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FORMULATION DEVELOPMENT AND EVALUATION OF TYROSINE KINASE INHIBITOR IMATINIB LOADED ORGANOGEL

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ABSTRACT

This study explores the development and evaluation of a transdermal delivery system for Imatinib mesylate using a pluronic lecithin organogel (PLO). Imatinib, a tyrosine kinase inhibitor used in treating chronic myeloid leukemia and gastrointestinal stromal tumors, suffers from poor oral bioavailability and gastrointestinal side effects. To address these issues, reverse micelles were formulated using lecithin in isopropyl myristate, then transformed into a gel using Pluronic F127. The resulting PLO was characterized for physicochemical properties including pH, viscosity, drug content, spread ability, and in vitro drug release. The optimized formulation showed homogeneity, ideal pH (6.6), appropriate gel strength, high drug content (90.83%), and sustained release over 8 hours (46.02%). Morphological studies confirmed Nano-sized, spherical particles with an encapsulation efficiency of 47%. This organogel system shows promise as a stable, effective, and patient-friendly alternative for topical Imatinib delivery in cancer therapy.

Keywords: *Imatinib, Organogel, Transdermal Delivery, Reverse Micelles, Controlled Release.*

1. INTRODUCTION

Cancer remains one of the leading causes of morbidity and mortality globally, with chronic myeloid leukemia (CML) being a particularly prevalent haematological malignancy. Imatinib mesylate, a first-generation tyrosine kinase inhibitor (TKI), revolutionized the treatment of CML and gastrointestinal stromal tumors (GISTs) due to its targeted inhibition of the BCR-ABL oncoprotein **(Druker et al., 2001).** Despite its clinical success, oral administration of imatinib is associated with systemic side effects, variable bioavailability, and poor patient compliance due to gastrointestinal disturbances **(Peng et al., 2004)**. These limitations highlight the need for alternative delivery systems to enhance therapeutic efficacy and reduce adverse effects. Organogels, semi-solid systems composed of an organic liquid phase entrapped in a three-dimensional network formed by gelators, have gained attention as promising carriers for hydrophobic drugs **(Fang et al., 2008).** Their thermo-reversible nature, ease of preparation, and ability to enhance skin permeability make them ideal for transdermal or topical drug delivery. Incorporating imatinib into an organogel could provide a localized and sustained release formulation, minimizing systemic exposure while maintaining therapeutic levels at the target site. This study aims to develop and evaluate an imatinib-loaded organogel with an emphasis on physicochemical characterization, drug release behaviour, and stability. The goal is to optimize the formulation for improved drug delivery and patient outcomes while expanding the application of organogels as a viable platform for TKI administration.

2. MATERIAL AND METHOD

2.1 Preformulation studies

Preformulation studies involve physical, chemical and biological characterization of the new drug substances in order to develop stable, safe and effective dosage form. Preformulation testing encompasses all studies enacted on drug compound in order to produce useful information for subsequent formulation of a stable and bio-pharmaceutically suitable drug dosage form.

2.2 Melting point

The melting point of the drug was determined by capillary tube method. Thin walled capillary melting point tubes are used to hold the samples. The tube was sealed at one end using Bunsen burner and the open end was filled with imatinib mesylate. The drug filled capillary tube was placed in the melting point apparatus and the temperature was raised gradually. The temperature at which drug started to melt was noted.

2.3 Solubility study

Saturation solubility of pure drug was tested in water, phosphate buffer pH 7.4 and isopropyl myristate. An excess amount of drug was added to 10 ml of each solvent separately and shaken in a water bath shaker for 24 h at room temperature. The mixture was then filtered using 0.22 µm filter and the filtrate was suitably diluted. The absorbance of the solution was measured at 289 nm using a UV spectrophotometer (UV-1650 PC; Shimadzu Corporation) to determine the solubility of imatinib mesylate.

2.4 Determination of lambda max

To facilitate the spectrophotometric analysis of imatinib mesylate, a series of stock solutions were prepared. Initially, Stock Solution A was prepared by dissolving 100 mg of imatinib mesylate in 100 mL of phosphate buffer (pH 7.4), resulting in a concentration of 1000 µg/mL. From this, 10 mL of Stock Solution A was further diluted to 100 mL with the same buffer to obtain Stock Solution B, with a concentration of 100 µg/mL. Subsequently, 1 mL of Stock Solution B was diluted to 10 mL to yield Stock Solution C, having a final

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concentration of 10 µg/mL. Stock Solution C was then subjected to UV-Visible spectrophotometric analysis using a double beam spectrophotometer. The solution was scanned in spectrum mode across a wavelength range of 200 to 400 nm to determine the analytical wavelength (λmax) for imatinib mesylate, which would be used for further quantitative analysis.

2.5 Construction of calibration curve

2.5.1 Standard curve of imatinib mesylate in phospahte buffer ph 7.4

Standard stock solutions of imatinib mesylate were prepared by dissolving 100 mg of imatinib mesylate in 100 ml of phosphate buffer pH 7.4. 1 ml of this stock solution was diluted to 10 ml by using the same solvent to produce a concentration range of 100 mcg/ml. From this stock solution (100 mcg/ml) further dilutions were made to produce 5, 10, 15, 20 and 25 mcg/ml. These solutions were analysed in the UV spectrometer at 289nm. A calibration curve was plotted with the concentration on the x-axis and the absorbance at y-axis. The regression coefficient was calculated.

