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Water hyacinth (*Eichhornia crassipes*)-derived cellulose nanofibril/methyl cellulose nanocomposite-based transdermal film for controlled release of Diclofenac sodium

Abstract

The members of the Pontederiaceae family, water hyacinth (*Eichhornia crassipes*) is an aquatic plant high in natural fibers containing cellulose nanofibrils (CNFs). Extracted by homogenization, grinding, and refining, CNFs—high-aspect-ratio nanoscale fibers with biocompatibility and unusual chemical structure—are Their uses in systems of medication delivery have attracted a lot of interest recently. This work focuses on the creation of CNF-based transdermal films for the controlled release of diclofenac sodium, a nonsteroidal anti-inflammatory medication (NSAID) generally used for arthritis, pain, and musculoskeletal diseases. Just half of orally given diclofenac sodium enters systemic circulation due to its limited bioavailability and hepatic first-pass metabolism. By means of continuous drug release, transdermal films provide an alternate drug delivery method that increases therapeutic efficacy, lowers systemic adverse effects, and improves patient compliance. Various matrix transdermal films were developed in this work with varied CNF ratios and assessed for drug penetration and release via the skin. In the process of film development, CNFs provide a good matrix material that guarantees regulated drug diffusion. Among the other benefits the transdermal films offer are lower dose frequency, better self-administration, and steady therapeutic drug levels over a longer length of time. The aim of this work is to develop and assess CNF-based transdermal films to attain a constant and efficient medication concentration for extended therapeutic efficacy.

Keywords: Cellulose nanofibrils, transdermal drug delivery, diclofenac sodium, drug release, controlled drug delivery, water hyacinth.

1. Introduction

Water Hyacinth is a member of the Pontederiaceae family, specifically the species *Eichhornia crassipes* [1]. Water hyacinths are aquatic plants native to South America, primarily in the Amazon basin. They have been grown in Australia since 1895 and have been found in Asian countries since the early 20th century [2]. White-handed mussels (WH) can infiltrate ecosystems, adapt to different environments, and reproduce quickly. They spread from one place to another due to shared waterways, bird legs, and human activity. The ideal conditions for WH development and reproduction are acidic to neutral pH, quiet, and low water depth. The water body's nutrient concentration is crucial for WH growth. WH reproduces asexually through solons and budding, and sexually through seed formation. They can grow on freshwater bodies and on stolon's, creating offspring plants[3, 4]. This water hyacinth composed by natural fibers which contain specially carbon fibers[5–7], fiberglass[8] etc. The interest of cellulose nanofibrils is enhance day by day. Cellulose nanofibrils (CNFs) are high aspect ratio nanoscale cellulose fibers that are usually several micrometres long and 5 to 50 nm in diameter. They come from the cell walls of plants and have been attracting interest because of their special qualities and possible uses [9]. They typically have a greater aspect ratio than CNCs and contain crystalline chains of cellulose as well as amorphous areas with tangling between the fibrils. Dimension, strength, aspect ratio, and crystallinity are the primary factors that distinguish CNFs from CNCs[10]. CNF extraction process has been done by different chemical treatment procedure. Basically, cellulose nanofibrils are obtained from water hyacinth by different procedure like grinding, refining and homogenization etc. CNFs are basically biocompatible and it has unique molecular structure which gain attraction day by day in pharmaceutical industry[11, 12]. In the film formation CNFs work as a matrix material to deliver the drug. There are different types of thin film which are formulated by different technologies such as multilayer thin film drug delivery system, prolonged release drug delivery system in the film, mouth dissolving film etc[13]. Diclofenac sodium is nonsteroidal anti-inflammatory agent which is used for arthritis, pain, inflammation, musculoskeletal disorders etc[14]. This has low bioavailability and short biological half-life and it undergoes hepatic fast pass metabolism, that is why only 50% drug can reach to the systematic circulation. Diclofenac sodium used in small dose, so it can be easily formulated in transdermal film[12, 15]. Transdermal film has various advantages such as it reduced frequency dosing, self-administration, prolonged drug level, small dose of drug required, better patient compliance etc[16–18].

In the present research study main objective was to formulate different matrix transdermal film with various ratio of CNFs which contain diclofenac sodium and perform the different evaluation study to check the release of the drug through the skin to gain a therapeutically effective drug level for long duration of time from transdermal film.

2. Experimental Work

2.1 Materials

Water hyacinth was collected from the nearby water bodies, Sodium Hydroxide, Sodium Chlorite, Sodium Bisulphite, Methyl Cellulose are purchased from Loba Chemie Pvt. Ltd. Sulphuric acid has been purchased from Nice Chemicals (p) ltd, Diclofenac Sodium gifted from Aarti Drugs Ltd.Tarapur Bioser. M.H.

2.2 Methodology

2.2.1 Extraction of CNFs from water hyacinths

At first, water hyacinth is collected from nearby water bodies and then it is being heated at room temperature and let it dry. The dry water has is then collected and the steam is cut and collected. The steam is further dried at hot air oven. Then the water hyacinth is then grinded using a mixer grinder. Then the sample is being stored in an air tight container. 30gm of grinded water hyacinth is taken and treated with 50% NaOH. The 30gm of the sample is mixed with 50% NaOH in a beaker. The beaker is then kept in water bath for 2 hours maintaining a temperature of 70 ° C. Then the sample is rinsed the sample is then arranged with distilled water for several times repeatedly. This is done to wash off the extra chemical. Then it is kept in Petri-dish in the hot air oven for 24 hours. Then the dried sample was bleached by treating it with 7% NaClO₂. The sample and NaClO₂ is taken in a beaker and kept in water bath for 2 hours maintaining a temperature of 70 ° C. After 2 hours, it is rinsed well repeatedly with distilled water and kept in the Hot air oven for overnight to dry. Then the sample is again treated with 14% NaOH for 2 hours and kept in the water bath. The temperature of the water bath was maintained at 70 ° C. Then it is treated with 5% Sodium Bisulphate to bleach and kept for 2 hours. After that, it was kept it in the Hot air oven to dry overnight. Then it was treated with 14% H₂SO₄ and kept for 2 hours. Then the product that was obtained was the lignin free CNF, as shown in Figure 01.

