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FORMULATION AND EVALUATION OF OXICONAZOLE NANOSPONGE GEL

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Abstract

Background: Oxiconazole nitrate is a broad spectrum imidazole antifungal agent. Poor solubility of this drug caused low bioavailability that limits the antifungal efficiency. Due to their low efficiency as drug delivery many conventional dosage form such as cream and ointment need high concentration of active ingredient for effective therapy, which may cause side effect.

Materials and Methods: In this study nanosponge was prepared using hydroxyl ethyl cellulose and poly vinyl alcohol by emulsion solvent diffusion method. The entrapment efficiency of particle size has found in the range of 100nm-1µm and 55% - 88% respectively. Based on the characterization, nanosponge with least particle size and highest entrapment efficiency was selected for gel formulation.

Results and Discussion: Four different formulations of gel were prepared by using carbopol 934 with varying the concentration of penetration enhancer and various evaluation studies

were carried out. The in vitro release study showed that the nanosponge loaded gel formulation with higher concentration of penetration enhancer showed greater drug release.

Conclusion: while compared with conventional gel. Based on the stability study carried out, it was concluded that formulation was stable at ambient conditions.

Keywords: *Oxiconazole, Imidazole, Nanosponge gel, Antifungal formulation, Carbopol-934, Kinetic mechanism, Prolonging release.*

1. Introduction

Nowadays targeting the delivery of drugs is the major problems for researchers- how to get the drug in right place in the body and how to control the release of drug to prevent overdoses [1]. The development of new complex called nanosponge which offers controlled drug delivery. Nanosponge is a developing technology for topical drug delivery. Nanosponge is about the size of virus which can be filled with a wide variety of drugs. These nanosponges can circulate around the body until they experience the specific target site and stick on the surface and begin to release the drug in a controlled and predictable manner [2].

Nanosponges are made of microscopic particle with many pockets, in which a large variety of substance can be encapsulated. These are capable of carrying both lipophilic and hydrophilic molecule and of improving the solubility of poor water soluble substances. Due to their aqueous solubility, which allow the use of these systems effectively for drugs with poor solubility [3]. Nanosponge is three dimensional networks with a backbone of degradable polyester. The long length polyester strands are mixed with cross linker. These crosslinkers have affinity for certain portion of the polyester. They cross link segment of polyester to form spherical shape that has many cavities. In these cavities drugs can be encapsulated. The polyester is chemically biodegradable which means that when it breaks up in the body, the drug can be released on a known schedule [4, 5].

When compared to other nanoparticle delivery system, major advantage of this system is predictable release. Many other nanoparticle delivery systems, when they reach the target site unload most of their drug in rapid and uncontrolled fashion. This is called burst effect and makes to determine effective dosage level. Whereas when nanosponges reach their target site, they

adhere to surface and start releasing the drug in a controlled and predictable manner [6]. Nanosponge can be prepared by using Emulsion solvent diffusion method [7]. Nanosponge prepared from hyper cross linked β cyclodextrin [8] and Solvent method [3, 9]. Several researchers had formulated many antifungal nanosponges for Voriconazole [10], Lemongrass loaded ethyl cellulose nanosponge with a topical hydrogel [11], Miconazole nitrate nanosponge [12] Econazole nitrate nanosponge [7 &13] Griseofulvin hydrogel formulated by Shishu, V Aggarwal (2006) [14]. Oxiconazole nitrate emulgel formulated [15].

Oxiconazole is a broad spectrum imidazole antifungal agent; it is used to treat skin infections such as athlete's foot, jock itch and ringworm. This medication is also used to treat a skin condition known as pityriasis (tinea versicolor). Oxiconazole inhibits the cytochrome P450-dependent demethylation of lanosterol. This prevents the synthesis of ergosterol which is a crucial component of fungal cell membrane. By disrupting fungal cell membrane synthesis and integrity, oxiconazole alters fungal cell membrane permeability, promotes loss of essential intracellular components and eventually inhibits fungal cell growth [16, 17] It is poorly soluble in water (0.00191mg/ml).soluble in methanol; sparingly soluble in ethanol, chloroform, and acetone. Molecular weight is 429.126 g/mol and its melting point was 137^0 C.

Chemical Structure ($C_{18}H_{13}ON_3Cl_4$)

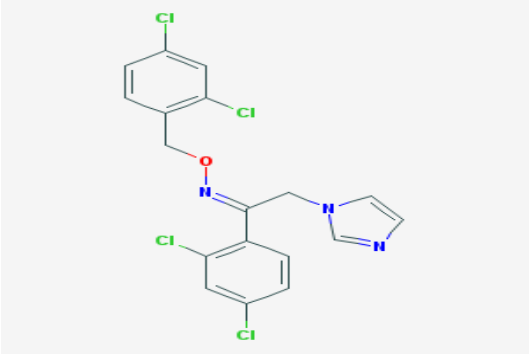

Fig 1.1 structure of oxiconazole nitrate

In the present study, an attempt was made to develop Nanosponge gel delivery system for lipophilic drug Oxiconazole nitrate by using emulsion solvent diffusion method as proposed by Sharma and Pathak, 2011 [7] (Figure 1).

2. Materials and methods

Chemicals

Oxiconazole nitrate, β-cyclodextrin, Polyvinyl Alcohol, Dichloromethane, Hydroxyl Ethyl Cellulose, Carbopol 934, Trietholamine, Propylene Glycol (Sigma Aldrich, Bangalore) peptic digest of animal tissue, agar, yeast extract, dextrose (Hi-media, Mumbai), distilled water.

Instrumentation

Magnetic stirrer (Rolick plus), UV Visible spectrophotometer (model 1601,PC,Shimadzu,Japan), FTIR Spectrophotometer (Shimadzu IR Prestigue 21 Specrophotometer, Japan), Hot air oven (Kemi,India), Scanning electron microscope (JEOL, Model J SM-6490 LA), Viscometer (Brookfield,USA), Stability testing Chamber (infra Model-Ihm678-ji), Sonicator(Remi, India),Incubator(Kemi,India),Electronic balance(infra-digi, India), P^H meter(Systronics, India).

Preformulation Studies:

Delivery of any drugs needs a suitable dosage form to achieve optimum therapeutics efficiency. During the development of such dosage forms it required to know the basic propertiesof the drug molecule. The classical preformulation studies require characterization in solid state as well as in solution form. In this study, the preformulation studies conducted are solubility analysis physical characterization like colour, odor and FTIR study (Figure 2).

