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# FORMULATION AND EVALUATION OF SAXAGLIPTIN-LOADED TRANSFEROSOMAL ORAL THIN FILMS FOR ENHANCED PERMEABILITY

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**Abstract:**
*The present research work on the formulation, development, and evaluation of Fulvestrant Solid Lipid Nanoparticles (SLNs) was successfully completed. Different formulations were prepared and evaluated to develop an effective sustained-release nanoparticulate drug delivery system for Fulvestrant. The prepared formulations exhibited satisfactory physicochemical characteristics with good stability and compatibility between the drug and excipients. All the pre-compression parameters, including angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio, were found to be within the acceptable IP limits, indicating good flow and compressibility properties of the powder blend. Similarly, all post-compression parameters such as hardness, friability, weight variation, thickness, drug content, and in-vitro drug release were also found to comply with IP standards. Among all the formulations, F4 formulation was considered as the optimized formulation based on its superior evaluation parameters and drug release profile. The F4 formulation showed a maximum cumulative drug release of 98.41% over a period of 48 hours when compared to other formulations, indicating an effective sustained-release behaviour and better formulation performance. Thus, the developed Fulvestrant Solid Lipid Nanoparticle formulation demonstrated enhanced drug release characteristics and may improve the bioavailability and therapeutic efficacy of Fulvestrant. The study concludes that SLNs are a promising and efficient carrier system for the controlled delivery of Fulvestrant and can be further explored for advanced pharmaceutical applications.*

***Keywords:*** *Fulvestrant Solid Lipid Nanoparticle*

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## INTRODUCTION:

### NOVEL DRUG DELIVERY SYSTEM

1For many decades treatment of an acute disease or a chronic illness has been mostly accomplished by delivery of drugs to patients using various pharmaceutical dosage forms including tablets, capsules, pills, suppositories, creams, ointments, liquids, aerosols and injectables, as drug delivery systems are the primary pharmaceutical products commonly seen in the market, even though these drug delivery system ensure a prompt release of drug, it is necessary to take this type of drug several times a day to achieve as well as to maintain the drug concentration with in the therapeutically effective range needed for the treatment. This results in significant fluctuations in drug level. In the past two and a half decades several advancements have been made. They have resulted in the development of new techniques for drug delivery. These techniques are capable of controlling the rate of drug delivery, sustaining the duration of therapeutic activity and targeting the delivery of drug to a cell or tissue. Recently pulsatile drug delivery system is gaining importance. These advancements have led to the development of several novel drug delivery systems that could revolutionalise the method of medication and provides a number of therapeutic benefits.

**Novel drug delivery system can be broadly divided into two classes:**

Sustained release drug delivery system.
Controlled release drug delivery system.

### SUSTAINED RELEASE DRUG DELIVERY SYSTEM:

Sustained release drug delivery system is described as a pharmaceutical dosage form formulated to retard the release of a therapeutic agent such that its appearance in the systemic circulation is delayed and/or prolonged and its plasma profile is sustained in duration. The onset of its pharmacological action is often delayed and the duration of its therapeutic effect is sustained (e.g. coated granules).

### CONTROLLED RELEASE DRUG DELIVERY SYSTEM:

Controlled release drug delivery system has a meaning that goes beyond the scope of sustained drug release. It implies a predictability and reproducibility in the drug release kinetics. The release of drug ingredients from a controlled release drug delivery system proceeds at a rate profile that is not only predictable kinetically but also reproducible from one unit to another.

**Controlled release drug delivery system can be classified into four categories:**

Rate-Preprogrammed drug delivery system.
Activation-Modulated drug delivery system.
Feedback-Regulated drug delivery system.
Site-Targeting drug delivery system.

### RATE-PREPROGRAMMED DRUG DELIVERY SYSTEM

In this system, the release of drug molecules from the drug delivery system has been preprogrammed at specific rate profiles. This was achieved by system designing which controls the molecular diffusion of drug molecules in and/or across the barrier medium with in or surrounding the delivery system. (e.g.) implants, transdermal system3.

### ACTIVATION – MODULATED DRUG DELIVERY SYSTEM

The release of the drug molecule from this delivery system is activated by some physical, chemical or biochemical process and/or facilitated by the energy supplied externally. The rate of drug release is then controlled by regulating the process applied or energy input.

Based on the nature of the process applied or the type of energy used, these activation modulated drug delivery system can be classified in to three categories:

Physical–e.g.: Osmotic pressure activated drug delivery system-
osmotic pump4, iontophoresis activated drug delivery system
Chemical- e.g.: pH activated drug delivery system6
Biochemical-e.g.: Enzyme activated drug delivery system7

### FEED BACK –REGULATED DRUG DELIVERY SYSTEM

The release of the drug molecule from the delivery system is activated by a triggering agent, such as biochemical substance in the body and regulated by its concentration viz. some feed back mechanisms. The rate of drug release is then controlled by the concentration of triggering agent detected by a sensor in the feed back regulated mechanism. E.g. bio-responsive drug delivery system, glucose triggered insulin delivery system8.

### SITE-TARGETING DRUG DELIVERY SYSTEM

In this system the drug molecules are circumventing the other tissues and moving towards the specific diseased site and get released. This will enhance the therapeutic effectiveness and reduces the toxicity to other healthy tissues and improve the treatment spectrum e.g. Niosomes, Microspheres.

## METHODOLOGY:

**Analytical Method Development**

**Identification and Characterization of Drug**
**Preparation of reagents:**

**Preparation of 0.2M NaOH Solution**
Dissolved 4g of Sodium hydroxide pellets in to 1000mL of Purified water and mixed

**Preparation of pH 6.8 Phosphate buffer**
Dissolved 6.805 g of Potassium dihydrogen phosphate in to 800mL of purified water and mixed added 112mL of 0.2M NaOH solution and mixed. Diluted to volume 1000mL with purified water and mixed. Then adjusted the pH of this solution to 6.8 with 0.2M NaOH solution.

**a) Determination of absorption maxima**
A solution containing the concentration 10 µg/ ml drug was prepared in 6.8 phosphate buffer UV spectrum was taken using Lab India Double beam UV/VIS spectrophotometer (Lab India UV 3000+). The solution was scanned in the range of 200 – 400 nm.

**b) Construction of standard graph**
100 mg of Saxagliptin was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000µg/mL) 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10µg/ml). From this stock solution aliquots of 0.5 ml, 1.0 ml, 1.5 ml, 2.0 ml, 2.5 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 5, 10, 15, 20 and 25 µg/ml respectively. The absorbance of each concentration was measured at respective ($\lambda_{max}$) i.e., 213nm.

**Organoleptic properties:**
Take a small quantity of sample and spread it on the white paper and examine it visually for color, odour and texture.

**Determination of Saxagliptin Melting point**
The melting point of Saxagliptin was determined by capillary tube method according to the USP. A sufficient quantity of Saxagliptin powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Saxagliptin in the tube passed into liquid phase**.**

**Determination of Saxagliptin Solubility**
Determination of solubility of drug by visual observation. An excess quantity of Saxagliptin was taken separately and adds in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the Table.

**Preformulation Studies**
The objective of Preformulation studies is to develop an elegant, stable, effective and safe dosage form by establishing kinetic rate profile, compatibility with the other ingredients and establish physicochemical parameter of new drug substances. It is the determination of those physical and chemical properties, which are considered as important factor in development of a newer dosage form. A Preformulation study is a phase which is initiated once the new entity is introduced. It deals with studies of physical characteristics, analytical properties and its methods, chemical properties, and pharmaceutical behavior related to molecule. It is a very important aspect of developing medicines. This study gives idea about of new molecule properties, related to interactions with different solvent medium, ingredients used in developments of dosage form and some intrinsic chemical reactivity. At various stages of development, it is essential to understand the physicochemical characteristics of compounds. Data obtained from such studies forms an important fact for understanding the potential pharmacokinetics and pharmacological behavior of a drug in humans and animals. Such studies are useful during manufacture, transport and storage. The different parameters i.e. the measurement of solubility and dissolution rate. It also involves such as IR, UV, DSC, powder X-ray diffraction etc. according to the nature of compound. This study also gives idea about morphological characteristics of molecule or compounds by using SEM studies (Khan et al., 2013). Thus, in order to establish optimum condition for developing suitable drug delivery system Preformulation studies are important. In the present work, Preformulation studies were conducted on the drug Saxagliptin by adopting following methods.

