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Preparation and in Vitro Evaluation of Biophytum Sensitivum-Loaded Cellulose Acetate Films for Diabetic Wound Management

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Abstract: Diabetic wound healing presents a significant clinical challenge in the expanding medical sector due to impaired blood circulation, neuropathy, protracted tissue regeneration, and increased susceptibility to persistent infection. Traditional wound dressings often fail to provide the multifunctional environment required for effective diabetic wound management. In this study, a biodegradable polymer-based wound dressing film incorporated with Biophytum sensitivum with a common name Mukkutti extract was developed to address these limitations. The plant extract which is rich in anti-inflammatory, antioxidant, and antimicrobial phytochemicals, was successfully integrated into a cellulose acetate thin-film matrix. The resulting film, loaded with phytochemicals, exhibited improved physicochemical stability, uniform surface morphology, and enhanced mechanical integrity compared to the polymer control. Spectroscopic and structural analyses confirmed effective interactions between polymers and phytochemicals, along with a uniform distribution of bioactive substances throughout the film. Additionally, the developed dressing exhibited considerable antimicrobial activity against both Gram-positive (Staphylococcus aureus) and Gram-negative (Escherichia coli and Pseudomonas aeruginosa) bacteria and supports cell viability towards 3T3 mouse fibroblast cell lines. Overall, the findings suggest that the developed film possesses a combination of physicochemical and biological properties relevant to wound management at an in vitro level. However, this study is limited to preliminary evaluation, and further investigations involving wound-specific functional parameters such as water vapor transmission, degradation behavior, extract release kinetics, and in vivo validation are required to establish its suitability for diabetic wound healing applications.

Keywords: Diabetic Wound Healing, Polymeric Wound Dressing, Biophytum Sensitivum, Cellulose Acetate Film, Phytochemical Delivery, Antimicrobial Activity, Cytocompatibility

1. Introduction

Diabetes mellitus affects more than 600 million people, and the rate is increasing in the upcoming years. Diabetic wounds are the major health concern associated with mobility and tissue deformities [1, 2] Normal wound healing is dynamic and has defined phases such as hemostasis, the inflammatory phase, the proliferative phase, and the maturation phase. In contrast, although a diabetic wound goes through the same four phases of healing, these phases are frequently impaired and dysregulated [3, 4] The complex pathophysiology associated with diabetes mellitus is a major global health challenge to the medical society [5-7]. As a result, diabetic foot ulcers (DFUs) account for a significant proportion of hospitalizations, lower-limb amputations, and wound-related mortality worldwide [8, 9] Management of the wound helps to overcome the amputation. Diabetic wound healing is highly challenging to medical society, as it provides a hyperglycemic environment, which impairs angiogenesis and provides polymicrobial infection due to the growth of biofilms [10] Effective wound healing requires a balanced microenvironment that supports moisture retention, gas exchange, immune regulation, and tissue regeneration [11, 12]. However, conventional dressings such as cotton gauze and bandages fail to maintain an optimal wound bed, lack antimicrobial protection, and often promote dehydration or maceration of tissues and cannot provide the moist condition essential for wound healing [13-15]. Furthermore, chronic wounds frequently develop biofilms formed by opportunistic pathogens such as Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, and Candida albicans, which further inhibit healing and increase the risk of systemic infection [16-18]. This underscores the urgent

need for advanced wound dressings capable of providing physical protection while actively modulating the biological wound environment. This can be provided using a thin film with lower contact angles that facilitates a hydrophilic environment [19]. Natural polymer shows good candidature for developing next-generation wound dressing, as it can meet the specific needs like biocompatibility and biodegradability [20-23].

Polymeric wound dressings have attracted significant attention owing to their adaptability, adjustable mechanical properties, biocompatibility, and ability to deliver therapeutic compounds in a controlled manner [24-26]. Thin polymeric films provide uniform thickness, transparency for monitoring wounds, conformability, and prolonged release of bioactive agents [27]. Natural polymers like chitosan, gelatin, alginate, and pectin exhibit natural biocompatibility and bioactivity, whereas synthetic polymers such as polyvinyl alcohol (PVA) and polyethylene glycol (PEG), offer mechanical strength and structural stability [28-31]. Combining plant extracts with polymeric matrices enhances the therapeutic value of wound dressings by improving antioxidant activity, antimicrobial efficacy, and tissue repair. In recent years, plant-based polymeric films have gained attention as promising wound dressings due to their inherent antimicrobial, antioxidant, and biocompatible properties. Various natural and synthetic polymer systems incorporating herbal extracts have demonstrated effectiveness in promoting wound healing, primarily through infection control and moisture retention. However, most of these systems are designed for general wound management and do not specifically address the multifactorial pathophysiology of diabetic wounds. As a result, there remains a critical need for the development of multifunctional wound dressings that are specifically tailored to the pathological environment of diabetic wounds. Medicinal plants are rich in bioactive compounds such as flavonoids, phenolics, terpenoids, and alkaloids, which exhibit antimicrobial, antioxidant, anti-inflammatory, and pro-angiogenic properties. Incorporating these phytochemicals into biomaterial-based dressings holds great potential for managing diabetic wounds, where multiple healing barriers like microbial colonization and oxidative damage are addressed simultaneously [32]. Biophytum sensitivum (Mukkutti), a traditional medicinal plant used in South India and Ayurvedic medicine to treat inflammation, wounds, ulcers, and infections [33]. contains bioactive flavonoids, phenolic acids, and polysaccharides, which contribute to its pharmacological effects [34]. Extracts of B. sensitivum possess strong antioxidant activity, scavenging free radicals such as superoxide and hydroxyl radicals, enhancing endogenous antioxidant enzymes (catalase, SOD, glutathione peroxidase), and inhibiting lipid peroxidation [35]. The plant also demonstrates antimicrobial activity against Gram-positive, Gram-negative, and fungal pathogens common in chronic wound infections [36] Incorporating B. sensitivum into polymer-based thin films offers a novel strategy for diabetic wound management by providing mechanical protection, moisture balance, and sustained phytochemical release [24, 27]. Moreover, integrating plant extracts into biopolymer matrices improves flexibility, tensile strength, biodegradability, and drug-release characteristics [37, 38]. Characterization of these films involves mechanical testing involves thickness measurement, surface morphology observed through scanning electron microscopy, SEM, moisture absorption assessed by degree of swelling and phytochemical cytotoxicity all crucial for evaluating biomedical suitability [39-41]. In addition to physicochemical analyses, antimicrobial evaluation against clinically relevant wound pathogens, such as S. aureus, P. aeruginosa, and E. coli, is critical for determining the therapeutic significance of formulated films [42–44]. Studies have shown that plant-loaded polymeric films can inhibit microbial growth, prevent biofilm formation, and reduce wound microbial load in vitro and in vivo. Despite extensive research on herbal wound-healing agents and polymer-based dressings, there remains limited literature on B. sensitivum-loaded thin films specifically developed for diabetic wounds. Therefore, the present study aims to develop polymeric thin films infused with the extract of Biophytum sensitivum, evaluate their physicochemical and mechanical properties, characterize their phytochemical release behavior, and assess their antimicrobial potential against major wound pathogens. This integrated approach may contribute significantly towards the development of a multifunctional wound dressing tailored for diabetic wound management [45].