Standard graph preparation

The stock solution (100µg/ml) was prepared by dissolving 10mg of the oxiconazole nitrate in methanol in a 100 ml volumetric flask. From the stock solution, 2ml, 4ml,6ml,8ml, 10ml was taken and diluted to 100ml with methanol to get 2,4,6,8,10 µg/ml of solution.Absorbance was measured at 212 nm by using the UV Spectroscopy. Calibration curve of drug was obtained by plotting a graph between concentration on X-axis and absorbance on Y-axis [18].

FTIR spectroscopy

Hydroxy ethyl cellulose loaded and oxiconazole nanosponge were subjected to FTIR for compatibility study. FTIR was conducted using a Shimadzu IR prestigue 21 spectrophotometer to detect drug-exicipient interaction. The spectrum was recorded in the region of 240-12500cm^{-1} [19].

Formulation of Oxiconazole Nitrate Loaded Nanosponge -Emulsion Solvent Diffusion Method

Formulation of Oxiconazole nanosponge

Nanosponge prepared by using varying proportion of hydroxyl ethyl cellulose and poly vinyl alcohol. The disperse phase consists of required quantity of hydroxyl ethyl cellulose and oxiconazole nitrate dissolved in dichloromethane was slowly added to a specific quantity of poly vinyl alcohol in the aqueous continuous phase. Then the mixture was stirred at 1000 rpm for 2 hrs on magnetic stirrer. The nanosponge formed were collected by filtration and dried in an oven at 40^0c for 24 hrs. Dried nanosponges were stored in vacuum desiccator to remove the residual solvent [20]. **Table 1**.

Formulation of Oxiconazole nanosponge comprised following common ingredients were present in the F1, F2 and F3 formulations, all three of the formulations contains hydroxyl ethyl cellulose (F1 contains 500 mg, F2 holding 1 gram and F3 consists 2 grams), Poly vinyl alcohol taken each 1 gram in all the formulations, similarly Oxiconazole nitrate taken each 100 mg in all the formulations, likely each 150 ml of distilled water was mixed in all the formulations and each 20 ml of Dichloromethane had taken in all the formulations. Concern, evaluation, particle size, drug entrapment efficiency, drug content and incorporation of oxiconazole nanosponge in to gel, in addition, Oxiconazole nanosponge gel has compared with conventional gel.

Preparation of gel containing nanosponge

Gel forming polymer carbopol 934 is soaked in water for 2hrs and then dispersed by agitation with aid of magnetic stirrer to get a uniform dispersion. The stirring was stopped and allowed to stand for 15 minutes to expel the entrapped air. To this aqueous solution, 2% v/v triethanolamine is slowly added. At this stage, prepared nanosponge and penetration enhancer (propylene glycol) is added to get nanosponge gel **Table 2**. [21].

Evaluation of Nanosponges:

Loading efficiency The loading efficiency can be determined by dissolving the nanosponge in a suitable solvent, sonicated to break the complex, diluted suitably and analyzed by UV spectrophotometer [22].

Microscopy studies

Scanning electron microscopy and transmission electron microscopy can be used to study the microscopic aspect of the drug, nanosponge and the product (drug/nanosponge complex) [23].

Fourier transforms infrared (FTIR) analysis:

FTIR was conducted to verify the possibility of interaction of chemical bonds between drug and polymer .Samples was scanned in the range of 400-4000 cm-1 and carbon black reference [23].

Zeta potential

Zeta potential is a measure of surface charge. It can be measured by using additional electrode in the particle size equipment [24].

In vitro drug release study

Drug release can be studied using multi compartment rotating cell with dialysis membrane using Franz diffusion cell. The donor phase consists of drug loaded nanosponge complex in distilled water. The receptor phase consist the same medium. The receptor phase is withdrawn completely after fixed time intervals, suitably diluted with distilled water and then analyzed by UV spectrophotometer [25,26].

Entrapment efficiency

The entrapment efficiency of nanosponges were determined by adding 10ml of phosphate buffer 7.2 in to100mg of nanosponge and sonicated in a bath sonicator and filtered. 1 ml of filtrate is made up to 10 ml with phosphate buffer is assayed spectrophotometrically at 212 nm. The amount of entrapped drug was calculated from the equation Gaber, D. A., 2023 [22].

$$\boldsymbol{Entrapment\ Efficiency}\ (\%\ \boldsymbol{EE}) = \frac{\boldsymbol{Actual\ content\ in\ nanosponge}}{\boldsymbol{Theoretical\ drug\ content}} * \mathbf{100}$$

Scanning Electron Microscopy

Analytical scanning electron microscopy can be used to study the average particle size, morphology, microscopic aspect of nanosponge. The shape and surface characteristics of oxiconazole nanosponge gel were determined by SEM (scanning electron microscopy)[23].

Evaluation of Gel Containing Nanosponge

Evaluation of gel loaded nanosponges:

Determination of Viscosity

The viscosity of prepared gel was measured by Brookfield viscometer. Viscosity was measured at 100rpm using spindle number [27].

Determination of pH:

The pH of gel formulation was noted using calibrated P^H meter.1gm of oxiconazole nanosponge loaded hydrogel was uniformly dispersed in 100ml of distilled water and kept for 2 hours at room temperature. Then P^H of dispersion was measured at 25 ± 1^0C. [27].

Estimation of Drug content:

The percentage drug content was estimated by weighing 100mg of hydrogel and extracting with 5ml of 0.1M HCl using mechanical stirrer. The volume was made up to 10ml and filtered and then diluted to 100ml and the concentration was determined spectrophotometrically at 212nm [28].

***In-vitro* drug release study**

The oxiconazole nanosponge loaded gel was permeated through an semi permeable egg membrane. 100mg gel was placed in the donor compartment. The receptor medium was filled with phosphate buffer pH 7.2 and constantly stirred with a small magnetic stirrer.1ml of sample were withdrawn at 0,1,2,3,4,5,and 6^{th} hour and replaced with fresh receptor solution. The samples withdrawn were analyzed spectrophotometrically at 212nm. The amount of drug release was calculated and the percentage of cumulative amount of drug released was plotted against time [29].

Kinetic of drug release:

The in vitro release profiles were fitted to four different kinetics models to see which one had the strongest correlation with the experimental release results. The zero-order kinetic model was derived by plotting cumulative% drug release vs. time, the first-order kinetic model by plotting log of% drug remaining vs. time, the simplified Higuchi model by plotting cumulative% drug release vs. square root of time, and the Korsmeyer-Peppas model by plotting log cumulative% drug release vs. log time. The rate constant and correlation values for each model were determined using a linear regression fit [30]. The release data were further fitted into Ritger-Peppas empirical equation because these kinetic models typically fail to explain the drug release mechanism from polymeric matrices that experience swelling and/or erosion throughout the dissolving process. **The equation which is used to describe drug release mechanism is: Mt/mα = ktn,** Where, Mt/mα is the fraction release of the drug,'t' is the release time, 'k' is the constant, which indicates the properties of the macromolecular polymeric system, and 'n' is the release exponent indicative of the mechanism of release. The 'n' value was used for the analysis of drug release mechanism from drug loaded nanosponge gel. The 'n' value was determined for all batches of drug loaded nanosponge gel by graphical method [31].

