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Preparation and in-vitro evaluation of surface functionalized diatoms microcapsules for drug delivery of ciprofloxacin.

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Abstract
Diatomaceous earth is considered as a natural and cost-effective alternative for synthetic mesoporous materials. Diatoms are biocompatible materials with potential drug carrying capacity. In this research we have focused on microcapsule drug delivery system. The aim of the research is to explore the surface functionalization of diatom microcapsules and their impact on the drug loading and release characteristics of water insoluble drugs. Ciprofloxacin was used as the model. It is an antimicrobial drug. Our focus is on to coat the microcapsule drug with diatoms rather than polymer. As polymers has drawbacks like high cost for the synthesis and low drug-loading capacity. The surface modification on diatoms was performed with 3- Phosphonopropanoic acid.Ciprofloxacin is used in drug loading for drug incorporation in microcapsules. To demonstrate covalent grafting of monolayer 3- Phosphonopropanoic acid on the surfaces of the diatoms, extensive characterizations were carried out utilisingDifferential scanning calorimetry (DSC), Fourier transforms infra-red spectrum (FT-IR), Scanning electron microscopy (SEM), Ultraviolet- visible spectroscopy (UV), stability studies. The *in-vitro* studies were done by Franz diffusion cell apparatus. The surface modificationby covalent attachment of selected 3-Phosphonopropanoicacid with COOH-terminated group was successfully performed and proven by these characterization techniques (DSC, TGA, and SEM). Thus the current review proves that diatoms is a promising drug carrier in drug delivery systems, intending to present the various strategies to improve targeted delivery through surface functionalization.

I. Introduction

In this research we have focused on microcapsule drug delivery system. Microcapsules is a small tiny capsules that contain a drug or core material surrounded by a coating, shell or membrane. It has desirable characteristics such as provides protection from environment (i.e) oxidation, achieve controlled release, target release, constant and prolonged therapeutic action, enhance solubility of poorly soluble drugs, reduce the dosing frequency.

In the drug loading process, ciprofloxacin drug is used. It is an antimicrobial drug. It is rapidly absorbed orally and undergoes first pass metabolism. It has bactericidal activity in the blood & good tissue penetrability. It is concentrated in the lungs, sputum and muscles. It is primarily excreted in the urine. It belongs to the category of class iv drugs in the BCS classification (low solubility and low permeability). It is hydrophilic in nature.

Diatoms are used for surface functionalization. Diatomaceous earth is otherwise called as kieselguhr powder, it comes from fossilized seaweed. It is safe for us so it has become a popular supplement due to its numerous health benefits good for teeth, skin and nails. It is used in manufacturing of products such as toothpaste, skin exfoliator. The mineral present in diatomaceous earth is silica, which helps to treat skin problems such as itching, boils, acne. Silica also improves our body's calcium absorption, contributing to the health of our teeth and nails, bones and improves ligament and joint health.

The design of this microcapsules dosage form produces sustained release, so that physicians

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can achieve the following therapeutic benefits: frequency of drug administration can be reduced, patient compliance is improved, and drug administration is made more convenient. It is used to treat bone, skin infections.

Our research goal is to coat the microcapsule drug with diatoms rather than polymer because polymer has the drawbacks like high cost for the synthesis, low drug-loading capacity whereas diatoms is naturally available, easy for surface modification. Surface functionalization are performed using diatomaceous earth and 3-phosphonopropionic acid. Ciprofloxacin is used in drug loading for drug incorporation in microcapsules. The following characterization studies were carried out: Differential scanning calorimetry (DSC), Fourier transforms infra-red spectrum (FT-IR), Scanning electron microscopy (SEM), Ultraviolet- visible spectroscopy (UV), stability studies. The *in-vitro* studies were done by Franz diffusion cell apparatus. The *in-vitro* kinetics studies were performed for drug loaded diatom. They were subjected to various release kinetics such as Zero order, first order, Higuchi, Koresmeyer-peppas, Hixson-crowell.

II. Materials And Methods

The raw material ciprofloxacin was purchased as a gift sample from Kniss Laboratories Pt. Ltd, Gerugambakkam. Diatomaceous earth was supplied by Sigma – Aldrich, India. The solvent 3-Phosphonopropanoic acid with a technical grade of 94% was purchased from Merck, India. The concentrated hydrochloric acid was acquired from EMPLURA and it is diluted to 0.1N HCl by SRIHER laboratory. Tween 20 was purchased from Merck Specialities pt. Ltd., Germany. Toluene and Phosphate buffer was obtained from Fisher Scientific.

Surface Functionalization of Diatomaceous Earth:

A mixture of concentrated sulphuric acid and concentrated nitric acid were taken in the ratio of 1:3 in a beaker respectively. To the mixture 3 gm of powdered diatom was weighed, added and mixed well. The mixture is allowed to sediment. The sedimented diatoms mixture has an acidic pH. By repeated rinsing of the mixture with water of volume of 1000ml for 4 -5 times,the acidic pH has converted into neutral pH (7.0). Whatman filter paper was used to filter the mixture once the desired pH has been reached. After filtration the residue was collected and transferred to a china dish. The residue was dried using hot plate. Finally, the functionalized diatom was obtained.

Drug Loading:

A mixture of 0.1 gm of 3-Phosphonopropanoic acid, 0.1 gram of ciprofloxacin, 5 ml of 0.1N Hcl and 5 ml of Toluene were taken in a beaker. In a sonicator, sonicate the substance for 15 minutes to obtain an even dispersion. Then add a drop of Tween 20 and Diatoms. Sonicate for an additional 2-3minutes for attaining a clear solution. The mixture was maintained undisturbed for 24 hours. The mixture was filtered by using a Whatman filter paper. The obtained residue was scraped and transferred to a china dish. The residue was dried using a hot plate for a minute. The final product was obtained.

EXPERIMENTAL METHODOLOGY

DETERMINATION OF SOLUBILITY PROFILE:

One of the key factors in achieving the optimum drug concentration in the systemic circulation for the desired (expected) pharmacological response is solubility, the phenomenon of solute dissolving in solvent to produce a homogeneous system. The main issue in developing formulations for new chemical entities as well as for generic drugs is low water solubility.

The solubility of ciprofloxacin in water, methanol, ethanol, Hydrochloric acid was carried out as per IP monograph.

Table: 1: Solubility Specification

Descriptive term	Approximate volume of solvent in milliliters per gram of solute
Very soluble	less than 1
Freely soluble	from 1 to 10
Soluble	from 10 to 30
Sparingly soluble	from 30 to 100

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Slightly soluble	from 100 to 1000
Very slightly soluble	from 1000 to 10,000
Insoluble or practically insoluble	more than 10,000

UV SPECTROSCOPIC METHOD FOR ESTIMATION OF CIPROFLOXACIN

Procedure: Preparation of standard stock solution:

Accurate quantity of 10 mg ciprofloxacin was taken in 10 ml volumetric flask and was dissolved by using HCl up to 10 ml to produce 1mg/ml of solution. [STOCK A]. Take 1ml of stock A in 10ml volumetric flask and dissolved by using HCL up to 10ml [STOCK B].

Scanning:

A series of concentration i.e., 2,4,6,8,10µg/ml were prepared by using above stock B solution and scanned between 200-400 nm. The absorption maxima obtained was 277 nm was selected and used for further studies.