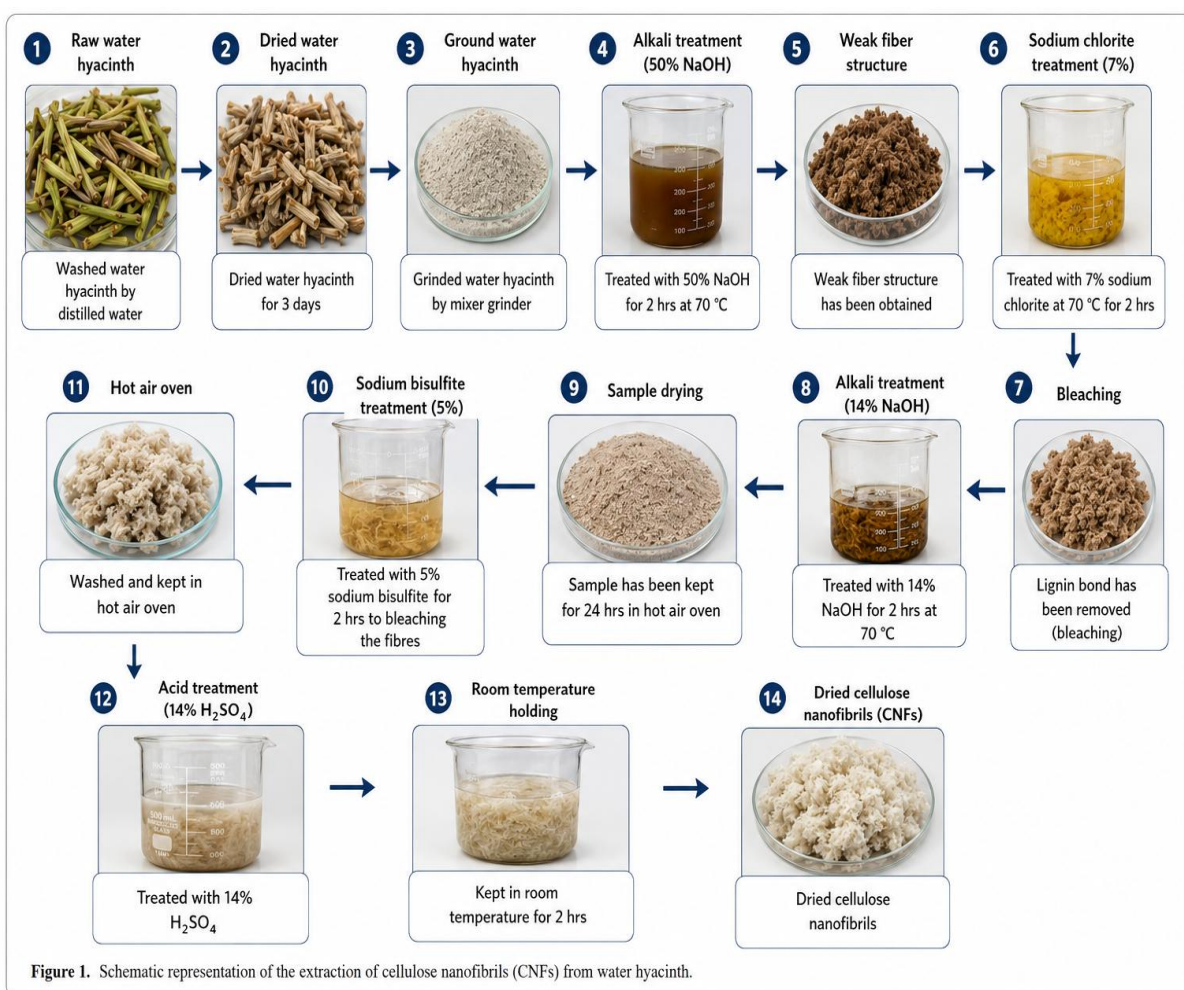


Figure 1. Schematic flow diagram illustrating the extraction and preparation of cellulose nanofibrils (CNFs) from water hyacinth (*Eichhornia crassipes*) through sequential alkali treatment, bleaching, acid hydrolysis, drying, and purification processes.

2.2.2 Preparation of CNF-Based Transdermal Film using Diclofenac sodium

Nanocomposite films were prepared as per the formulation shown in Table 1 (Formulation trial batches of Transdermal Film using CNF). As shown in Figure 2, a 2% w/v methyl cellulose solution was prepared by dissolving the required quantity of methyl cellulose in 100 ml of distilled water under continuous stirring. Separately, the drug diclofenac sodium was dissolved in dimethyl sulfoxide (DMSO) to obtain a clear drug solution. Cellulose nanofibers (CNFs) of varying concentrations (3%, 6%, 9%, and 12% based on the polymer weight) were then dispersed into the drug solution and kept for 24 hrs. under gentle stirring to facilitate drug adsorption onto the CNF surface. The drug-loaded CNFs were subsequently incorporated into 20 ml portions of the methyl cellulose solution, which were distributed into five 100 ml beakers

labeled F1(do not contain CNF) but F2, F3, F4, and F5, corresponding to different CNF concentrations. Each mixture was stirred magnetically for 2–3 hours, followed by sonication for 1.5 hours to ensure homogeneous dispersion. The prepared dispersions were cast into Petri dishes and dried at 45–50 °C. The resulting drug-loaded CNF–methyl cellulose films were carefully peeled off and stored in a desiccator for further characterization.

Table 1. Formulation trial batches of Transdermal Film using CNF

Sr. No	Formulation	2%(w/v) methyl cellulose solution (ml)	% of CNF with respect to weight (mg) of methyl cellulose	Diclofenac Sodium (mg)
01	F1	20	0	100
02	F2	20	3	100
03	F3	20	6	100
04	F4	20	9	100
05	F5	20	12	100

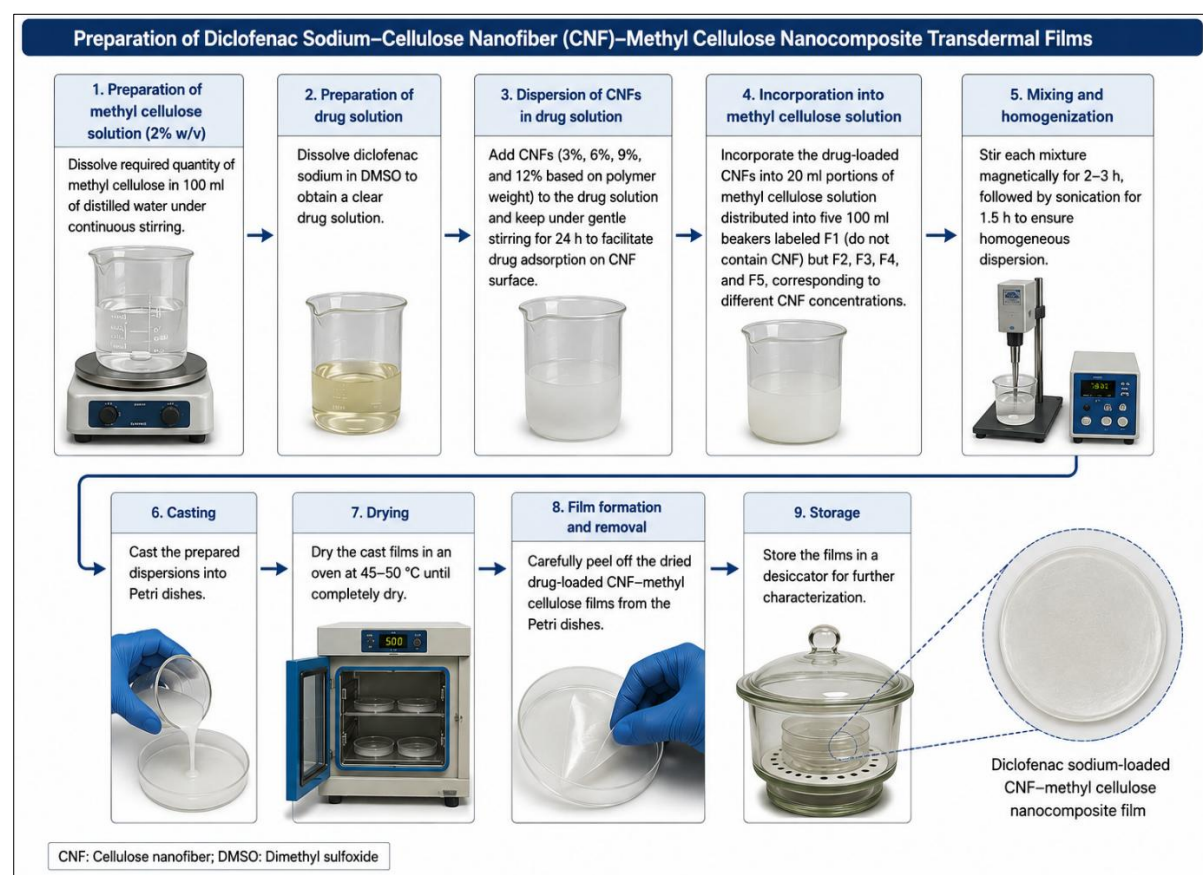


Figure 2. Schematic representation of the preparation of diclofenac sodium-loaded cellulose nanofiber (CNF)–methyl cellulose nanocomposite transdermal films, including polymer solution preparation