Swelling studies

Dried gel were weighed accurately and kept immersed in 10ml of phosphate buffer of pH 7.2. Gels were taken carefully at 1, 2, 4, 6, 8, 10, 12, and 24 hours intervals. Blotted with filter paper and weighed accurately. Increase in weight was determined as time increases. The percentage swelling was calculated from the equation of % swelling = wet weight – dry weight /wet weight *100 [32].

Anti microbial activity

The antimicrobial studies ascertained the microbial activity of the formulation against *candida albicans* fungus. This can determine by sabouraud dextrose agar diffusion test. Petridish containing 20ml of saboraud dextrose agar medium were seeded with fungal strains. Well were cut and different concentration of optimized formulation were added. The plates were incubated at 37^0 C for 48 hrs. The zone of inhibition was measured [33, 34].

Procedure for preparation of media

Compositions of media are peptone (10 gm), dextrose (40 gm), agar (15gm). Suspend the 65 g of the medium in one liter of purified water. Heat with frequent agitation and boil for one minute to completely dissolve the medium and kept in Autoclave at 121^0 C for 15 minutes. Then cool to 45^0 C and pour in to petridish [35].

The optimized formulation were kept for stability studies for 3 months at room temperature (30 ± 2°C), at refrigerator temperature (4 ±2°C) and at accelerated condition (40±2°C, 75%RH) in programmable environmental test chamber to determine physical and chemical stabilities. The formulation was evaluated visually and for entrapment efficiency and drug release after 15, 30, 45, 60 and 90 days [36].

3.Results

Pre Formulation Studies

Fourier transforms infrared (FTIR) analysis:

Hydroxy ethyl cellulose and oxiconazole nanosponge were subjected to FTIR for compatibility study. FTIR conducted using a Shimadzu IR prestigue 21 spectrophotometer to detect drug-exicipient interaction. The spectrum was recorded in the region of 240-12500 cm^{-1} was shown in **Figure 4** and **5.** The Fourier transform infrared spectroscopy (FT-IR) study has done to verify the originality of the sample of oxiconazole nitrate recorded through FT-IR had compared with standard molecular functional group of Oxiconazole nitrate. The functional group frequencies of attained sample of the drug have matched with reported range shows that the sample was genuine one. The IR spectrum of drug exhibited distinctive peaks at 1378.20 (cm-1) due to C=N stretching. The peaks at 1514.19(cm-1) is due to the C=C stretching and at 632.68 (cm-1) is due to the C-Cl stretching. The peak at 2925.17 (cm-1) is due to the C-H (methylene) stretching. The peak at 1378.20 (cm-1) is due to N-O stretching.

Standard graph preparation

The stock solution was prepared by dissolving 10mg of the Oxiconazole nitrate in methanol in a 100ml volumetric flask. From the stock solution, solutions containing 2,4,6,8, 10µg/ml were

prepared by appropriate dilution. The UV Spectroscopy of oxiconazole nitrate was performed at 212nm. The standard graph of drug was plotted by taking the concentration of the drug solutions on the X- axis and the corresponding absorbance values on Y-axis (Figure 3).

Formulation of nanosponge

The nanosponges of three different ratios were prepared using the polyvinyl alcohol and hydroxylethyl cellulose as a polymer by solvent emulsion diffusion method are shown in **Figure 6.**

Evaluation of Nanosponge *In-vitro* characterization of nanosponge

Scanning electron microscopy

SEM analysis of nanosponge illustrated in figures 7, 8 and 9. The scanning electron microscopy was performed to determine the particle size, shape, morphology. The particle size of three different nanosponge formulations was found in the range between 100nm-1µm. From the scanning electron microscopy images, it was evident that the surface of nanosponge is porous. The presence of pores was due to the impression of diffusion of the solvent dichloromethane.

Drug entrapment efficiency

Drug entrapment efficiency was determined for three different nanosponge formulations was listed in **Table 3**. The variation in the entrapment efficiency was due to changes in the concentration. The formulation F3 showed highest percentage of drug entrapment efficiency 55% at absorbance of 0.893, F2 entrapped 75% (0.644), whereas F3 got 88% (0.413). The formulation having least particle size and highest percentage of entrapment efficiency was taken to formulate gel.

Formulation of Nanosponge Gel

Oxiconazolenanosponge gel was prepared using carbopol 934 as a gelling agent **Figure 10**. Carbopol 934 was soaked in water, to this triethanolamine was added; finally penetration enhancer was added to the formulations.

Evaluation of OxiconazoleNanosponge Gel

***In-vitro* characterization of Oxiconazole nanosponge gel**

Determination of pH, Viscosity & Swelling studies

The viscosities of different formulation of gel were ranged between 5753-12100 cps. The viscosity variation is based on the varying the concentration of gelling agent at the **pH** range of 6.72-7.15, this range of **pH** avoids the risk of irritation upon application to the skin. The Viscosity of different formulations and its corresponding P^H were given in bract as NF1 5753 (6.72); NF2- 9708 (6.84); NF-3 29853 (6.85); NF-4 12100 (7.15). The **pH** and Viscosity of different formulation and swelling studies of all formulation were carried out in phosphate buffer of **pH** 7.2. In the present study, swelling studies of all formulation were carried out in phosphate buffer of P^H 7.2. When gel come contact with buffer, this buffer penetrates in to gel and become swell and allow the drug to dissolve and drug gets released. The percentage swelling of different hydrogel formulations within 24 hours were NF1-73%; NF2- 82%; NF3- 90.27%;NF4- 94.16%. NF4 formulation showed highest swelling index within 24 hours. Higher the percentage of swelling, higher will be the drug release. Hence from the swelling study it was confirmed that NF4 formulation showed higher drug release. The drug content of the four formulations was determined. The table shows the drug content. The NF4 formulation shows the 0.478 mg of drug content **Table 4.**

***In vitro* drug release study**

In vitro drug release study was carried out in phosphate buffer 7.2 using egg membrane. *In vitro* drug release from of four different formulations was determined. In these four formulations, NF4 formulation showed highest percentage of drug release. The NF4 formulation showed drug release of 56.21% at 6^{th} hour. The release of oxiconazole nitrate from the NF4 formulation may be attributed to the solubility of drug within the gel matrix due to permeation enhancers. The permeation enhancer consequently facilitated the drug to release from the gel in to the test media. **Table 5** and **Figure 11** Table1, 2, 3, and 4 and figure -6 shows percentage cumulative amount of drug release.