Preparation of calibration curve:

A standard solution containing 1mg/ml of Ciprofloxacin was prepared. The absorbance of the solution was measured at 277 nm against blank. All spectral absorbance measurement was made on by using Shimadzu UV–visible spectrophotometer.

CHARACTERIZATION STUDIES:

DSC ANALYSIS:

The DSC measurements were carried out in a nitrogen environment. NETZSCH DSC 204F1 phoenix calorimeter was used. An aluminium pan served as the control and two milligrams of each sample (Functionalized diatoms, diatom, and diatom with ciprofloxacin) were weighed and sealed in the pan. Indium was used to calibrate the device, and nitrogen gas was used to purge it. Under nitrogen flow rates of 20ml/min, the sample was heated at a rate of 10℃/min from 20℃ to 400℃.

SCANNING ELECTRON MICROSCOPY:

Field emission scanning electron microscopy was used to characterise the structural differences between diatoms before and after Ciprofloxacin loading. The diatom was initially taken on the slide in powder form and placed on the base plate to prepare the sample for the polarising. A vacuum is passed to lessen conduction. To get low and high - resolution images, the microscope was run at an accelerating voltage of 30kV, at normal incidence, a working distance of 20mm, and various scales.

FOURIER TRANSFORMS INFRA-RED SPECTRUM(FTIR) STUDIES:

To characterize the functional groups, FTIR spectra of pure drug, diatoms and characterized diatoms were compared to each other. The samples were measured from 4000 to 400cm^{-1} using Bruker FTIR spectrophotometer. Samples of diatoms were mixed with KBr in the ratio 1:3 and were pressed as pellet mechanically. The formulated exfoliant was lyophilized which was taken for studying IR analysis using attenuated total reflectance. The spectrum scanning range was from 400 to 4000/cm and resolution *in-situ* 1/cm.

***IN-VITRO* STUDIES:**

PREPARATION OF CELLOPHANE MEMBRANE:

By taking a cellophane membrane of size 8cm×8cm (length×breadth) and soaking it in a glycerine solution. Initially, a small amount of glycerine is taken in a beaker and a single layer of cellophane sheet is added. Repeat the procedure for two more layers and allow it to soak for 24 hours so that the sheet becomes sensitive and acts as a semi-permeable membrane.

IN-VITRO RELEASE:

For *In-vitro* studies, the Franz diffusion cell apparatus is used. It is jacketed Franz cell with a 9mm orifice diameter, flat ground joint, and 5ml receptor volume.

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Image of Franz diffusion cell apparatus

The apparatus consists of two compartments known as receptor and donor compartment. The receptor compartment is filled with 0.1N HCl of volume 27ml, stirring bar is placed in the receptor chamber, and the prepared cellophane membrane is placed in between the compartments and secured by using the clamps. The cellophane membrane serves as a semi- permeable membrane. The donor compartment is brimmed with final product (drug+ diatoms+ solvent) of 2g in 2ml. the whole set-up was placed on the magnetic stirrer and then the sample is collected and replaced with the buffer, this condition is known as sink condition.105mlml of sample is collected for each interval from 0minutes to 24 hours. The collected sample is observed under UV spectrophotometer at 277nm with 0.1N HCl as blank solution.

IN-VITRO DRUG RELEASE KINETICS STUDIES:

The outcomes of the *In-vitro* release profiles obtained for each formulation were plotted using the following modalities of data treatment

- Zero order kinetics model (Cumulative % drug released versus time)
- First order kinetic model (Log cumulative % drug remaining versus time)
- Higuchi plot (Cumulative % drug release versus square root of time)
- Kores Meyer-peppas model (Log cumulative % drug release versus log T)
- Hixson-Crowell model (Cube root of drug % remaining versus time)

ZERO ORDER KINETICS:

The following equation would predict a zero-order release.

$$\mathbf{A_t = A_0 - K_0 t}$$

Where,

A_t = Drug released at time 't'
A_0 = Initial drug concentration
K_0 = Zero-order rate constant

In this cumulative % drug released was plotted against time.

FIRST ORDER KINETIC:

The following equation would predict a First order release

$$\mathbf{Log\ C = Log\ C_0 - kt/2.303}$$

Where,

C = amount of drug remained at time 't'
C_0 = Initial amount of drug
K = First order rate constant (h-1)

When the data is plotted as log cumulative percent drug remaining versus time it yields a straight line, indicating that the release follows first order kinetics. The constant 'K' can be obtained by multiplying 2.303 with a slope value.

KORESMEYER-PEPPAS MODEL:

Koresmeyer- peppas model was used in order to understand the mode of release of drug from swellable matrices.

The following Peppas Law equation was used to fit the data:

$$\mathbf{Mt/M = Ktn}$$

Where,

Mt/M = Fraction of drug release at time 't'
K = Constant incorporating the structural and geometrical characteristic of the drug/ polymer system.
n = Diffusion exponent related to the mechanism of the release

when the data is plotted as log of drug released vs log time, a straight line is obtained. The slope equal to 'n' and the value of 'K' can be obtained from y-intercept.

For fickian release n=0.5 while 0.5<n<1.0 indicates anomalous (non-fickian) transport and n=1 indicates case II diffusion reading to zero-order release.

HIXSON- CROWELL MODEL:

Data obtained from the *In- vitro* release studies were plotted as cube root of % remaining vs time.

$$\mathbf{W_0\ 1/3 - W_t\ 1/3 = K_t}$$

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Where,

W_0 = Initial amount of drug release at time 't'

W_t= Remaining amount of drug at time 't'

K = constant incorporating the surface-volume relation.

- From this data we can get the release of various kinetic models.
- Zero, Higuchi, first order kinetics indicates the order of release of drug i.e, release is dependent on time (first) / square of time (Higuchi)/ independent of time (zero).
- Peppas model indicates the mechanism of drug release i.e, release of drug from the formulation by diffusion, erosion, swelling and may by the combination of diffusion and swelling.
- Hixon Crowell model indicates that the release of drug is by diffusion.
- The values obtained in correlation indicates the regression coefficient values of the respective kinetic models in order to cross verify the formulae the graphs are also plotted in the individual charts.
- Greater the regression coefficient greater the linearity towards the kinetic model for the peppas equation.

III. Result and discussion

DETERMINATION OF SOLUBILITY PROFILE

Calibration Curve of Ciprofloxacin in 0.1N HCl

Calibration graph of ciprofloxacin was plotted by measuring the absorbance of different concentrations of drug in 0.1N HCl using UV spectrophotometer. In the graph of concentration Vs Absorbance, a linear correlation was observed which indicated that both were directly proportional i.e. with increase in concentration there is an increase in the absorbance value indicating linearity, thereby obeying Beer's law. Ciprofloxacin obeys Beer's law within the concentration range of 2-10 µg/ ml of drug in 0.1N HCl with slope of 0.111 x+0.008 and R2 value was 0.998 as shown in the Figure 18.

