

## Formulation and Characterization of Tofacitinib Loaded Nanofiber Hydrogel

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Date of Submission: 25-10-2025

Date of Acceptance: 05-11-2025

### ABSTRACT

The present study focuses on the formulation and characterization of a Tofacitinib-loaded PVA/PVP electrospun nanofiber hydrogel designed for the topical treatment of psoriasis. Tofacitinib, a Janus kinase (JAK) inhibitor, suffers from poor dermal penetration and notable systemic toxicity when administered orally. To overcome these limitations, nanofibers were fabricated using the electrospinning technique with an optimized drug-to-polymer ratio of 1:5, followed by their incorporation into a Carbopol-based hydrogel matrix. The prepared nanofibers exhibited uniform, bead-free morphology and high drug entrapment efficiency ( $98.76 \pm 0.04\%$ ), as confirmed by SEM and FT-IR analyses. Hydrogel formulations (F1–F6) were evaluated for pH, viscosity, spreadability, drug content, and in-vitro release. The optimized formulation (F3) demonstrated ideal physicochemical properties (pH  $6.4 \pm 0.1$ ; viscosity  $\approx 4500$  cps) and a biphasic release profile, providing sustained Tofacitinib release of  $\approx 99\%$  over 4.5 hours. The developed nanofiber-hydrogel composite enhances drug retention, promotes controlled diffusion through psoriatic skin, and minimizes systemic absorption, addressing the key drawbacks of conventional therapy. This novel delivery platform presents a promising, patient-friendly, and efficient approach for localized management of psoriasis with reduced adverse effects.

**KEY WORDS:** Tofacitinib, Nanofiber hydrogel, Psoriasis, Electro spinning, Controlled release, Topical drug delivery.

### I. INTRODUCTION

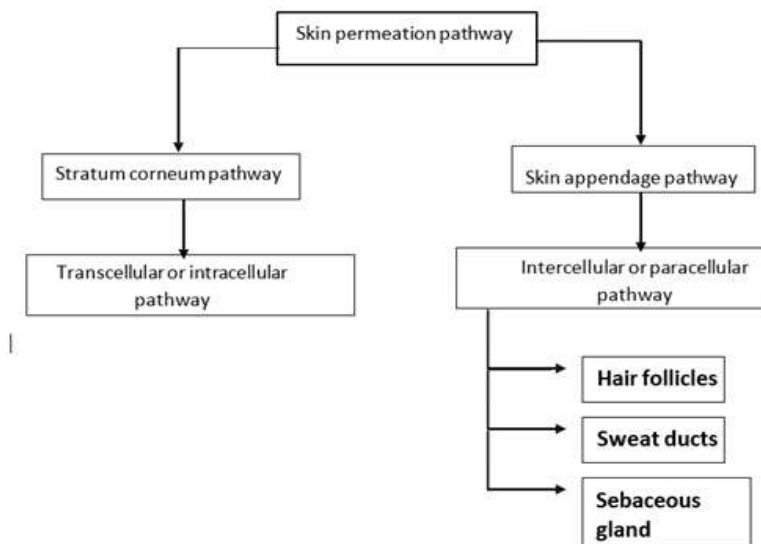
The skin, being the largest organ of the human body, serves as a vital barrier that protects against a wide range of chemical, physical, and biological insults. Skin-related disorders are among

the most common global health concerns, affecting individuals across all age groups and ethnic backgrounds. These conditions often arise from a complex interplay of intrinsic and extrinsic factors. Although several therapeutic options are available, most conventional treatments are limited by undesirable side effects and poor drug penetration through the skin. Consequently, there has been an increasing scientific interest in developing novel, safe, cost-effective, and more efficient therapeutic systems for the management of chronic inflammatory skin diseases such as psoriasis and atopic dermatitis.

Topical drug delivery remains a preferred route for treating dermatological disorders due to its ability to deliver drugs directly to the target site while minimizing systemic exposure and associated adverse effects. Furthermore, with appropriate optimization, transdermal systems can also provide systemic therapeutic benefits. However, traditional topical formulations frequently exhibit limited skin permeability and local irritation, reducing their overall clinical efficacy. These limitations have encouraged researchers to explore advanced nanotechnology-based delivery platforms capable of enhancing drug penetration, improving therapeutic outcomes, and achieving sustained localized action.

Among such nanotechnological innovations, electrospun nanofibers have gained remarkable attention owing to their unique physicochemical and structural attributes, including a high surface-area-to-volume ratio, mechanical strength, flexibility, biodegradability, and excellent oxygen permeability. Their resemblance to the native extracellular matrix (ECM) facilitates skin repair and regeneration while allowing for controlled and sustained drug release, positioning them as a superior alternative to conventional topical delivery systems.

### SKIN PERMEATION PATHWAY

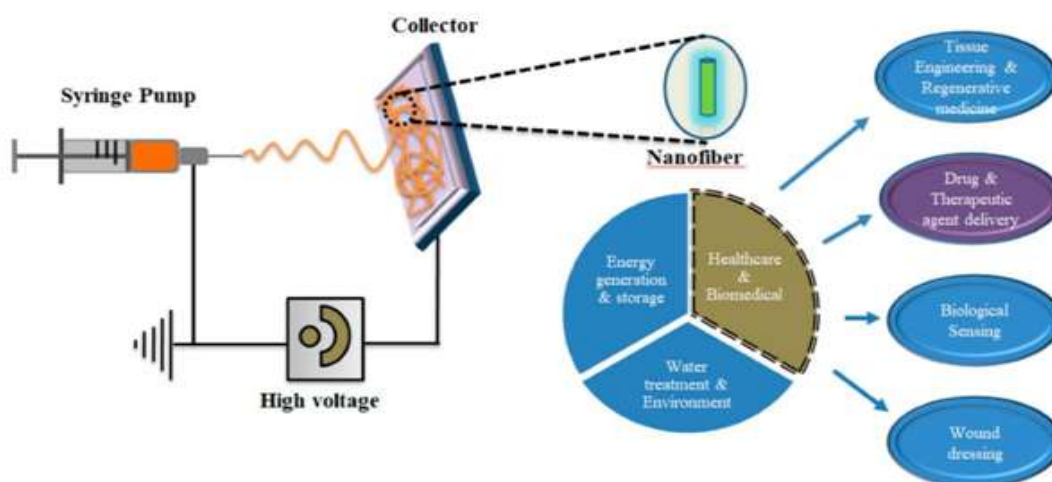


### ELECTROSPINNING NANOTECHNOLOGY

Electro spinning is one of the most versatile and widely adopted techniques for fabricating nanofibers due to its simplicity, cost-effectiveness, and ability to produce uniform ultrafine fibers. Polymeric nanofiber mats can be engineered to encapsulate single or multiple drugs, enabling targeted delivery, enhanced protection of active molecules, and improved therapeutic performance. Such systems also support controlled drug release, reducing dosing frequency and minimizing systemic

side effects associated with conventional immediate-release formulations.