3. Characterization

3.1 Attenuated Total Reflectance Fourier Transform Infrared Spectrophotometer

Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) spectroscopy was employed to investigate the chemical structure and intermolecular interactions of cellulose nanofibers (CNF) and CNF/methylcellulose nanocomposites using a Shimadzu IRSpirit-T spectrometer equipped with a diamond ATR crystal. Spectra were recorded in the range of 4000–400 cm^{-1} with a resolution of 4 cm^{-1} and an average of 32 scans per sample at room temperature[19].

3.2 Field Emission Scanning Electron Microscopy (FeSEM) analysis of CNFs and transdermal film

To investigate the surface morphology and microstructural features of cellulose nanofibres (CNFs) and their methylcellulose-based nanocomposites, scanning electron microscopy (SEM) was conducted using a ZEISS EVO 18 SERIES instrument. For CNF analysis, a dilute aqueous dispersion was prepared by sonicating 1 mg of CNFs in 100 mL of distilled water for 1 hour to ensure uniform dispersion. A small drop of the resulting suspension was then carefully cast onto a clean silicon slide and allowed to air dry under ambient conditions for 24 hours. The dried samples were subsequently sputter-coated with a thin layer of gold to enhance conductivity prior to SEM imaging. For cross-sectional analysis of methylcellulose films and CNF/methylcellulose nanocomposites, each sample was manually torn to produce a rough fracture surface, thereby exposing the internal structure. These fractured pieces were then mounted onto SEM stubs, sputter-coated with gold, and examined under the same ZEISS EVO 18 SERIES SEM. The micrographs obtained provided detailed insights into the surface morphology of CNFs and the internal structural organization of the nanocomposite films[20].

3.3 DLS (Dynamic Light Scattering) Study

The hydrodynamic particle size of cellulose nanofibrils (CNF) was determined using a Zetasizer Nano series ZS, dynamic light scattering (DLS) instrument (Malvern Instruments, Malvern UK). The concentration of cellulose nano fibrils (CNF) in water (as the solvent) was 1000 ppm[21].

3.4 Zeta Potential

Dynamic Light Scattering (DLS) analysis was conducted to determine the hydrodynamic particle size of the cellulose nanofiber (CNF) dispersion. The measurement was performed at IIT Kharagpur Central Research Facility, using a Zetasizer Nano ZS instrument (Malvern Instruments, Malvern, UK). Aqueous CNF dispersion at a concentration of 1 g/L was prepared and analysed under standard conditions. The instrument utilized backscattered light at an angle of 173° to evaluate the Brownian motion of the dispersed nanoparticles, enabling calculation of the hydrodynamic diameter based on the Stokes-Einstein equation. The analysis provided essential information regarding the average particle size distribution and colloidal stability of the CNF suspension in water[22].

3.5 Mechanical properties

The mechanical properties of the prepared methylcellulose and CNF/methylcellulose nanocomposite films were evaluated using a Zwick Roell Z010 universal tensile testing machine. Five specimens from each film type were cut into rectangular strips with dimensions of 22 mm in length and 5 mm in width. Tensile testing was performed at room temperature with a constant crosshead speed of 5 mm/min. The measurements were conducted to assess parameters such as tensile strength, elongation at break, and Young's modulus, providing insight into the mechanical reinforcement effect of CNFs within the polymer matrix.

3.6 X-Ray diffraction (XRD) analysis

Nanocellulose and the prepared nanocomposites were characterized using an X-ray diffractometer (X-PERT-PRO, PANalytical) equipped with CuK α radiation ($\lambda = 1.5406$ Å), operating at 40 kV and 30 mA. Diffraction patterns were recorded over a 2θ range of 5° to 60° at a scan rate of 2° min⁻¹. The crystallinity index (CrI) of nanocellulose was determined using Equation (1), as described in previous studies.

$$\text{Crystallinity index} = [(I_{\text{Crystalline}} - I_{\text{Amorphous}})/I_{\text{Amorphous}}] \times 100 \quad [1]$$

Where, $I_{\text{Crystalline}}$ is the height of the crystalline contribution peak (at 2θ of approximately 22.57°) and $I_{\text{Amorphous}}$ is the amorphous contribution at 18.29°

4. Evaluation of transdermal film

4.1 Thickness of the transdermal film

The thickness of films was measured by Digital Vernier Calipers (Make: Zhart) with least count 0.001mm. The thickness uniformity was measured at five different sites and average of five readings were taken with standard deviation[23].

4.2 Weight variation of transdermal film

Three films of 2x2 cm² were cut from different area of petriplate and weighed on electronic weighing balance[24].

4.3 Folding Endurance

Three samples, each of F1, F2, F3, F4 and FS formulations were repeatedly folded at the same point until the sample broke. This was carried out for the three specimens of each sample and the average value was taken. The folding cycles endured by each tested sample specimen without breakage was considered to be the folding endurance value of that sample[25].

4.4 Surface pH

Transdermal film was left to swell for 1 hour on the surface of agar plate. It is prepared by dissolving 2% (w/v) agar in warmed isotonic phosphate buffer of pH 6.8 under stirring. Then it poured the solution into the petridish allowed to stand till gelling at room temperature. Then the surface pH was measured by means of pH paper placed on the surface of the swollen film[26].

4.5 Swelling Index

Film samples were cut into uniform disk shapes and weighed prior to immersion in phosphate buffer solution (pH 7.4). The samples were then immersed, and their weights were recorded at predetermined time intervals over a 24-hour period. Before each measurement, excess buffer adhering to the film surface was gently removed using filter paper. The swelling ratio of the transdermal films was calculated using Equation[27].

The swelling index was calculated by,

$$S = (X_t - X_0) / X_0 \dots\dots\dots (4)$$

Where, S = Swelling Index, X_t = Weight of film after t time, X_0 = Initial weight of film.

4.6 Drug Loading Efficiency

Diclofenac sodium, used as a model drug, was incorporated into the CNF/methylcellulose matrix via the solvent evaporation method. Disk-shaped films were immersed in 10 mL of diclofenac sodium solution (10 mg mL⁻¹) for 24 hours. After immersion, the swollen films were removed, rinsed with 10 mL of distilled water to eliminate surface-adhered drug, and subsequently dried in an oven at 37 °C for 24 hours. The concentration of the unabsorbed drug remaining in the solution was determined spectrophotometrically using a Shimadzu

UV-Visible Spectrophotometer (Model 1780) at 276 nm. The drug loading efficiency (DL%) was calculated using Equation [4].

$$\text{Drug Loading (\%)} = \frac{\text{Amount of drug loaded into the film}}{\text{Initial amount of drug}} \times 100$$

4.7 In vitro drug release and kinetics study

In the present study the in-vitro release of drug from the matrix transdermal film was studied by Franz diffusion cell using plasma dialysis membrane. Here the cell has been made by two different chamber that is donor and receptor compartment. Total system surrounded by water which is continuously circulated by motor and the temperature must be maintained 37 °C. The donor compartment filled with phosphate buffer (pH 7.4) solution. and upside of donor compartment dialysis membrane (LA390, width 25.27 mm diameter 15.9mm and capacity 1.99 ml cm⁻¹) has been placed and the film placed on the membrane. After the system has been maintained the sample has been taken with proper duration of time by the help of needle from the donor compartment which is under continuous stirring process by the help of magnetic stirrer. After the collection of samples with duration of time observed under the UV-Spectroscopy at 276nm to check the release of drug from the film[28].