2.6 FT-IR Spectroscopy

To verify the possible interaction between drug and excipients, FT-IR study was conducted. FT-IR spectrum of pure drug (imatinib mesylate), surfactant (lecithin) and the mixture of drug and excipients were performed with FT-IR spectrophotometer using KBr pellets disc method. The sample were scanned over the range of 4000-400cm-1

2.7 Determination of CMC (Critical Micellar Concentration)

The CMC of the lecithin (surfactant) in isopropyl myristate was determined by drop count method using stalagmometer. The clean and dry stalagmometer is placed in the vertical position and held fixed. The number of drops between the uppermost (A) on the upper stem and lowermost (B) on the lower stem which fixes the volume (V) of the liquid is counted. The different concentration of stock solution 0.4%(v/v), 0.8%(v/v), 1.2%(v/v), 1.6%(v/v) and 2% (v/v) of lecithin in isopropyl myristate was prepared .The liquid was sucked above mark A and the number of drops of liquid falls between the marks A and B was counted. The surface tension of different concentration was determined using the formula,

$$\gamma 2 = \frac{n2\rho 1}{n1\rho 2} \times \gamma 1$$

γ2 = surface tension of the liquid to be determined γ1 = surface tension of IPM
n1= no of drops of IPM n2 = no of drops of water ρ1 = density of IPM
ρ2 = density of waterA graph of concentration (%v/v) v/s surface tension (dynes/cm) was plotted and the critical micellar concentration of the surfactant was determined **(Zhang et al., 2004; Vrignaud et al., 2012).**

2.8 Optimization of lecithin concentration

Various concentrations of lecithin in isopropyl myristate above the CMC were considered for optimizing reverse micelles. Different concentrations [Listed in Table 1] were prepared by adding measured quantity of lecithin into IPM under continuous stirring. Measured quantity of distilled water was added into lecithin IPM solution and stirred for 1 hr and the temperature was maintained at 80°C throughout the process to obtain uniform and stable reverse micelles. Reverse micelles formed was confirmed when lecithin-isopropyl myristate solution is transparent, homogenous and stable **(Mackeben and Muller, 2000).**

Table 1: Optimization of Lecithin concentration

FORMULATION CODE	COMPOSITION		
	IPM(ml)	Lecithin(ml)	WATER(ml)

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F1	10	1	0.3
F2	10	2	0.3
F3	10	4	0.3

2.9 Preparation of imatinib mesylate loaded reverse micelles

From the above optimization process, formulation containing 10%(v/v) lecithin in IPM was used to load the drug. 10 mg of imatinib mesylate was accurately weighed and dissolved in 0.3 ml of distilled water. This solution was added by means of microlitre syringe to the lecithin IPM solution and stirred for about 2 hrs to achieve complete micellar solubilization of the drug using magnetic stirrer. The temperature was maintained at 80°C throughout the process **(Lyu and Wang, 2000).**

2.10 Characterization of the imatinib mesylate loaded reverse micelles

2.10.1 Determination of morphology

The morphology of the prepared imatinib mesylate loaded reverse micelles was studied by observing under Phase Contrast Microscopy. It is an optical microscopy technique that converts phase shifts in light passing through a transparent specimen to brightness changes in the image. The morphology of the prepared reverse micelles was determined by placing the sample in slide and focusing at 100X magnification.

2.10.2 Particle size determination and polydispersity indexi (pdi) by zetasizer

The mean particle size and PDI of the prepared reverse micelles was determined by Zetasizer (nano ZS90, Malvern instruments) at 25˚ C. The samples were kept in the polystyrene cuvette and the readings were found out at the fixed angle.

2.10.3 Drug encapsulation efficiency

Encapsulation efficiency was determined by centrifugation method. Imatinb mesylate loaded reverse micelles were centrifuged at 13,000 rpm for 10 mins at controlled temperature using ultra centrifuge. The supernatant was recovered using micropipette and analyzed by UV Spectrophotometer at 289 nm. The percentage of the drug encapsulated was calculated by using the formula,

$$EE = \frac{\text{Amount of encapsulated imatinib mesylate}}{\text{Total amount of imatinb mesylate added}} \times 100$$

2.10.4 Transmission electron microscopy

TEM provides morphologic, compositional and crystallographic information of the nanoparticles. The optimized formulation containing imatininb mesylate loaded reverse micelles was analyzed for its surface morphology. One drop of imatinib mesylate loaded reverse micelles was deposited on a film-coated copper grid and it was stained with one drop of 2% (w/v) aqueous solution of phosphotungstic acid. Excess of solution was drained off with a filter paper and then grid was allowed to dry for contrast enhancement. The sample was then examined by Transmission Electron Microscopy.

2.11 Optimization of concentration of pluronic f127

The optimized imatinb mesylate loaded reverse micelle [F1] was converted in to organogel using pluronic F127 as stabilizer. Various concentration of pluronic F127 such as 10%.20% and 30% w/v was used to obtain gel with suitable characteristics. Weighed amount of pluronic F127 was dispersed in cold water and the mixture

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was kept overnight at 2-4°C in a refrigerator for the complete dissolution of pluronic F127. It was then observed for gelling behavior.