Table: 2: Calibration Curve:

S.NO	CONCENTRATION (mcg)	ABSORBANCE (nm)
1	0	0
2	2	0.2422
3	4	0.4676
4	6	0.6537
5	8	0.8949
6	10	1.1253

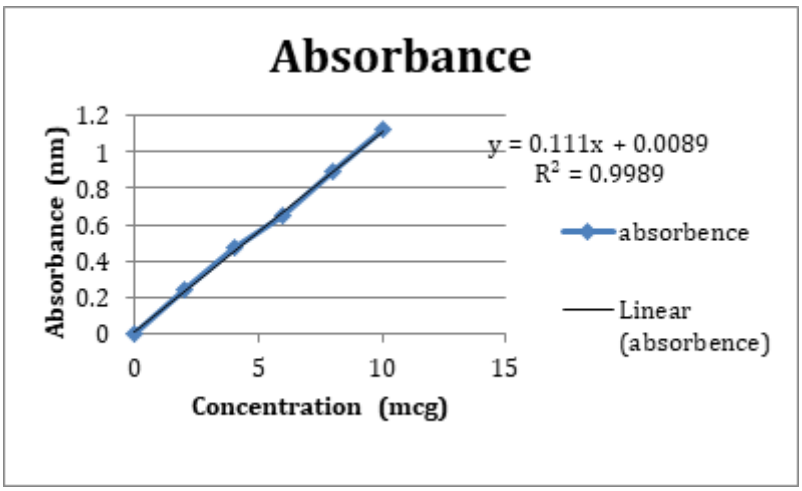

Fig: Linearity graphof ciprofloxacin by UV spectrophotometer

LINEARITYGRAPH: The drug samples were analyzed by UV spectroscopy (277 nm) using HCL as solvent. Which obey the Beer-Lambert law shown in fig

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EVALUATION OF DRUG LOADED DIATOMS

Differential Scanning Calorimetry

DSC is crucial in ascertaining phase transitions that Ind might undergo during encapsulation and storage in diatom microcapsules. DSC is essential for determining any phase transitions that ciprofloaxacin may experience during its storage and encapsulation in diatom microcapsules (Figure 19). The elimination of chemisorbed or structural water from the bulk mineral structure is thought to be the cause of the large endothermic peak of the pure Diatom, which is indicated at 82.5°C. A DSC graph of ciprofloxacin demonstrates a prominent endothermic peak for its melting in the stable crystalline form at 341.7°C. The drug structure breaking down during the melting of the stable form of the crystalline is largely to blame for the endothermic changes observed in the temperature range of 82 to 150°C. Pure Diatom has a melting point that peaked at 82.5 °C. 3-Phosphonopropionic acid has a melting point that peaked at 150.1°C . Ciprofloxacin has a melting point that peaked at 341.7°C.

Coincidently, the melting temperatures for both the ciprofloxacin and phosphonic acid structures are quite similar or marginally lower, rationalizing the occurrence of various functionality/structure-mediated, endothermic transitions in the temperature range 154–163°C for the surface functionalized, drug-loaded DE samples.

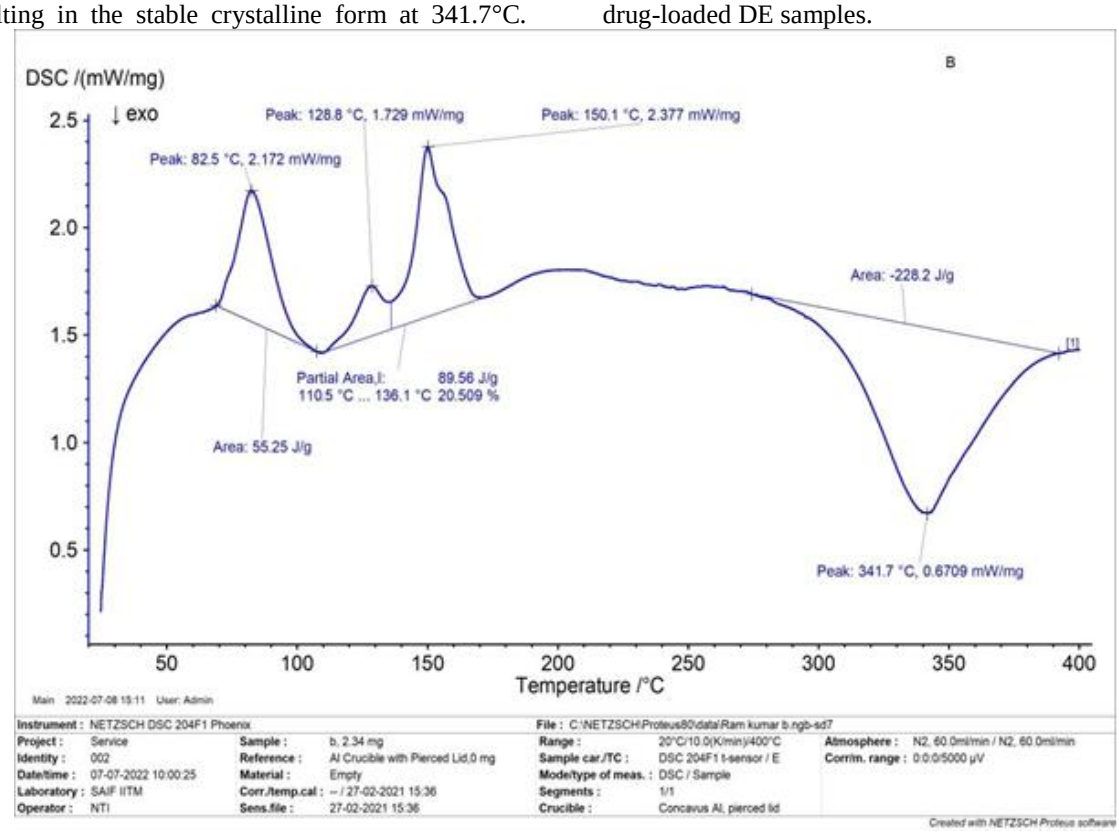

Fig: DSC Result of drug with diatoms and solvent

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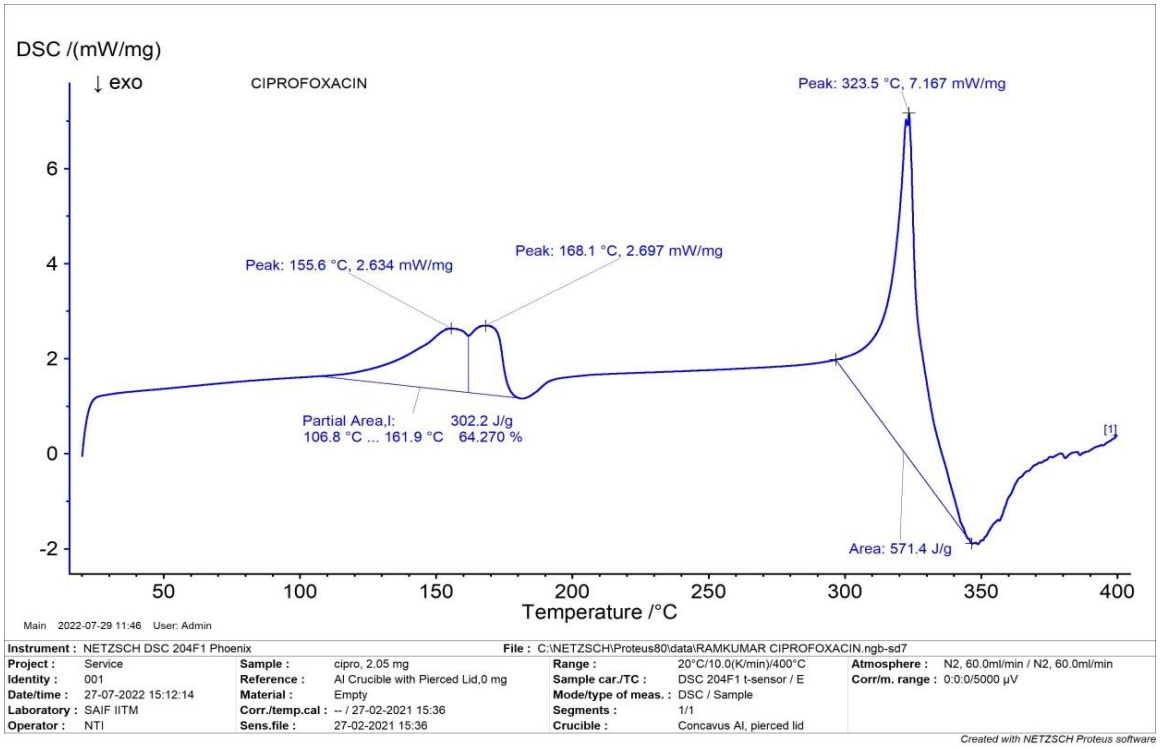