5. Result & Discussion

5.1 Organoleptic Evaluation

Organoleptic properties of cellulose nanofibrils are observed below Table 02 which is dissolved in water and extracted from water hyacinth. The sample was observed to be off-white in color, odourless, and irregular in shape. It exhibited good solubility characteristics, being almost completely soluble in water, which indicates its suitability for formulation development and potential ease of administration in aqueous systems.

5.2 Characterization Study

5.2.1 Dynamic Light Scattering (DLS) Study

The hydrodynamic particle size of cellulose nanofibrils (CNF) was determined using a Zetasizer Nano series ZS, dynamic light scattering (DLS) instrument (Malvern Instruments, Malvern UK). We determined the mean hydrodynamic size of the nanoparticles, which was 95.79 nm, and their range, which was 10 to 350 nm[21], as illustrated in Figure 3.

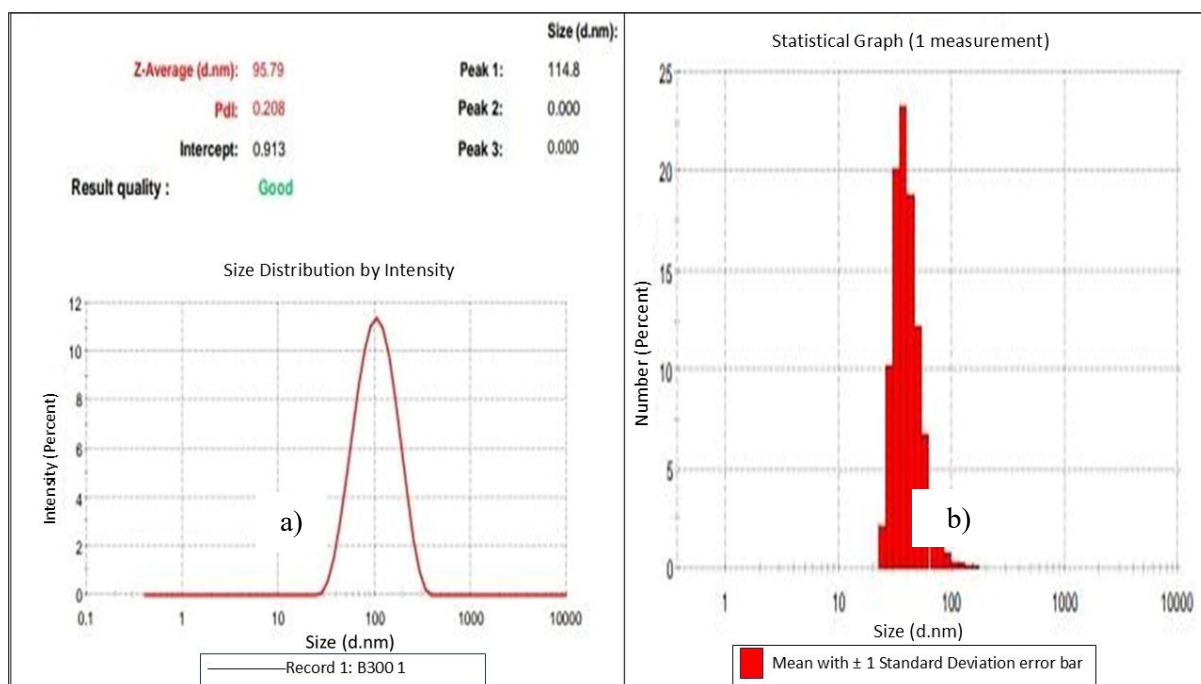


Figure 3. Dynamic light scattering (DLS) analysis showing the particle size distribution of cellulose nanofibrils (CNFs). The sample exhibited a mean hydrodynamic diameter (Z-average) of 95.79 nm with a polydispersity index (PDI) of 0.208, indicating a relatively narrow size distribution. The intensity distribution curve and corresponding statistical histogram confirm the nanoscale size range of the prepared CNFs.

5.2.2 Zeta Potential study

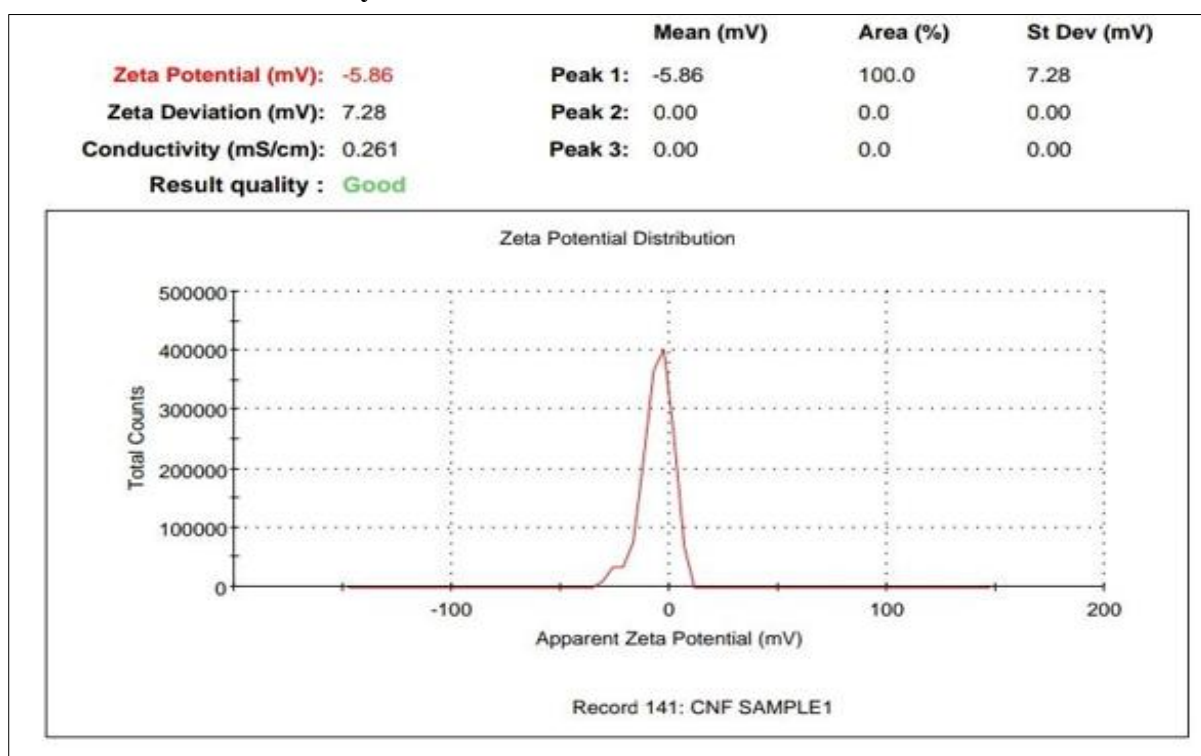


Figure 4: Zeta potential distribution profile of the prepared cellulose nanofibrils (CNFs) determined by electrophoretic light scattering. The CNFs exhibited a mean zeta potential of -5.86 mV with a zeta deviation of 7.28 mV, indicating a slightly negative surface charge and providing information on the colloidal stability of the nanofibril dispersion. The distribution curve shows a single dominant peak, suggesting a relatively homogeneous particle population.