**PREPARATION OF TRANSFERSOMES**

**Methods of preparation of transfersomes**
Soya-phosphatidylcholine, span 80 and Saxagliptin (5mg) were dissolved alcohol. Then solution was put in a round bottom flask. These were then dissolved by shaking. Thin film was then formed by keeping it in the rotator vaccum evaporator at 400ºC. Final traces of solvent are removed under vacuum. The deposited lipid film is hydrated with the appropriate buffer by rotation at 60 rpm for 1 hour at room temperature. The resulting vesicles are swollen for 2 hours at room temperature. The multilamellar lipid vesicles (MLV) are then sonicated at room temperature. This thin film was then hydrated by phosphate buffer saline to get the transferosome.

**Table: Formulation chart**

| S.No. | Formulation code | PC:S (mg) | Drug (mg) |
|---|---|---|---|
| 1 | F1 | 300:40 | 1000 |
| 2 | F2 | 600:80 | 1000 |
| 3 | F3 | 900:120 | 1000 |
| 4 | F4 | 300:40 | 1000 |
| 5 | F5 | 600:80 | 1000 |
| 6 | F6 | 900:120 | 1000 |

**SP=Span 80, PC=Phosphatidylcholine**

**CHARACTERIZATION OF TRANSFERSOMES**

**Particle Sizes, PDI, Zeta Potential:**

The mean particle length and polydispersity index (PDI), that's a degree of the distribution of transfersomes, was decided the usage of dynamic light scattering (Delta Nano C, Beckman counter), and Zeta capability becomes anticipated on the premise of electrophoretic mobility under an electric powered field, the use of zeta Sizer Nano ZS (Malvern Instruments, UK). Samples had been diluted with the distilled water before measurement and measure at a hard and fast angle of $165^0$c for the particle size and poly dispersity index (PDI) analysis. For the Zeta ability measurement, Samples have been diluted as 1:40 ratio with filtered water (v/v) before analysis. Average particle size, PDI, and zeta potential have been then measured in triplicate

**ENTRAPMENT EFFICIENCY**

The entrapment efficiency was determined by using direct method. Detergents are used to break the transfersomes membranes1 ml of 0.1% Triton X-100(Triton X-100 dissolved in phosphate buffer) was added to 0.1 ml Transfersomes preparations and made up to 5 ml with phosphate buffer then it was incubated at 37°C for 1.5 hrs to complete breakup of the transfersomes membrane and to release the entrapped material. The sample was filtered through a Millipore membrane filter (0.25) µm. and the filtrate was measured at 213nm for Saxagliptin. The amount of Saxagliptin was derived from the calibration curve.

**The entrapment efficiency is expressed as:**

$$\text{Percentage Entrapment Efficiency} = \frac{\text{Amount entrapped}}{\text{Total amount added}} \times 100$$

**Preparation of Saxagliptin-Loaded Transferosomal Oral Thin Films**

The solvent casting method was employed for the preparation of Saxagliptin-loaded transferosomal oral thin films with slight modifications. The required quantity of Carbopol was accurately weighed and slowly dispersed in the required quantity of purified water under continuous stirring to obtain a uniform polymeric dispersion. The concentration of Carbopol was varied according to the formulation design, ranging from 1.5% to 2.5%.

The prepared polymeric dispersion was allowed to hydrate under continuous stirring. Glycerol was incorporated as a plasticizer, followed by the addition of the required quantity of sucralose as a sweetening agent. The mixture was stirred using a magnetic stirrer at approximately 250 rpm for 12 h at room temperature to ensure uniform dispersion and complete hydration of the polymer.

The previously prepared Saxagliptin-loaded transferosomal dispersion was then added gradually to the hydrated polymeric solution with continuous stirring. The resulting mixture was homogenized using a high-speed homogenizer for approximately 5 min to achieve uniform distribution of the transferosomal vesicles throughout the film-forming solution. The formulation was subsequently allowed to stand overnight to facilitate complete homogenization and removal of entrapped air bubbles.

The deaerated film-forming solution was then uniformly cast onto a polyethylene terephthalate (PET) release liner using a calibrated film applicator. The cast film was allowed to dry at room temperature for approximately 24 h to facilitate gradual evaporation of the aqueous solvent and formation of a uniform film. After complete drying, the film was carefully peeled from the release liner and cut into the required dimensions corresponding to the desired dose of Saxagliptin.

The prepared Saxagliptin-loaded transferosomal oral thin films were individually wrapped in aluminium foil to protect them from environmental conditions and stored in a desiccator at room temperature until further characterization and evaluation.

**Table: Composition of Saxagliptin-loaded transferosomal films (each film contains 5 mg/mL of Saxagliptin)**

| Ingredients(mg) | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Polyvinyl alcohol (mg) | 50 | 100 | 150 | - | - | - |
| Maltodextrin (mg) | - | - | - | 50 | 100 | 150 |
| Carbopol (%) | 1.5 | 2 | 2.5 | 1.5 | 2 | 2.5 |
| D.W | qs | qs | qs | qs | qs | qs |
| Citric Acid (mg) | 10 | 10 | 10 | 10 | 10 | 10 |
| Cross Povidone (mg) | 15 | 15 | 15 | 15 | 15 | 15 |
| Mannitol (mg) | 15 | 15 | 15 | 15 | 15 | 15 |
| Total weight | 100 | 100 | 100 | 100 | 100 | 100 |

Drug = Gabapentin, PG = Propylene glycol

TRANSFERSOMES FILMS EVALUATIONS

***In-vitro* Unfolding Behavior of the Film:**

The prepared polymeric film was folded into 00 capsules. *In vitro* unfolding study was carried out in 900 mL of 0.1N HCL using USP type I apparatus at a constant temperature of 37 ± 5 ºC at 50 rpm to examine their unfolding behavior. Baskets were removed after an interval of 2 h,4 h and 8 h, respectively.

**Folding Endurance of Film:**

The folding endurance of the film was determined by repeatedly folding the film at the same place at three different positions until it breaks at the places of folding.

**Drug Content:**

Drug content was determined by dissolving the film in 100 mL 0.1N HCL and kept for 24 h and intermittently shaken to dissolve completely, and the absorbance was measured at 213nm using UV spectrophotometer.

**Swelling Index:**

The swelling properties of the film can be determined by placing the film in USP dissolution test apparatus I in 900 mL of 0.1 N HCL. The film should be removed periodically from the dissolution medium after draining free water by blotting, and film weight gain should be measured on an electronic balance. The Swelling index can be calculated by formula.

**Swelling index = (swelling wt of film-initial wt of film) / (initial wt of film) × 100**

***In-vitro* Dissolution Studies:**

*In-vitro* drug dissolution study was carried out in 900 mL 0.1N HCL using USP dissolution apparatus I (Paddle type) at 37 ± 0.5 ºC at 100 rpm. The film was inserted into the capsule and submerged in a dissolution medium. Aliquot of 5 mL was withdrawn at a particular time interval and analyzed using UV spectrophotometer at a given λ max 213 nm. Sink conditions should be maintained throughout experiment**.**

***IN VITRO* DRUG RELEASE**

**Diffusion Study for Saxagliptin Transfersomes**

The *in vitro* release of Saxagliptin from the transfersomes formulations were studied by open ended cylinder method. This diffusion cell apparatus consists of a glass tube with inner diameter of 2.5cm, open at both ends. One end tied with artificial membrane, which serves as a donor compartment. This study is performed for determining the permeation rate. The time needed to attain permeation flux at steady state and the information from *in vitro* studies was used to optimize the formulations. Studies of drug release from transfersomes gel formulation were performed using the *in vitro* diffusion method at $37^0$C, 100 rpm, within a period of 24hr. A weighed amount of prepared transfersomes gel formulation was poured in to the glass cell and diffused against phosphate buffer pH 6.4 as a diffusion medium. Aliquots were taken at regular intervals and analyzed

spectrophotometrically at 213nm using phosphate buffer pH 6.4 as blank.

**Application of Release Rate Kinetics to Dissolution Data:**
Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

**Zero order release rate kinetics:**
To study the zero–order release kinetics the release rate data ar e fitted to the following equation.

F = K o t

Where, 'F' is the drug release at time't', and 'K o ' is the zero order release rate constant. The plot of % drug release versus time is linear.

**First order release rate kinetics:** The release rate data are fitted to the following equation

Log (100-F) = kt. A plot of log cumulative percent of drug remaining to be released vs. time is plotted then it gives first order release.

**Higuchi release model:** To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

F = k t1/2

Where, 'k' is the Higuchi constant.

In higuchi model, a plot of % drug release versus square root of time is linear.

**Korsmeyer and Peppas release model:**
The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer-Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

M t / M ∞ = K t n

Where, M t / M ∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case I I transport), n=1; and for supercase II transport, n > 1. In this model, a plot of log (M t / M ∞) versus log (time) is linear.

**Fourier Transform Infrared (FTIR) spectroscopy:**
The formulations were subjected to FTIR studies to find out the possible interaction between the drug and the excipients during the time of preparation. FT IR analysis of the pure drug and optimized formulation were carried out using an FT IR spectrophotometer (Bruker FT-IR - GERMANY).