Fig: 20DSC result of ciprofloxacin

Structural characterization of diatom structures:

SEM images of the diatom microcapsules obtained by purification of the raw DE material are shown in Figure 1(a), confirming their usual structure and demonstrating distinct and separated diatom structures (frustules) free of aggregations and minor cracked portions. The main species of diatom with a cylindrical structure and a circular hole on one side and closed end on the other side were discovered to be Aulacoseira sp...Each diatom frustule has a hollow center, a well-defined size range, and a unidirectional, orderly arrangement of micro-nano-sized porous structures. The length of the diatom structure ranged from 10 to 20 mm, and its diameter was between 4mm and 6mm. Diatom structures, including pores that demonstrate their monolayer coating, do not show any topographical alterations after surface modifications. However, following drug loading (ciprofloxacin), the majority of the pores were shown to be closed completely or partially (Figure 1(b)). This is explained by the fact that monolayer alteration with phosphonic acids does not cause multi-layered drug adsorption on the diatom surface.

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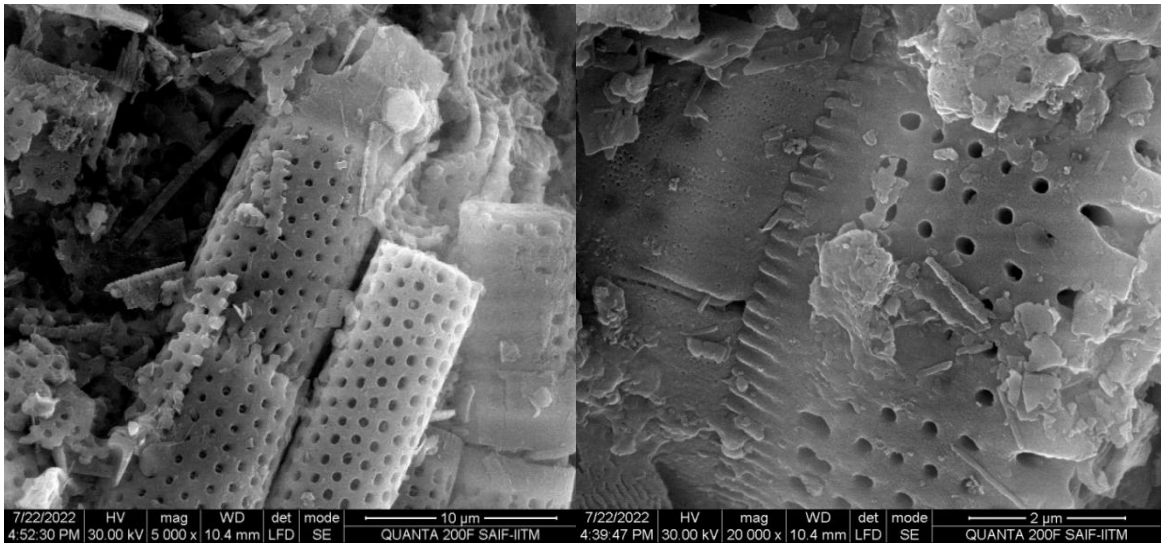

Fig 1(a) SEM image of functionalized diatoms

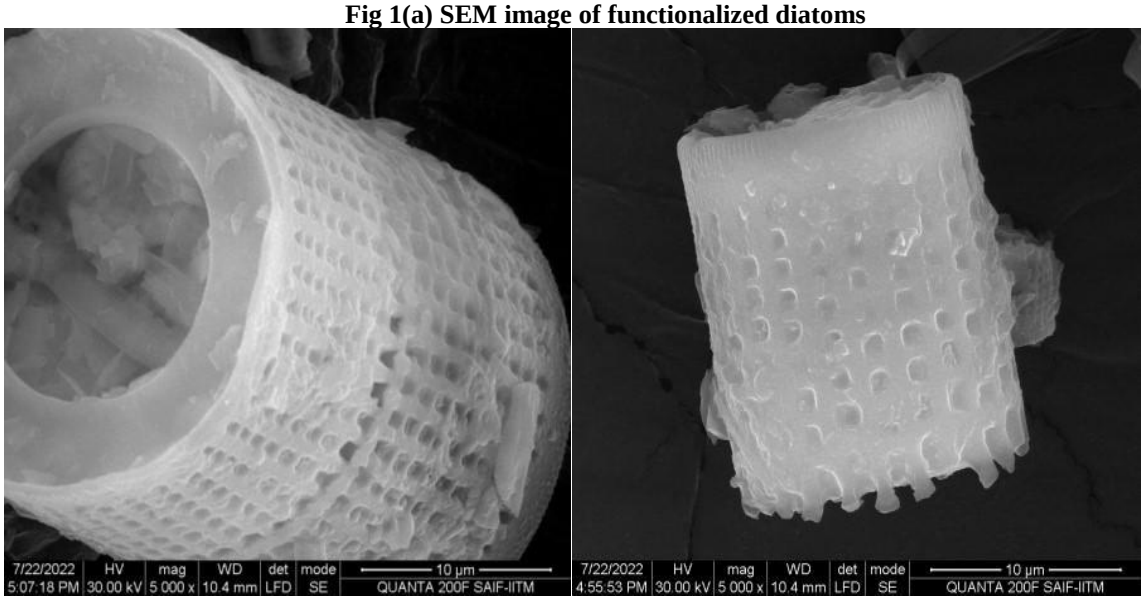

Fig 1(b) SEM images of diatoms microcapsules

***IN-VITRO* STUDIES:**

In-vitro drug release developed for diatoms by ciprofloxacin drug was carried out by Franz diffusion cell method. The glass diffusion cell (Kesharychein type) was used to release studies. 2g of the finished product in 2ml of water was placed in the donor compartment, and a cellophane membrane was placed between them and clamped together, and kept in a magnetic stirrer for 24 hours. The sample was withdrawn for every 0minutes,15 minutes, 30 minutes, 45 minutes,60 minutes, 90 minutes, 120minutes, 180minutes, 240minutes, 300minutes, 360 minutes, and 1440minutes respectively, and analyzed by UV spectrophotometer at 277nm using a 0.1N HCl buffer the % amount is calculated. The cumulative drug release was found to be 97.86% in 1440 minutes(24hour). A 4-hour initial burst was followed by a steady discharge that lasted between 24 hrs. On all samples, a sharp initial rise in drug concentration brought on by drug release elution from the diatoms' outer surfaces is seen. Due to drug molecules loosely adhering to the porous silica walls, there was a large drug concentration gradient between the bulk solution-drug interfaces. When DE was functionalized with 3-Phosphonopropionic acid, the burst release was significantly reduced from 80% in bare DE to 50%,