Theoretical models of electrokinetic and electroacoustic events can be used to compute zeta potential. When an electric field is applied over a dispersion, particles are drawn to the opposite charge electrode to be measured. Electrophoretic light scattering and microelectrophoresis are two experimental methods. Smoluchowski or Huckel theory is used to convert the particle mobility, which is determined by the frequency shift of an incident laser beam, to ZP. The zeta potential of CNF has been measured from IIT Kharagpur by using of Malvern Instrument. We determine the zeta potential of the cellulose nanofibrils was -5.86 , by using Dynamic Light Scattering[22], as illustrated in Figure 4.

5.2.3 ATR-IR Spectra Study

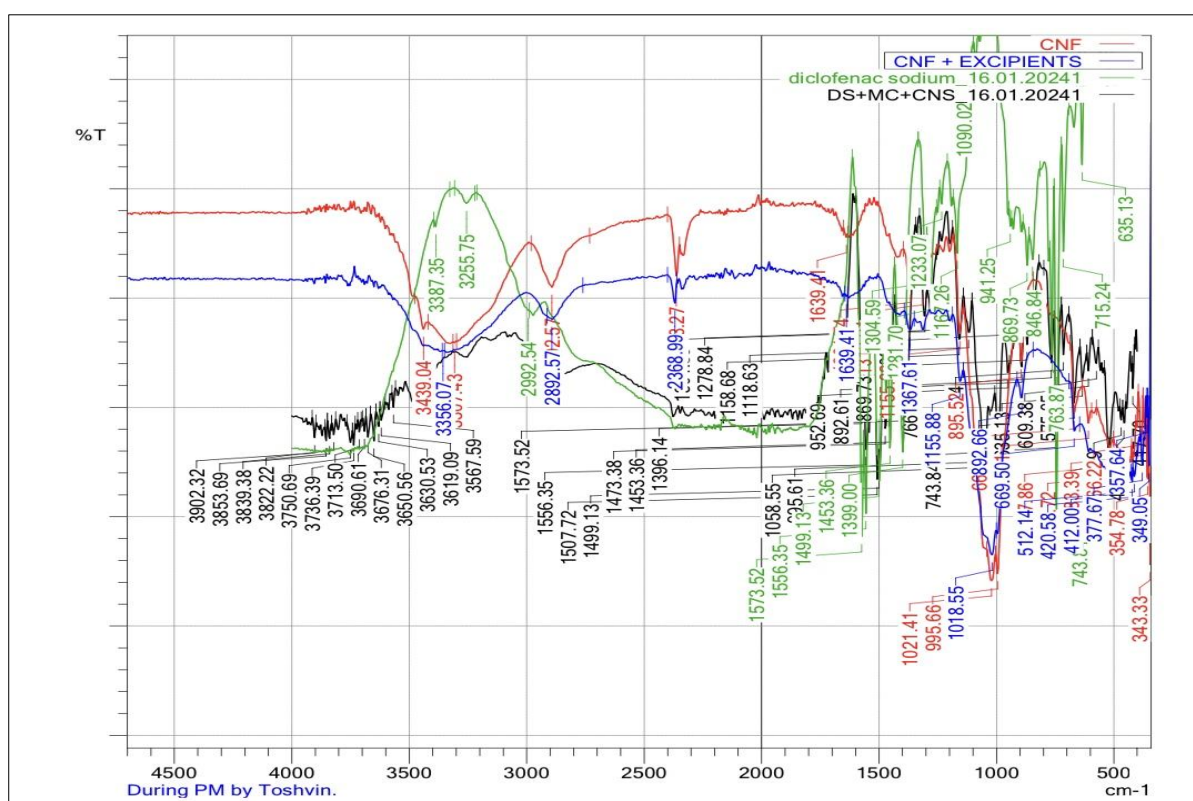


Figure 5. ATR-IR Spectra of CNF, Diclofenac Sodium, Physical mixture of CNF with excipients and drug loaded in transdermal film

ATR-IR helped to identify the compatibility studies drug with CNF and polymer, as illustrated in figure 04. Also, it helps to determine the functional groups which are present in cellulose nanofibrils. It shows no chemical interaction between diclofenac sodium with CNF and polymer. The materials are observed under the ATR-IR of SHIMADZU was used to evaluate the changes in chemical bond of water hyacinth before and after treatment with alkaline & acidic solution. For the C=C stretching, O-H stretching, C=O stretching, C-H stretching, N-H stretching shows different peak such as 1090 cm^{-1} , 1167 cm^{-1} , 3387 cm^{-1} , 1722 cm^{-1} , 2930 cm^{-1} , 3387 cm^{-1} , 3255 cm^{-1} observed in diclofenac sodium drug and CNF which has been showed on Figure 5. These peaks were proved that they are compatible with each other and ideal for preparation of transdermal film[19].