**Differential Scanning Calorimetry:**
The possibility of any interaction between the drug and the Excipients during preparation of SLN was assessed by carrying out thermal analysis of optimized formulation using DSC. DSC analysis was performed using Hitachi DSC 7020, on 5 to 15 mg samples. Samples were heated in sealed aluminum pan at a rate of 10°C/min conducted over a temperature range of 30 to 350°C under a nitrogen flow of 50 mL/min.

**SEM (Scanning Electron microscope) studies**
The surface morphology of the layered sample was examined by using SEM (Hitachi, Japan). The small amount of powder was manually dispersed onto a carbon tab (double adhesive carbon coated tape) adhered to an aluminum stubs. These sample stubs were coated with a thin layer (30Å) of gold by employing POLARON-E 3000 sputter coater. The samples were examined by SEM and photographed under various magnifications with direct data capture of the images onto a computer.

**Powder X-ray Diffraction (PXRD) Studies**
The prepared mixtures were also analyzed using X-ray powder diffractometer (PXRD) which confirms the formation of the new solid phases. The difference in the 2 theta lines confirms the formation of the new solid phases as no two solids have same 2 theta lines, thus revealing the formation of new solid phases. It also reveals the information about the crystal structure, chemical composition, and physical properties of the material and also helps in structural characterization. This technique detects changes in the crystal lattice and is therefore a powerful tool for studying polymorphism, pharmaceutical salts, and cocrystalline phases. Spectra of PXRD were taken on a sample stage Spinner PW3064. The samples were exposed to nickel filtrate Cukœ radiations (40 KV, 30 mA) and were scanned from 10° to 40°, 2Θ at a step size of 0.045° and step time of 0.5 s.

## RESULTS AND DISCUSSION:

**Organoleptic properties**

**Table: Organoleptic properties**

| S NO. | Properties | Observed Results |
|---|---|---|
| 1 | State | Solid |
| 2 | Colour | White |
| 3 | Odor | Odorless |
| **Melting point determination** | | |
| 4 | Reported Melting Point | Observed Melting Point |
| | 107°C to 110°C | 109.3 °C |

**Solubility studies**

**Table: Solubility studies of drug in different solvents**

| S NO. | Solvents | Solubility of Saxagliptin |
|---|---|---|
| 1 | Water | Freely soluble |
| 2 | Methanol | Moderately soluble |
| 3 | Acetonitrile | Sparingly soluble |
| 4 | Dimethyl formamide | Soluble |
| 5 | pH 6.8 Phosphate Buffer | Soluble |
| 6 | Ethanol | Soluble |

Initially the drug was tested by UV to know their significant absorption maximum which can be used for the diffusion study of the drug.

**Analysis of drug:**

**A. UV scans:**

The lambda max of Saxagliptin was found to be 213nm.

UV-vis spectra of Saxagliptin were measured from 200 to 800 nm and 213 nm was used as the optimum wavelength throughout the experiment.

**B. construction of calibration curve:**

**Table:** Standard graph of Saxagliptin

| Concentration (µg/ml) | Absorbance (at 213 nm) |
|---|---|
| 0 | 0 |
| 5 | 0.128 |
| 10 | 0.254 |
| 15 | 0.368 |
| 20 | 0.478 |
| 25 | 0.591 |

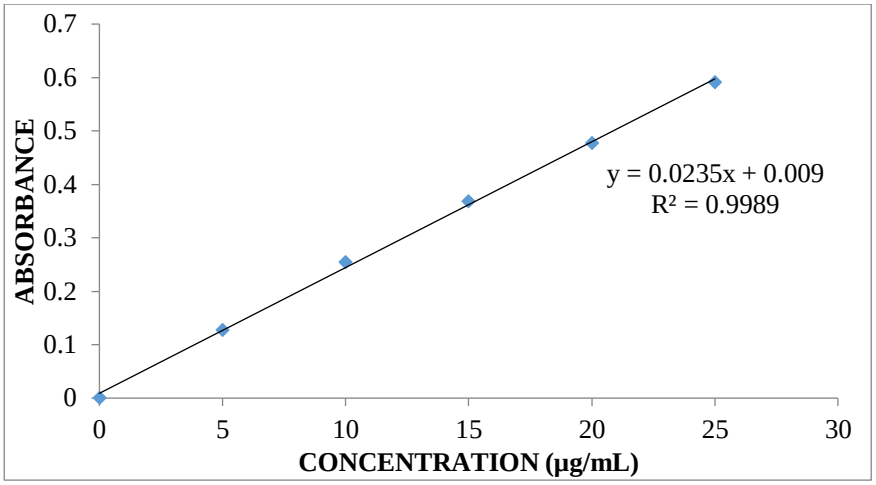



**Figure: Standard calibration curve of Saxagliptin**

Standard graph of Saxagliptin was plotted as per the procedure in experimental method and its linearity is shown in Table and Fig. The standard graph of Saxagliptin showed good linearity with $R^2$ of 0.9989, which indicates that it obeys "Beer-Lamberts" law.

**Characterization of Transfersomes:**

**Table:** Percentage yield, Drug Content, Entrapment Efficiency of all Transfersomes formulations

| FORMULATION | Particle Sizes | PDI | Zeta Potential | Entrapment Efficiency | Drug content |
|---|---|---|---|---|---|
| F1 | 541.31 | 0.540 | -15.12 | C | 89.25 |
| F2 | 425.19 | 0.312 | -19.56 | 91.30 | 92.15 |
| F3 | 305.98 | 0.201 | -33.01 | 92.09 | 97.65 |
| F4 | 621.87 | 0.475 | -14.20 | 85.90 | 86.14 |
| F5 | 539.09 | 0.356 | -21.61 | 90.53 | 90.75 |
| F6 | 482.10 | 0.315 | -22.85 | 93.18 | 93.69 |

Transfersomes were subjected in to laser particle counter (L.P.C) for characterizing size distribution of transfersomes. Its shows that the particle size range 200-700nm, 200-600nm, and 200-700 nm range for Saxagliptin transfersomes of 1:1, 1:2, and 1:3 ratios respectively. It is shown in Table.

The transfersomes were subjected to microscopic examination (S.E.M) for characterizing size and shape of the transfersomes. Microscopic examination revealed, spherical small unit-lamellar vesicles size.

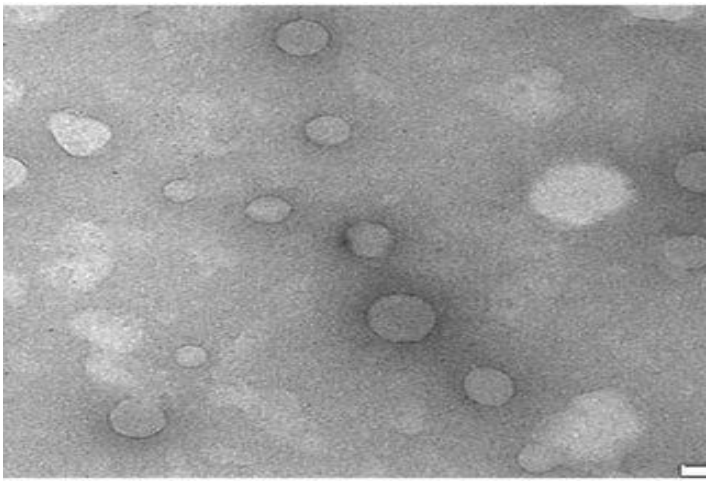


**Fig: SEM Photograph of Saxagliptin Transfersomes (Formulation-3)**

**ENTRAPMENT EFFICIENCY**

The formulation variables were altered and optimized to obtain the transfersomes with maximum drug entrapment, desired transferosomal size and stability. Increased in

the lipid concentration compared to drug entrapment with increase in quantity of lipid a greater number of transfersomes per ml of the transferosomal dispersion were formed, resulting in to an increased percent drug entrapment.

However, further increase in the lipid concentration had no proportionateincrease in percentage drug entrapment due to approaching system saturation.

Here 1:1, 1:2, and 1:3 ratios were used to prepare transfersomes. The percentage entrapment of transfersomes was found to be F1-87.43, F2- 91.30, F3-92.09, F4-85.90, F5-90.53and, F6-93.18 respectively and 1:3 ratio found to have more entrapment efficiency compared to other formulations. It is shown in Table.

Increasing the sonication time resulted in to reduction in percent drug entrapment; the decrease in percent drug entrapment is due to leakage of the drug during sonication.

Sonication brings about size reduction by breaking large transfersomes to smaller ones and in doing so, leakage of small quantities of drug from the transfersomes occur. Hence sonication time was optimized to 30 min, and further reduction in the size by increasing sonication time was not attempted.