Table 1 shows the comparison between various herbal polymeric films and the present cellulose acetate thin film incorporated with *Biophytum sensitivum.* While numerous herbal polymeric films have been reported for wound healing, most systems focus on general wound repair without addressing the multifactorial pathology of diabetic wounds. In contrast, the present study introduces a cellulose acetate-based thin film incorporating *Biophytum sensitivum*, designed through a mechanism-driven approach targeting oxidative stress, microbial infection, and moisture imbalance. The formulation demonstrates enhanced structural integration, high swelling capacity (230%), significant antioxidant and antimicrobial activity, and cytocompatibility, thereby offering a multifunctional dressing platform specifically relevant to diabetic wound management. This integrated therapeutic and material design distinguishes the present work from existing herbal film systems.

2. Materials and Methods

2.1 Material synthesis

2.1.1 Materials

Cellulose acetate Extra Pure (Loba Chemie Pvt. Ltd, CAS NO.: 9004-35-7); the plant *Biophytum sensitivum (Mukkutti)* sample has been collected from the alluvial region of the Palakkad district in Kerala, India; glacial acetic acid (Loba Chemie Pvt. Ltd, CAS NO.: 64-19-7); ethanol (Sigma-Aldrich, CAS-No.: 64-17-5; ≥99.5%). All chemicals used in current research were procured from commercial suppliers and were of laboratory grade.

2.1.2 Preparation of Plant Extract

Biophytum sensitivum, commonly known as *Mukkutti*, an *Oxalidaceae* family found in marshy places of South India, is preferred for the current study. The plant is believed to exhibit ayurvedic characters like antibacterial, antioxidant, anti-inflammatory, and anti-tumor activity, along with immune modulation, which is believed to be most preferable for wound healing [46, 47]. The leaf extract of *Biophytum sensitivum* was used as a therapeutic agent in the polymer film. After washing to remove dust, the leaves of *Biophytum sensitivum* were shade dried. The dried leaves were then powdered using mortar and pestle, which was then subjected to extraction using ethanol as the solvent. Approximately 2 g of the powdered material was macerated in ethanol in a 1:10 (w/v) ratio and kept on a rotary shaker for 48–72 hours at room temperature. The extract was then filtered through Whatman No. 1 filter paper, and the filtrate was concentrated to obtain a semisolid crude extract. The concentrated extract was stored at 4°C in airtight containers until further use.

2.1.3 Preparation of Phyto-infused thin film

To make the controlled release of extract and protect its bioactive compound, the biologically derived polymeric bed needs to act as a drug delivery matrix. The skin tissue engineering approach involves fabrication using thin film, which helps to maximize the wound closure time and avoid scar tissue formation [48] For complete regeneration of tissue and restoration of its function, natural polymers can be used; they resemble the human extracellular matrix with biocompatibility. However, most natural polymers have a fast degradation capacity, which results in poor adherence and lacks the multifunctional effect of wound dressing [49]. These can be addressed when the natural polymers combine with plant extract to develop the thin film. The plant extract-embedded polymers act as molecular absorptive filters and help to improve the partial thickness of wound dressings that protect the impregnated therapeutic agent [50].

Figure 1 represents the schematic flow diagram of thin film production using cellulose acetate and phytocompound induced thin film production. Natural polymer cellulose with acetate ion forms the semisynthetic polymer and cellulose acetate (CA) naturally have an ability to form uniform crack free film even at low concentration. This uniformity forms strong intermolecular hydrogen bonding and dipole interaction with mechanically stable flexible thin film.

Table 1. Comparison table against recent herbal film systems and the present study

Study (Year)	Polymer System	Herbal Component	Key Functional Outcomes	Diabetic Relevance	Key Limitation
Lopes *et al.,* 2024 [51]	Various (alginate, chitosan, cellulose)	Essential oils / plant extracts	Antimicrobial, biocompatibility, fibroblast migration	Not specific	Poor targeting, limited bioavailability
Priya *et al.,* 2024 [52]	Polysaccharide films	Various plant extracts	Swelling, antibacterial, anti-inflammatory	General wound only	No disease-specific validation
Ali *et al.,* 2024 [53]	Composite biopolymer films	Bioactive additives	Moisture retention, antimicrobial, mechanical strength	Not targeted	Focus on material, not therapeutic mechanism
Jangra *et al.,* 2025 [54]	Biopolymer matrices	Herbal bioactives	Antioxidant, antimicrobial, wound closure	Limited	Lack of standardized multifunctional validation
Present Study	Cellulose acetate thin film	*Biophytum sensitivum*	Antioxidant + antimicrobial + swelling (230%) + biocompatibility	Diabetic wound-focused	—