5.2.4 Field Emission Scanning Electron Microscopy (Fe-SEM):

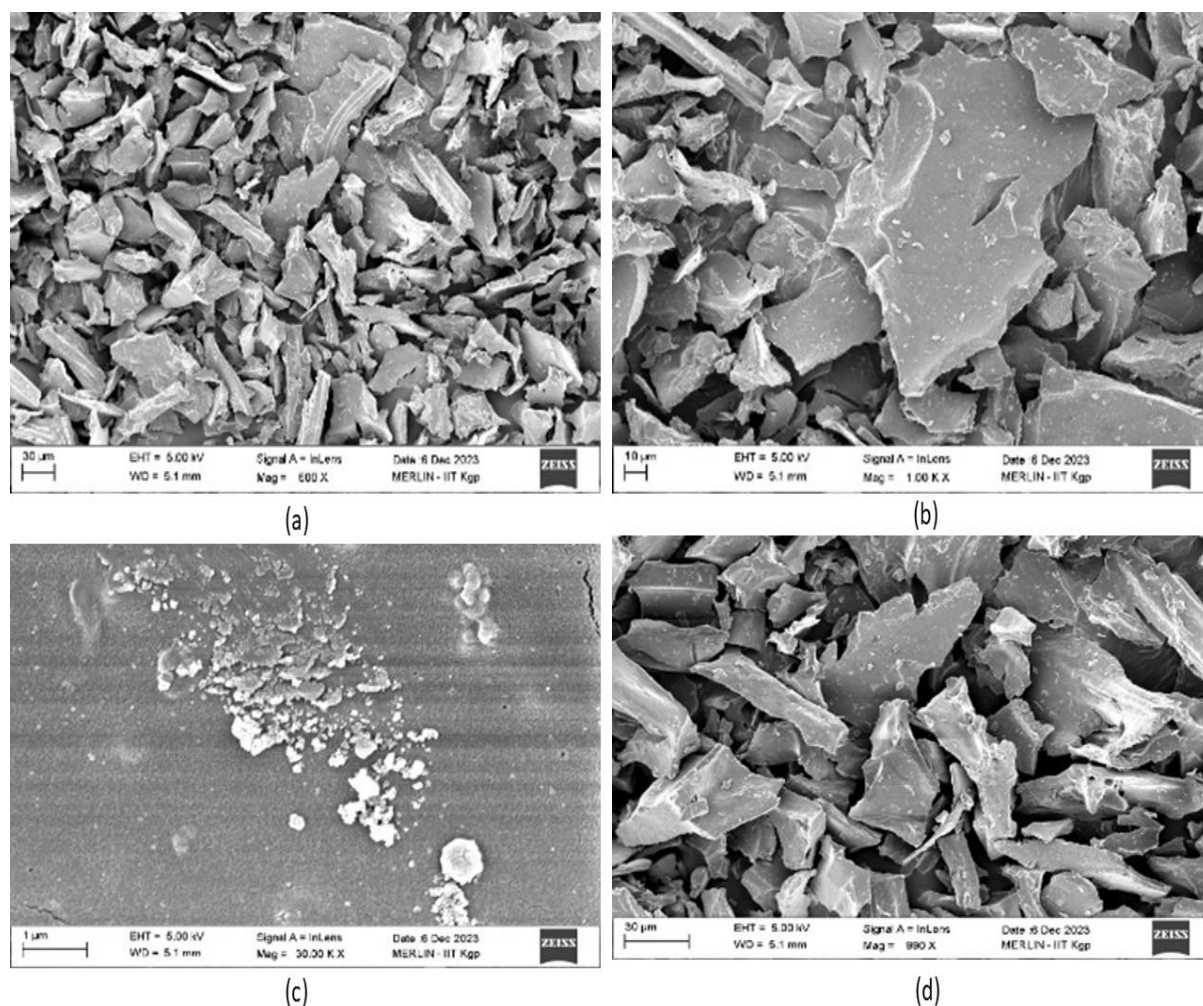


Figure 6. Field Emission Scanning Electron Microscopy (FESEM) images of cellulose nanofibrils (CNFs) isolated from water hyacinth at different magnifications. The micrographs reveal the surface morphology and fibrillar structure of the extracted cellulose, showing irregular fibrous fragments,

layered sheet-like particles, and aggregated nanocellulose domains formed after chemical treatment. Images (a–d) demonstrate the progressive defibrillation and structural modification of water hyacinth fibers, confirming the successful isolation of cellulose-rich nanofibrillar material suitable for nanocomposite film fabrication.

Fe-SEM study has been showed in the Figure 6, which gave the morphological characteristics of cellulose nanofibrils after the extraction from water hyacinth. These micrographs showed that CNFs were in irregular structure. The tiny particles of different extracted CNF observed under Fe-SEM. It showed rough, sharp, needle structure of nanofibrils [20].

5.3 Evaluation parameters of Transdermal Film

5.3.1 Thickness, weight variation, folding endurance, % of drug content, surface pH

The thickness, weight variation, folding endurance, % of drug content and surface pH of different formulation of film was calculated and results given below in Table 2.

Table 2. Effect of different concentration of % of CNF with respect to weight (mg) of methyl cellulose on different formulation film

Formulation code	Thickness (mm)	Weight Variation (mg)	Folding Endurance	Surface pH	% of drug content
F1	0.09 ±1.5	18.25 ±1.05	245	5.21	91±1.54
F2	0.65 ±1.2	19.25 ±1.38	250	5.32	92±1.61
F3	0.77 ±1.3	18.25 ±1.14	230	5.45	93±1.37
F4	0.83 ±1.5	19.52 ±1.32	300	5.50	93±1.92
F5	0.93 ±1.2	20.26 ±1.22	255	5.45	95±1.28

The thickness of films was measured by Digital Vernier Calipers (Make: Zhart) with least count 0.001mm. The thickness uniformity was measured at five different sites and average of five readings were taken with standard deviation which is showed in the Table 02. The thickness of the transdermal films varied from 0.09mm to 0.98mm[23]. Three films of 2x2 cm² were cut from different area of petriplate and weighed on electronic weighing balance which is denoted in Table 02. The weight variation of the films varied from 18.25mg to 20.26mg[24]. Folding endurance of all different formulation films were observed in Table 02. All films folding endurance came below 300 and 300 which proved that all formulated films were good in

nature[25]. Drug content uniformity of film means that how much drug has been uniformly distributed in the formulation. The film size 2x2 cm² were cut down and placed in a volumetric flask. Then the film has been dissolved with the phosphate buffer (pH 7.4) for 24 hours under the continuous stirring process by the help of magnetic stirrer. After 24 hours the solution has been taken from volumetric flask and check at 276 nm by using UV-visible spectrophotometer. From the absorbance the drug content has been came which is showed in the Table 02 [25].

The graphs present below in Figure 7 represent the thickness, weight variation, folding endurance, surface pH, and drug content of the formulated films, demonstrating the effect of increasing cellulose nanofibril (CNF) concentration on film characteristics. Data are expressed as mean $\pm$ standard deviation (SD).