In this technique, a high-voltage electric field is applied to a polymer solution delivered through a syringe needle toward a grounded or oppositely charged collector. When the electrostatic force surpasses the surface tension of the polymer droplet, it elongates into a Taylor cone and ejects a fine jet. As the jet travels through the electric field, it undergoes rapid stretching and solvent evaporation, forming continuous nanofibers that are deposited onto the collector as a thin, uniform mat.



### OVERVIEW OF ELECTROSPINNING

### PRINCIPLE OF ELECTROSPINNING

Electro spinning is a simple and efficient technique for producing ultrafine polymeric nanofibers with controlled morphology. Its low cost, scalability, and versatility make it ideal for fabricating advanced drug delivery systems. Polymeric nanofiber mats enable targeted and sustained drug release, improving therapeutic efficacy and patient compliance while reducing systemic toxicity. The process involves applying a high-voltage electric field to a polymer solution, causing the charged droplet to form a Taylor cone and eject a fine jet. As the solvent evaporates during flight, continuous nanofibers are deposited onto a grounded collector, forming a uniform fibrous mat.

### METHODS OF ELECTROSPINNING

Electro spinning techniques are classified based on their processing methods, including blend, coaxial, emulsion, melt, and gas-jet electro spinning. In blend electro spinning, the drug is directly mixed with the polymer solution to form uniform fibers with sustained release properties. Coaxial electro spinning produces core-shell fibers using dual syringes, enabling controlled or zero-order release profiles. Emulsion electro spinning utilizes oil-in-water or water-in-oil emulsions for efficient drug encapsulation and prolonged delivery. Melt electro spinning employs molten polymers instead of solvents, reducing toxicity and simplifying fabrication. Gas-jet electro spinning uses pressurized gas to aid fiber formation, providing better control over fiber diameter and uniformity.

### APPLICATIONS OF ELECTROSPINNING

Electrospun nanofibers offer several advantages for pharmaceutical and biomedical applications. Their high surface-area-to-volume ratio enables efficient drug loading and controlled release at the target site. The process allows solvent evaporation without heating, preserving drug stability. The resulting polymeric mats are biocompatible, porous, and free from residual solvents, reducing microbial contamination risks. Moreover, nanofibers can absorb exudates, maintain skin moisture, and mimic the extracellular matrix, thereby accelerating wound healing and improving therapeutic outcomes.

### DISEASE PROFILE

Psoriasis is a chronic, systemic, immune-mediated condition marked by the formation of erythematous, thickened, scaly, and pruritic skin plaques, which may also be painful. It is an

inflammatory skin disorder primarily influenced by genetic predisposition and the ageing process.

Psoriasis is a chronic immune-mediated disorder primarily driven by the dysregulation of the immune system and over activation of the JAK-STAT and Th17 pathways. The disease begins with the activation of dendritic cells, which release cytokines such as IL-12 and IL-23, stimulating T-cell differentiation into Th1 and Th17 subsets. These T cells secrete pro-inflammatory cytokines including IL-17, IL-22, TNF- $\alpha$ , and IFN- $\gamma$ , leading to abnormal keratinocyte proliferation and reduced differentiation. This creates a self-amplifying inflammatory loop between immune cells and keratinocytes, resulting in epidermal hyperplasia and plaque formation. The JAK-STAT signaling cascade further enhances cytokine transcription, maintaining chronic inflammation. Thus, psoriasis represents a complex interaction between genetic susceptibility, immune activation, and cytokine-mediated signaling.

### DRUG PROFILE

Generic Name: Tofacitinib

Chemical Class: Janus kinase (JAK) inhibitor

Molecular Formula:  $C_{16}H_{20}N_6O$

Mechanism of Action: Tofacitinib selectively inhibits JAK1 and JAK3, blocking the JAK-STAT signaling pathway. This reduces pro-inflammatory cytokine activity, leading to suppression of immune-mediated inflammation in conditions such as psoriasis.

Therapeutic Use: Management of moderate to severe plaque psoriasis, psoriatic arthritis, and rheumatoid arthritis.

Dosage Forms: Oral tablets, topical formulations (in development/research for dermatologic use)

#### Pharmacokinetics:

- Absorption: Well-absorbed orally with moderate bioavailability
- Distribution: Widely distributed; protein binding ~40%
- Metabolism: Hepatic via CYP3A4 and CYP2C19
- Elimination: Primarily renal excretion; half-life ~3 hours

Common Adverse Effects: Headache, infections, diarrhea, elevated liver enzymes, hyperlipidemia, increased risk of thrombosis.

Special Considerations: Requires monitoring of liver function, lipid profile, and complete blood counts; caution in immunocompromised patients.

## II. METHODOLOGY

### a) PREFORMULATION STUDIES

#### Organoleptic evaluation

The organoleptic characters of drug was evaluated and recorded by using descriptive terminology. Following organoleptic properties were studied: colour, odour, and texture.

#### Determination of the solubility of tofacitinib

Solubility test of Tofacitinib was performed by using various solvents that include Dimethyl Sulfoxide, ethanol, distilled water, glycerin, methanol, propylene glycol, HCL, a combination thereof.

### b) PREPARATION OF STANDARD CALIBRATION CURVE

#### Estimation of absorption maxima ( $\lambda$ -max)

Tofacitinib 10  $\mu$ g/mL standard stock solution was prepared by accurately weighing 100 mg of Tofacitinib and transferring it to a 100 mL volumetric flask. The drug was dissolved in DMSO, and the volume was made up to the mark with the water to obtain a concentration of 1000  $\mu$ g/mL (Stock 1). From this solution, 1 mL was precisely transferred into another 100 mL volumetric flask, and the volume was made up to the mark with water to obtain a concentration of 10  $\mu$ g/mL (Stock 2). The resulting solution was scanned over the wavelength range of 200–400 nm against a blank using a UV-visible spectrophotometer to determine the wavelength of maximum absorbance ( $\lambda$ max) for the pure drug.

#### Preparation of standard curve

An accurately weighed amount of Tofacitinib (equivalent to 100 mg) was transferred into a 100 mL standard volumetric flask and dissolved using a small quantity of DMSO. The volume was then made up to the mark with DMSO to obtain a stock solution having a concentration of 1000  $\mu$ g/mL (Stock Solution 1). From this solution, 1 mL was withdrawn and diluted to 100 mL with water to obtain Stock Solution 2 (10  $\mu$ g/mL). From Stock Solution 2, 2 mL, 4 mL, 6 mL, 8 mL, and 10 mL were pipetted out and each was diluted to 100 mL with water to obtain final concentrations ranging from 2–10  $\mu$ g/mL. The absorbance of these solutions was measured using a UV-visible spectrophotometer at  $\lambda$ max 285 nm. A calibration curve was then plotted with concentration on the X-axis and absorbance on the Y-axis.