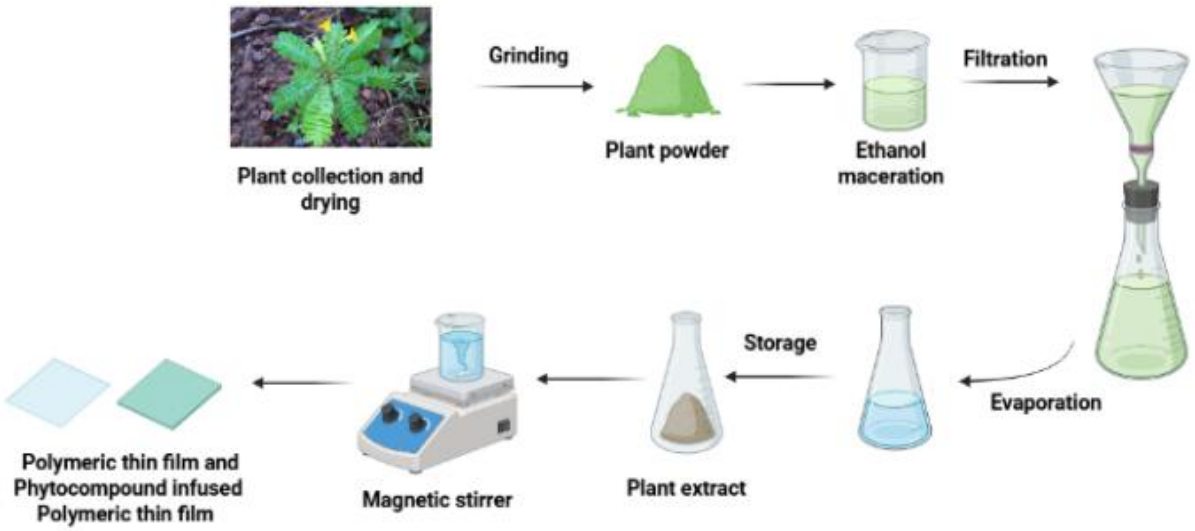

Figure 1. Schematic representation of phytocompound induced thin film production.

The polymer solutions were prepared by dissolving the 20g of CA in 100ml of glacial acetic acid under constant stirring at 50°C –60°C until complete dissolution was achieved. Followed by, 2 ml of *Biophytum sensitivum* crude extract was incorporated into the polymer solution under constant stirring. By this the effective extract loading corresponds to 0.2g lead equivalent to 20g polymer i.e. 10mg crude extract equals per gram of cellulose acetate. Plasticizers such as glycerol were added in concentrations of 2% v/v to improve film flexibility. The final mixture was poured onto sterile glass petri plates or teflon-coated trays and allowed to dry at room temperature for 24–48 hours. After complete solvent evaporation, the thin films were carefully peeled off and cut into standardized dimensions (1cm × 1 cm) for further analyses. All films were stored in sterile containers under desiccated conditions until further use. A comprehensive physicochemical characterization of the developed polymeric thin film incorporated with *Biophytum sensitivum* plant extract were systematically assessed using XRD (X-Ray diffraction), SEM (Scanning electron Microscopy), Fourier Transform Infrared (FTIR) spectroscopy and UV-Visible spectroscopy that confirms the successful incorporation, uniform distribution, structural stability, and biological relevance of *Biophytum sensitivum* within the polymeric thin film, supporting its suitability for diabetic wound healing applications.

2.2 Characterization

2.2.1 X ray Diffraction (XRD) Analysis

X-ray diffraction (XRD) analysis was performed to evaluate the crystalline structure and phase behavior of the polymeric thin films and to analyse the influence of *Biophytum sensitivum* extract incorporation on the polymer matrix. Diffraction patterns of the control and phytochemical-loaded films were recorded using a fixed goniometer system (ARL EQUINOX 3000, Thermo Fisher Scientific Ltd.) equipped with a curved position-sensitive X-ray detector (CPS120). Monochromatic Cu $K\alpha_1$ radiation was used as the X-ray source. Data acquisition was carried out in asymmetric geometry, with diffraction patterns collected over a 2θ scanning range of 0°–120° at room temperature. The acquired diffractograms were examined to identify characteristic diffraction peaks, evaluate changes in crystallinity, and determine structural modifications generated by the incorporation of phytochemical constituents within the polymeric thin film.

2.2.2 Scanning electron Microscopy (SEM) Analysis

Scanning electron microscopy (SEM) was used to examine the surface morphology and microstructural features of the polymeric thin films. This was analysed using Hi Resolution Scanning Electron Microscope (Thermoscientific Apreo S). The obtained micrographs were analyzed to assess surface uniformity, porosity, and the distribution of phytochemical constituents within the polymer matrix. The uniform crack free substrate strongly influences the cell adhesion and reinduces the epithelial formation at wounded site.

2.2.3 FTIR spectroscopic Analysis

Fourier Transform Infrared (FTIR) spectroscopy was carried out to identify the functional groups present in the polymeric thin films and to evaluate possible interactions between the polymer matrix and the incorporated phytochemicals. FTIR spectra of the CA polymer film and phytochemical-loaded films were recorded using a Shimadzu, IRTracer 100 FTIR spectrometer in the wavenumber range of 4000–400 cm^{-1} at room temperature. The thin film samples were analysed directly using the attenuated total reflectance (ATR) mode.

2.2.4 UV–Visible Spectroscopic Analysis

UV–Visible spectroscopy was employed to evaluate the optical and electrical properties of the film. This provides details on structure, composition and quality of the film. When UV visible light passes through the thin film it results in light absorbance, light transmittance and reflectance. The UV absorbed data gives the optical band gap which relates to electronic structure, phase purity and effect of phytochemical distribution in the thin film. Shift in band gap often shows the changes in crystallinity, particle size and interfacial interaction between the phytocompound and the polymer. The absorption edge helps to determine the density defect and structural disorder. The spectra of polymeric thin film without incorporated phytochemical and the phytochemical-loaded films were recorded using a Shimadzu, UV 3600 PLUS UV–Visible spectrophotometer over the wavelength range of 200–800 nm at room temperature.