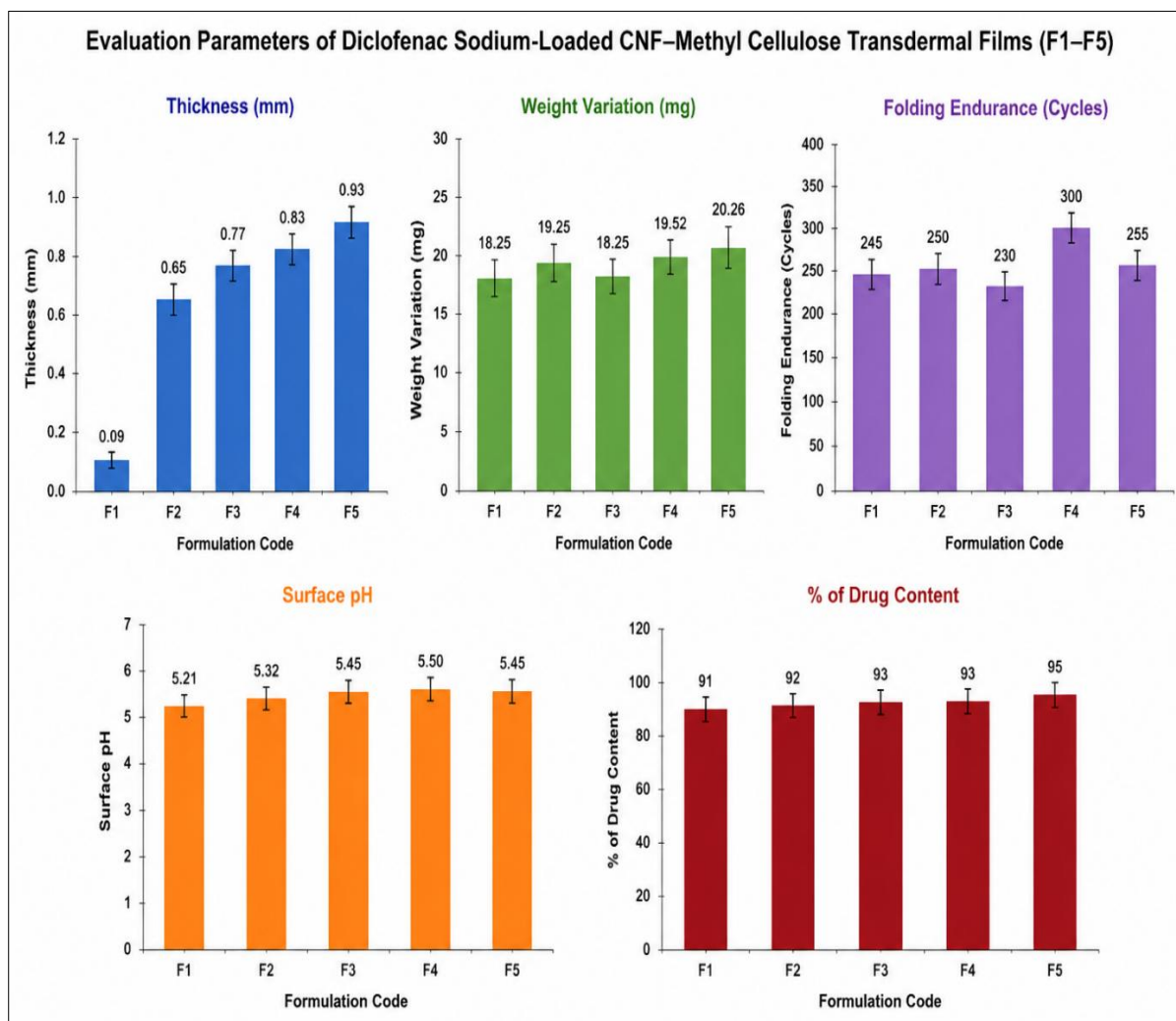


Figure 7. Comparative bar diagrams illustrating the physicochemical and mechanical evaluation of diclofenac sodium-loaded CNF–methyl cellulose transdermal films (F1–F5)

5.3.2 Swelling study

For swelling studies films were cut down in 2x2 cm² size from different places and weighed properly. Then the films were taken and placed on the coverslip which was placed on the petridish. Then distilled water has been given on the coverslip for the 05,10,15,20,60 seconds according to different time interval. Due to the methyl cellulose and CNF which is hydrophilic in nature when they came to contact with distilled water the films were started swelling. Thus, the weight of films was enhanced due to absorbed the water. The Figure 8 showed the order of swelling ratio of film[27].

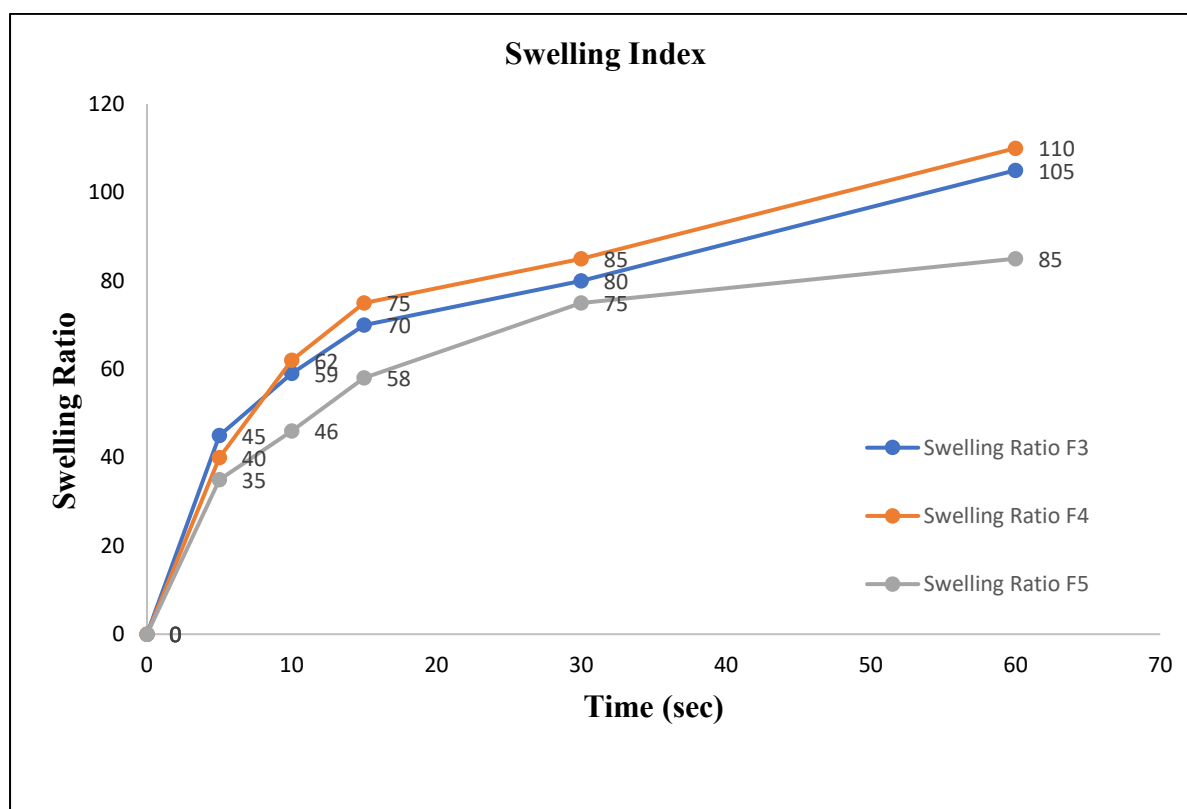


Figure 8 Swelling behavior of diclofenac sodium-loaded CNF–methyl cellulose transdermal films (F3–F5) as a function of time. The swelling ratio increased progressively with immersion time for all formulations, indicating water uptake and matrix hydration. Formulation F4 exhibited the highest swelling ratio (110% at 60 s), followed by F3 (105%) and F5 (85%), suggesting that CNF concentration significantly influences the swelling characteristics and moisture absorption capacity of the transdermal films.

5.3.3 “In-vitro” drug release study

The comparative evaluation of the drug release profiles among the formulations (F1–F5), as shown in Table 03 (“In-vitro” drug release study discussion), indicates that the variation in

release rates can be attributed to differences in polymer concentration, excipient composition, and matrix characteristics.

Table 3. In vitro cumulative percentage drug release of diclofenac sodium from CNF–methyl cellulose transdermal film formulations (F1–F5) at different time intervals (mean $\pm$ SD).

Time (hrs)	% Cumulative Drug Release				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	26.8743 $\pm$ 0.5	26.1499 $\pm$ 0.5	25.6429 $\pm$ 0.3	23.6871 $\pm$ 0.2	21.8037 $\pm$ 0.2
2	31.2206 $\pm$ 0.4	29.7718 $\pm$ 0.2	28.3231 $\pm$ 0.2	25.5704 $\pm$ 0.4	22.9627 $\pm$ 0.3
3	39.1887 $\pm$ 0.2	35.5668 $\pm$ 0.3	33.3213 $\pm$ 0.4	29.7718 $\pm$ 0.6	24.7012 $\pm$ 0.3
4	45.4183 $\pm$ 0.5	43.9696 $\pm$ 0.4	40.2753 $\pm$ 0.3	33.3213 $\pm$ 0.4	25.1358 $\pm$ 0.4
5	51.7204 $\pm$ 0.3	48.0985 $\pm$ 0.3	46.0703 $\pm$ 0.5	37.3778 $\pm$ 0.3	26.2224 $\pm$ 0.3
6	57.8776 $\pm$ 0.3	53.3865 $\pm$ 0.5	51.9377 $\pm$ 0.3	42.0862 $\pm$ 0.3	29.7718 $\pm$ 0.2
7	65.2662 $\pm$ 0.4	59.2539 $\pm$ 0.5	58.2398 $\pm$ 0.5	48.7505 $\pm$ 0.5	30.6411 $\pm$ 0.5
8	76.3491 $\pm$ 0.3	66.5701 $\pm$ 0.3	60.8475 $\pm$ 0.4	54.1108 $\pm$ 0.3	32.5969 $\pm$ 0.5

Formulation F1, which showed the highest cumulative release (76.35% at 8 hours), likely contained a lower concentration of release-retarding polymer or a higher proportion of hydrophilic excipients, facilitating rapid water penetration and drug diffusion. F2 and F3 demonstrated moderately sustained release (66.57% and 60.84%, respectively), suggesting a balanced polymer-to-drug ratio that slowed the release compared to F1 but still ensured effective drug diffusion. F4 exhibited a slower release pattern (54.11%), which could be due to a higher concentration of release-controlling polymer, leading to increased matrix density and reduced drug mobility. F5 showed the lowest release (32.59% at 8 hours), likely resulting from the presence of a high proportion of retarding polymer or stronger polymer–drug interactions, which restricted water uptake and hindered drug diffusion. These observations, illustrated in Figure 9, highlight that the concentration and type of polymers, as well as the excipient composition, play a crucial role in modulating the drug release kinetics across formulations.