Drug content

In vitro drug release studies results have shown that the drug content of the four formulations was determined by using spectrophotometry analysis were NF-1: 0.381mg (0.2960); NF2: 0.3413mg (0.439); NF3: 0.3601mg (0.465); NF4: 0.3712mg (0.478). The NF4 formulation shows the 0.478mg of drug content.

Kinetic data modeling studies

The data obtained from the in vitro release study was used for kinetic modeling. This was done to find out the mechanism of release from gel.

Zero order kinetics

The graphs were plotted with % drug release on Y-axis and time on X-axis. The Zero order rate constant (K_0) for four formulation NF1, NF2, NF3, NF4 were determined from the slope (K_0 = slope*2.303), which was found to be 16.29, 17.71, 19.90, 20.51 respectively. The regression coefficient (R^2) value ranges between 0.912-0.979.

First order kinetics

The graphs were plotted between log percentage drug remaining on Y-axis and time in hours in X-axis. The first order rate constant for the formulations NF1, NF2, NF3, NF4 were determined from the slope which were found to be 0.0921, 0.0951, 0.1151, 0.1197 respectively. The regression coefficient value ranged between 0.964-0.988.

Higuchi's model

The graphs were plotted between cumulative amount of drug released on Y-axis and square root of time on X-axis. The regression coefficient lies between 0.974-0.992.

Korsemeyer-peppa's model

The graphs were plotted between log percentage drug released Vs log time yields slope n (diffusion exponent). The regression coefficient ranged between 0.955-0.982.

In vitro drug release study data of all four formulations were subjected to goodness of fit test by linear regression analysis according to Zero order, and first order kinetics, Higuchi's and

Korsemeyer- Peppas model to ascertain the mechanism of drug release. The result of linear regression analysis including rate constant and regression coefficients are listed in **Table 6**.

The korsemeyer –Peppas release exponent ranged between 0.629-0.729. In drug release profile of all four formulations, the release mechanism is assumed to be non fickian diffusion are shown in **Figure 12**.

Anti fungal studies

The anti fungal activity of optimized formulation was determined against *Candida albicans.* The anti fungalactivity was carried out at different concentration (0.0, 0.2mg, 0.3mg, 0.4mg). The zones of inhibition control and drug were 0.0, 1.0, 1.1, 1.5, cm respectively **Table 7.**

Stability studies

The stability studies of drug formulation were monitored under different temperature sources, and the percentage of drug content was found for freshly prepared (duration of 1 to 6 days) formulation at room temperature as 92.547°F and 91.574°F, 91.120°F, 90.838°F, 90.388°F, 90.123°F for the duration of the 7th, 15th, 30th, 60th, and 90th days, and in the same duration, the drug formulation was kept under refrigerator temperature and in accelerated condition. The percentage drug content was evaluated and shows that there are no significant changes in the drug content during storage. Hence, based upon the stability studies carried outfor 3 months, it was concluded that the optimized formulation is stable under ambient conditions. The percentages of drug contents were estimated at 92.547, 91.801, 91.631, 90.892, 90.688, 90.493, and 92.547, 91.505, 91.089, 91.004, 90.789, 90.549 respectively **Table 8**.

4. Discussion

Oxiconazole nitrate is a broad spectrum of imidazole antifungal agent. Poor solubility of oxiconazole caused low bioavailability that limits the antifungal efficiency. Due to their low efficiency as drug delivery many conventional dosage form such as cream and ointment need high concentration of active ingredient for effective therapy, which may cause side effect. [37]. Nanosponge delivery systems have potential to slow down the release of active ingredient from topical formulation. Nanosponge can be effectively incorporated in to hydrogel for prolonged

release, retention of dosage form on the skin, reducing the toxicity, improving the patient compliance by prolonging dosing intervals.

In this study nanosponge were prepared by emulsion solvent diffusion method. A victorious effort was made to formulate Nanospongegel of Oxiconazole nitrate **(NF1-NF4)**. It was prepared by using varying proportion of hydroxyl ethyl cellulose and poly vinyl alcohol, and Oxiconazole nitrate dichloromethane, Carbopol 934 and Trietholamine and Propylene glycol. The drug is poorly soluble in water (0.00191mg/ml) but soluble in methanol, sparingly soluble in ethanol, chloroform, and acetone. Its Molecular weight is 429.126 g/mol and its melting point was identified as 143°C and it correlate with standards 141°C -143°C shows that the drug sample is genuine [38].

The infrared spectral analysis of the acquired Oxiconazole nitrate was matched with the standard IR values of Oxiconazole nitrate. FT-IR investigations demonstrated no interaction between the chosen medication and polymers. The standard calibration curve of Oxiconazole nitrate in phosphate buffer pH 6.8 has taken by using UV-Spectrophotometery, the curve was identified to be linear in the Beer's vary between 4 and 14µg/ml at 212 nm. The formulation has gone under various quality control evaluations such as pH, viscosity, spread ability, extrudability, and *in-vitro* drug release. Nanosponge gel formulation NF4 shown potential report in respect of spreadability, viscosity, In-vitro drug release, therefore it was chosen as optimized Nanosponge gel formulation. The optimized Nanosponge gel formulation illustrated better anti-fungal activity. From the above report has shown that Oxiconazole Nanosponge gel formulation was effectively formulated.

The particle size and entrapment efficiency found in the range 100 nm-1µm and 55%-88% respectively. Based on the characterization, nanosponge with least particle size and highest entrapment efficiency was selected for gel formulation. Four different formulation of gel were prepared by using carbopol 934 with varying the concentration of penetration enhancer. Various evaluation studies were carried out. The in vitro release study of nanosponge loaded gel showed that the formulation with higher concentration of penetration enhancer and also greater drug release while with conventional gel. Based on the stability study carried out, it was concluded that formulation was stable at ambient conditions. Among all batches, F4 was optimized based

on particle size, SEM, zeta potential, and in vitro drug release profile. The particle size, SEM, PDI, and zeta potential of all NS formulations developed were acceptable and adequate. The average entrapment efficiency of most Oxiconazole nitrate NS was found to be better than 80%, with the improved formulation F4 achieving 92.72% entrapment. Release kinetics experiments revealed that drug release from the nanosponge follows non-Fickian diffusion.

Conclusion

In conclusion, the oxiconazole nanosponge gel delivery system shows promise for improving drug solubility and bioavailability, achieving controlled release over 12 hours, and optimizing formulation with high drug entrapment efficiency. Compared to conventional gels, it offers enhanced drug release capabilities and potential clinical benefits such as reduced side effects and improved patient compliance. Further clinical studies are warranted to validate its efficacy and safety in practical use.