2.2.5 DPPH Assay of plant extract

The antioxidant activity of the plant extract was evaluated using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay. A 0.1 mM DPPH solution was prepared by dissolving DPPH in methanol and kept protected from light. The concentrated plant extract was diluted with methanol to obtain different concentrations (25, 50, 100, 200, and 400 µg/mL).

For the assay, 100 µL of each extract concentration was mixed with 100 µL of DPPH solution in a 96-well microplate. Methanol mixed with DPPH solution served as the negative control, while Ascorbic acid was used as the positive control. A blank containing methanol alone was also prepared. The reaction mixture was incubated in the dark at room temperature for 30 minutes to allow the antioxidant compounds in the extract to react with the DPPH radicals. After incubation, the absorbance was measured at 517 nm using a microplate reader. All experiments were performed in triplicate.

The percentage of DPPH radical scavenging activity was calculated using the following formula:

$$\%\ \text{Inhibition} = \frac{A_c - A_s}{A_c} \times 100 \quad (1)$$

Where A_c represents the absorbance of the control and $A_s$represents the absorbance of the sample.

2.2.6 Thickness Measurement

The thickness of the developed polymeric thin films was determined as a part of the mechanical behavior analysis using a digital micrometre thickness gauge. Film samples were cut into uniform sections, and thickness measurements were recorded at multiple randomly selected points across each film to account for surface variations and ensure accuracy. The micrometre was applied with minimal and consistent pressure to avoid film deformation during measurement. The average thickness value was calculated from the recorded measurements and reported as the representative thickness of the film. This measurement was used to assess film uniformity and to support the evaluation of mechanical integrity relevant to wound dressing applications.

2.2.7 Swelling Behavior

The swelling behavior of the plant extract-loaded thin film and the control polymeric thin film composed of Cellulose acetate was evaluated to determine their absorption capacity. Pre-weighed dried film samples were immersed in Phosphate Buffered Saline (PBS, pH 7.4) at room temperature. At predetermined time intervals (30 min, 1 h, 2 h, 4 h, 8 h, and 24 h), the samples were carefully removed from the medium, gently blotted with filter paper to remove excess surface liquid, and weighed to determine the swollen weight.

The swelling degree (SD) of the films was calculated using the following equation:

$$SD(\%) = \frac{W_w - W_d}{W_d} \times 100 \quad (2)$$

where W_d represents the initial dry weight of the film and W_w represents the weight of the swollen film at each time interval. All measurements were performed in triplicate, and the results were expressed as mean ± standard deviation.

2.2.8 Antimicrobial Susceptibility Test

The antimicrobial study was done using disc diffusion method. The antimicrobial efficacy of the plant-based thin films was assessed against clinically important wound pathogens including, *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli.* The cultures were obtained from a certified microbial culture repository and maintained on nutrient agar. The antimicrobial potential of thin films was assessed using the disc diffusion method. Overnight cultures of the test organisms were adjusted to 0.5 McFarland standard and uniformly spread on Muller–Hinton agar plates. Thin film samples of uniform diameter of 3mm were aseptically placed on the inoculated agar surface and incubated at 37°C for 24 hours. The antimicrobial susceptibility test was performed in triplicates (n=3) for each pathogen. The zone of inhibition surrounding each film was measured in millimetre to determine antimicrobial activity. Films without plant extracts served as negative control, and standard antibiotics, that is gentamicin (50µg/disc), is served as positive control.

2.2.9 In vitro cytocompatibility assessment (MTT assay)

The cytocompatibility of the plant extract and plant extract-loaded thin film was evaluated using the MTT assay on 3T3 mouse fibroblast cell lines. Cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum (FBS) and 1% antibiotic solution and incubated at 37 °C in a humidified atmosphere with 5% CO_2.

For the assay, cells were seeded into a 96-well plate at a density of approximately 1 × 10^4 cells per well and allowed to attach for 24 h. The plant extract was prepared in culture medium and tested at different concentrations (25, 50, and 100 µg/mL). For the thin film group, films were cut into small sterile pieces of uniform diameter 2mm and sterilized (ethanol washing followed by 3 times PBS rinsing and UV exposure) prior to treatment. The sterilized films were then directly placed in the wells containing cells.

After treatment, cells were incubated for 24 h under standard culture conditions. Subsequently, the medium was removed and 100 µL of MTT solution (0.5 mg/mL in serum-free medium) was added to each well, followed by incubation for 3–4 h at 37 °C to allow formation of formazan crystals. The MTT solution was then carefully removed, and the formed crystals were dissolved using dimethyl sulfoxide (DMSO).

The absorbance was measured at 570 nm using a microplate reader. Cell viability (%) was calculated relative to the untreated control using the formula:

$$\text{Cell viability (\%)} = \frac{\text{Absorbance of treated cells}}{\text{Absorbance of control cells}} \times 100 \quad (3)$$

All experiments were performed in triplicate, and results were expressed as mean ± standard deviation.

3. Results and Discussion

3.1 X-ray Diffraction (XRD) Analysis

The crystalline or amorphous nature of cellulose acetate polymeric thin films play a crucial role in understanding structural modifications induced by the incorporation of *Biophytum sensitivum* plant extract. Cellulose acetate is the semisynthetic polymer derived from natural polymer cellulose where all hydroxyl (-OH) groups on the anhydroglucose unit are replaced by acetyl (-$OCOCH_3$) groups. Polarity, solubility, and packing are the main parameters to consider while making thin films with CA. The excessive hydrogen bonds in the cellulose when subjected to partial acetylation preserves the chain stiffness and the dipole-dipole interaction promotes short range of ordering but prevents perfect crystallization and results in semi crystalline to amorphous structure.