### c) DRUG AND EXCIPIENT COMPATIBILITY STUDIES

To determine whether there is any interaction between the drug and excipients, compatibility studies are carried out. This was done to look for any modifications to the drug's chemical composition following its combination with excipients. The technique to examine the compatibility between drugs and polymers is infrared spectroscopy analysis. The FTIR spectra of Tofacitinib, carbopol 934, plain gel and Tofacitinib loaded Nanofiber hydrogel will be subjected to infrared analysis in order to observe any interaction. The samples will be scanned from 400  $\text{cm}^{-1}$  to 4000  $\text{cm}^{-1}$  and will be recorded using the KBr disk.

### d) FORMULATION OF TOFACITINIB LOADED NANOFIBERS INTO HYDROGEL

#### Preparation of electro spinning solutions

PVA (12 % w/v) and PVP K-90 (8 % w/v) were separately dissolved in ethanol under magnetic stirring until clear solutions were obtained. The two polymeric solutions were then combined and homogenized to form a uniform PVA/PVP blend. Accurately weighed Tofacitinib (10g) and PVA/PVP polymer blend (1:5 drug: polymer ratio) were incorporated into the mixture under constant stirring to obtain a clear, homogeneous electro spinning solution.<sup>[50, 51]</sup>

#### Electro spinning process

The mixture of drug polymer solution will be loaded in a 10 mL syringe. The flow rate will be maintained at a constant feeding rate of 750  $\mu\text{L h}^{-1}$  controlled by a syringe pump. A high voltage of 16–18 kV will be applied to the metallic needle having an inner hole diameter of 0.5 mm. A horizontal collector containing an aluminum foil has been fixed at a distance of 18 cm away from the needle tip to collect the nanofibers. All the electro spinning procedures were conducted at the optimum conditions (temperature 24  $\pm$  1  $^{\circ}\text{C}$ , relative humidity 68  $\pm$  3%). The prepared nanofibers were dried at 40  $^{\circ}\text{C}$  under vacuum to ensure complete removal of organic residual solvents and moisture.

#### Preparation of electro spun nanofiber gel

Antipsoriatic gel was going to be prepared using dispersion method. Carbopol 934/940 was dispersed in water and was left for an hour to ensure complete hydration and swelling of polymer. Weighed quantity of electro spun

nanofibers equivalent to 3.03g of tofacitinib were added to the polymer solution with continuous stirring to ensure the homogenous dispersion of electro spun fibers throughout the gel. Methyl and propylparaben were added to prevent the microbial growth in the gel. Tri-ethanolamine was added in a

sufficient quantity to the polymer–fiber mixture for neutralization and formation of clear homogenous gel. The gel was stored in the refrigerator until further evaluation.

S.No	INGREDIENTS	F1	F2	F3	F4	F5	F6
1	Carbopol934	0.5g	-	1g	-	1.5g	-
2	Carbopol940	-	0.5g	-	1g	-	1.5g
3	Methotrexate nanofiber	3.03g	3.03g	3.03g	3.03g	3.03g	3.03g
4	Triethanolamine	1.5g	1.5g	1.5g	1.5g	1.5g	1.5g
5	MethylParaben	0.015g	0.015g	0.015g	0.015g	0.015g	0.015g
6	Propylparaben	0.012g	0.012g	0.012g	0.012g	0.012g	0.012g
7	Distilled Water	Upto 50ml	Upto 50ml	Upto 50ml	Upto 50ml	Upto 50ml	Upto 5ml

**COMPOSITION OF TOF NANOFIBRE LOADED HYDROGEL**

e) CHARACTERISATION OF TOFACITINIB LOADED NANOFIBERS INTO HYDROGEL

(i) Nanofiber Characterisation Surface Morphological studies

Surface morphology of the drug loaded electro spun nanofibers was studied using SEM. A small piece of nanofibrous mat was affixed on the stub and the sample was subjected to gold coating in an inert atmosphere to render it electrically conductive. Images were obtained at an excitation voltage of 5–15kV. The distribution of fibers in the carbomer gel was observed using SEM. The electro spun nano-fibers loaded gel was subjected to imaging in the same pattern as that of nanofibers.

Elemental analysis studies

Elemental analysis of the nanofiber sample was carried out using an Energy-Dispersive X-ray Spectroscopy (EDX) system attached to the Scanning Electron Microscope (SEM) to identify and confirm the presence of key elements. The EDX analysis was performed using an EDAX APEX system attached to the SEM. The instrument was operated at an accelerating voltage of 10 kV, with a live time of 81.8 seconds, and a resolution of 128.3 eV. The take-off angle was set at 37.2°. During the analysis, the electron beam was focused on a specific region of the nanofiber sample to excite the atoms, resulting in the emission of characteristic X-rays used for elemental identification.

The emitted X-rays were detected and processed using EDAX APEX software, which generated a spectrum for elemental identification.

In the spectrum, the X-axis represented the energy of the X-rays in kilo-electron volts (keV), while the Y-axis indicated the intensity (counts). Distinct peaks corresponding to different energies were used to identify the elements present.

Loading efficacy of nanofibers

The drug content in the nanofibers was estimated by dissolving Methotrexate loaded nanofibers (2 mg) in a suitable solvent (1 ml DMSO) and was analyzed spectrophotometrically at 285 nm. Drug loading was estimated using the following equation,

$$\text{Loading efficiency (\% w/w)} = \left( \frac{\text{Amount of drug present in nanofibers}}{\text{Amount of nanofibers taken}} \right) \times 100$$

(ii) Nanofibre loaded gel characterization Physical appearance and homogeneity

The appearance and clarity of the gel will be assessed visually after settling the gels in a transparent container to observe the presence of lumps and phase separation.

Measurement of viscosity

The measurement of the viscosity of the prepared hydrogel will be done by Brookfield viscometer. 20 g of hydrogel will be added to a beaker followed by the addition of a viscometer spindle in the same beaker. Readings on the viscometer dial will be observed after rotating the spindle at different speeds like 0.5, 2.5, and 5 RPM.

#### Measurement of pH

The measurement of pH of the prepared hydrogel will be identified by using digital pH meter. Approximately 0.5 g of various hydrogels will be dispersed in 20 mL of distilled water and stirred for 30 minutes using a magnetic stirrer at room temperature; the pH sensor probe electrode will be immersed into the dispersed gel, and the pH of the formulation will be read from the digital display.

#### Determination of spreadability

100 mg of the sample was kept at the center of a glass slide. The slide was covered with another slide and the slides were pressed between fingers until no more expansion of the circle formed by the gel between the slides is observed. The diameter of the circle formed by the gel is measured in centimeter.

#### % Drug Content of Hydrogel

One gram of gel was accurately weighed and put into a (100 mL) volumetric flask containing 50mL of phosphate buffer solution (PBSpH5.4). Afterward, the gel mixture was sonicated for 15 min to ensure uniform drug solubility within the solution. Further, the resultant solution was filtered with the aid of a membrane filter of pore size 0.45 $\mu$ m. Finally, the absorbance was taken at  $\lambda$  max of 285nm alongside PBS (pH 5.4), which was considered blank to compare by using an ultraviolet (UV) visible spectrophotometer.