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Conflicts of interest: None

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Table 1: Composition of Oxiconazole nanosponge formulation

Ingredients	F1	F2	F3
Hydroxyl ethyl cellulose	500 mg	1 g	2 g
Poly vinyl alcohol	1g	1 g	1g
Oxiconazole nitrate	100 mg	100 mg	100 mg
Distilled water	150 ml	150 ml	150 ml
dichloromethane	20 ml	20 ml	20 ml

Table 2: Composition of oxiconazole nanosponge gel

Ingredient	NF1	NF2	NF3	NF4
Carbopol 934	150 mg	150 mg	150 mg	150 mg
Trietholamine	0.25 ml	0.25 ml	0.25 ml	0.25 ml
Propylene glycol	-	-	1 ml	5 ml

Oxiconazole nitrate	100mg	-	-	-
Oxiconazole nanosponge	-	100 mg	100 mg	100mg
Distilled water	10 ml	10 ml	10 ml	10 ml

Table 3: Drug entrapment efficiency

Formulation	Absorbance	Drug entrapment efficiency
F1	0.413	88%
F2	0.644	75%
F3	0.893	55%

Table 4: pH, Viscosity and Swelling index

Formulations	Viscosity	pH	Swelling index	Drug content (mg)
NF1	5753	6.72	73%	0.381
NF2	9708	6.84	82%	0.439
NF3	9853	6.85	90.27%	0.465
NF4	12100	7.15	94.16%	0.478

Table 5: *In-vitro* drug release study of formulation NF1 to NF4

Time (hrs)	PERCENTAGE CUMULATIVE AMOUNT OF DRUG RELEASE			
	NF1	NF2	NF3	NF4
0	0	0	0	0
1	14.54	12.38	15.62	17.66
2	18.29	24.76	28.99	32.90
3	24.43	31.62	37.59	42.55
4	31.25	34.70	42.13	46.700
5	38.35	41.91	48.91	51.18
6	45.85	48.79	54.09	56.21

Table 6: Kinetic data modeling studies

Formulation	Zero order		First order		Higuchi's	Korsemeyer-Peppas	
	K	R^2	K	R^2	R^2	R^2	n
NF1	16.29	0.979	0.0921	0.976	0.951	0.955	0.652
NF2	17.71	0.962	0.0951	0.982	0.985	0.978	0.729
NF3	19.90	0.947	0.1151	0.988	0.992	0.982	0.678
NF4	20.51	0.912	0.1197	0.964	0.974	0.964	0.629

Table 7: Zone of inhibition study for Oxiconazole loaded Nanosponge gel NF4

Microorganism	Volume added (mg)	Zone of inhibition (cm)
Candida albicans	Control	0
	0.2	1
	0.3	1.1
	0.4	1.5

Table 8: Stability study (drug content)

Temperature	Room temperature % drug content	Refrigerator % drug content	Accelerated condition % drug content
Freshly prepared	92.547	92.547	92.547
7th day	91.574	91.801	91.505
15th day	91.120	91.631	91.089
30th day	90.838	90.892	91.004
60th day	90.388	90.688	90.789
90th day	90.123	90.493	90.549