Further, the diffraction pattern obtained for the phytocompound-infused polymeric cellulose acetate thin film is shown in Figure 2. The XRD diffractogram of *Biophytum sensitivum* infused CA film exhibits two prominent diffraction peaks at 2θ = 7.230° and 9.373°, both showing strong and high intensity. These peaks significantly show the different diffraction behavior due to the reorganization of the polymer matrix induced by phytocompound incorporation. Compared to the CA thin film that shows a reflection at 7.347° shown in Figure 3, the slight shift towards lower 2θ indicates inter-chain (d-spacing) spacing by intercalation of phytocompounds and strong hydrogen bond interactions between cellulose acetate and the bioactive compound in the plant extract. The increased intensity shows reinforced short-range ordering rather than crystallinity. This replicates the phytocompound, which played a dominant ordered structure.

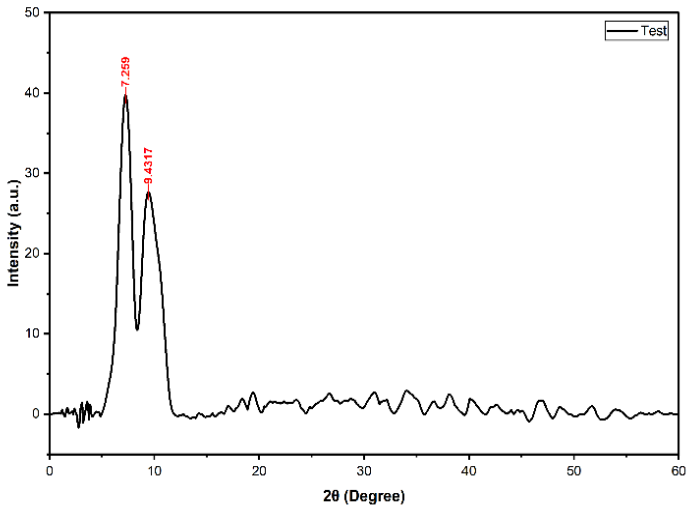

Figure 2. Phytocompound infused Polymeric thin film diffraction Pattern (2θ Vs I)

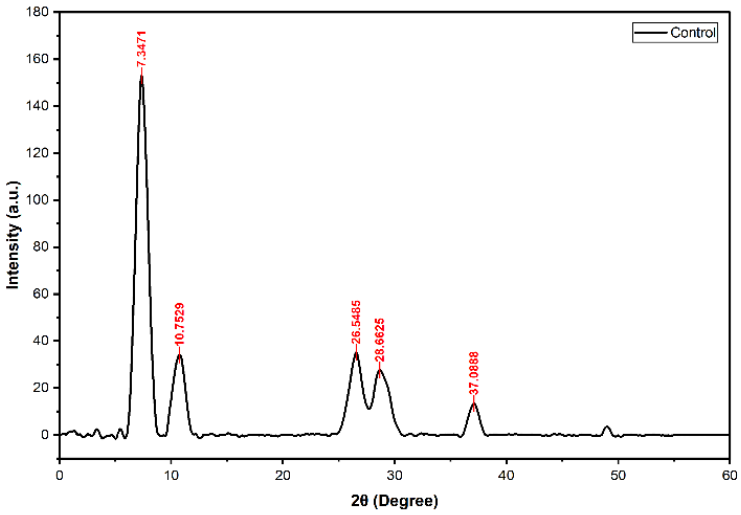

Figure 3. Polymeric Thin film Diffraction Pattern (2θ Vs I)

The second peak at 2θ = 9.373° shows a shift from 10.951° obtained for the CA thin film. This shifting shows the structural relaxation of the polymer chain and the plasticizing effect of the infused phytocompound. The shift or presence of peaks alone does not confirm inter-chain spacing changes or structural reorganization. However, the combination of reduced intensity and peak broadening is consistent with a relative decrease in crystallinity and increased structural disorder in the film. Thus, the obtained diffraction pattern in Figure. 3 reveals that the CA film converted to a more homogeneous, amorphous dominant phase, which favors a stable CA polymer phytocompound stable complex. This modified architecture favors bioactive retention, flexibility, and controlled release, which supports faster wound healing.

3.2 Scanning Electron Microscopy (SEM) Analysis

SEM micrographs were obtained for both the control polymeric thin film without phytochemical incorporation and the *Biophytum sensitivum*–loaded film to evaluate surface morphology and structural modifications induced by the bioactive extract. Surface morphology provides critical insights into film uniformity, porosity, and features relevant to wound dressing performance.

Figure. 4 shows the scanning electron microscopy image of the CA polymer thin film at (A) 5000X magnification and (B) 10000X magnification, which exhibits a relatively smooth and continuous surface, confirming the good film-forming ability of the polymer matrix. The homogeneous film production is shown by the flat, uniform surface. This is because the solvent evaporation occurs slowly during the solvent casting process, allowing the CA chain to reorganize, establish effective packing, and reduce surface roughness. The limited porosity shows the controlled solvent evaporation rate and helps to enhance barrier property. The absence of cracks suggests the solubility nature of CA, and uniform chain entanglement results in this complete solubility nature. This continuous crack-free surface promotes mechanical integrity. The compact and dense packing shows the strong intermolecular interactions within CA, which restricts excessive chain mobility, and the dense structure implies the semi-crystalline nature of CA. Thus, the obtained SEM image shows the dense and compact smooth surface morphology, which provides mechanical strength, acts as a protective barrier, and supports controlled swelling and diffusion, a critical parameter needed in wound dressing.

Figure. 5, the scanning electron microscopy image of CA thin film infused with *Biophytum sensitivum* phytochemical at (A) 5000X magnification and (B) 10000X magnification, shows a uniform modified surface with increased roughness and well-distributed microporous features. The increased surface roughness is due to the strong molecular interaction between CA and phytochemicals like phenols and flavonoids present in *Biophytum sensitivum* extract. These bioactive compounds disturb the regular packing and lead to localized chain rearrangement and introduce surface heterogeneity. The roughness shows that the phytochemicals are integrated within the polymer matrix rather than adsorbed onto the surface of the matrix. The uniform micropore distribution shows the partial phase relaxation achieved by solvent evaporation. The localized solvent interacts with phytochemicals and acts as temporary spacers and creates voids as the solvent diffuses out. The absence of agglomerates and cracks shows the complete miscibility of CA and *Biophytum sensitivum* extract. The obtained results confirm that incorporation of *Biophytum sensitivum* extract significantly alters the surface morphology of the polymeric thin film, promoting a favorable microenvironment for controlled bioactive release and supporting its potential application as a wound dressing material.