#### In-vitro drug release and permeation studies

100 mg of the electrospun tofacitinib loaded nanofibers was weighed and suspended in the dissolution medium (PBS pH-5.4), to study the release pattern of the drug from the fibers. The release study was conducted at 37  $\pm$  0.5  $^{\circ}$ C and 100 rpm. Aliquots of 1 ml each were withdrawn and replaced by an equal amount of

fresh dissolution medium at regular intervals of time (60min) to maintain a constant volume. The collected samples were analyzed using UV spectrophotometer for drug release using pH 5.4 phosphate buffer as blank at a wavelength of 285 nm.

In-vitro permeation study of electrospun nanofiber loaded gel was carried out using dialysis method. A semi permeable egg membrane was isolated from egg using 20% HCl. The isolated membrane was repeatedly washed to remove the debris of the eggshell using distilled water and immersed in phosphate buffer (pH5.4) for 24 hours. 1g of the gel was accurately weighed and placed on the egg membrane and tied to one end of the open ended cylinder (donor compartment) and was immersed in a beaker containing 100 ml of buffer (receptor compartment). This diffusion system was maintained at 37  $\pm$  0.5  $^{\circ}$ C and 100 rpm. Aliquots were withdrawn at regular intervals of time and were analyzed spectrophotometrically at 285 nm.

### III. RESULT AND DISCUSSION

#### a) PREFORMULATION STUDIES ORGANOLEPTIC EVALUATION

The colour, odour, and texture of the Tofacitinib were characterized.

- Color: White or off – white
- Odor: Odorless
- Texture: Crystalline powder

#### DETERMINATION OF SOLUBILITY OF TOFACITINIB

The solubility of Tofacitinib was determined in various solvents. It was observed that the solubility of Tofacitinib was freely soluble in dimethyl sulfoxide (DMSO), slightly soluble in propylene glycol (PG) and very slightly soluble in ethanol.

SL.NO	SOLVENT	SOLUBILITY
1.	Dimethyl Sulfoxide (DMSO)	Freely soluble
2.	0.1 M HCL	Freely soluble
3.	Propylene Glycol (PG)	Slightly soluble
4.	Ethanol	Very slightly soluble
5.	Phosphate buffer pH 5.4	Soluble
6.	Phosphate buffer pH 7.4	Insoluble
7.	H <sub>2</sub> O	Slightly soluble

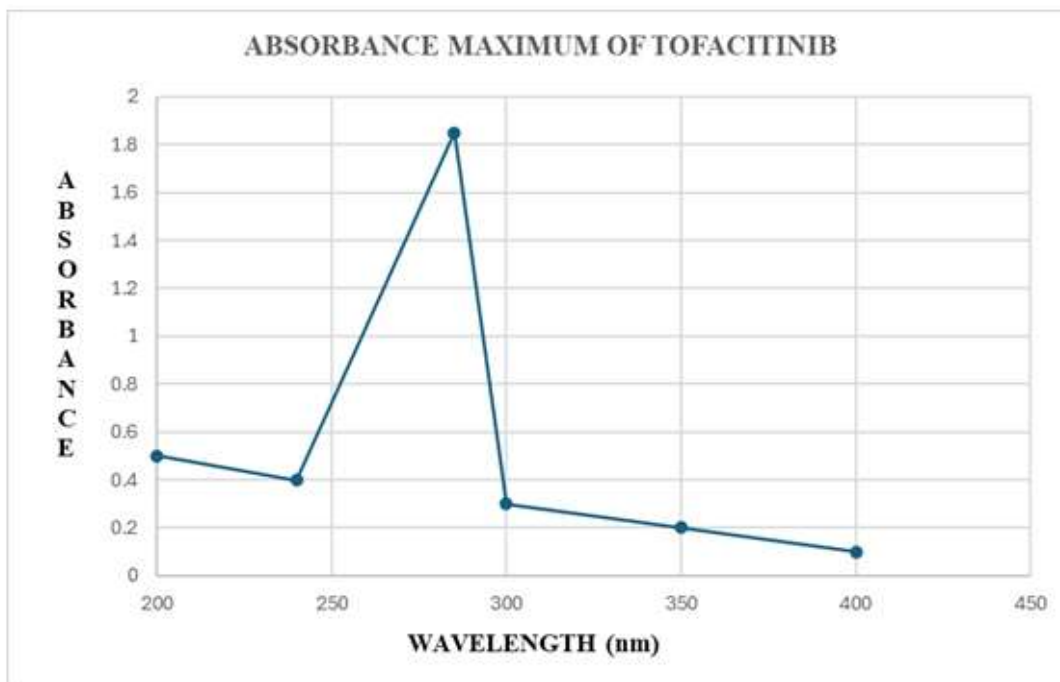
#### b) SPECTROMETRIC IDENTIFICATION OF TOFACITINIB

Estimation of absorption maxima ( $\lambda$ -max):

The absorption maximum ( $\lambda$ max) of Tofacitinib was determined by scanning a diluted solution of the drug (10  $\mu$ g/mL) prepared in DMSO

(Dimethyl Sulfoxide). A standard stock solution of Tofacitinib (1000 µg/mL) was first prepared by accurately weighing 100 mg of the drug and dissolving it in DMSO in a 100 mL volumetric flask. From this, 1 mL was transferred into another 100 mL volumetric flask and diluted with DMSO to obtain a concentration of 10 µg/mL. The

resulting solution was scanned in the wavelength range of 200–400 nm using a UV-visible spectrophotometer against a water blank. The spectrum obtained showed a maximum absorbance ( $\lambda_{max}$ ) at **285 nm**, which was selected as the detection wavelength.



**TOFACITINIB EXHIBITS MAXIMUM ABSORBANCE OF 1.823 AT 285nm**

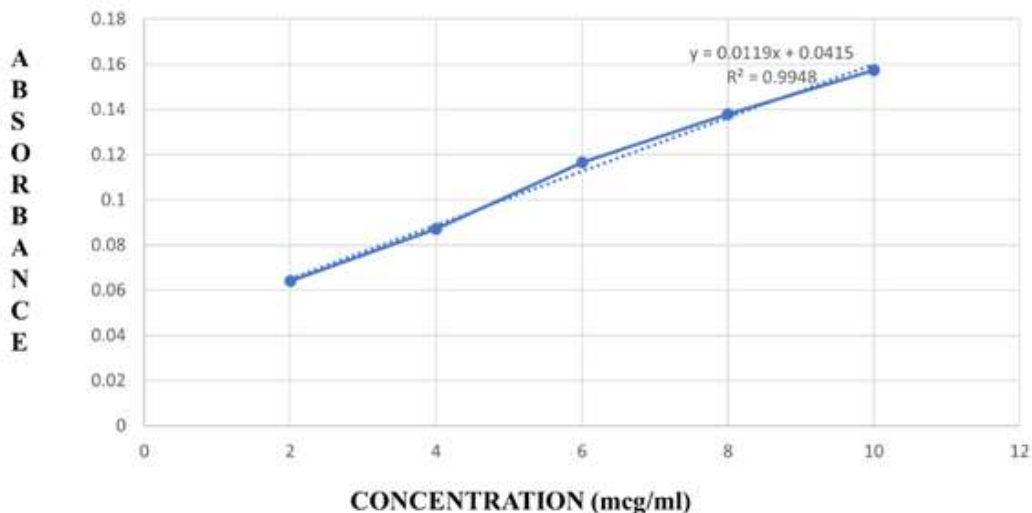
**CALIBRATION OF TOFINPHOSPHATE BUFFER pH5.4:**