2.12 Preparation of the pluronic lecithin organogel (plo)

PLO was prepared by mixing aqueous phase and oil phase. The optimized amount of pluronic F127 (30 % w/v) was considered as aqueous phase. Optimized imatinib mesylate loaded reverse micelles (F1) was considered as oil phase. 70% of aqueous phase [pluronic F127] was added drop by drop to 30% of oil phase with continuous stirring using mechanical stirrer **(Pawar et al., 2014; Dorothee et al., 2004).**

2.13 characterizationof prepared pluronic lecithin organogel (plo)

2.13.1 Organoleptic examination

The formulation was evaluated for its organoleptic properties i.e colour ,odour ,texture and phase separation as well as feels upon application (greasiness, stiffness and tackiness).

2.13.2 Homogeneity test

100 mg of the prepared organogel was pressed between the thumb and index finger in order to check if there are any coarse particles being attached or detached from the finger.

2.13.3 Determination of ph:

The pH of the prepared PLO was measured by using pH meter (Systronics,pH system 361).The pH meter was calibrated using standard 7.4 phosphate buffer solution and the electrodes was immersed in organogel and the readings were recorded. The study was performed in triplicate and the average pH values were noted.

2.13.4 Determination of viscosity

Viscosities of the formulated pluronic lecithin organogel were determined using Brookfield Viscometer with Spindle no.7 at 25° with the spindle speed of 10 rpm. Viscosity measurement for gels was replicated three times and the mean values were recorded.

2.13.5 Bloom strength

The bloom strength of the prepared PLOs was determined by using Texture Analyser TA-XT Plus., equipped with 5kg load cell using a cylindrical probe 0.5" diameter as fixture. The sample in the container was placed centrally on the platform beneath the cylindrical probe. After calibrating the height of the probe, the test was commenced. A trigger force of 10gm was used for the study.

2.13.6 Spreadability

The spreadability of the formulated PLOs was determined by Texture Analyser TA-XT Plus equipped with 5 kg load cell using spreadability rig as fixture. This fixture consists of a heavy duty platform, male cone and a female cone. The heavy duty platform was placed on the base of the machine and locked in the desired positioning by tightening the screws. An empty female cone sample holder was placed in the base holder. The male cone probe was attached above the female cone such that the male cone fits almost all the way to the female cone sample holder and proper care was taken to align the cones in this position. The height of the male cone was calibrated against the female cone so that the starting point was 25.0mm above the female cone (2mm form the tip of the male cone and the sample). After calibration the sample was placed on the female cone holder and the test was run. The values of firmness (g) and the work of shear (g/s) were noted down by running macros.

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2.13.7 Drug content

Drug content for the optimized batch(PLO-3) was calculated by dissolving 100mg of gel in 100 ml of phosphate buffer pH 7.4 and filtered through 0.45µm. after filtration the drug content was found out by taking absorbance at 289 nm.

2.14 *In-vitro* diffusion for pluronic lecithin organogel

In-vitro diffusion studies were carried out through cellophane membrane. The one end of open cylinder i.e the donor compartment was tied with a semi-permeable membrane containing 2g of the formulation. The receptor compartment consisted of 50 ml of 7.4 phosphate buffer which was kept at continuous stirring using magnetic stirrer at room temperature for about 8 hrs. Sample was withdrawn at specified time intervals and replaced with fresh volume of buffer solution. It was then analyzed by UV spectrophotometer at 289 nm **(Jhawat et al., 2016).**

3. RESULTS

3.1 PREFORMULATION

3.1.1 Melting Point

The physical property such as melting point helps in the identification of the sample and also to establish its purity. The melting point was determined by capillary tube method and the result was found to be 219°C. Reported melting point of imatinib mesylate in USP monograph is 226°C which indicates the drug sample is pure.

3.1.2 Solubility Studies

Solubility of imatinb Mesylate in water, phosphate buffer pH 7.4 and isopropyl myristate was determined by shake flask method and the results are indicated in table 2.The results indicate that imatinib mesylate is highly soluble in water when compared to other solvents.

Table 2: Solubility of Imatinib Mesylate

SOLVENTS	CONCENTRATION(MG/ML)	INFERENCE
Water	200mg/ml	Highly soluble
7.4 Phosphate Buffer	23mg/ml	Partially soluble
Isopropyl Myristate	Insoluble	Insoluble

3.1.3 Determination of Lambda Max

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Lambda max for the diluted stock solutions of imatinib mesylate was scanned in the UV spectrometer region ranging from 200-400 nm. The maximum wavelength was seen at 289nm.

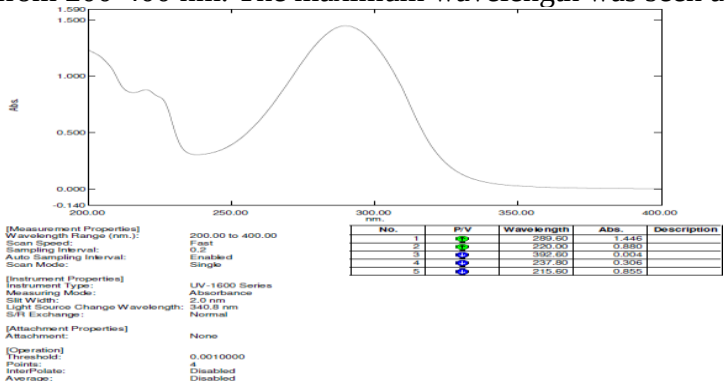

Fig 1: Lambda max of Imatinib Mesylate

3.2 Construction of the calibration curve

Calibration curve was constructed in the concentration range of 5-25 mcg/ml. The absorbance values corresponding to the construction were shown in table 3 and the regression value (R2) was found to be 0.999 from the graph.