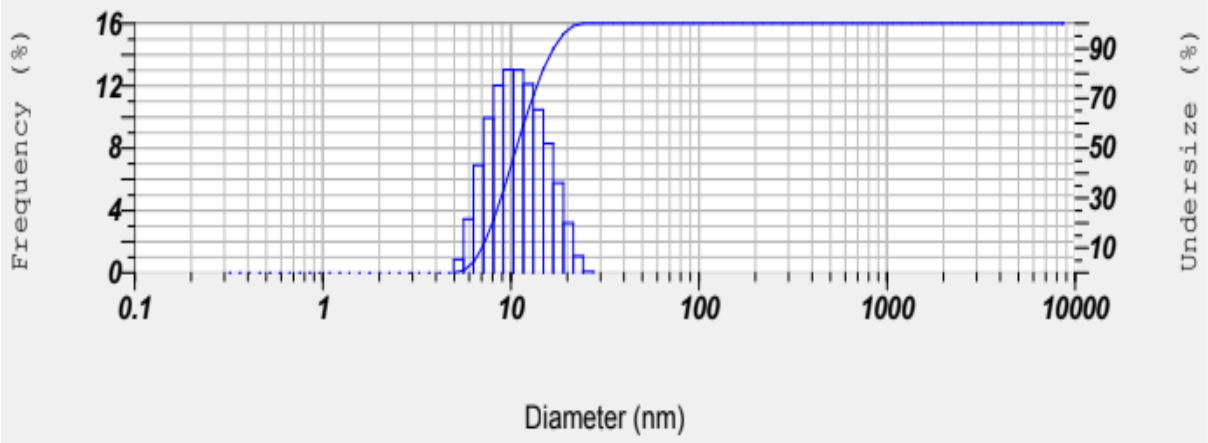



**Fig: Particle size of F3 Formulation**

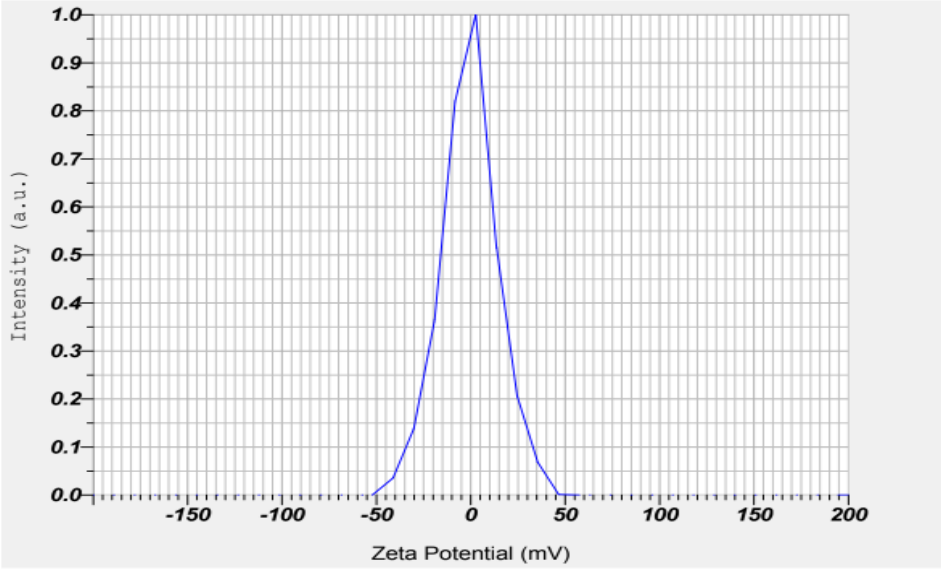



**Fig: Zeta Potential of F3 Formulation**

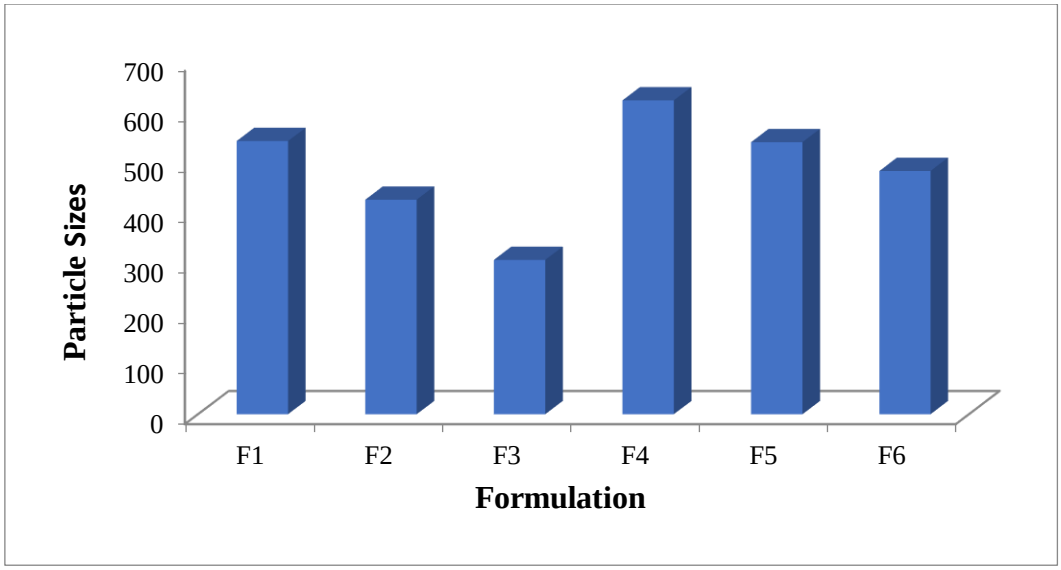



**Fig: Particles size graph of Saxagliptin Transfersomes (All Formulation)**

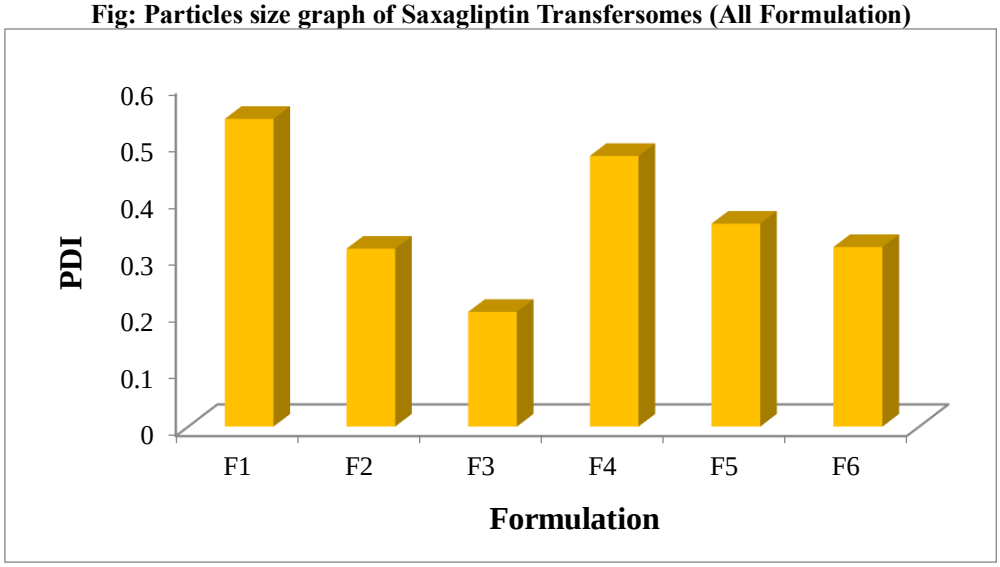



**Fig: PDI graph of Saxagliptin Transfersomes (All Formulation)**

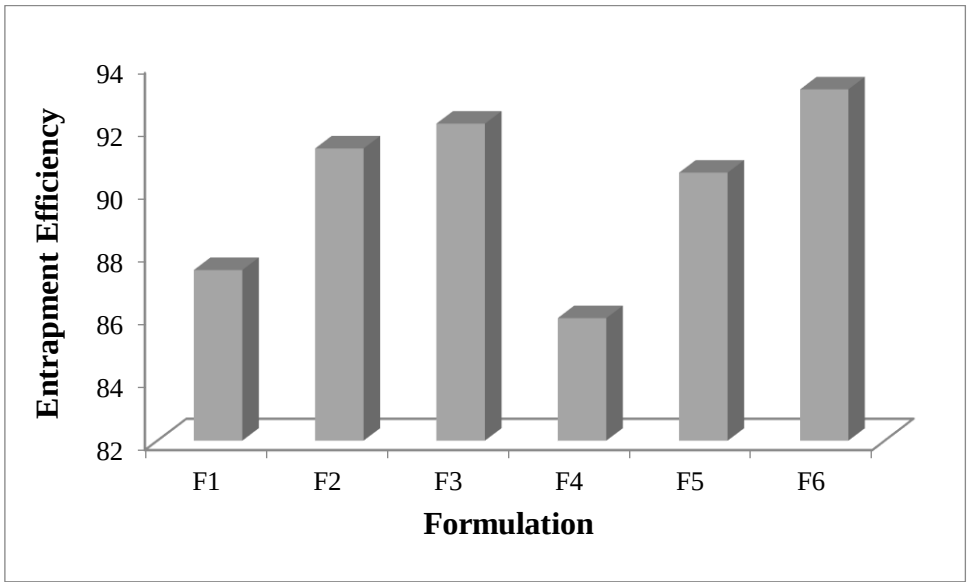



**Fig: Entrapment efficiency graph of Saxagliptin Transfersomes (All Formulation)**

**Table: *In vitro* dissolution studies of F1-F6 Transfersomes formulations in percentage**

| Time (hour) | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 1 | 18.42 | 30.14 | 48.14 | 31.15 | 12.45 | 10.18 |
| 2 | 20.92 | 27.90 | 53.06 | 41.03 | 20.43 | 18.14 |
| 4 | 24.86 | 36.98 | 68.19 | 53.19 | 36.96 | 25.94 |
| 6 | 40.78 | 47.56 | 71.47 | 65.42 | 53.09 | 38.37 |
| 8 | 45.05 | 54.71 | 79.99 | 69.71 | 62.14 | 45.19 |
| 10 | 50.11 | 65.98 | 86.03 | 74.86 | 70.27 | 52.24 |
| 12 | 54.59 | 70.35 | 90.38 | 79.90 | 73.19 | 68.83 |
| 18 | 58.62 | 89.99 | 96.60 | 84.61 | 78.34 | 70.14 |
| 24 | 71.14 | 92.47 | 98.12 | 87.55 | 85.15 | 77.72 |

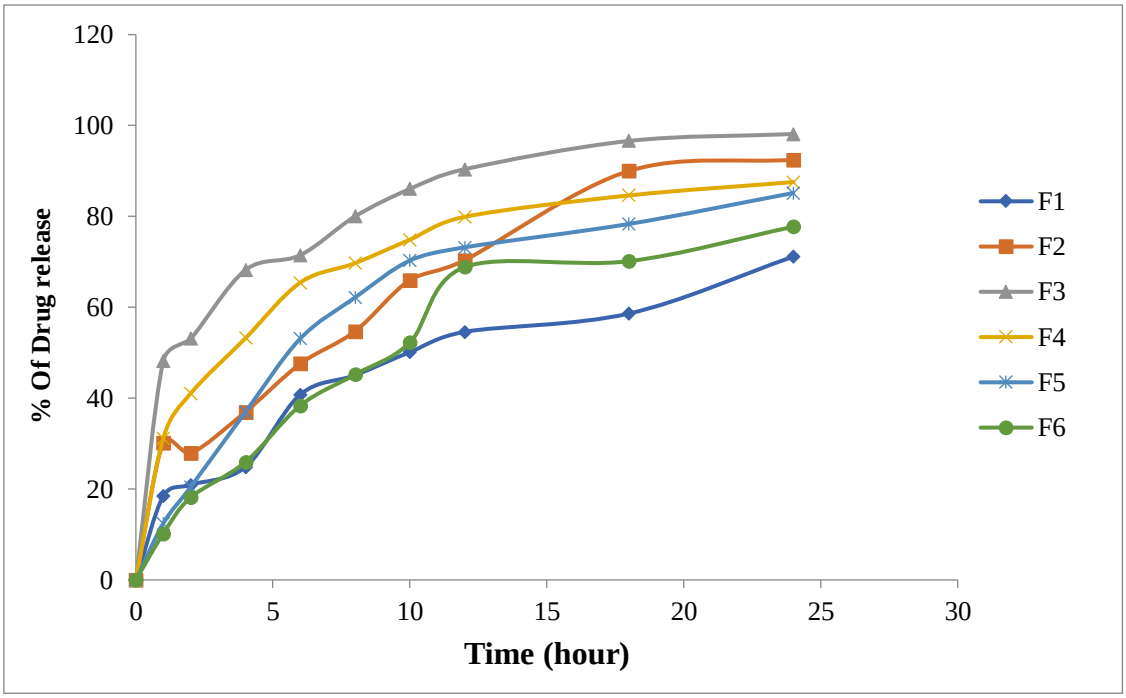



**Fig: *In vitro* dissolution studies of F1-F6 Transfersomes formulations in percentage**

*In vitro* drug release study of the selected Transfersomes (F1, F2, F3, F4, F5 and F6) was carried out. The Transfersomes exhibited 24 hours sustained release pattern. Fifty percent of the incorporated amount of drugs was found to be released during the first 2 hours, followed by a slowed release of 98.12% of the drug up to 24 hours. The Saxagliptin Transfersomes F3 showed a better release profile of 98.12 % by 24 hours. The prolonged release at 24 hours can be attributed to slow diffusion of drug from lipid matrix. The results of *in vitro* drug release are depicted in above Table.