The standard calibration curve of Tofacitinib was prepared using DMSO as the solvent. The absorbance was measured at the  $\lambda_{max}$

of 285 nm. The correlation coefficient was found to be 0.9948, indicating good linearity. Tofacitinib was found to obey Beer-Lambert’s law within the concentration range of 2–10 µg/mL. The calibration plot of Tofacitinib in DMSO is shown.

SL.NO	CONCENTRATION (µg/ml)	ABSORBANCE
1.	2	0.0641
2.	4	0.0872
3.	6	0.1166
4.	8	0.1379
5.	10	0.1574

**ESTIMATION OF TOFACITINIB MEASURED AT 285nm IN UV SPECTROSCOPY**



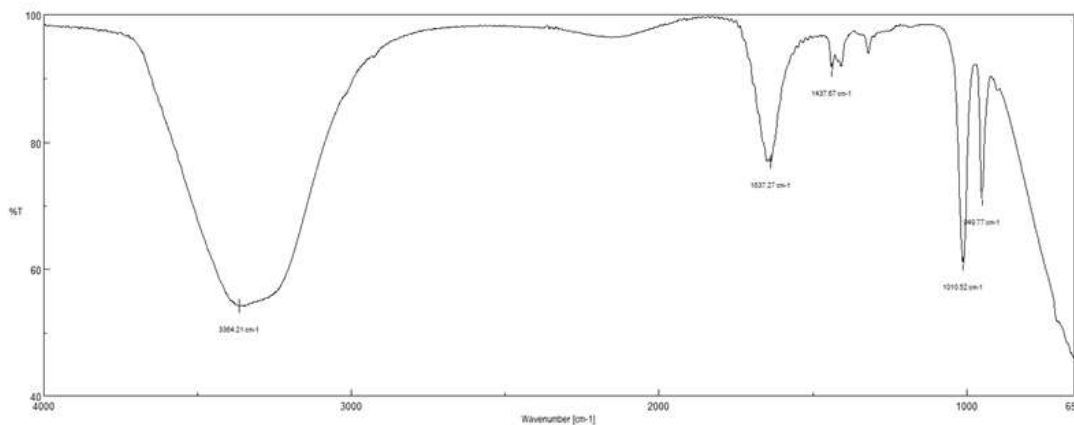
**CALIBRATION CURVE OF TOFACITINIB**

**c) DRUG AND EXCIPIENT COMPATIBILITY STUDIES**

Fourier Transform Infra-Redspectroscopic (FT-IR) studies:

The FT-IR study was conducted to confirm the compatibility between drug and the excipients used in the preparation of Tofacitinib

nanofibre loaded hydrogel formulation to identify the possible interactions. FT-IR spectrum was performed for pure drug (Tofacitinib), excipients (carbopol, plain gel and Tofacitinib nanofibre loaded gel).



**FT-IR SPECTRUM OF TOFACITINIB NANOFIBRE LOADED HYDROGEL**

**CHARACTERISTIC PEAKS OF TOFACITINIB NANOFIBRE LOADED HYDROGEL**

SL.NO	WAVE NO.	FUNTIONAL GROUP
1	3335	O-H / N-H STRETCHING
2	2920	Aliphatic C=O
3	1636	Amide C=O
4	1240	C-O / C-N
5	553	Tofacitinib fingerprint
6	---(absent)	-COOH

The FTIR spectrum of the Tofacitinib-loaded nanofiber hydrogel confirms successful drug incorporation and chemical stability. The amide C=O stretch of Tofacitinib appears at  $1636\text{ cm}^{-1}$  (within the typical  $1680\text{--}1650\text{ cm}^{-1}$  range), and the characteristic aromatic fingerprint peak is observed at  $553\text{ cm}^{-1}$ , both matching the pure drug, indicating no degradation occurred during electro spinning or gel formulation.

The broad O–H / N–H band centered at  $\sim 3335\text{ cm}^{-1}$  reflects overlapping hydroxyls from PVA, PVP, Carbopol, and the drug's N–H, suggesting hydrogen bonding and physical entrapment rather than chemical reaction. The C–O / C–N stretch at  $1240\text{ cm}^{-1}$  confirm the presence of nanofiber polymers within the hydrogel matrix. Notably, the –COOH peak of Carbopol at  $1713\text{ cm}^{-1}$  is absent indicating physical entrapment and hydrogen bonding with Tofacitinib without chemical degradation.

Overall, the spectrum shows all characteristic drug, polymer, and gel peaks with minor shifts or broadening, confirming that the drug is physically incorporated, chemically intact, and well distributed within the hydrogel network, supporting its suitability for controlled topical delivery.

#### FORMULATION OF TOFACITINIB NANOFIBRE

The mixture of drug polymer solution will be loaded in a 10 ml syringe. The flow rate will be maintained at a constant feeding rate of  $750\mu\text{l h}^{-1}$  controlled by a syringe pump. A high voltage of 16–18kV will be applied to the metallic needle having an inner hole diameter of 0.5mm. A horizontal collector containing an aluminium foil has been fixed at a distance of 18cm away from the needle tip to collect the nanofibers. All the electro spinning procedures were conducted at the optimum conditions (temperature  $24 \pm 1^\circ\text{C}$ , relative humidity  $68 \pm 3\%$ ). The prepared nanofibers were dried at  $40^\circ\text{C}$  under vacuum to ensure complete removal of organic residual solvents and moisture



**TOFACITINIB NANO FIBROUS MAT**

#### FORMULATION OF TOFACITINIB NANOFIBRE LOADED HYDROGEL:

The Tofacitinib loaded hydrogel were prepared by dispersion method using different concentration of polymers such as carbopol 934 (0.5% - 2.5%) and carbopol 940 (0.5% - 2.5%) with triethanolamine (0.5% - 1.5%), water, methyl paraben and propyl paraben.