Table 3: Standard graph data of Imatinib Mesylate at phosphate buffer pH 7.4

CONCENTRATION (mcg/ml)	ABSORBANCE AT 289 nm
5	0.184
10	0.356
15	0.544
20	0.703
25	0.905

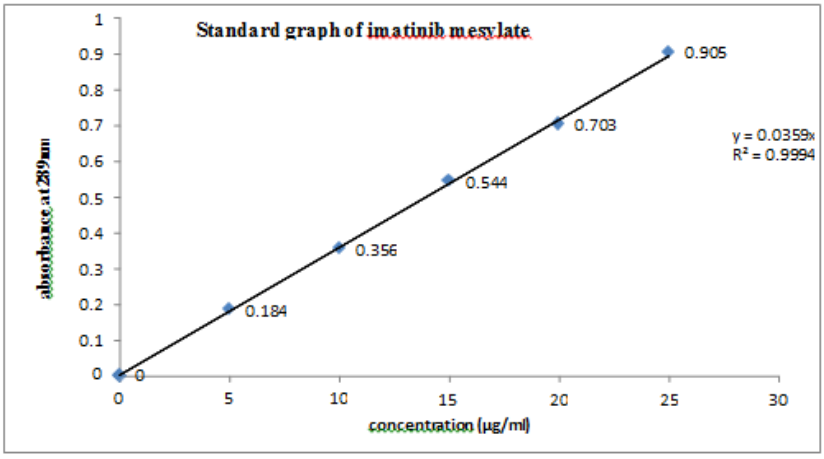

Fig 2: Calibration curve of Imatinib Mesylate in phosphate buffer pH 7.4

3.3 FT-IR spectroscopy

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Drug-excipients compatibility was checked by comparing the IR spectra of pure drug, excipients and the physical mixture of the drug and excipients. FT-IR spectra of the drug excipient mixture retained the characteristic functional peaks of the drug and it was ensured that there was no interaction between the drug and the excipients.

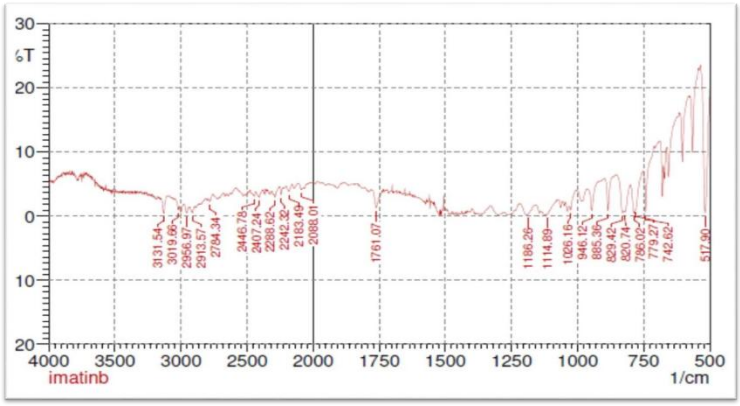

Fig 3: FT-IR data of imatinib mesylate

SL NO	WAVE NUMBER cm-1	FUNCTIONAL GROUP
1	2913.57	C-H Stretching
2	1761.07	C=O Stretching
3	2088.62	C≡N Stretching

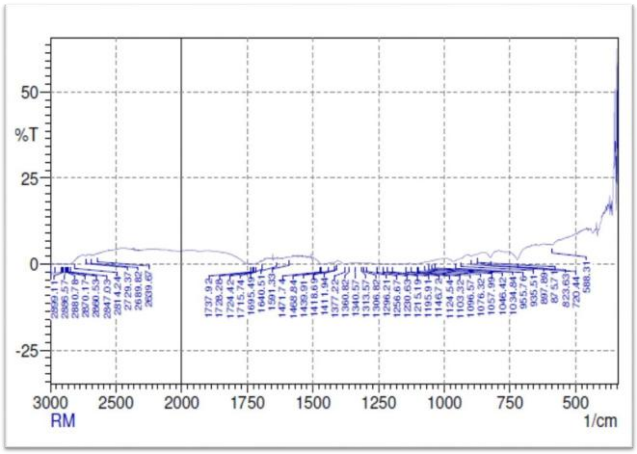

Fig 4: FT-IR of physical mixture

SL NO	WAVENUMBER cm-1	FUNCTIONAL GROUP
1	2899.11	C-H Stretching
2	1715.74	C=O Stretching
3	1360.82	C-N Stretching

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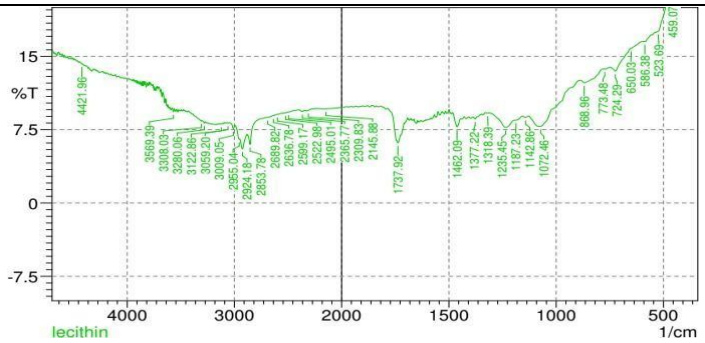

Fig 5: FT-IR of Lecithin

SL NO	WAVE NUMBER	FUNCTIONAL GROUP
1	2924.18	C-H Stretching
2	1737.92	C=O Stretching
3	1072.46	C-N Stretching