**_IN-VITRO_ TESTS OF FILM:**

**TABLE: *IN-VITRO* EVALUATION RESULTS FOR ALL FORMULATIONS:**

| Code | Visual Appearance | *In vitro* unfolding behavior (min) Mean ± S.D (n=3) | % Drug content Mean ± S.D (n=3) | Folding endurance (times ± S.D) (n=3) | Swelling index (%) Mean ± S.D (n=3) |
|---|---|---|---|---|---|
| **F1** | Transparent | 15±0.57 | 98.8±0.23 | 179±0.26 | 104.1 ±0.16 |
| **F2** | Transparent | 14±0.12 | 96.3±0.69 | 180±0.14 | 95.3 ±0.28 |
| **F3** | Transparent | 17±0.36 | 99.1±0.46 | 181±0.62 | 98.1 ±0.30 |
| **F4** | Transparent | 14±0.47 | 97.9±0.16 | 178±0.96 | 100.0 ±0.41 |
| **F5** | Transparent | 15±0.61 | 98.3±0.93 | 178±0.40 | 99.9 ±0.65 |
| **F6** | Transparent | 12±0.92 | 97.1±0.77 | 184±0.62 | 98.2 ±0.44 |

***In- Vitro*-dissolution studies**

Dissolution profiles from films of Saxagliptin were carried out in USP dissolution apparatus-II. The results are reported in the table.

**Table: *In vitro* drug releases for F1 to F6 formulations**

| TIME (H) | CUMULATIVE PERCENT DRUG RELEASED | | | | | |
|---|---|---|---|---|---|---|
| | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** |
| 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 0.5 | 35.6 | 15.9 | 25.6 | 33.60 | 17.86 | 10.31 |
| 1 | 52.8 | 25.6 | 36.7 | 38.19 | 20.62 | 15.10 |
| 2 | 69.4 | 35.6 | 48.5 | 49.52 | 27.31 | 22.68 |
| 3 | 78.3 | 52.8 | 52.3 | 53.96 | 30.53 | 30.78 |
| 4 | 88.4 | 69.4 | 69.4 | 60.37 | 37.94 | 35.48 |
| 5 | 96.6 | 78.3 | 78.4 | 67.82 | 48.36 | 41.94 |
| 6 | | 88.4 | 87.3 | 72.65 | 53.78 | 46.87 |
| 7 | | 96.6 | 92.5 | 79.29 | 60.33 | 52.10 |
| 8 | | | 95.2 | 81.66 | 63.39 | 60.87 |
| 9 | | | 98.3 | 84.25 | 67.59 | 65.85 |
| 10 | | | | 90.33 | 71.48 | 70.32 |
| 11 | | | | 96.21 | 76.55 | 73.92 |
| 12 | | | | 99.10 | 84.95 | 79.40 |