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indicating that hydrophilic surfaces favor stronger drug adsorption on modified diatoms as well as better drug containment inside silica pores and matrices, leading to slower release kinetics. This is explained by electrostatic forces such as induced dipole-dipole attractions in the drug molecules that were physically adsorbed to the active carboxyl-terminated PA (3-Phosphonopropionic acid) or silane-terminated (amino rich) SAM-grafted diatoms, as well as weak secondary intermolecular bonding such as Van der Waals. Diatoms' drug release mechanism is primarily controlled by the diffusion of medicines through their porous features. Since the silica lattice of diatoms has a relatively high surface area (31 m^2/g) and low porosity (0.052 cm^3/g), the diffusion of ciprofloxacin into the HCL environment is a surface-dependent process. A zero-order model can be used to fit the delayed release that occurs from the second day until the completion day. Given that diatoms' solvent-accessible surface area is unchanging and there is no degradation during the release period, the drug's rate of release is essentially constant. These findings support the use of diatom surface functionalization to modify the efficiency of drug loading and release. The choice of changes with the proper functional groups can lead to stronger interactions with drug molecules and the potential creation of stimuli-responsive release, leading to further advancement (pH, temperature, radio frequency).

Si.no	Time in mins	% of Cumulative drug release(Drug +diatoms)	% of drug release (ciprofloxacin)	% of bare diatom release
1	0	0	0	0
2	15	2.69	6.36	15.63
3	30	9.01	12.66	48.36
4	45	16.99	24.32	71.36
5	60	22.01	41.52	89.46
6	90	24.56	60.45	99.02
7	120	31.69	75.62	
8	180	39.07	89.22	
9	240	43.92	98.99	
10	300	50.23		
11	360	58.96		
12	1440	97.86		

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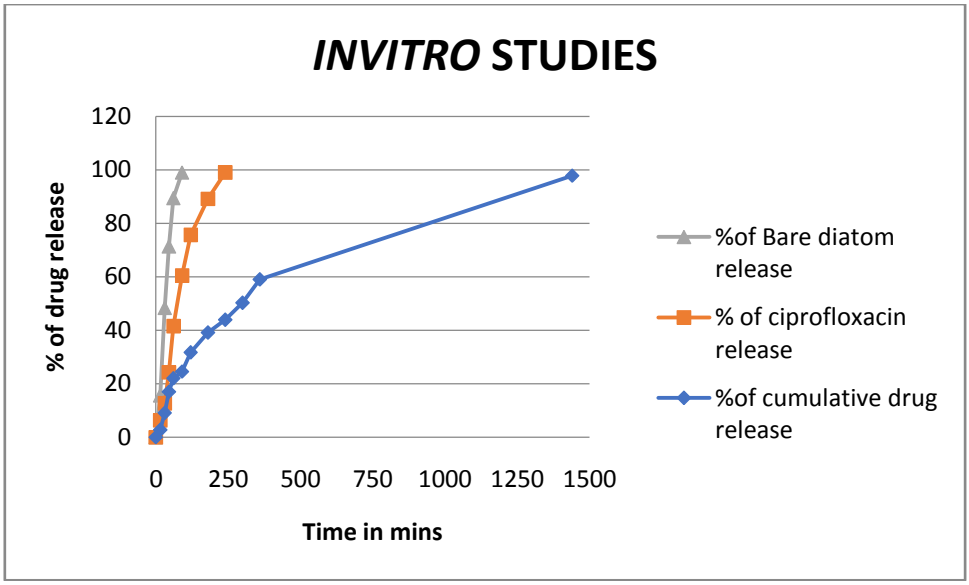

Fourier Transforms Infra-Red Spectrum (FTIR) Studies:

The presence of functional groups was confirmed by using FT-IR (Instrument BRUKER). The readings were obtained between 400 cm-1 to 4000 cm-1. FT-IR study was carried out for drugs and various excipients. The results showed various stretching, bending and rocking vibration based on the groups present. The reaction between the drug ciprofloxacin, diatoms and the solvent 3-phosphonopropionic acid produces physical changes but no functional changes.

Table : Interpretation of FT-IR Spectrum of Drug, Diatoms And Functionalized Diatoms:

SI NO	DRUG	DIATOMS	DRUG+DIATOMS+SOLVENT	VIBRATION
1	3371.65	3361	3367.05	O-H Stretching
2	2683.57		2684.86	C-H Stretching
3	2616.66		2619.54	C-H Stretching
4	2463.17		2464.14	C-H Stretching, -COOH
5		2110.23	2118.02	C≡X
6	1617.84	1635.29	1617.23	C=O Stretching, N-H Bending
7	1446.15		1440.81	O-H Bending
8	1340.79		1345.78	C-H Bending
9	1308.97		1301.14	C-H Bending
10	1267.04		1262.76	C-H Bending, O-H Bending
11	1186.33		1180.47	O-H Bending, C-N Stretching
12	1023.56	1051.91	1004.09	C-O Stretching
13	942.03		929.51	C-N Stretching
14	829.11		827.87	N-H Rocking, C-H Rocking
15	804.53		792.82	N-H Rocking, C-H Rockng
16		795.48	792.82	C-H Rocking
17	749.83		742.68	N-H Rocking
18	561.24		594.64	C-H Rocking

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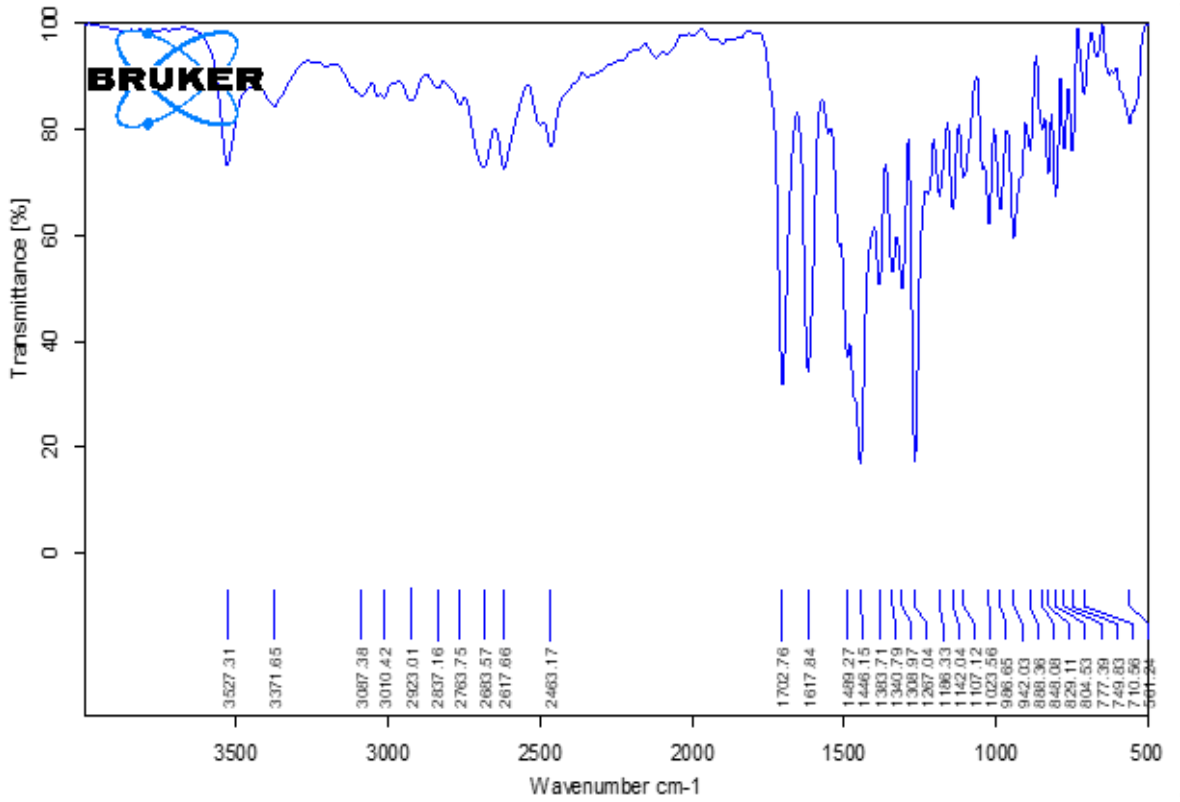