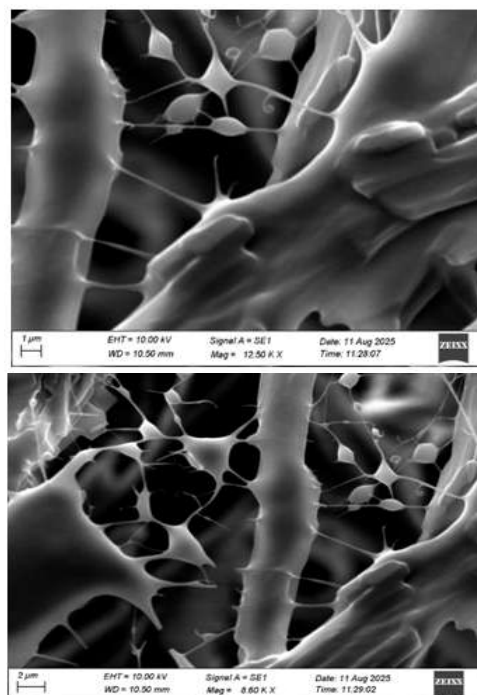


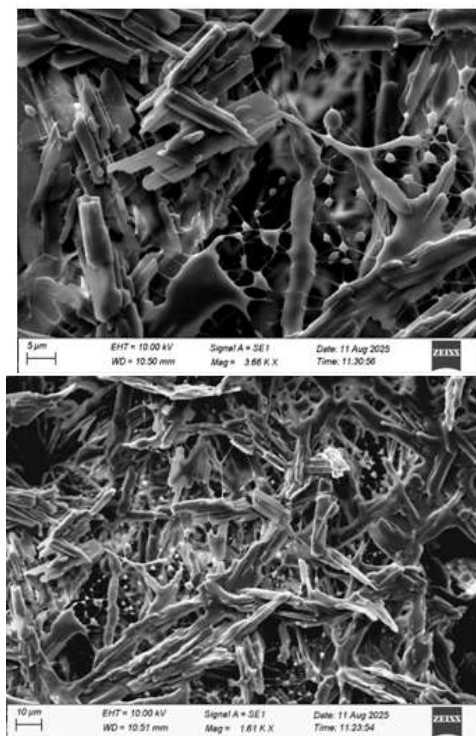
#### FORMULATION OF TOFACITINIB NANOFIBRE LOADED HYDROGEL (F1 – F6)

#### e) CHARACTERIZATION OF TOFACITINIB NANOFIBRE LOADED HYDROGEL NANOFIBRE CHARACTERIZATION

Determination of Surface morphology of Tofacitinib nanofibres and Nanofibre loaded hydrogel:

The nanofibre shape and morphology of Tofacitinib nanofibrous mat observed under SEM and the results were shown.





**SEM IMAGES OF TOF NANOFIBER**

Using scanning electron microscopy (SEM) image, evaluation of the surface, and shape of prepared nanofibers were performed. The SEM analysis revealed improvement in the

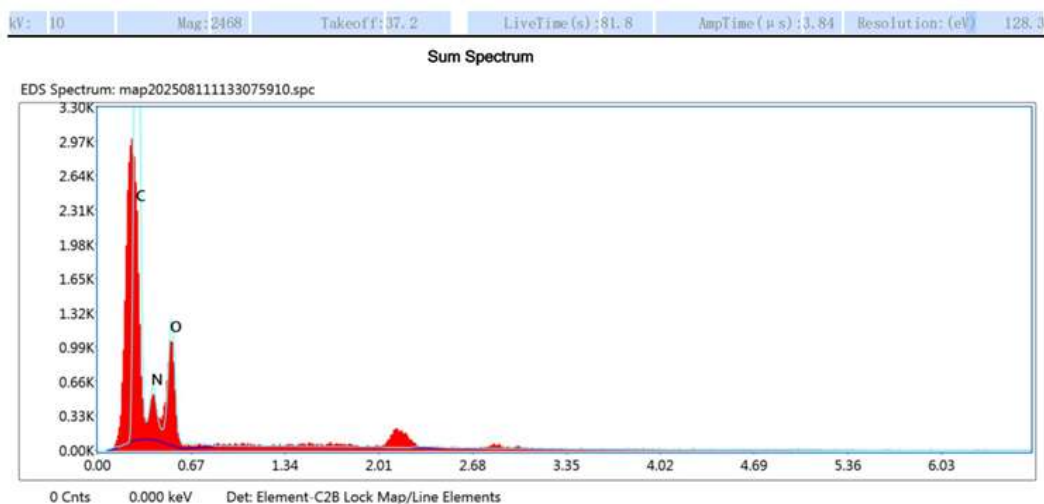
nanofibrous mat surface shape and homogeneity of nanofibers. The SEM morphology of nanofibers indicated very smooth, fine, flexible, porous, and mesh-like structures that formed inter connected-structured nanofibrous mats.

No other assorted structure was seen on the surface of the nanofibers indicating that drug have been completely incorporated into the nanofibrous mats.

Elemental analysis study:

The EDX spectrum of the Tofacitinib-loaded nanofiber hydrogel is shown in Figure 25. The analysis revealed the presence of Carbon (C), Oxygen (O), and Nitrogen (N) as the primary elements. The quantitative data are presented.

The weight percentages were found to be C: 56.81%, O: 27.23%, and N: 15.96. The significant carbon content is due to the organic backbone of these polymers, while the oxygen component comes from hydroxyl (-OH) groups present in PVA and carbonyl (C=O) groups present in PVP. Importantly, the detection of nitrogen confirms the successful encapsulation of Tofacitinib within the nanofiber matrix. Since PVA and PVP lack nitrogen, its presence can only be attributed to the drug molecule, which contains nitrogenous heterocyclic groups.



**EDX SPECTRUM OF TOFACITINIB-LOADED PVA/PVP NANOFIBERS SHOWING MAJOR PEAKS FOR CARBON, OXYGEN, AND NITROGEN. THE PRESENCE OF NITROGEN CONFIRMS SUCCESSFUL DRUG INCORPORATION INTO THE POLYMERIC NANOFIBER MATRIX. PEAKS MARKED WITH “K” REPRESENT K-SHELL EMISSION LINES TYPICAL OF LIGHT ELEMENTS.**

ELEMENT	WEIGHT %	ATOMIC %
C (Carbon)	56.81%	62.47%
N (Nitrogen)	15.96%	15.05%
O (Oxygen)	27.23%	22.48%

**Elemental Composition of Tofacitinib Nanofiber**

The absence of any metallic or foreign elemental peaks indicates that the nanofiber formulation is free from contamination and inorganic impurities.

EDX analysis confirmed the successful incorporation of Tofacitinib into the electro spun nanofiber system, with a clean elemental profile free from foreign impurities.

Loading efficacy of nanofibres:

The loading efficiency of tofacitinib in the nanofibers was determined by dissolving a known amount of nanofibers in dimethyl sulfoxide and

analyzing the drug content spectrophotometrically at 285nm. The loading efficiency was calculated using the standard formula. The Tofacitinib-loaded nanofibers showed a loading efficiency of 98.76% w/w, indicating successful incorporation of the drug into the nanofiber matrix.

**NANOFIBRE LOADED GEL CHARACTERIZATION:**

Physical appearance and homogeneity:

The physical appearance and homogeneity of the TOF NF loaded hydrogel were observed visually and the results were shown.