Figure Caption

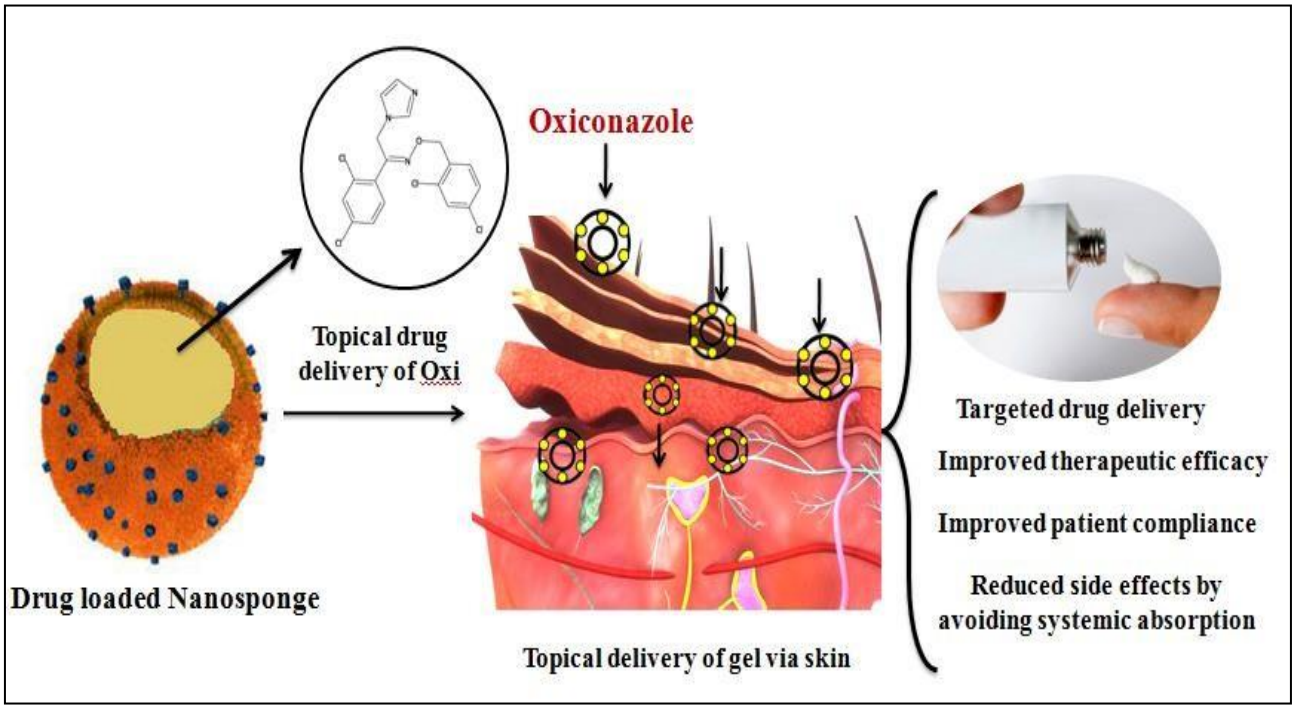

Fig.1: Graphical representation of Drug loaded nanosponge via topical delivery

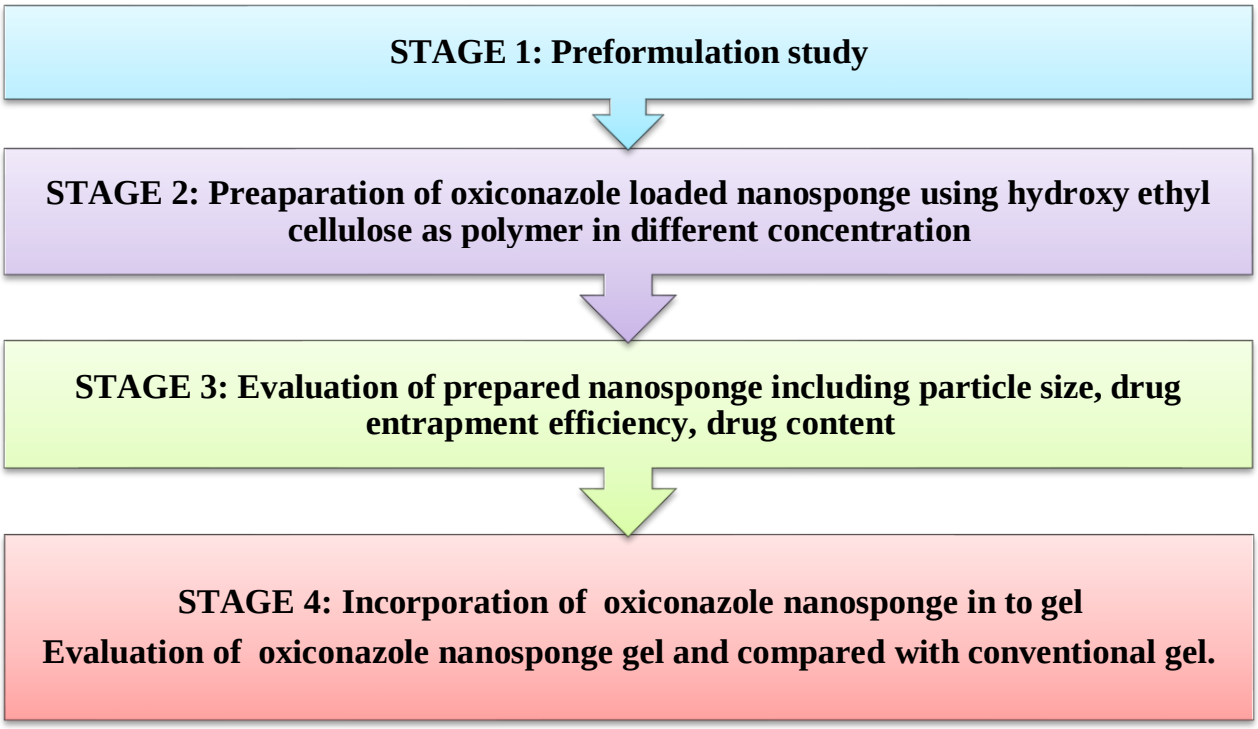

Fig.2: Plan of work for oxiconazole nanosponge loaded gel

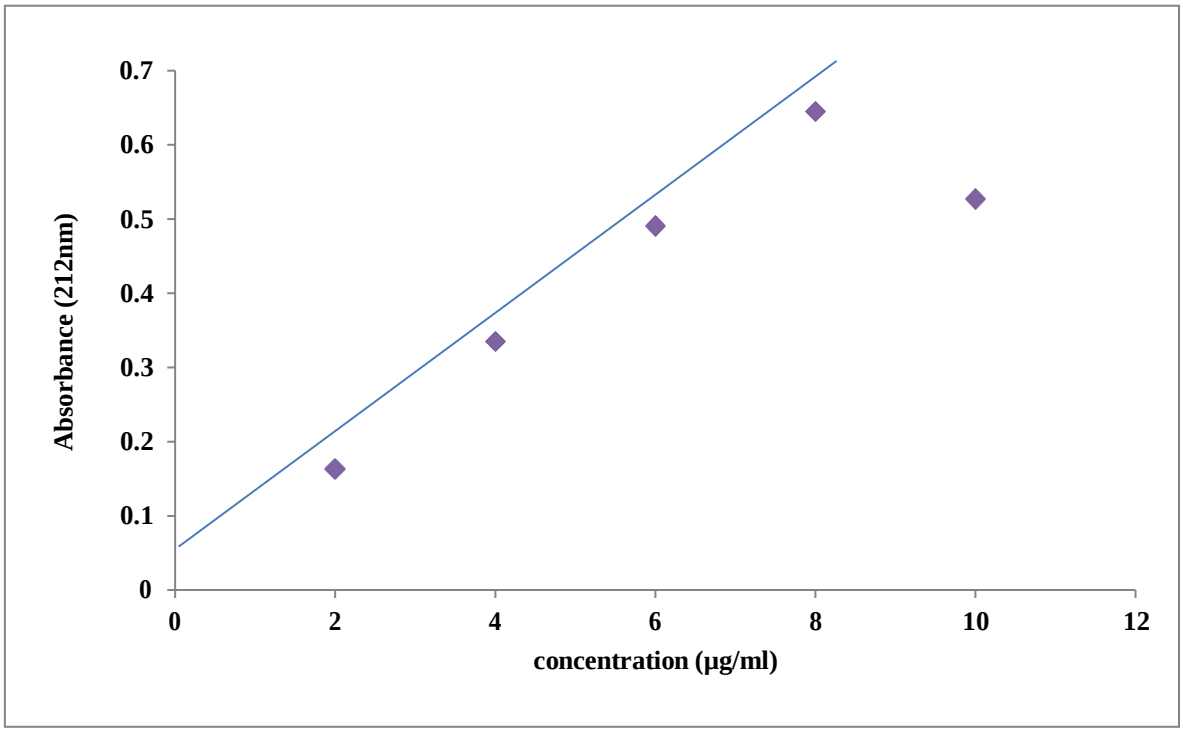

Fig.3: Standard graph of Oxiconazole Nitrate