Fig: FT-IR Of Ciprofloxacin

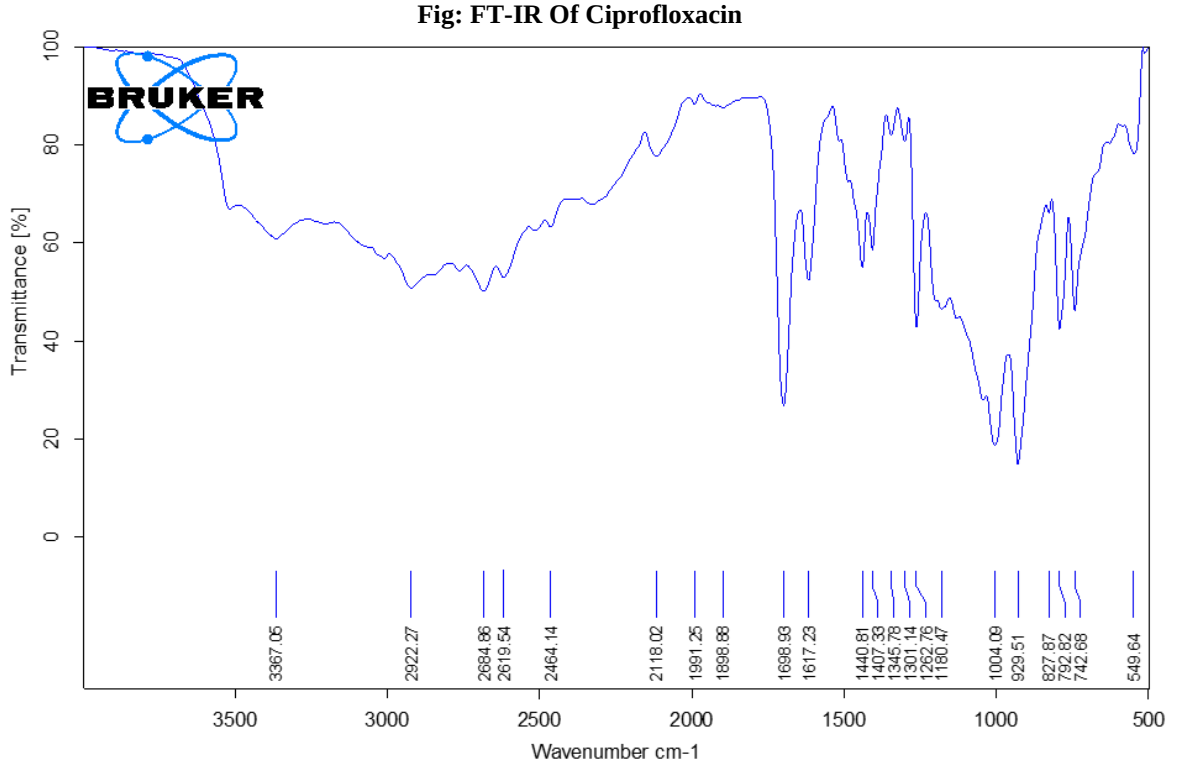

Fig: FT-IR Of Drug with Diatom and Solvent

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***In-vitro* drug release kinetics:**

Table 5:Kinetics data of invitro drug release for drug-loaded diatom

CUMULATIVE (%) RELEASE Q	TIME in mins (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	% Drug Remaining	Cube root of drug % remaining
9.01	30	5.477	1.263	1.477	1.959	90.99	0.144
22.01	60	7.746	1.343	1.778	1.892	77.99	0.369
24.56	90	9.487	1.390	1.954	1.878	75.44	0.416
31.69	120	10.954	1.501	2.079	1.834	68.31	0.554
35.23	150	12.247	1.547	2.176	1.811	64.77	0.626
39.07	180	13.416	1.592	2.255	1.785	60.93	0.707
41.01	210	14.491	1.613	2.322	1.771	58.99	0.749
43.92	240	15.492	1.643	2.380	1.749	56.08	0.814
46.95	270	16.432	1.672	2.431	1.725	53.05	0.884
50.23	300	17.321	1.701	2.477	1.697	49.77	0.963
54.82	330	18.166	1.739	2.519	1.655	45.18	1.080
58.96	360	18.974	1.771	2.556	1.613	41.04	1.192
97.86	1440	37.947	1.991	3.158	0.330	2.14	3.353