SL.NO	PHYSICALCHARACTERS	TOFHIDROGEL
1.	Colour	Transparent
2.	Glossiness	Good
3.	Homogeneity	Good

The prepared TOF hydrogel (F1–F6) was transparent in color and showed high homogeneity with no lumps. The gel was flexible, and non-tacky in texture.

**Measurement of viscosity**

The viscosity of developed formulations (F1 – F6) was evaluated by using Brookfield viscometer. The viscosity of the formulation was shown.

SL.NO	FORMULATION CODE	VISCOSITY (CPS)±S.D
1.	F1	3900 ± 0.021
2.	F2	3800 ± 0.024
3.	F3	4500 ± 0.015
4.	F4	4100 ± 0.018
5.	F5	4900± 0.02
6.	F6	5000 ± 0.023

The rheogram revealed that the addition of nanofiber to the carbopol did not show much variation in the viscosity of the gel. The ideal viscosity for a hydrogel is between 3000 and 5000, there all the formulations (F1 –F6) possess good viscosity. The physical evaluation of the gel after the analysis indicated that the applying high shear rate did not break or deformed the gel. This suggests that the formulation had good gel strength.

**Measurement of pH:**

The optimum pH of the hydro gel should be between 4 and 6, which is similar to the pH of the skin. Considering the psoriatic lesion cure and skin regeneration purposes, the observed pH should match the skin pH. Moreover, a pH between 4 and 6 has been reported as being ideal for proliferation of fibroblasts, regeneration of keratinocytes, and curing of psoriatic lesions. The pH value of the TOF-loaded hydro gel formulation was determined by a pH meter and the result is shown.

SL.NO	FORMULATION CODE	pH±S.D
1.	F1	5.1±0.015
2.	F2	5.6±0.044
3	F3	5.3±0.024
4	F4	5.4±0.034
5	F5	5.3±0.04
6	F6	5.5±0.019

The pH of all the formulations was within the acceptable range. Hence, the prepared hydrogel was suitable for application with a minimum tissue irritation risk. This was considered to be close to the pH of the skin and was considered assat is factory for application with minimal risk of irritation or discomfort due to acidic pH.

Measurement of Spreadability:

The spreadability of the gels were determined by measuring the diameter of the gelthat spreads over the glass slides. The results were shown.

SL.NO	FORMULATION CODE	SPREADABILITY±S.D(cm)
1.	F1	5.37±0.20
2.	F2	5.22±0.150
3.	F3	5.56±0.23
4.	F4	5.38±0.25
5.	F5	5.81±0.15
6.	F6	5.54±0.26

This shows that the hydrogel's spreadability increased as polymer concentration decreases. Formulation made with higher concentrations carbopol 940 (F2, F4, F6) had less

spreadability while compared to carbopol 934 (F1, F3, F5).

Drug content of TOF NF Hydrogel

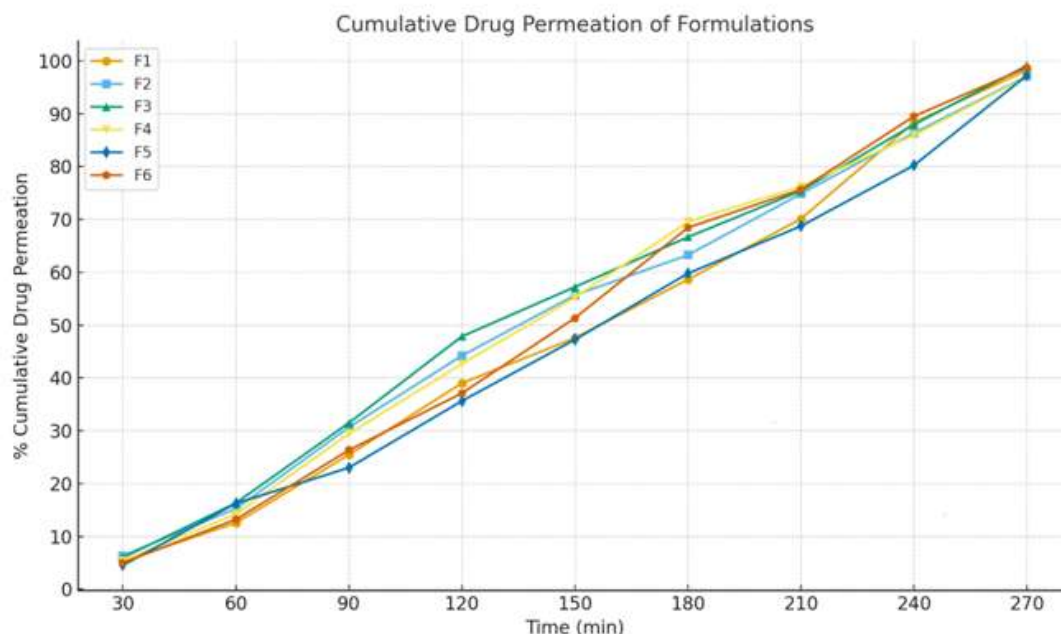
SL.NO	FORMULATION CODE	DRUG CONTENT(%)±SD
1.	F1	97.26±0.12
2.	F2	96.64±0.45
<b>3.</b>	<b>F3</b>	<b>98.72±0.32</b>
4.	F4	96.58±0.11
5.	F5	94.65±0.14
6.	F6	92.8±0.25

The drug content(%) of prepared hydrogel was evaluated, and values were between 92.8±0.25%

and 98.72±0.32% indicating a uniform distribution of the drug in the formulation.

In-vitro drug release of TOF Nanofibre loaded hydrogel

SL.NO	TIME (inmins)	%CUMULATIVE DRUG PERMEATION±SD					
		F1	F2	F3	F4	F5	F6
1.	30	5.326±0.12	6.352±0.12	5.987±0.12	5.411±0.21	4.5354±0.32	5.012±0.51
2.	60	12.568±0.11	15.258±0.25	16.325±0.31	14.256±0.15	16.254±0.42	13.221±0.21
3.	90	25.465±0.45	30.654±0.11	31.478±0.41	29.442±0.31	23.011±0.14	26.341±0.31
4.	120	38.998±0.24	44.215±0.31	47.856±0.2	42.651±0.21	35.641±0.12	37.112±0.11
5.	150	47.568±0.12	55.654±0.44	57.214±0.15	55.211±0.33	47.251±0.52	51.331±0.54
6.	180	58.625±0.54	63.258±0.13	66.654±0.13	69.554±0.56	59.771±0.41	68.447±0.23
7.	210	70.125±0.11	74.859±0.33	75.411±0.36	76.241±0.14	68.741±0.31	75.661±0.31
8.	240	88.335±0.31	86.368±0.22	87.951±0.25	85.954±0.14	80.236±0.34	89.521±0.21
9.	270	98.256±0.14	97.124±0.14	<b>99.121±0.14</b>	97.001±0.54	97.256±0.12	98.765±0.45