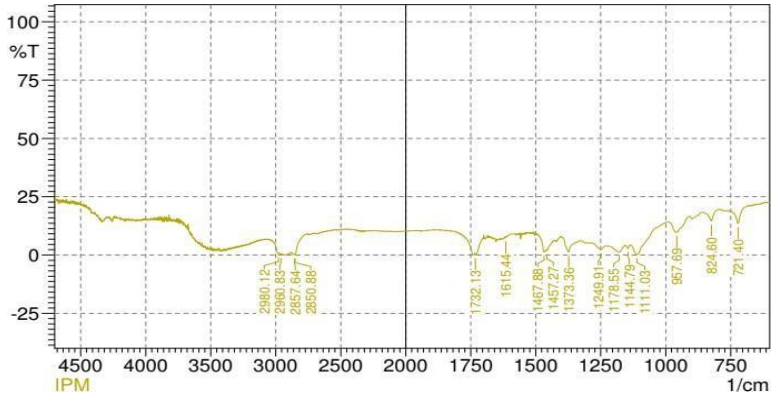

Fig 6: FT-IR of Isopropyl Myristate

SL NO	WAVE NUMBER	FUNCTIONAL GROUP
1	2850.64	C-H Stretching
2	1732.13	C=O Stretching
3	1249.91	CH3 Bending

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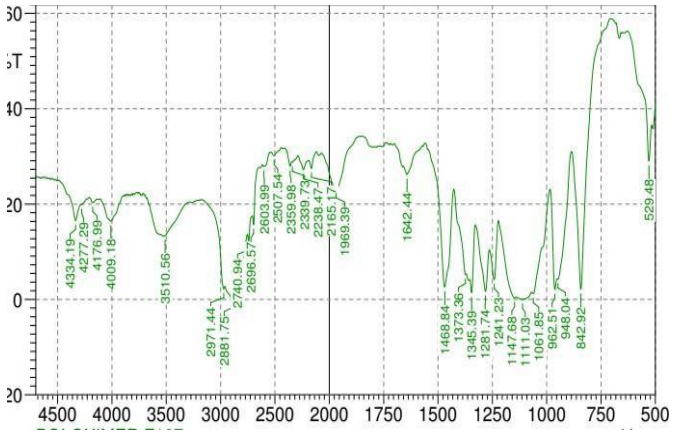

Fig 7: FT-IR of Pluronic F127

SL NO	WAVE NUMBER	FUNCTIONAL GROUP
1	2881.75	C-H Bending
2	1241.23	C-H3 Bending
3	1061.85	C-O Stretching

3.4 Determination of CRITICAL MICELLAR CONCENTRATION (CMC)

The CMC is the concentration of the surfactant in the bulk phase above which aggregates of molecules, so-called micelles, start to form. The CMC of various concentration of lecithin in isopropyl myristate such as 0.4%, 0.8%, 1.2%, 1.6% and 2% v/v was determined was drop count method. A graph of surface tension v/s concentration was plotted and the critical micellar concentration of the surfactant was found to be 1.6%.

Table 4: Determination of CMC

Concentration of lecithin in isopropyl myristate (%v/v)	Surface tension(dynes/cm)
0	29.7
0.4	26.84
0.8	25.72
1.2	25.05
1.6	25.05
2.0	25.01

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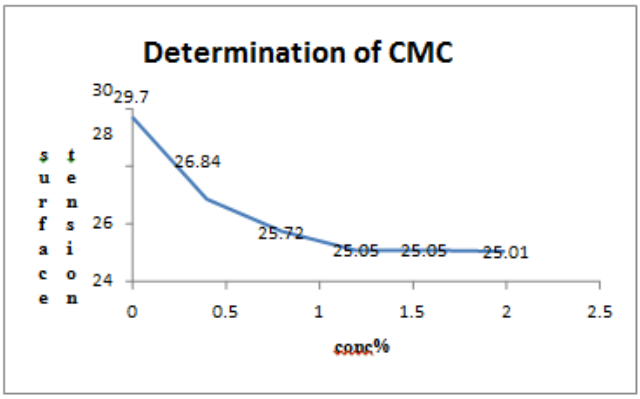

Fig 8: Determination of CMC

3.5 Formulation of reverse micelles

3.5.1 Optimization of lecithin concentration:

The concentration of the surfactant plays an important role in the formation of reverse micelles. Concentration above CMC such as 10%, 20% and 40% was used for preparing reverse micelles. Optimization of lecithin concentration was based on the parameters like transparency, physical stability, particle size and it was concluded that the formulation F1 showed best results when compared to the other. The results also indicate that when the concentration of the surfactant increases, there is increase in particle size and decrease in physical stability.

Table 5: Optimization of Lecithin Concentration

Formulation code	Composition				PARAMETERS			
	IPM (ml)	Lecithin (ml)	Water (ml)	IM (mg)	Homogeneity	Transparency	Physical stability	Particle Size (nm)
F1	10	1	0.3	10	Homogenous	Transparent	Stable	215.8
F2	10	2	0.3	10	Less Homogenous	Less Transparent	Less stable	633
F3	10	4	0.3	10	Least Homogenous	Least Transparent	Least stable	1125

3.5.2 Preparation of imatinib mesylate loaded reverse micelles

Suitable formula for preparing drug loaded reverse micelles was selected from the optimization process considering physical stability, transparency, homogeneity and particle size as an evaluating factor. Formulation F1 containing 10% v/v of lecithin was considered ideal. To this 10 mg of imatinib Mesylate dissolved in 0.3 ml of distilled water was added by means of microlitre syringe under continuous stirring for about 2hrs using magnetic stirrer at a temperature of 80°C.