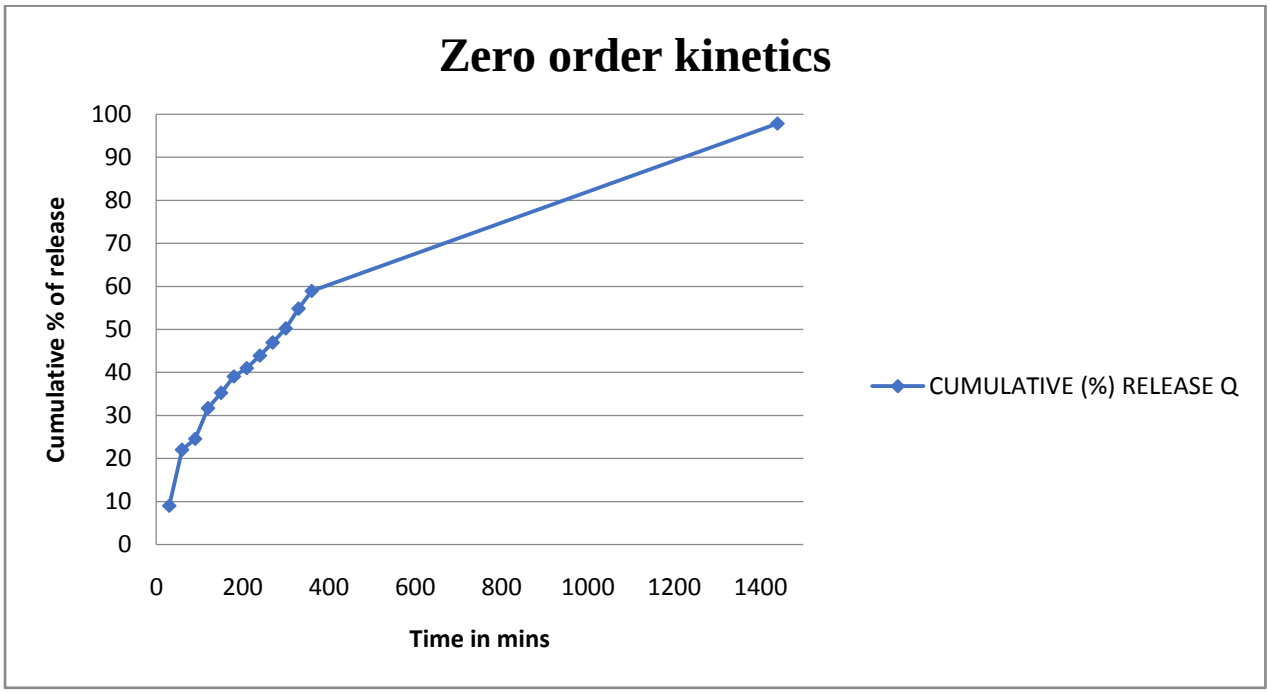

Fig: Zero-order release kinetics for the Drug loaded diatom

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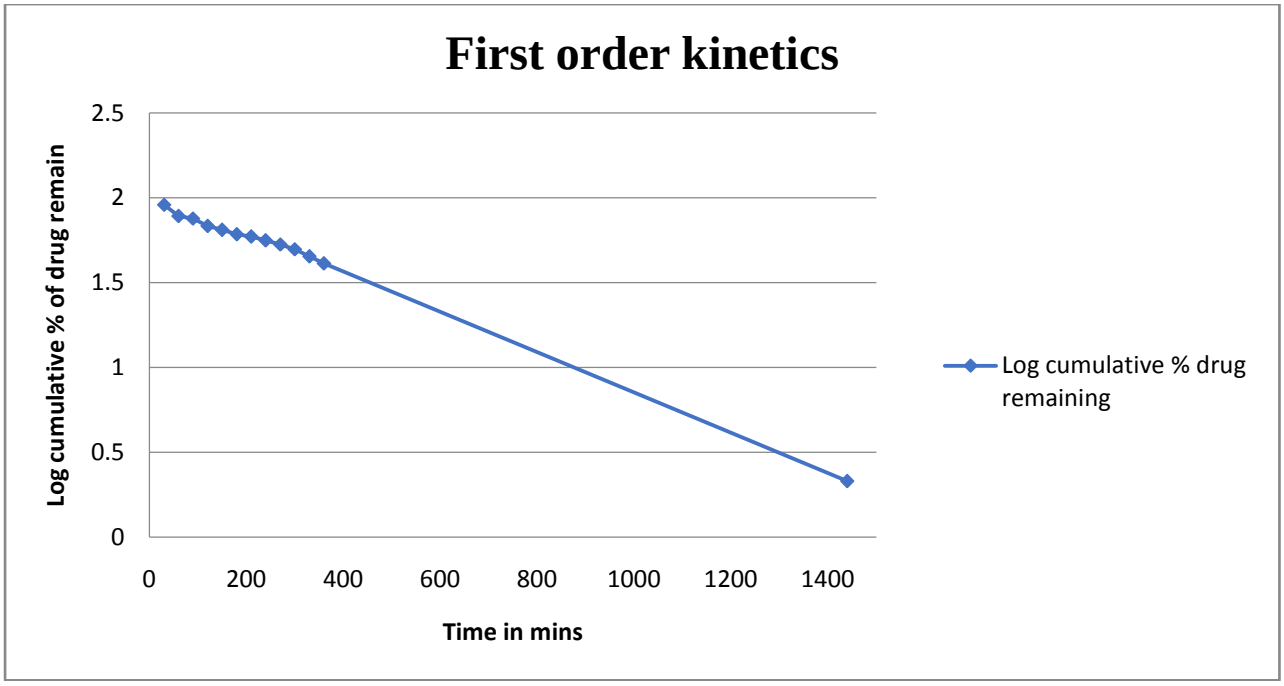

