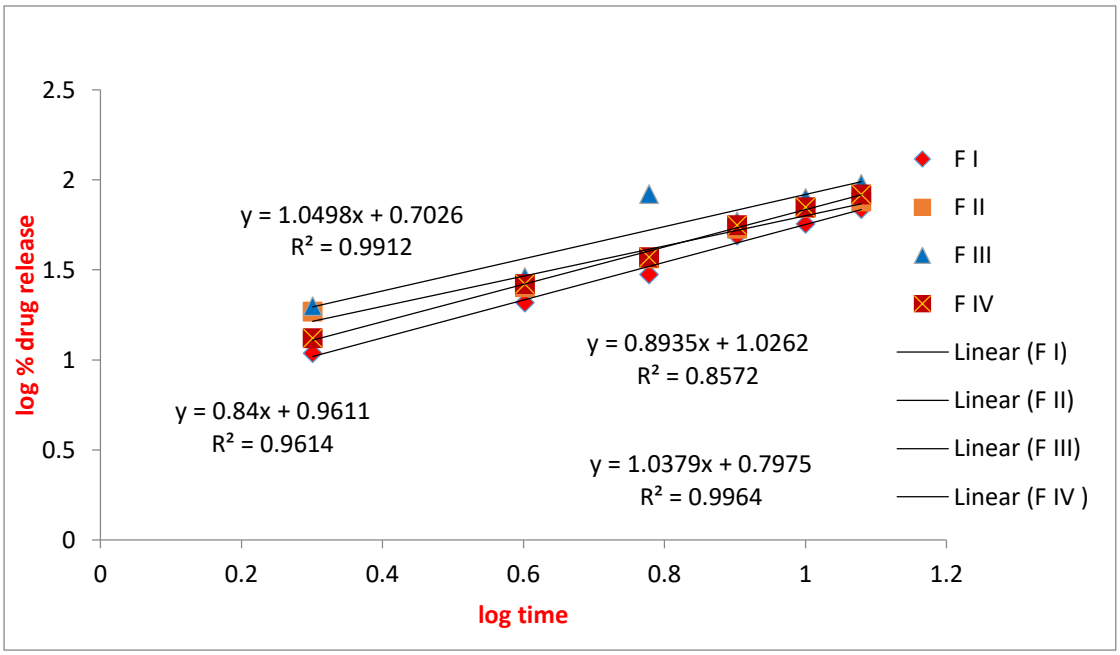

Figure No.9 Korsmeyer-Peppas Model for all four formulations

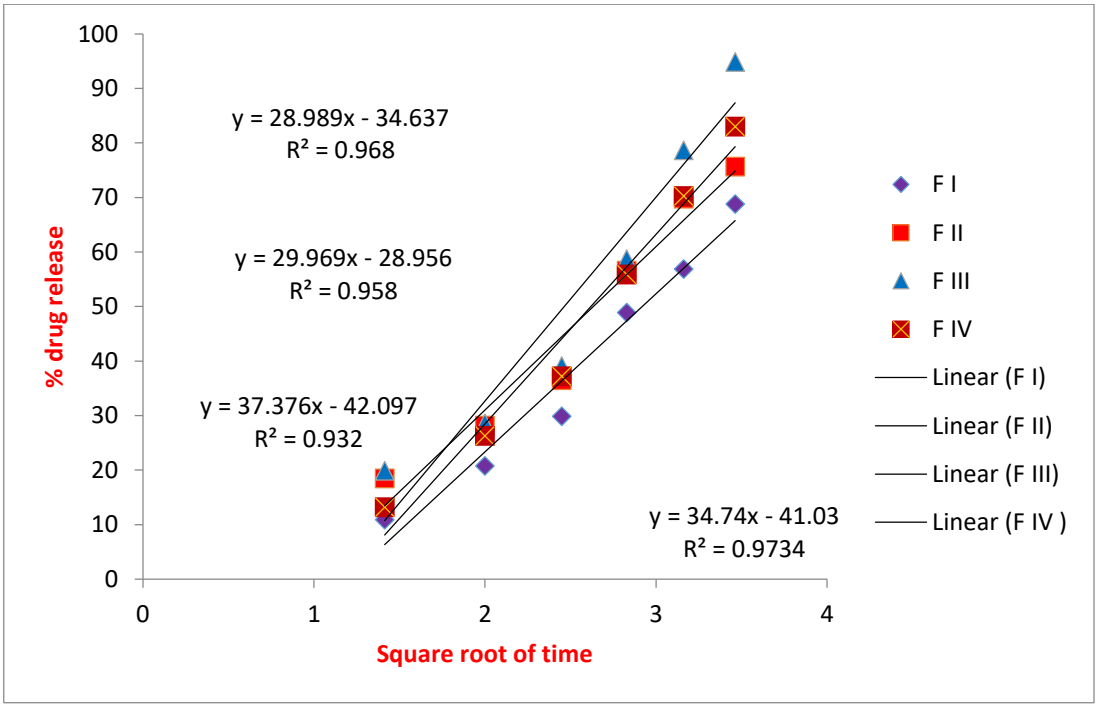

Figure No.10 Higuchi Model for all four formulations

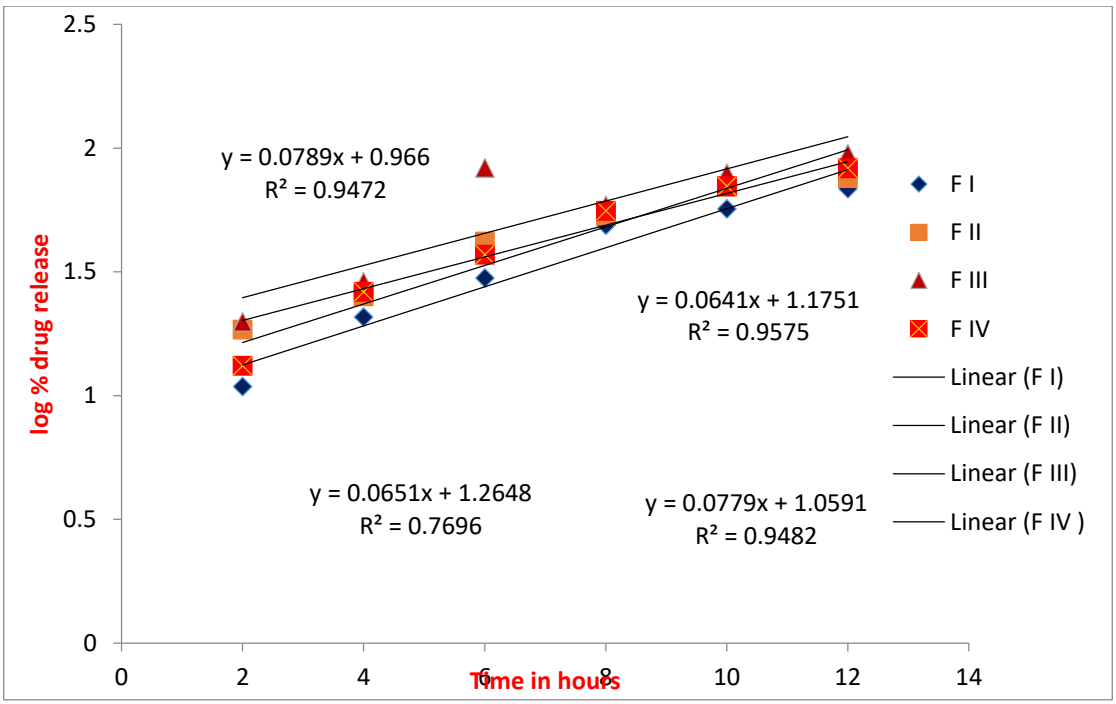

Figure No.11 First order Kinetics for all four formulations

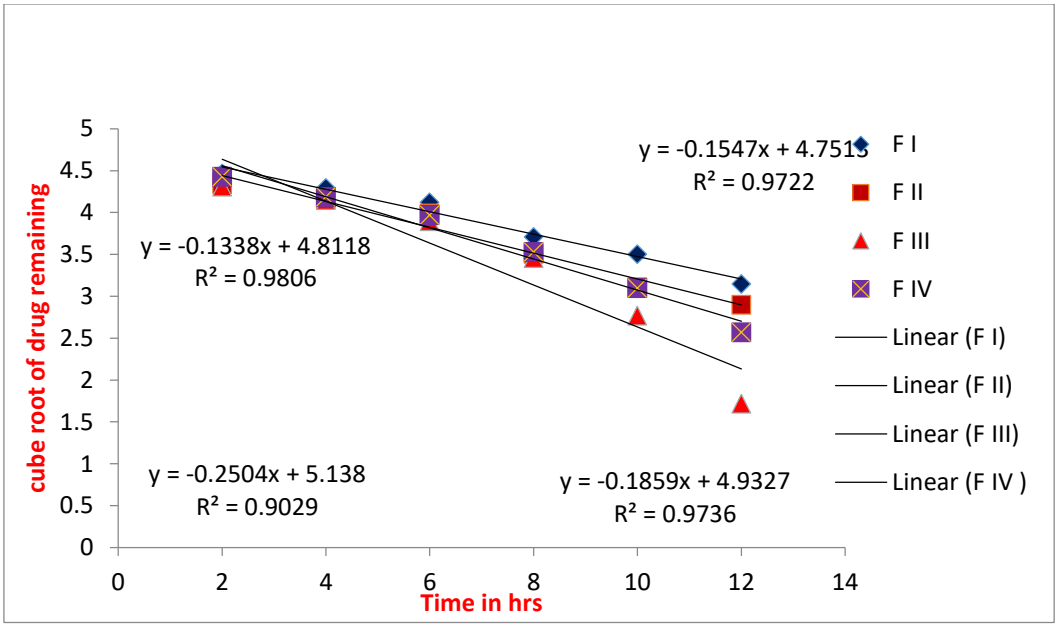

Figure No12 . Hixson Crowell Model for all four formulations

SUMMARY AND CONCLUSION

In the present study, Atorvastatin Calcium loaded Nano- sponges resulted in sustained release. The Nano- sponges prepared with ethyl cellulose were successfully incorporated. The polymer studied was found to be an efficient carrier for Atorvastatin Calcium Nanosponges showing diffusion controlled release. The Nanosponge systems have been found to have good potential for prolonged drug release and therefore can be beneficial for usein the treatment of hypercholesterolemia. Additional benefits such as dose reduction, reduced frequency of administration and avoiding related systemic side effects can be produced

The process involved the formulation of