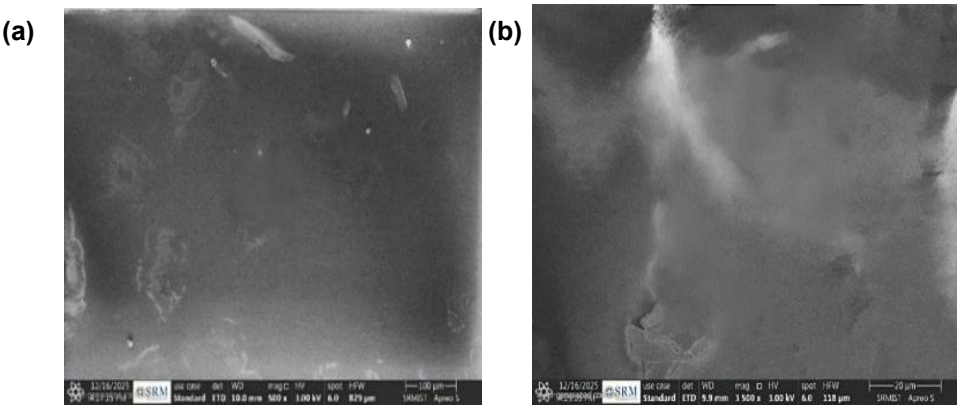

Figure 4. Surface Morphology of Polymeric Thin Film

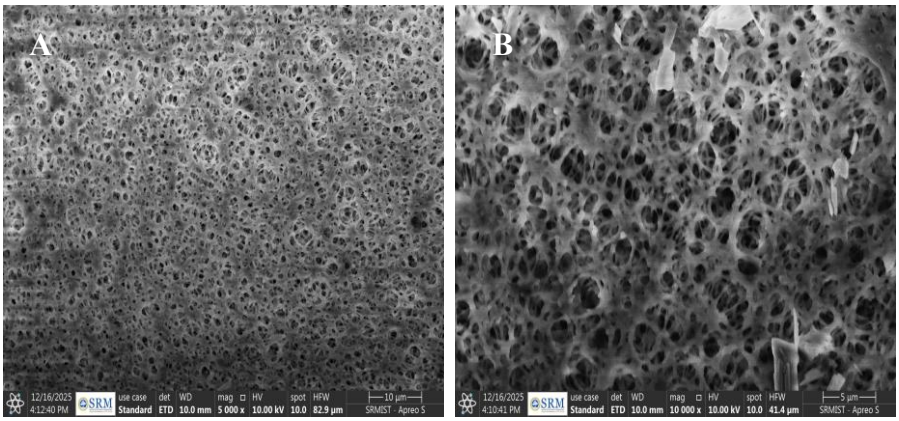

Figure 5. Surface Morphology of Phyto compound infused Polymeric thin film

3.3 FTIR spectroscopic Analysis

Fourier Transform Infrared Spectroscopy (FTIR) provides molecular-level information about the cellulose acetate polymer thin film and phyto compound-infused polymeric thin film. With the help of FTIR, the functional groups, chemical composition, and interaction of the thin film were identified.

The FTIR spectrum of cellulose acetate in Figure. 6 exhibits characteristic absorption bands at 3473.80 cm^{-1}, 3354.21 cm^{-1}, and 3250.05 cm^{-1}, showing the stretching of residual hydroxyl groups (O-H). This indicates that there is a hydrogen bond existing within the CA chain. This reflects the hydrophilicity of the film. The vibration band of 1739.39 cm^{-1} shows the C=O stretching vibration of ester (acetyl) groups and is evidence of the acetylation of cellulose and preservation of ester functionality in the film. The 1543.05 cm^{-1} band corresponds to C=C stretching and reflects possible interaction within CA through hydrogen bonds. The 1431.18 cm^{-1} stretching bond corresponds to CH_2 bending vibrations and reflects the stable structural integrity established by the cellulose acetate backbone. The 1381.03 cm^{-1} vibrational band corresponding to CH_3 symmetric bending of acetyl groups validates the presence of the acetyl group. The 1230.58 cm^{-1} band is attributed to C-O-C asymmetric stretching of ester linkage and strong dipole-dipole interaction. 1041.56 cm^{-1} vibrational band shows the characteristic C–O stretching of the pyranose ring in cellulose. 906.54 cm^{-1} corresponds to the β-1,4-glycosidic linkage in the glucose structure that favors the cellulose acetate structure. 661.58 cm^{-1} shows the bending of C–H. This skeletal vibration reflects the ordered vibration exhibited by the polymer chain. 609.51 cm^{-1} shows the deformation vibrations of O–C–O, showing the semi-crystalline nature of CA by local structural ordering. The flexibility and molecular rearrangement were indicated by skeletal bending vibrations of the polymer backbone at 466.77 cm^{-1}.

Further, Figure. 7 represents the FTIR transmission spectrum of the phyto compound-infused polymeric thin film. The vibrational band 3462.22 cm^{-1} shows O-H stretching attributed to the phenolic and alcoholic hydroxyl groups from *Biophytum sensitivum* phytochemicals, and the residual CA-OH groups indicate a strong hydrogen bond exists between cellulose acetate and phytochemical. 2939.52 cm^{-1} represents C-H stretching of aliphatic -CH_2 and CH_3 groups, showing the polymer backbone in addition to other alkyl groups in phytochemicals.

The presence of C=O stretching of ester groups in cellulose acetate is evidenced by 1739.79 cm^{-1}. The vibrational band 1548.84 cm^{-1} corresponds to aromatic stretching of C=C and supports the presence of phenolic or flavonoid compounds from *Biophytum sensitivum* interacting with CA. The structural stability of the CA backbone is shown by CH_2 scissoring vibration at 1436.97 cm^{-1}.