Fig: First-order release kinetics for the Drug loaded diatom

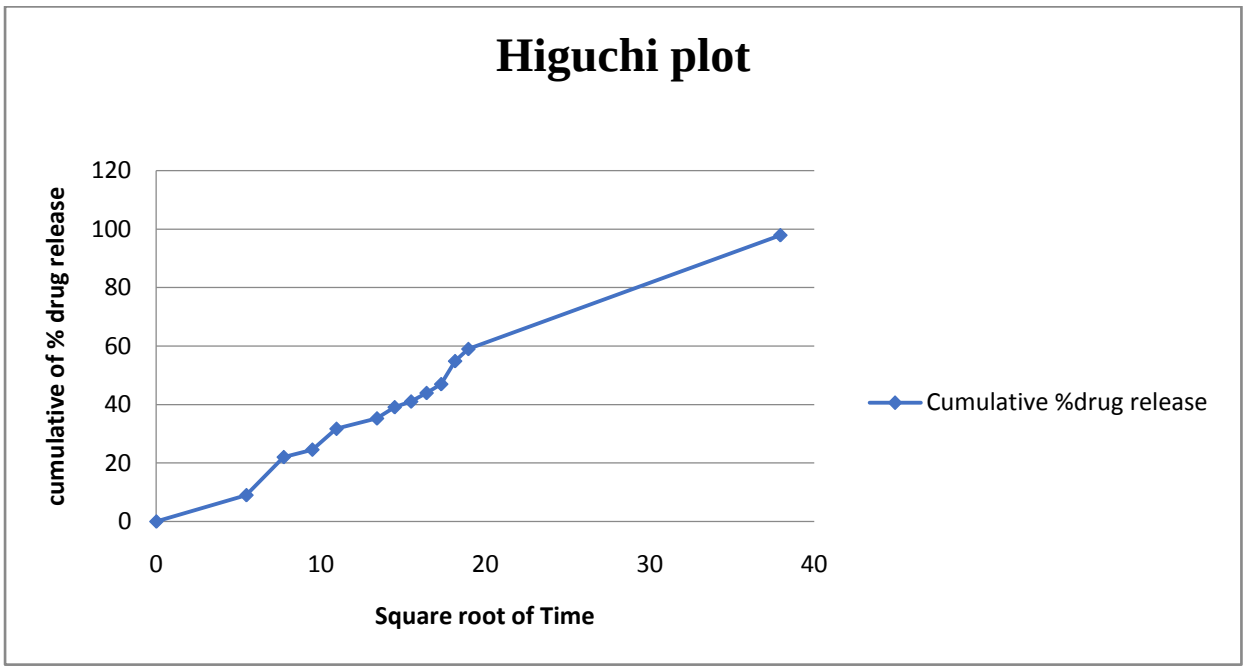

Fig: Higuchi release kinetics for the drug loaded diatom

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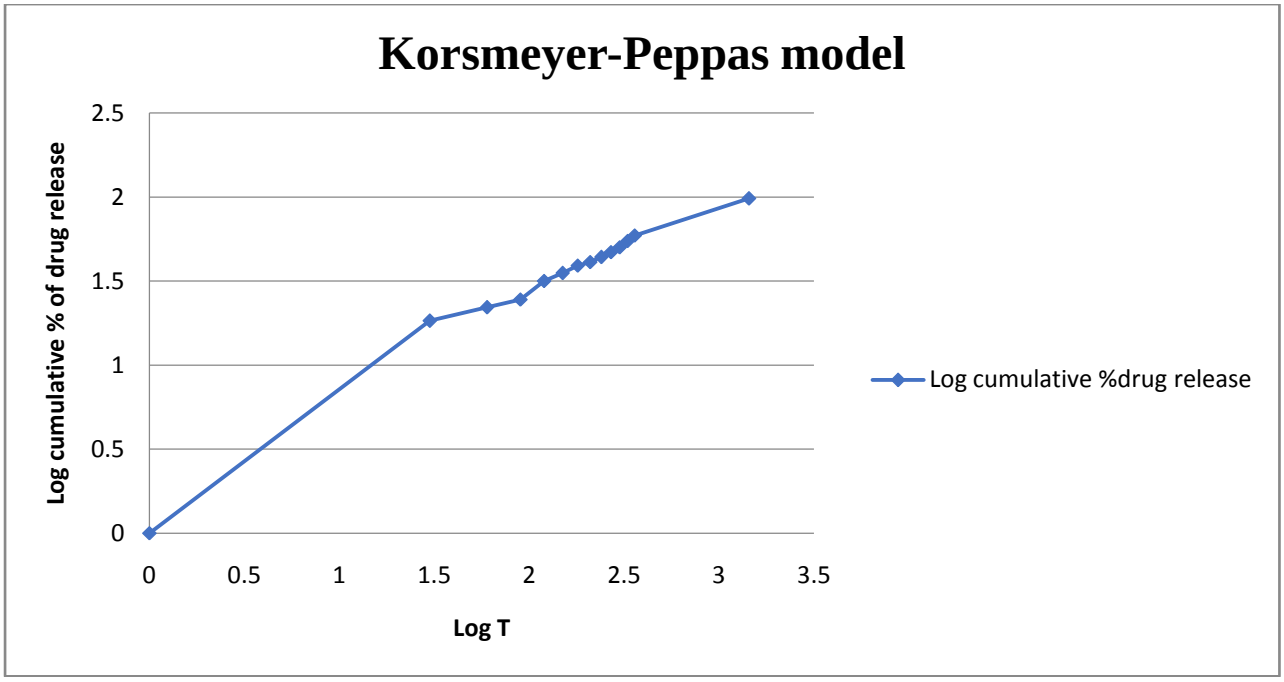

Fig: Peppas release kinetics for the Drug loaded diatom

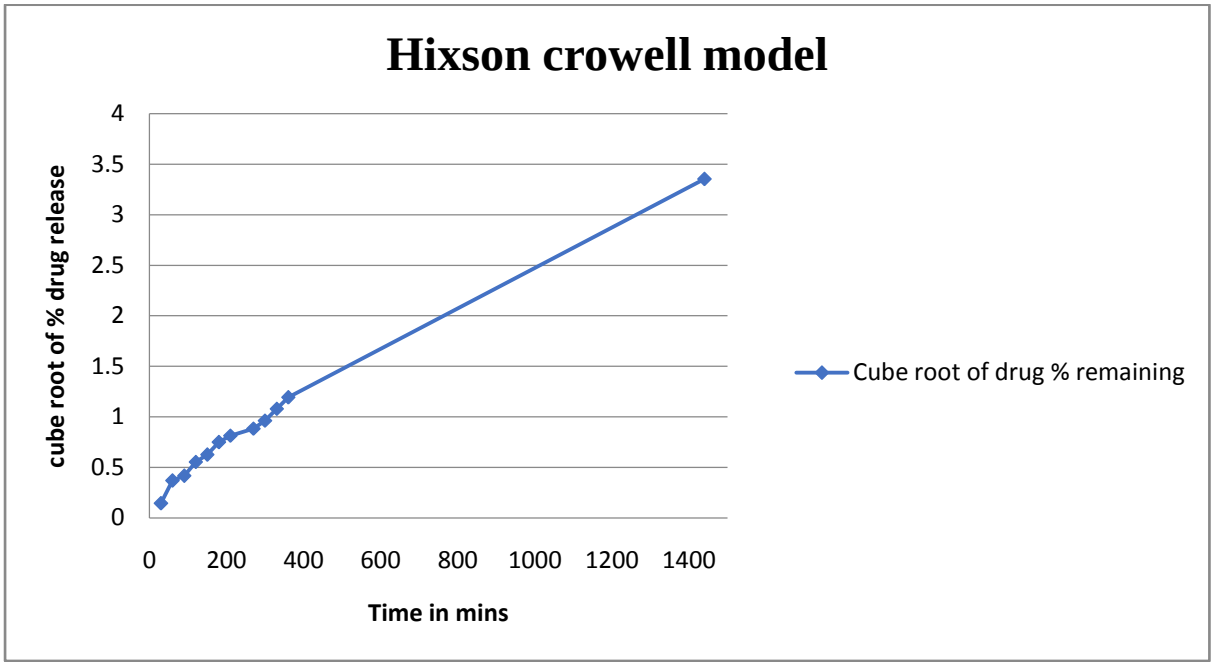

Fig: Hixson release kinetics for the drug loaded diatom

From the various mathematical models, the *in-vitro* kinetics studies were performed for drug loaded diatom microcapsule.

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COMPARATIVE KINETICS OF MICROCAPSULE:

Table : Comparative kinetics of microcapsule

From the various mathematical models, the *in-vitro* kinetics studies were performed for drug loaded diatom.

	RELEASE KINEITCS				
	ZERO	**HIGUCHI**	**PEPPAS**	**FIRST**	**Hixson Crowell**
	1	**2**	**3**	**4**	**5**
	R(CvT)	**R(CvRoot(T))**	**Log T vs Log C**	**TIME vs LOG % REMAINING**	**TIME Vs (Q1/3-Qt1/3)**
Slope	0.055	2.679	0.447	-0.017	0.002
Correlation	0.9146	0.9855	0.9824	-0.9979	0.9949
R^2	0.8364	0.9712	0.9652	0.9958	0.9898

They were subjected to various release kinetics such as Zero order, first order, Higuchi., Koresmeyer-peppas, Hixson-Crowell. Here the R^2 value was found to be highest in First order, hence it follows First order kinetics type of drug release mechanism.

IV. Conclusion

Unicellular diatom microalgaeare a promising natural resource of porous biosilica. Diatoms are attractive for industrial applications, especially in the field of biomedicine and pharmaceutical sciences. The study implies the importance of the formulation of drug using nanotechnology does not require a polymer but substance or compounds which will replace it. This study shows how surface modifications of diatom silica affect drug loading and release behaviour of water-insoluble drugs, using ciprofloxacin as a model. The surface modification by covalent attachment of selected and phophonic acids (2-phos) with COOH-terminated group was successfully performed and proven by several characterization techniques (DSC, TGA, and SEM). Determination of solubility, Differential scanning calorimetry, scanning electron microscopy, and Fourier transform infrared characterization techniques were used. Finally, diatom silica, as a low-cost, biocompatible, and natural material, has significant potential for use in implantable drug delivery, particularly in skin and bone infections. The current review focused on the use of diatoms in drug delivery systems, intending to present the various strategies to improve targeted delivery through surface functionalization. We are currently producing diatoms in powder form so that they can be diluted into suspension form for intravenous injections.

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