**%CUMULATIVE DRUG RELEASE CURVE OF TOF HYDROGELS**

Among all TOF-PVP/PVA-NF formulations (F1-F6), Formulation 3 (F3) provided better-regulated drug release for upto 4.5h. TOF-PVA/PVA-NF (F3) had an early burst release, with 16.32% ± 0.31% TOF released in 1h followed by a slow release, with 99.12% ± 0.14% TOF released up to 4.5h, suggesting a biphasic release pattern. This was due to the high hydrophilicity of the PVA as compared with that of the PVP polymer. An

early burst occurred with TOF- PVA/PVA-NF nanofibers as they exhibited rapid drug release within a few hours as the polymeric layers in nanofibers tend to degrade rapidly and release the drug; this would help to attain the minimum effective drug concentration necessary to provide the effective anti-psoriatic pharmacological effect in a very short duration. The percent release of TOF was 99.12±0.14 at 4.5h. The electro spun fibers

supplied TOF more slowly and smoothly, with the aligned group releasing it slightly faster. This is because PVP and PVA were used in TOF-PVA/PVP-NF, and a protracted release of active drug molecules from the narrow pores of the fibers was observed that would allow the same effect throughout the prolonged period. This may be because both PVA and PVP are hydrophilic. This confirms that it provide promising effect against psoriasis for up to 4.5hour.

#### IV. CONCLUSION

From the present investigation, it can be concluded that Tofacitinib-loaded PVA/PVP electro spun nanofiber hydrogel was successfully formulated and optimized as a potential topical delivery system for psoriasis.

The combination of nanofiber technology and hydrogel formulation enhanced drug entrapment, mechanical strength, and localized drug retention at the psoriatic site.

This novel system has the potential to deliver Tofacitinib directly to the epidermal and dermal layers, providing targeted inhibition of the JAK-STAT pathway, thereby reducing inflammation and keratinocyte hyper proliferation — the hallmark features of psoriasis. The importance of this project lies in its ability to minimize the systemic toxicity associated with oral Tofacitinib, which carries FDA warnings for serious infections, malignancy, and cardiovascular risks.

By offering localized delivery, this hydrogel may provide safer, sustained, and patient-compliant therapy, reducing the need for frequent dosing and avoiding first-pass metabolism. The nanofiber-based hydrogel also provides a biocompatible, moisture-retentive, and non-greasy platform, ideal for chronic skin conditions.

Overall, the study demonstrates that the Tofacitinib nanofiber hydrogel system is a scientifically sound and pharmaceutically viable approach for psoriasis management.

It successfully integrates high loading efficiency, controlled release, enhanced permeation, and patient convenience, positioning it as a next-generation topical JAK-inhibitor therapy for localized psoriasis treatment.

Further work involving ex-vivo skin permeation, in-vivo efficacy, and stability studies is recommended to establish its clinical safety and therapeutic potential.

#### REFERENCES

- [1]. Majtan J, Bucekova M, Jesenak M. Natural Products and Skin Diseases. *Molecules*. 2021 Jul 25;26(15):4489.
- [2]. Luraghi, A.; Peri, F.; Moroni, L. Electrospinning for drug delivery applications: A review. *J. Controlled Release* 2021, 334, 463–484.
- [3]. Li, D.; Xia, Y. Electrospinning of Nanofibers: Reinventing the Wheel. *Adv. Mater.* 2004, 16, 1151–117.
- [4]. Karthikeyan K, Sowjanya RS, Yugandhar ADV, et al. Design and development of a topical dosage form for the convenient delivery of electrospun drug loaded nanofibers. *RSC Adv.* 2015;5(66):52420-6. doi:10.1039/C5RA04438C.
- [5]. Galluzzo M, D'Adamio S, Servoli S, Bianchi L, Chimenti S, Talamonti M. Tofacitinib for the treatment of psoriasis. *Expert Opin Pharmacother.* 2016 Jul;17(10):1421-33. doi: 10.1080/14656566.2016.1195812. PMID: 27267933.
- [6]. Kumar S, Prasad M, Rao R. Topical delivery of clobetasol propionate loaded nanosponge hydrogel for effective treatment of psoriasis: Formulation, physicochemical characterization, antipsoriatic potential and biochemical estimation. *Materials Science and Engineering: C*. 2021 Feb 1;119:111605. <https://doi.org/10.1016/j.msec.2020.111605>
- [7]. Gürtler AL, Rades T, Heinz A. Electrospun fibers for the treatment of skin diseases. *Journal of Controlled Release*. 2023 Nov 1;363:621-40. <https://doi.org/10.1016/j.jconrel.2023.10.09>
- [8]. Thakur S, Anjum MM, Jaiswal S, Kumar A, Deepak P, Anand S, Singh S, Rajinikanth PS. Novel synergistic approach: tazarotene-calcipotriol-loaded-PVA/PVP-nanofibers incorporated in hydrogel film for management and treatment of psoriasis. *Molecular Pharmaceutics*. 2023 Jan 11;20(2):997-1014. <https://doi.org/10.1021/acs.molpharmaceut.2c00713>.
- [9]. Langley RGB. Psoriasis: epidemiology, clinical features, and quality of life.

- Annals of the Rheumatic Diseases [Internet]. 2005 Mar 1;64(suppl\_2):18–23. Available from: [https://ard.bmj.com/content/64/suppl\\_2/ii18](https://ard.bmj.com/content/64/suppl_2/ii18).
- [10]. Korman NJ. Management of psoriasis as a systemic disease: what is the evidence British Journal of Dermatology. 2019 Oct 15;182(4):840–8.
- [11]. Irmina Maria Michalek, Loring B, Swen Malte John, World Health Organization. Global report on psoriasis. Geneva, Switzerland: World Health Organization; 2016.
- [12]. Cada DJ, Demaris K, Levien TL, Baker DE. Tofacitinib. Hospital pharmacy. 2013May;48(5):413-24.
- [13]. Indian Pharmacopoeia 2018, Vol 1;239.
- [14]. S Abhijeet, U Madhawai, S Dhobale, S Jadhav, D Gaikwad. Method Development and Validation of Tofacitinib Bulk Drug By Using Uv Visible Spectrophotometer. Bull. Env. Pharmacol. Life Sci., Vol 10[2] January 2021 : 60-64.
- [15]. Thakur S, Anjum M, Jaiswal S, Kumar A. Novel synergistic approach: Tazarotene-Calcipotriol-Loaded PVA/PVP Nanofibers incorporated in Carbopol hydrogel film. Mol Pharm. 2023;20(2):997-1014. doi:10.1021/acs.molpharmaceut.2c00713
- [16]. Rani, Pooja, et al. "Preparation, Characterization, and Evaluation of Ketoconazole-Loaded Pineapple Cellulose Green Nanofiber Gel." International Journal of Biological Macromolecules, 1 Feb. 2024, pp. 130221–130221, <https://doi.org/10.1016/j.ijbiomac.2024.130221>. Accessed 3 Mar. 2024.