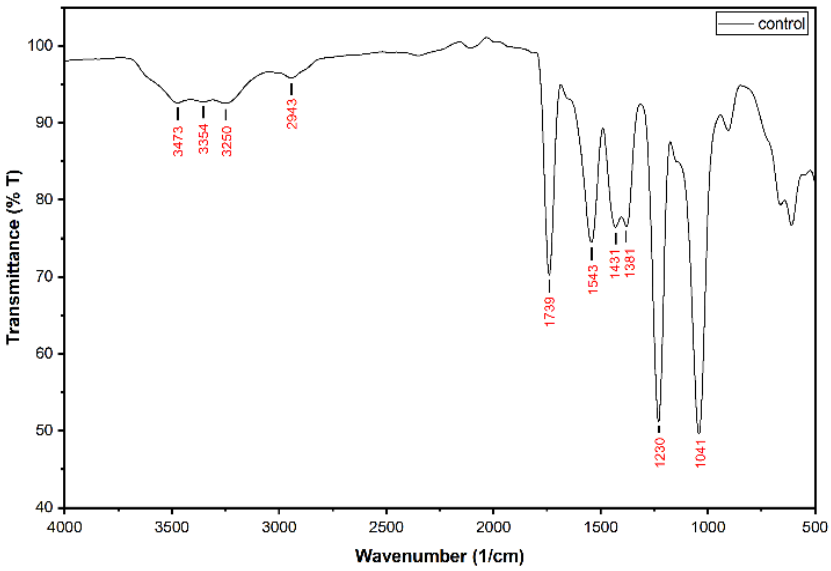

Figure 6. FTIR Transmission spectrum of Polymeric Thin film

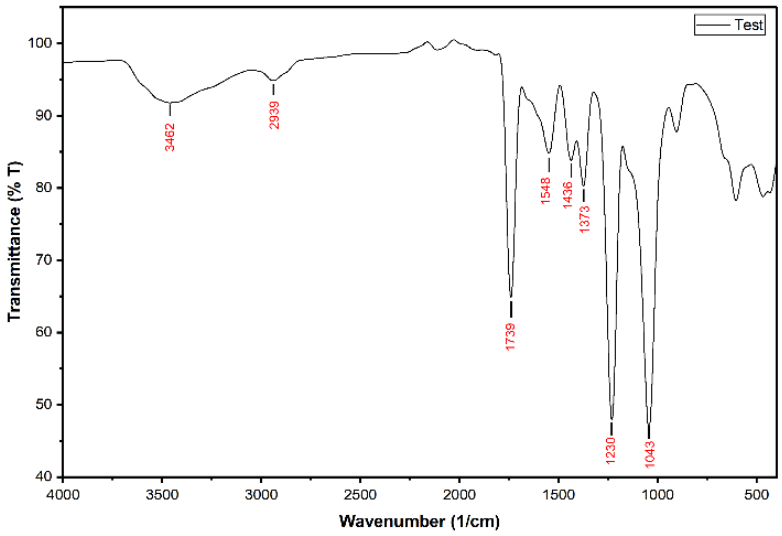

Figure 7. FTIR Transmission spectrum of Phyto compound infused Polymeric thin films.

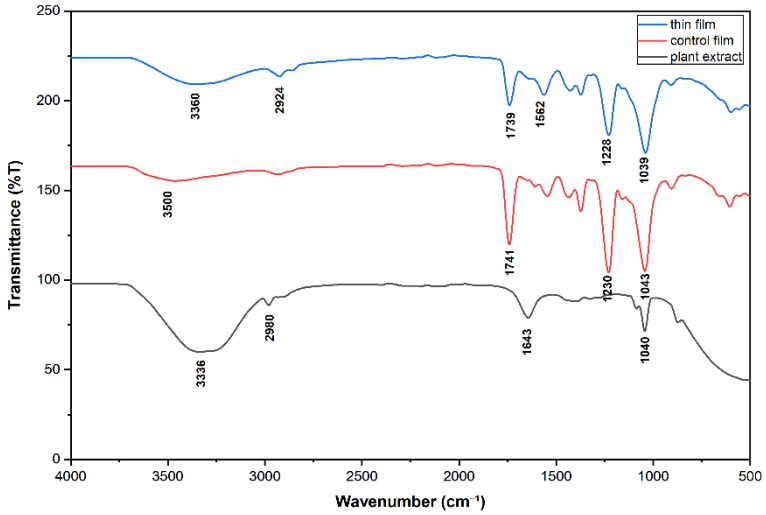

Figure 8. FTIR Analysis of plant extract-loaded thin film (Test), polymeric thin film (Control) and plant extract. The test spectrum was vertically shifted for clarity

Table 2. FTIR Analysis of polymeric thin film (Control) and plant extract-loaded thin film (Test)

Functional Group	Plant Extract (cm^{-1})	Control Film (cm^{-1})	Infused Film (cm^{-1})	Inference
O–H stretching	3336	3458	3360	Shift to lower wavenumber indicates hydrogen bonding between plant phytochemicals and polymer, confirming incorporation
C–H stretching	2980	No peak	2924	Presence in all samples confirms aliphatic backbone retained after incorporation
C=O (ester)	No peak	1741	1739	Peak retained with minimal shift indicates polymer structure remains stable
Aromatic C=C	1643	No peak	1562	Appearance/shift confirms presence of plant-derived aromatic compounds in film
C–O stretching	1040	1230–1043	1228–1039	Overlapping and broadening indicate phenolic/alcohol groups from plant incorporated into film
Peak Intensity (1000–1200 cm^{-1})	Moderate	Lower	Higher & broader	Increase in intensity confirms additional functional groups from plant extract

The band at 1373.32 cm^{-1} shows symmetric bending of CH_3 groups of acetyl moieties. C–O–C stretching of ester linkage was exhibited by 1230.58 cm^{-1}. 1043.49 cm^{-1} exhibits C–O stretching of the pyranose ring structure, and the β-glycosidic linkage vibration is represented by 904.61 cm^{-1}. The skeletal vibration exhibited by 603.72 cm^{-1}. The band at 466.77 cm^{-1} and 432.05 cm^{-1} indicates deformation mode and shows a dominant amorphous domain with a flexible structure. In contrast to the cellulose acetate polymer film, the *Biophytum sensitivum* extract-infused cellulose acetate film exhibits significant hydrogen bonding and molecular compatibility, as seen by the shift and broadening of the band from Figure. 7. Figure.8 shows the comparison of FTIR spectrum obtained for Plant extract, polymeric thin film that acts as control and the Plant extract loaded thin film a test sample. The FTIR spectral analysis was compared in Table 2.