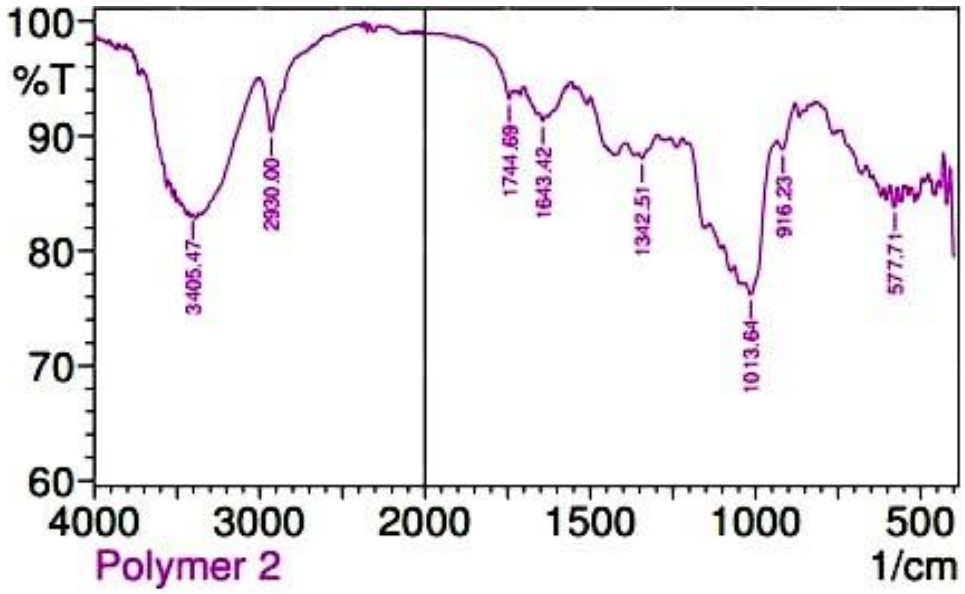

Fig.4: FTIR of hydroxyl ethyl cellulose

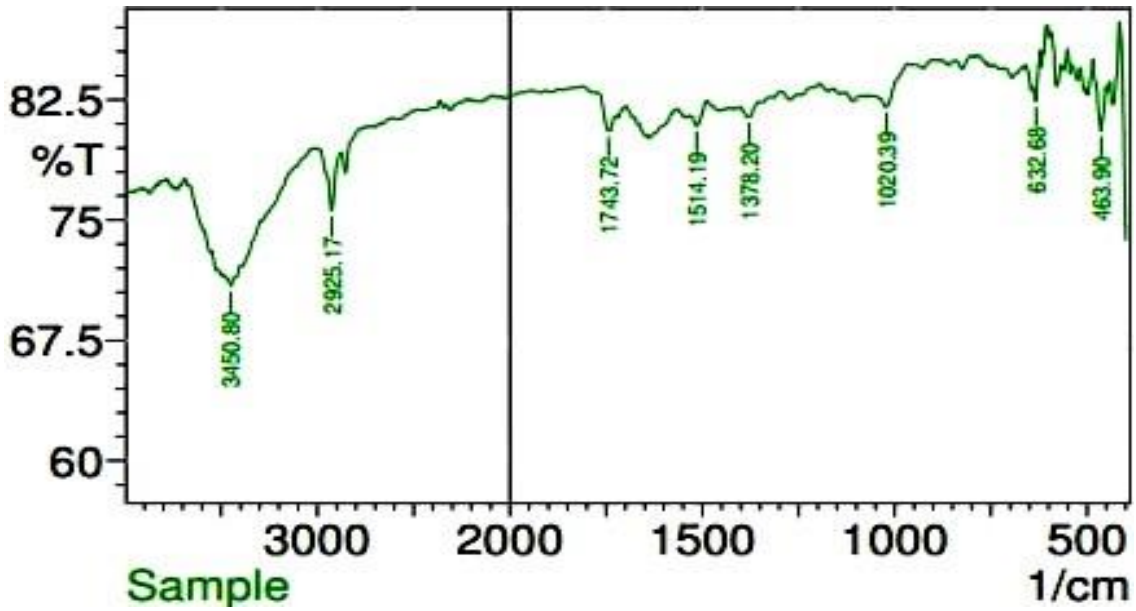

Fig. 5: FTIR of oxiconazole nanosponge

Fig. 6: Preparation of oxiconazole nanosponge

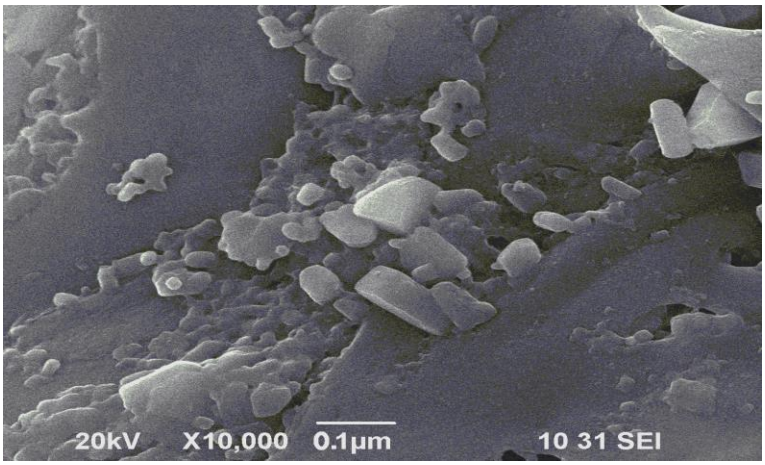

Fig.7: SEM analysis for Formulation-1

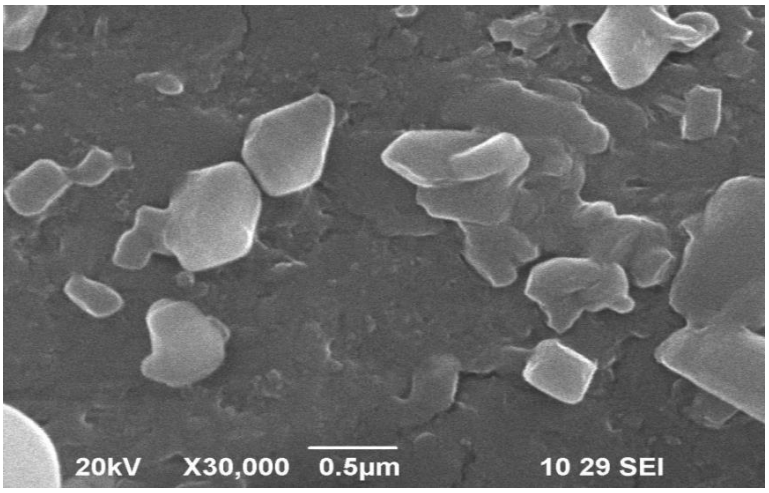