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Table 6: Preparation of drug loaded Reverse Micelles

Formulation code	Composition				PARAMETERS			
	IPM (ml)	Lecithin (ml)	Water (ml)	IM (mg)	homogeneity	transparency	Physical Stability	Particle Size (nm)
F1	10	1	0.3	10	homogenous	transparent	Stable	238.8

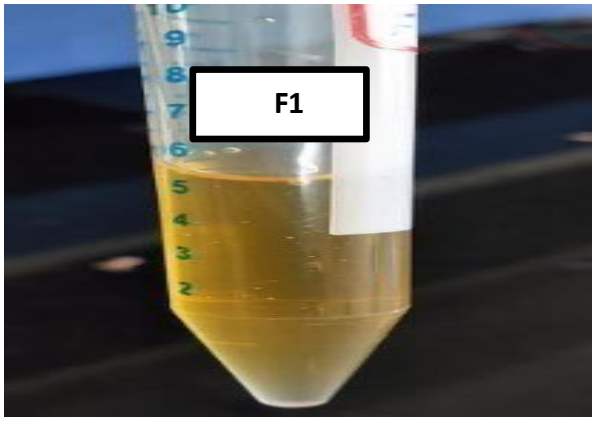

Fig 9: Optimized Imatinib Mesylate Loaded Reverse Micelles

3.6 Characterizations of the prepared reverse micelles

3.6.1 Determination of morphology

The morphology of reverse micelles was observed using Phase Contrast Microscopy under the magnification of 100X. Fig 18 represents the morphology of reverse micelles which shows spherical shape.

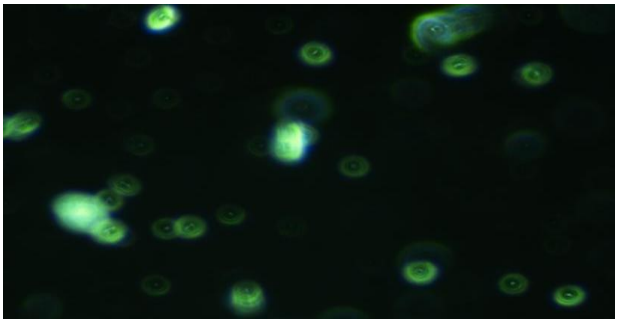

Fig 10: Formulated Imatinib Mesylate Loaded Reverse Micelle Morphology by PCM

3.6.2 DETERMINATION OF PARTICLE SIZE AND POLYDISPERSITY INDEX (PDI)

The mean particle size of the prepared reverse micelles was determined by Dynamic Light Scattering (DLS) method. The average particle size of the optimized formulation F1 was 238.8 nm and PDI is 0.389 which shows that the prepared imatinib mesylate loaded reverse micelles are homogenous without any aggregates.

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Fig 11: Particle Size and PDI of imatinib Mesylate loaded reverse micelles

3.6.3 Encapsulation efficiency

The encapsulation efficiency of the prepared imatinib mesylate loaded reverse micelles was carried out by centrifuge method. The encapsulation efficiency is the characteristics of surfactant drug and water. The encapsulation efficiency of the optimized batch was found to be 47%.

3.6.4 Transmission electron microscopy

The formulated reverse micelle was given for morphological analysis by TEM which showed the following results.

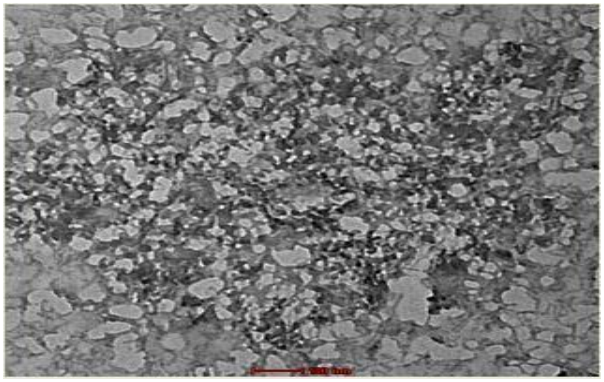

Fig 12: TEM image of Imatinib Mesylate Loaded Reverse micelles

3.7 Optimization of concentration of pluronic f127

Various concentration of pluronic F127 such as 10 %(w/v),20%(w/v) and 30% w/v was used to obtain gel with suitable characteristics. Weighed amount of pluronic F127 was dispersed in cold water and the mixture was kept overnight at 2-4°C in a refrigerator for the complete dissolution of pluronic F127.

Table 7: Optimization of Pluronic F127 concentration

FORMULATION CODE	CONCENTRATION OF PLURONIC F127 (%W/V)	PARAMETERS	
		GELATION	HOMOGENEITY

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PLO-1	10	No gelation	Less homogenous
PLO-2	20	Moderate gelation	Moderately homogenous
PLO-3	30	Complete gelation	Homogenous

3.8 Preparation of the pluronic lecithin organogel (plo)

Suitable formulation for preparing pluronic lecithin organogel was selected from the optimization process considering gelation and homogeneity as an evaluating factor. Formulation PLO-3 containing 30 % w/v of pluronic F 127 was considered to be ideal with suitable characteristics of gel and it was used for further characterization.