nanosponges through the emulsion solvent diffusion method. The method are simpler and production cost of method is less with subsequent evaluation including % yield, linearity assay, entrapment efficiency, SEM analysis, FTIR analysis, drug content and drug release kinetics and the mechanism . The compatibility of drug and polymer was determined by FT-IR analysis and the result of IR Spectroscopy shows drug and polymers are compatible to each other. There was no any interaction observed in the formulation The Percentage yield value of Atorvastatin calcium loaded Nanosponges was found to be 66.66 % to 89.33%. %. The drug entrapment efficiency observed for Atorvastatin calcium loaded nanosponges was 67.33% to 87.16%, indicating higher drug entrapment efficiency. Nanosponges were spherical in shape with even surface and spongy nature. The SEM micrographs revealed that formed nanosponges were having several fine surface voids. Moreover, no residual, intact crystals of drugs were seen on nanosponges surface, indicating formation of nanosponges matrix

The nanosponges size range is seem to be around 100 to 600 nm . The nanosponge formulation shows zero order drug release. The outcome of the study concluded that Ethyl cellulose is employed as polymer for oral drug delivery system. Nanosponges of Atorvastatin Calcium increases solubility and dissolution rate of drug. The emulsion solvent diffusion method is best method for preparation of nanosponges.

Overall this study resulted in better encapsulation, solubility and permeation of Atorvastatin Calcium loaded nanosponge. Nanosponges can be easily formulated into different dosage forms like parenteral, aerosols, buccal, sublingual, transdermal, topical, tablets and capsule due to its size and shape. For effective drug delivery, drug has to reach the target site instead of circulating throughout body. This is possible when drug is formulated in oral (tablet and capsules), Parenteral, transdermal dosage form. Hence, this study stated that nanosponge drug delivery systems are suitable candidates for oral, Parenteral and topical route and continuous and prolonged drug release which can be easily and effectively scaled up. Still Further research needed to optimise the formulation and to incorporate the Nanosponges into a possible route of administration

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