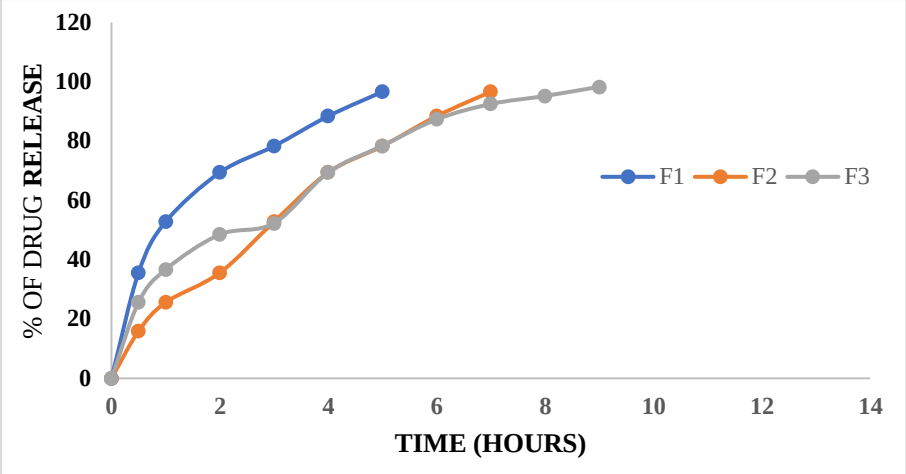



**Figure 8.6: Comparison curve of *Invitro* drug release for F1- F3 formulations**

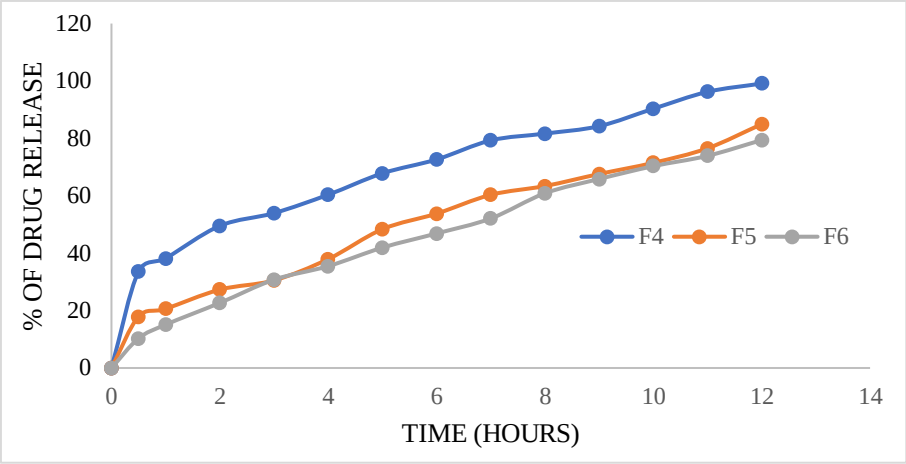



**Figure 8.7: Comparison curve of *Invitro* drug release for F4- F6 formulations**

*Invitro* dissolution study of formulations F1-F6 shown good drug release respectively up to 12hours. Among the all formulations F4 showed good dissolution property. F4 batch contain Maltodextrin and Carbopol as film forming polymer.

**Table: Release kinetics of optimized formulation**

| CUMULATIVE (%) RELEASE Q | TIME ( T ) | ROOT (T) | LOG( %) RELEASE | LOG ( T ) | LOG (%) REMAIN | RELEASE RATE (CUMULATIVE % RELEASE / t) | 1/CUM% RELEASE | PEPPAS log Q/100 | % Drug Remaining | Q01/3 | Qt1/3 | Q01/3-Qt1/3 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | | | 2.000 | | | | 100 | 4.642 | 4.642 | 0.000 |
| 33.6 | 0.5 | 0.707 | 1.526 | -0.301 | 1.822 | 67.200 | 0.0298 | -0.474 | 66.4 | 4.642 | 4.049 | 0.592 |
| 38.19 | 1 | 1.000 | 1.582 | 0.000 | 1.791 | 38.190 | 0.0262 | -0.418 | 61.81 | 4.642 | 3.954 | 0.688 |
| 49.52 | 2 | 1.414 | 1.695 | 0.301 | 1.703 | 24.760 | 0.0202 | -0.305 | 50.48 | 4.642 | 3.696 | 0.946 |
| 53.96 | 3 | 1.732 | 1.732 | 0.477 | 1.663 | 17.987 | 0.0185 | -0.268 | 46.04 | 4.642 | 3.584 | 1.058 |
| 60.37 | 4 | 2.000 | 1.781 | 0.602 | 1.598 | 15.093 | 0.0166 | -0.219 | 39.63 | 4.642 | 3.409 | 1.232 |
| 67.82 | 5 | 2.236 | 1.831 | 0.699 | 1.508 | 13.564 | 0.0147 | -0.169 | 32.18 | 4.642 | 3.181 | 1.461 |
| 72.65 | 6 | 2.449 | 1.861 | 0.778 | 1.437 | 12.108 | 0.0138 | -0.139 | 27.35 | 4.642 | 3.013 | 1.629 |
| 79.29 | 7 | 2.646 | 1.899 | 0.845 | 1.316 | 11.327 | 0.0126 | -0.101 | 20.71 | 4.642 | 2.746 | 1.895 |
| 81.66 | 8 | 2.828 | 1.912 | 0.903 | 1.263 | 10.208 | 0.0122 | -0.088 | 18.34 | 4.642 | 2.637 | 2.004 |
| 84.25 | 9 | 3.000 | 1.926 | 0.954 | 1.197 | 9.361 | 0.0119 | -0.074 | 15.75 | 4.642 | 2.507 | 2.135 |
| 90.33 | 10 | 3.162 | 1.956 | 1.000 | 0.985 | 9.033 | 0.0111 | -0.044 | 9.67 | 4.642 | 2.130 | 2.511 |
| 96.21 | 11 | 3.317 | 1.983 | 1.041 | 0.579 | 8.746 | 0.0104 | -0.017 | 3.79 | 4.642 | 1.559 | 3.082 |
| 99.1 | 12 | 3.464 | 1.996 | 1.079 | -0.046 | 8.258 | 0.0101 | -0.004 | 0.9 | 4.642 | 0.965 | 3.676 |