3.9 Characterization of prepared pluronic lecithin gel (plo)

3.9.1 Organoleptic examination

The prepared organogel was visually inspected for its organoleptic properties such as color, texture, appearance and phase separation. The results are tabulated in table 8 which indicates that formulated pluronic lecithin organogel has ideal characteristics of gel. No phase separation was observed after 72 hours which indicates the stability of the gel.

Table 8: Organoleptic evaluation of pluronic lecithin organogel

Formulation Code	Appearance	Color	Homogeneity	Phase Separation
PLO-3	Opaque	Off white	Homogenous	No phase separation

Fig 13: Pluronic lecithin organogel

3.9.2 Homogeneity test

Homogeneity test was performed to evaluate the ease of application of gel to the skin. The prepared pluronic lecithin organogel was evaluated for its homogeneity by pressing the gel between thumb and index finger. It shows that the gel is homogenous without any gritty particles.

3.9.3 Determination of ph

The pH of the organogel was determined by pH meter and the values are tabulated in table 9. The average pH value of pluronic lecithin organogel was found to be 6.6 which matches with the skin pH. It shows that the formulated organogel is compatible and it may not produce any skin irritation.

Table 9: Determination of pH

Formulation code	pH			Average
PLO-3	6.7	6.6	6.5	6.6

3.9.4 Determination of viscosity

Viscosity is an important property of gel which describes its resistance to the flow. This rheological property helps in determining consistency and also the diffusion rate of the drug from gel. The measurement of

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viscosity of the prepared gel was done with Brookfield viscometer with spindle no 7 and the results were found to be 2448cps. This high viscosity may be due to the formation of 3D network upon the addition of polymer (Pluronic F127) to the reverse micelles.

Table10: Determination of viscosity

Formulation code	Viscosity (cps)			Average
PLO-3	2448	2557	2669	2548 cps

3.9.5 BLOOM STRENGTH:

Bloom Strength is a measure of the ability of a colloidal dispersion to develop and retain a gel form. It is the force expressed in grams, necessary to depress by 4mm the surface of a gel with a standard 0.5" diameter cylinder probe. It is otherwise known as force required to rupture the gel. The bloom strength of gel indicates the resistance to penetration. For the formulated pluronic lecithin organogel, the value is 1.040kg. Since the bloom value was found to be high , therefore it was concluded that formulated pluronic lecithin organogel has good gel strength.

Table 11: Bloom Strength of Pluronic Lecithin Organogel

Force (gm)	Value
10	1.040 kg

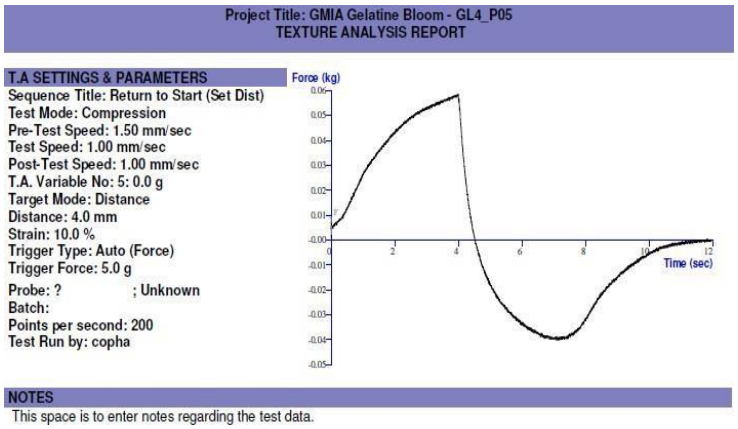

Fig 14: Bloom Strength of Pluronic Lecithin Organogel

3.9.6 Spreadability

Spredability of the formulated organogel was determined by using Texture analyzer. The firmness and work of shear obtained is mentioned in Table .The values of spreadability indicate that gel is easily spreadable with small shear.

Table 12: Spreadability of Pluronic Lecithin Organogel

Firmness	Work of shear
1849.56g	1779.799g.sec

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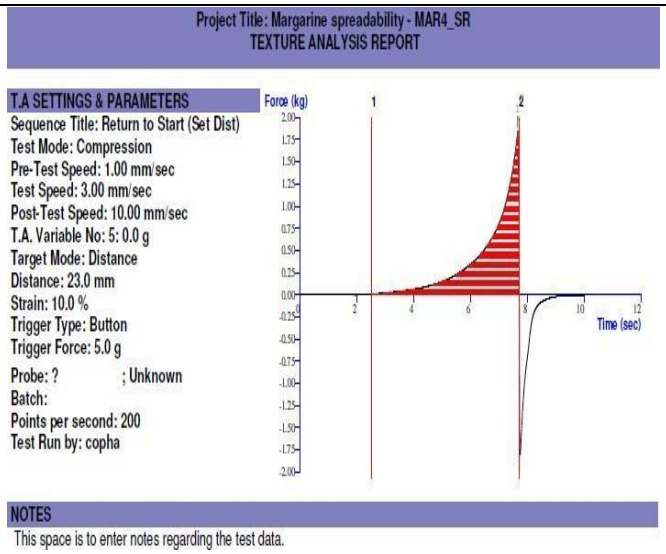

Fig 15: Spreadability of Pluronic Lecithin Organogel

3.9.7 Drug content

Drug content of the prepared organogel was determined by dissolving the gel in phosphate buffer pH7.4. The filtered sample was analyse sat 289 nm using spectrophotometer and the drug content was found to be 90.83%

3.10 In-vitro diffusion of pluronic lecithin organogel

In-vitro diffusion studies of formulated organogel was carried out through the cellophane membrane for about 8 hours using phosphate buffer pH 7.4 The values are tabulated in Table no and the graph was plotted by taking time on X- axis and percentage drug release on Y -axis. The results shows that formulated organogel shows sustained release (46.02 % for 8 hrs).