Fig. 8: SEM analysis for Formulation -2

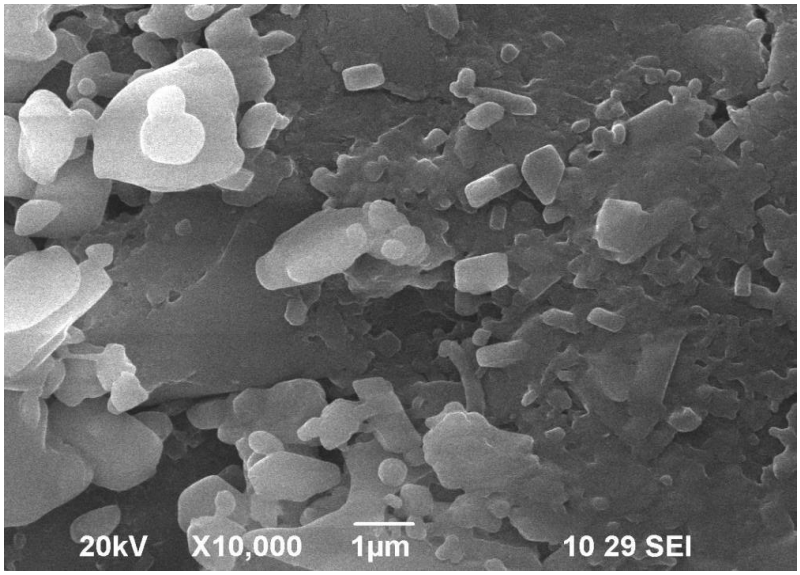

Fig.9: SEM analysis of Formulation-3

Fig. 10: Oxiconazole nanosponge gel

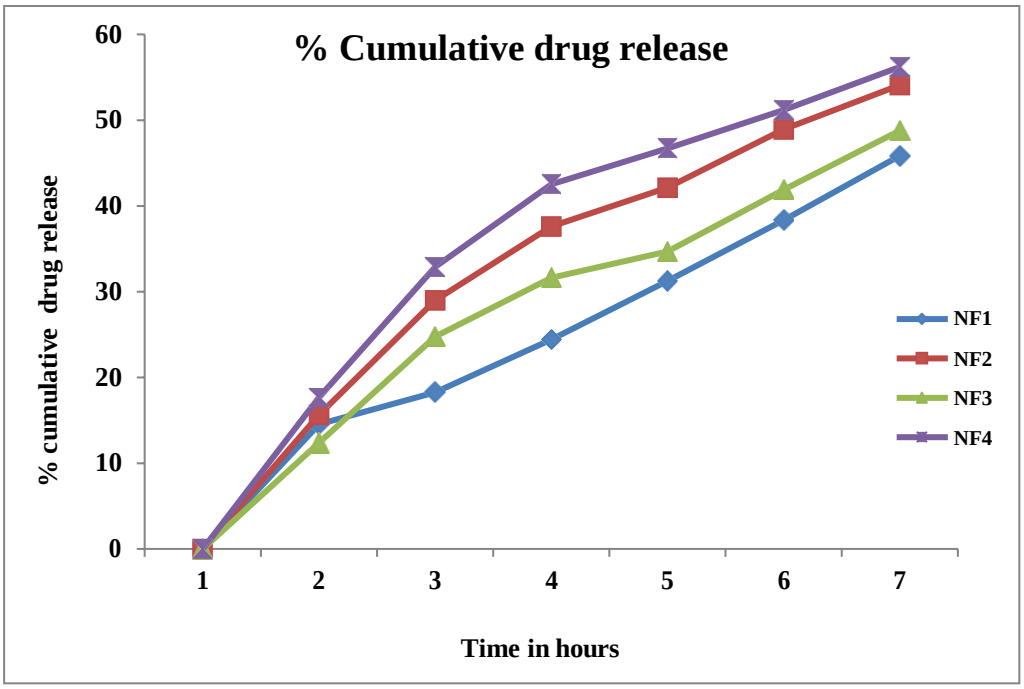

Fig.11: % **Cumulative amount of drug release Vs time**

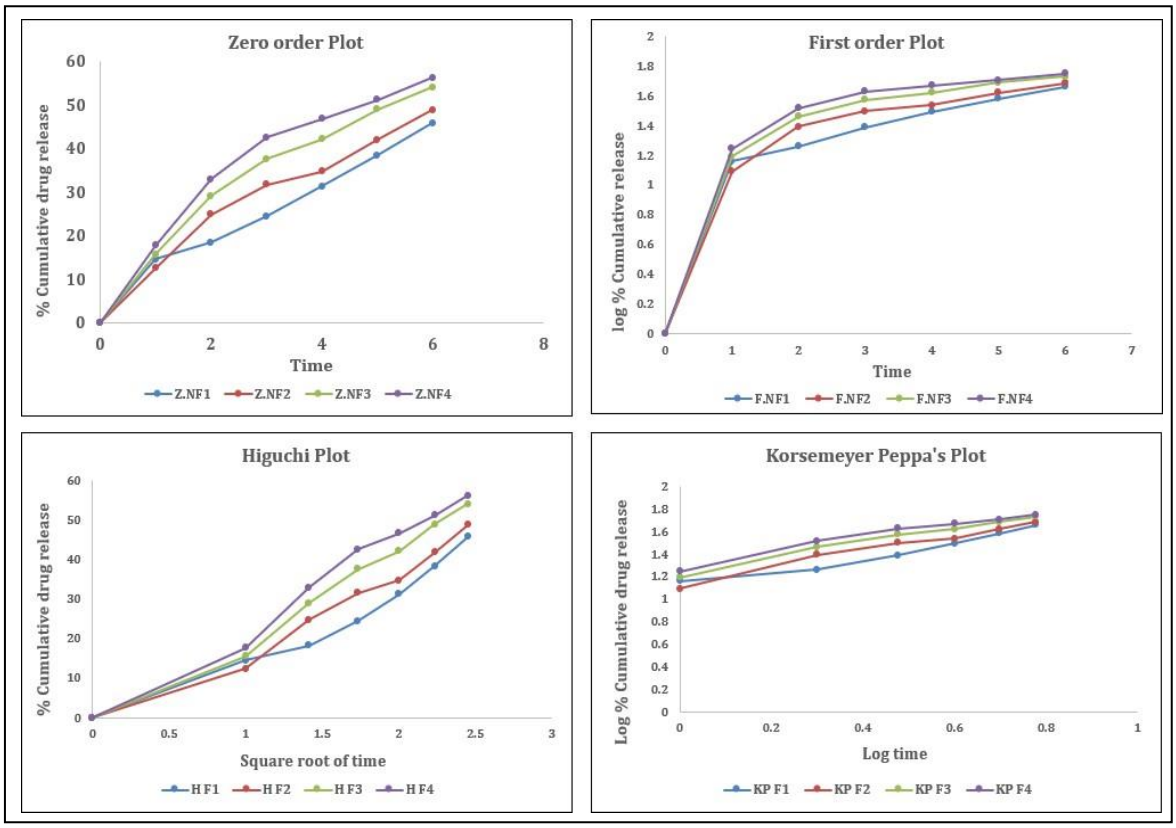

Fig. 12: Kinetic plot study for Oxiconazole nanosponge gel