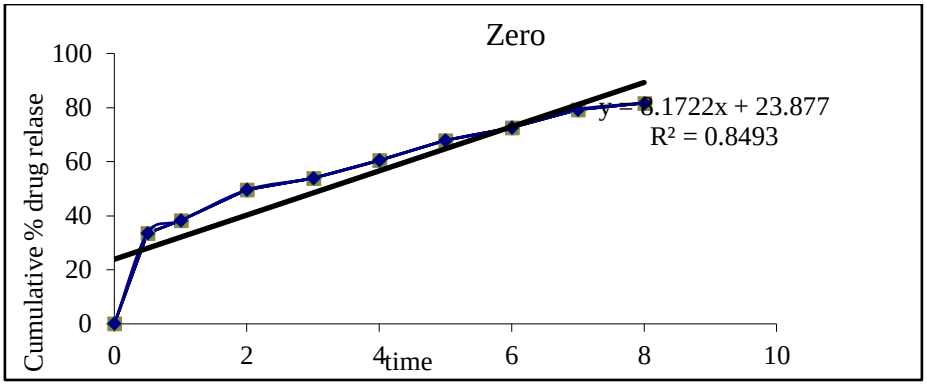



**Figure: Zero order release kinetics**

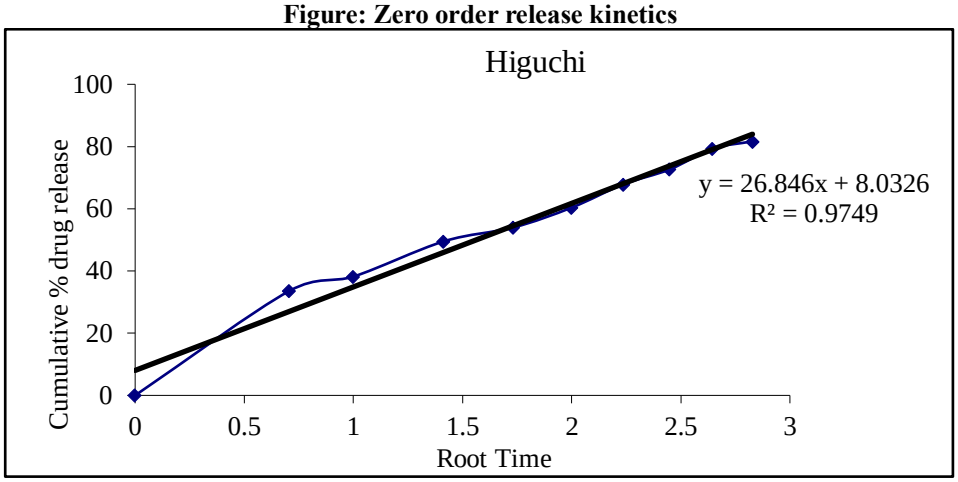



**Figure: Higuchi release kinetics**

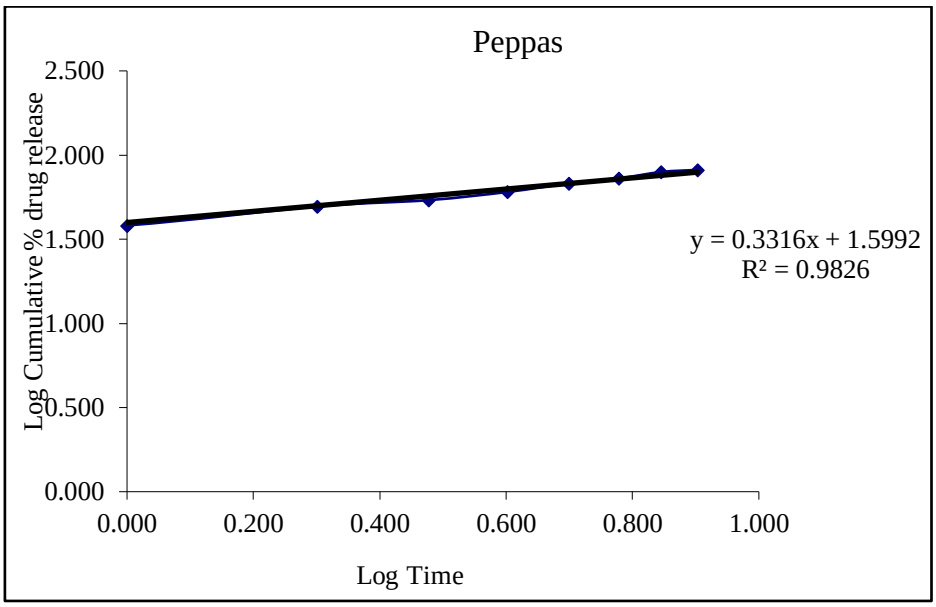



**Figure: Peppas release kinetics**

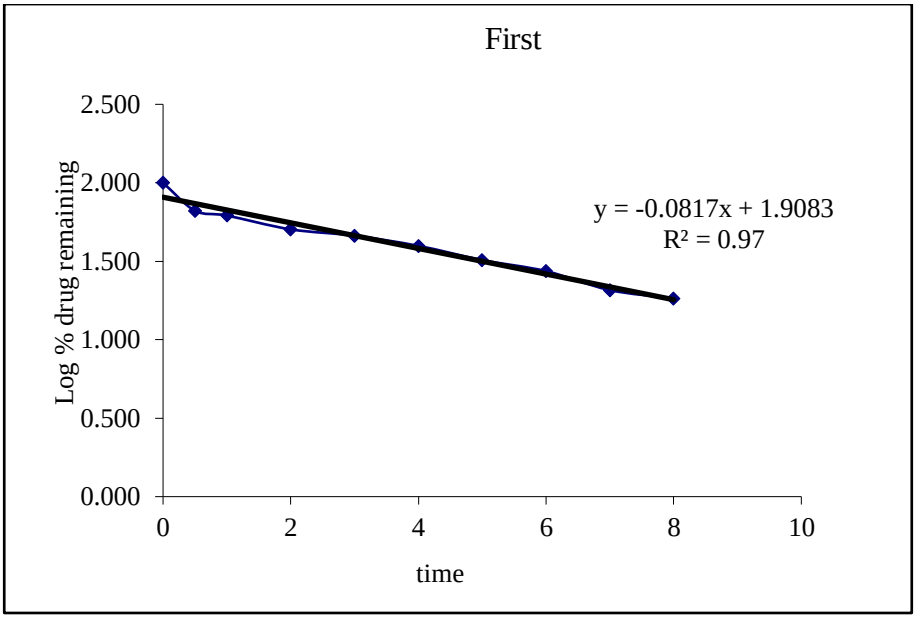



**Figure: First order release kinetics**

The prepared F4 optimized were subjected to the drug release kinetics and release mechanism. The formulations were studied by fitting the drug release time profile with the various equations such as Zero order, First order, Higuchi and Korsmeyer pappas.

The optimized formulation F4 was analyzed for the drug release mechanism. The best correlation coefficient value (0.9826) indicates the best release mechanism (Peppas release).

**FTIR**

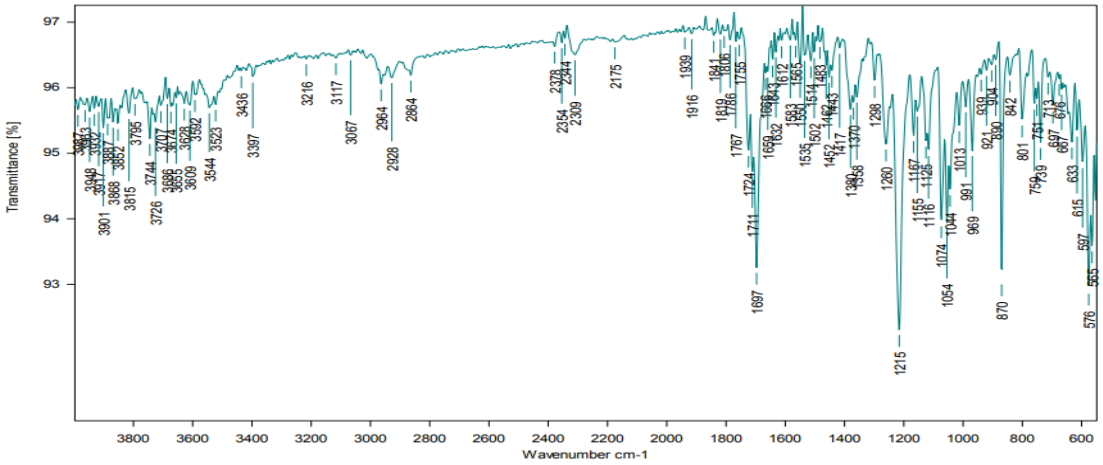



**Figure: Saxagliptin Pure drug FTIR**

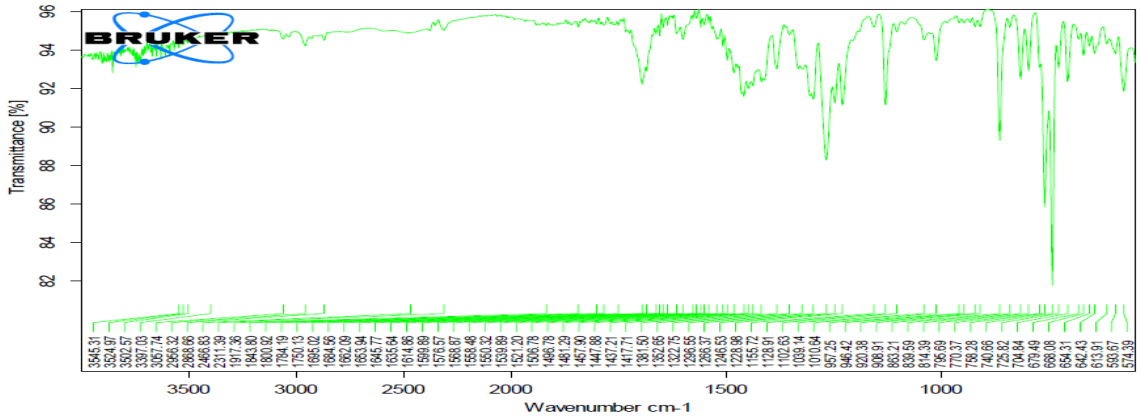



**Figure: Saxagliptin F4 optimized Film FTIR**

Infrared studies were carried out to confirm the compatibility between the lipid, drug, and selected excipients. From the spectra it was observed that there was no major shifting, as well as, no loss of functional peaks between the spectra of the drug and transfersomes gel. This indicated no interaction between the drug and other excipients.