Table 13: In-vitro diffusion of pluronic lecithin organogel

TIME (HOURS)	PERCENTAGE DRUG RELEASE (%)
0	0
1	6.32
2	9.58
3	15.45
4	23.53
5	28.90
6	34.14
7	36.87
8	46.02

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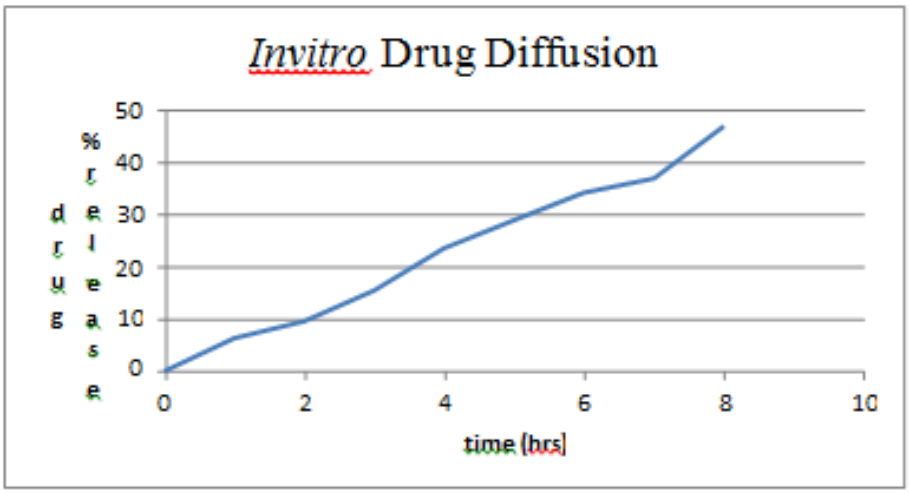

Fig 16: *In-vitro* diffusion of pluronic lecithin organogel

4. DISCUSSION

The present research work was aimed at preparing reverse micelle based pluronic lecithin organogel for controlled delivery of imatinib mesylate for its application in skin cancer. PLO consist of a 3D network of entangled reverse cylindrical micelles, the jelly-like phases, which in many solvents very effectively self-assemble into 3D networks, thereby turning a liquid into a gel. Topical drug treatment using pluronic lecithin organogel helps in avoiding systemic side effects associated with oral treatment of imatinib mesylate.

Imatinib mesylate is a tyrosine kinase inhibitor shows significant activity against dermatofibrosarcoma protuberans and metastatic melanoma [types of skin cancer]. Since Imatinib mesylate is BCS class I drug with high water solubility, incorporating this drug in carrier with significant encapsulation efficiency is a challenge. Hence reverse micelles with inner polar and outer non polar region was formulated to encapsulate imatinib meyslate. Lecithin and isopropyl myristate was used as surfactant and organic solvent to formulate reverse micelles. Cocnentration above CMC was considered for preparing reverse micelles.

Various batches of reverse micelles were prepared by varying the concentrations of lecithin (10%,20% and 40 % v/v) to obtain an optimal formulation with suitable thermodynamic stability transparency and particle size.The results shows that formulation containing 10 % v/v of lecithin in isopropyl myristate (F1) was found to be optimum with particle size of 238.8 nm. Entrapmement efficiency was determined by centrifuge method and the reuslts were found to be 47 %. The morphology of the reverse micelles was also confirmed by TEM. Imatinib mesylate loaded reverse micelle was converted in to organogel for gtopical delivery of drug using pluronic F 127 as polymer.

To prepare pluronic lecithin organogel, optimized reverse micelles containing imatinib mesylate was considered as oil phase and pluronic F127 dissolved in water as aqueous phase. Various concentration of pluronic F127 (30%w/v) was used to prepare organogel with suitable gelation. The optimized pluronic lecithin organogel was evaluated for organoleptic properties, pH, viscosity, bloom strength and spreadability. Pluronic lecithin organogel containing imatinib mesylate was found to be off white , homogenous and have pJH value 6.6 which is non –irritant. Bloom strength and spreadability value indicates the formulated gel has suitable gel strength and easily spreadable. Drug content of the gel was found to be 90.83%.In-vitro diffusion study shows using phosphate buffer pH7.4 as medium which shows controlled release over a period of 8 hours. Therefore, from the above study it may be concluded that reverse micelles based pluronic lecithin organogel will be effective in topical delivery of imatinib mesylate. Futher in vitro cell line studies need to be conducted to confirm the above hypothesis.

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5. CONCLUSION

In conclusion, the formulation and evaluation of Imatinib-loaded organogel demonstrated promising potential for enhancing the delivery of the tyrosine kinase inhibitor. The organogel system showed favorable physicochemical characteristics, stability, and sustained drug release, indicating its suitability as a novel transdermal or topical delivery platform. This approach could improve therapeutic efficacy, reduce systemic side effects, and provide better patient compliance for cancer treatment involving Imatinib.

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