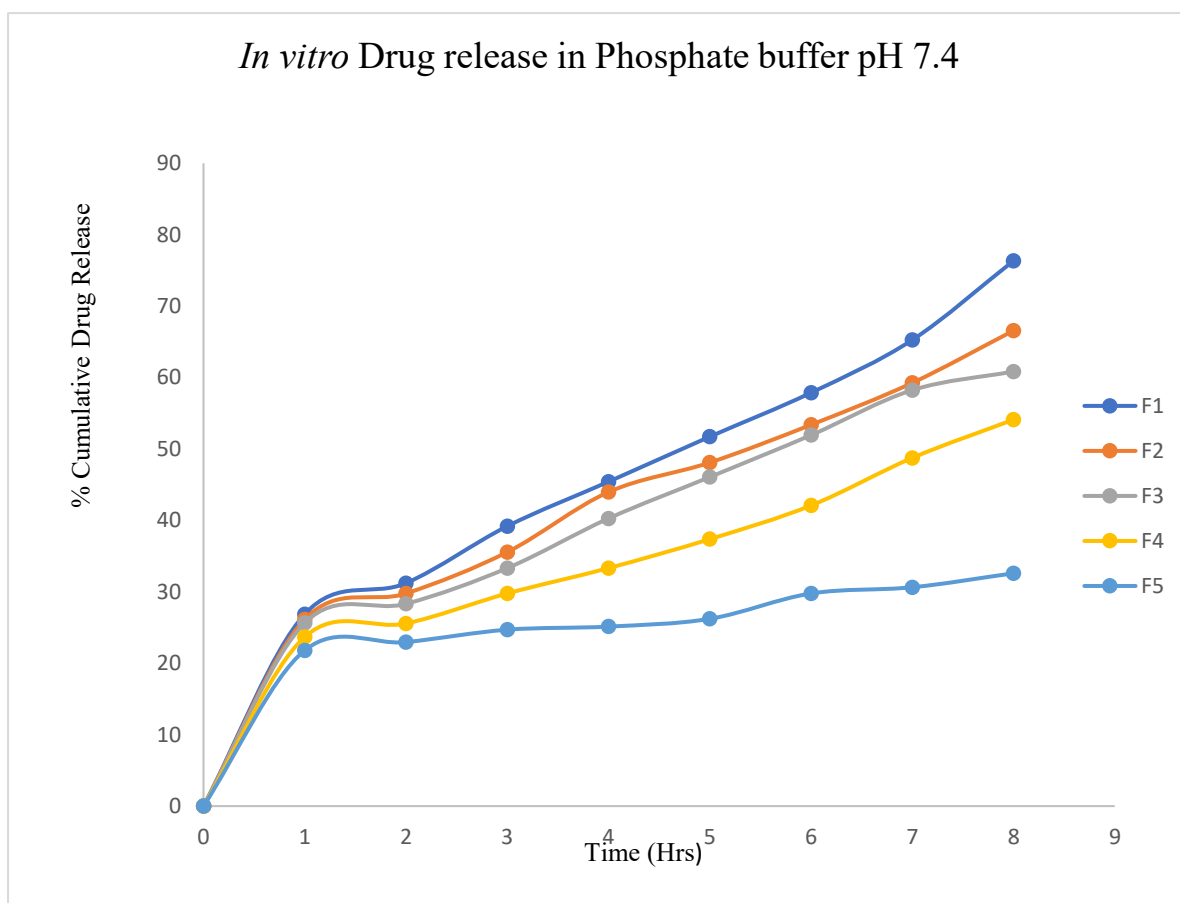


Figure 9. *In vitro* Drug release in Phosphate buffer pH 7.4

6. Future scope

The successful extraction of biocompatible cellulose nanofibrils (CNFs) from the invasive water hyacinth establishes a cost-effective, eco-friendly framework for polymer matrix development in pharmaceutical applications. Building upon the ideal characteristics observed in the F5 nanocomposite batch, future investigations should focus on performing *ex vivo* skin permeation studies using animal models to better replicate human skin barriers, as the current study relied solely on artificial plasma dialysis membranes. To transition this transdermal film toward clinical viability, comprehensive *in vivo* pharmacokinetic and pharmacodynamic evaluations are essential to track systemic drug concentration and validate prolonged anti-inflammatory efficacy over extended durations.

Additionally, further optimization of the film can incorporate safe chemical permeation enhancers or leverage modern cross-linking technologies to systematically fine-tune the hydration and diffusion kinetics of high-polymer batches like F5, which exhibited highly restricted drug mobility. Finally, the scaling potential of this green synthesis method should be explored by testing this CNF/methyl cellulose matrix with a broader spectrum of low-dose, short half-life drugs suffering from extensive first-pass metabolism, thereby maximizing the therapeutic and environmental utility of water hyacinth biomass

7. Conclusion

Water hyacinth is an invasive aquatic plant which has significant negative environmental impacts such as harmful aquatic life, reducing oxygen level in water etc. Though from this cellulose nanofibrils are obtained by different chemical treatment (treat with acidic and basic solution). This isolated CNF is cost effective and it's are basically biocompatible and it has unique molecular structure which gain attraction day by day in pharmaceutical industry. In the transdermal film formation CNFs work as a matrix material to deliver the drug. In, this research study it has been observed that CNF has favourable organoleptic properties and it can easily completely soluble in water which suggests a cost-effective homogenization cycle for producing films using cellulose nanomaterial. The average hydrodynamic dimension (d. nm) of the CNFs is clearly 196 nm according to the DLS result, although the size is approximately the same according to the FESEM. It is discovered that the zeta potential is -5.86 mV. The FESEM data show that the water hyacinth was successfully chemically defibrillated, reducing its length from mm to nm. The CNF is fashioned like a web of nanoscale needle-like threads crossing one another. The ATR-IR results verify that there is no interaction between methyl cellulose and CNF. After that the transdermal film has been produced by solvent casting method. In this film formulation diclofenac sodium drug has been used with CNF. After the preparation of formulation, it has been showed in ATR-IR study that they are compatible with each other. To determine the ideal conditions of films they are observed by different evaluation method such as weight variation, thickness, surface pH, and another many variable were checked. From the swelling index, thickness, folding endurance, surface Ph it has been shown that F5 batch had ideal characteristics.

8. Declaration Statement

Author Contribution: **S.P.:** Writing-original draft; **B.B:** Writing- review and editing; **P.P:** Data collection; **A.B:** Conceptualization; **B.D.:** Formal analysis.

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