**DIFFERENTIAL SCANNING CALORIMETRY**

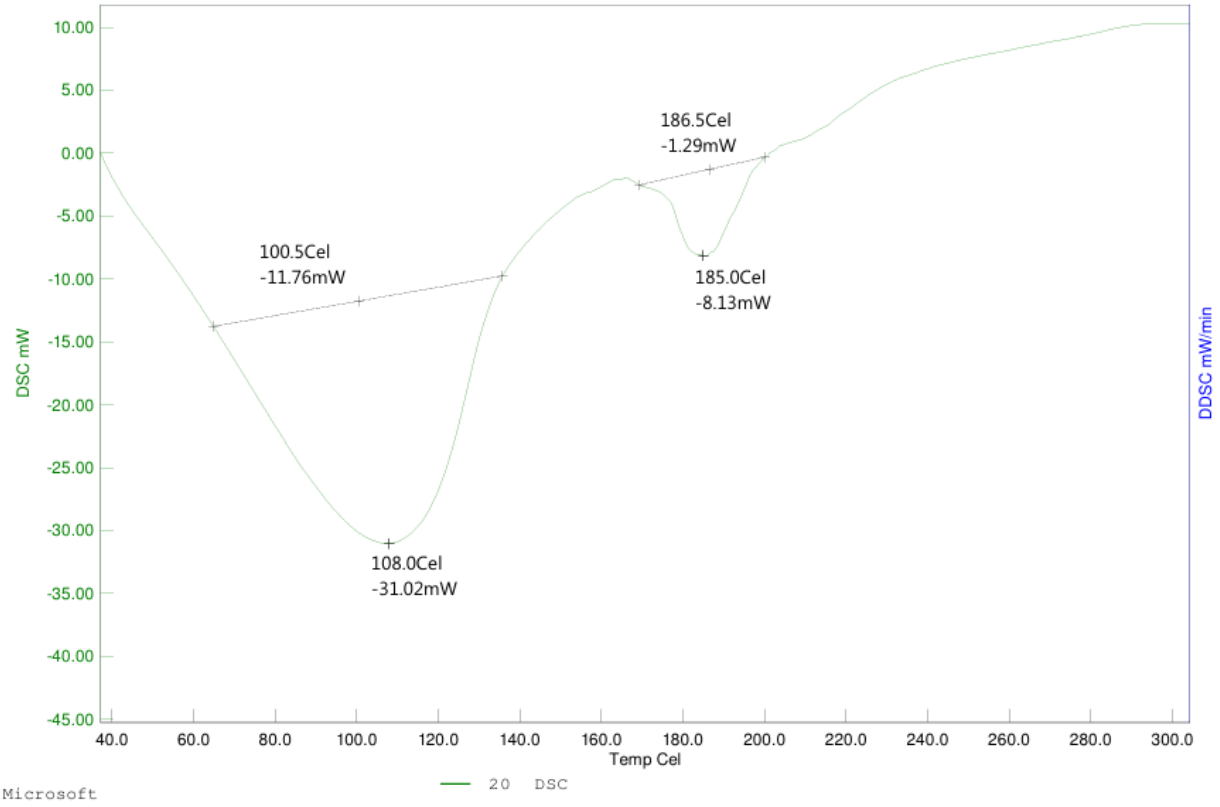



**Figure: Saxagliptin Pure drug DSC**

**XRD**

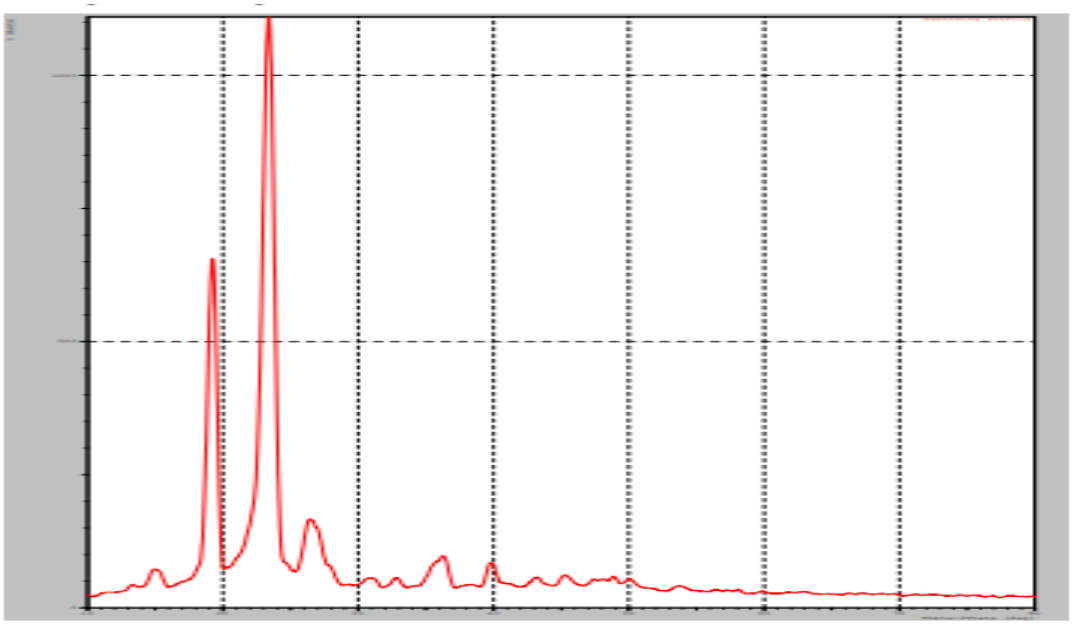


**Figure: Saxagliptin F4 optimized formulation**

**CONCLUSION:**

The present study was undertaken to formulate and evaluate Saxagliptin-loaded transferosomal oral thin

films. The prepared formulations were evaluated for physicochemical characteristics, entrapment efficiency, drug content, particle size, polydispersity index (PDI), zeta potential, in vitro unfolding behavior, folding endurance, swelling index, *in vitro* drug release, and drug–excipient compatibility. The UV spectrophotometric analysis of Saxagliptin showed a maximum absorption wavelength ((\lambda_{\max})) of 213 nm. The calibration curve exhibited good linearity, with a correlation coefficient ((R^2)) of 0.9989. Among the transferosomal formulations, F3 exhibited a particle size of 305.98 nm, a PDI of 0.201, an entrapment efficiency of 92.09%, and a drug content of 97.65%. The *in vitro* drug release study of the transferosomal dispersion showed a cumulative drug release of 98.12% at 24 hours for F3. The oral thin film formulations exhibited transparent appearance, satisfactory drug content, folding endurance, and swelling characteristics. Among the evaluated film formulations, F4 demonstrated a cumulative drug release of 99.10% at 12 hours. The release kinetic analysis of F4 showed the highest reported correlation coefficient for the Korsmeyer–Peppas model ((R^2 = 0.9826)), suggesting that the drug release profile was best fitted by this model among the models evaluated. FTIR analysis indicated that no major changes in the characteristic functional group peaks were observed between the pure drug and the optimized formulation, suggesting the absence of significant drug–excipient interactions. Overall, the study demonstrated the feasibility of developing Saxagliptin-loaded transferosomal oral thin films with sustained in vitro drug release and satisfactory evaluated formulation characteristics.

**REFERANCE:**


1. Remington 'The science and practice of pharmacy' 20th edition, VOLI: 903-905, 2001.
2. Y.W. Chien, Drug Development And Industrial Pharmacy 1983, 9:447-520, 1291-1330.
3. F. Teewes, Drug Development And Industrial Pharmacy 1983,9: 1331-1357.
4. J. M. Class., R.L.Stephan and S. C. Jacobson, Int. j. Dermatol, 19:519.
5. H.Sezahi and M. Hashida, Crc, Critical Reviews In "Therapeutic drug Carrier Systems", 1984, 1:1.
6. T.A Horbett, B.D Ratner, T.Kost and M.Sigh In " Recent Advances In Drug Delivery System" Plenum Press, New york. 1984, 209-220.
7. Joseph R. Robinson., Vincent H.L. Lee, "Controllrd Drug Delivery", 2nd edition, revised and expanded, 1987: 596-597.
8. S. P. Vyas, R.K. Khar. "Targeted and Controlled Druig Delivery Novel Carrier Systems", I edition, CBS Publishers, New Delhi, 2002:39-40, 42-46.
9. Welling pG, Dobrinska MR, In Robinson JR, Lee VHL, eds:"Controlled Drug Delivery", II edition, Marcel Dekker, Newyork.1987: 253.
10. Gregoriadis G, "Targeting of drugs", Nature. 1977: 407-411.
11. Gregoriadis G. In Gregoriadis C, Senior J, Trout A, eds: "Targeting ofdrugs", Plenum, New york. 1982: 155.
12. Tretise A, D.M. Brahmankhar, Sunil B. Jaiswal, "Biopharmaceutics and Pharmacokinetics", 2001: 360-363.
13. Wirth M, Hamilton G and Gabar F, "J.Drug Target", 6, 1998: 95-104.
14. Subheet Jain, Dipankar Bhadra, N. K. Jain. (2001)"Advances in Controlled and Novel Drug Delivery" 1st edition, CBS Publishers, New Delhi, 427.
15. Christophers, e.; Walff, H. H; Laurence, E.B. (1974) "The formation of epidermal cell columns", J. Invest. Dermatol., 62: 556-564.
16. Christophers, E.91988) In: The Skin of vertebrates, Spearman, R. I.C. ; Riley, P.A; (Eds.0, Academic Press, London, 137-139.
17. Juliano, R. L. (1980) "Drug Delivery Systems". Oxford universitypress. New york, 15.
18. Prausnitz, M. R. ; Allen, M. G. (1998) J. Pharm. Sci., 87(8): 925
19. Chowdary, K. P. R.; Naidu, R. A. S. (1995)"Transdremal drug delivery; areview of current status", Indian Drugs, 32(9): 414-422.
20. Barry, B. W. (1991)"LPP theory of Skin penetration enhancement", J.Control. Rel., 15: 237-248.
21.