From the transmission spectrum analysis discussed in Table 2 it is concluded that the increased peak intensities, band broadening, and minor peak shifts were observed clearly in the *Biophytum sensitivum* extract–infused cellulose acetate film compared to Cellulose acetate polymer film. The comparative table supports that it arises only from the phyto compound that is present in the plant extract not from the polymeric thin film. The detailed report on successful incorporation of functional components and the development of a chemically complex and interactive network within the thin film was explained at a molecular level.

3.4 UV–Visible Spectroscopic Analysis

UV Visible spectroscopy is the powerful technique to know the optical, chemical and functional behaviour of cellulose acetate polymer thin film compared with Biophytum sensitivum extract–infused cellulose acetate thin films.

The UV spectrum in Figure. 9 corresponds to the cellulose acetate polymer thin film. The UV-visible spectrum of the cellulose acetate polymer thin film was recorded in the 200-800 nm range and reveals a significant absorption in the UV area followed by a steady decline in absorption towards the visible region. There was no noticeable absorption peak in the visible region. 200-230 nm shows high absorption, revealing that the film shows maximum absorbance between 200 and 205 nm and starts to decrease up to 230 nm. From 230 nm, the absorption range gradually drops from 0.30 to 0.10 with no distinct peak. This shows the purity of cellulose acetate with a lack of conjugated chromophores, aromatic, or phenolic compounds. The visible spectrum exhibits uniform thickness, good optical transparency, and little light scattering starting at 400 nm. This demonstrates the homogeneity, lack of cracks, and smooth surface of the CA film.

Figure. 10 shows the UV-visible spectrum of the phyto compound-infused polymeric thin film. The absorbance was recorded in the wavelength range of 200-800 nm. The distinct absorption behavior shows the successful incorporation of *Biophytum sensitivum* phytochemicals into the CA matrix.

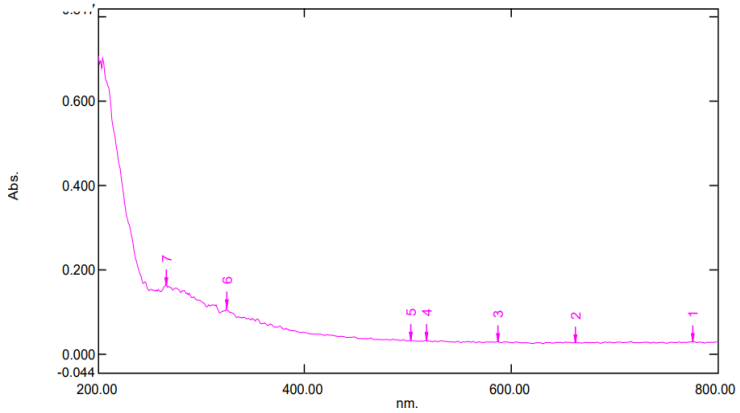

Figure 9. UV-Visible spectrum of Polymeric Thin film

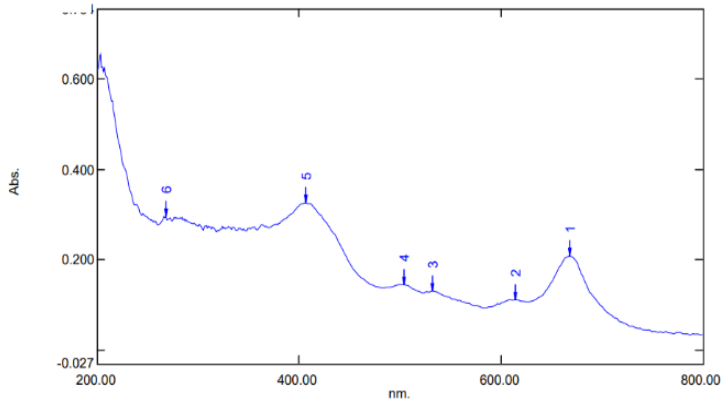

Figure 10. UV-Visible spectrum of Phyto compound infused Polymeric thin films.

The broad absorption plateau in the near 230-350 nm region shows the sustained absorption region with no sharp peak. This broad band implies the presence of phenolic compounds, flavonoids, and secondary metabolites found in *Biophytum sensitivum*. This demonstrates the strong hydrogen bonding interactions between phytochemicals and the CA polymer chain. A uniform dispersion of phytochemicals in CA polymer is shown by the lack of a distinct peak. The extended absorbance at the visible region between 350 and 450 nm shows a gradual decrease in absorbance, showing a higher value when compared to the CA polymeric film. The film maintains the measured transparency of light absorption, indicating uniform film thickness, lack of phase separation, and regulated optical transparency, as evidenced by the steady decrease in light absorption and stabilization in the visible range of 450–800 nm. Phytochemical-infused CA shows higher absorbance across UV and near-visible regions, indicating the ability to block harmful UV radiation. This shielding property is advantageous for diabetic wound healing, where the protection from UV-induced oxidative stress is highly essential.

3.5 DPPH Assay of plant extract

The antioxidant activity of the plant extract was evaluated using the DPPH radical scavenging assay. The results demonstrated that the extract exhibited concentration-dependent antioxidant activity. As the concentration of the extract increased from 25 to 200 µg/mL, a gradual decrease in absorbance was observed, indicating effective scavenging of DPPH free radicals by the bioactive compounds present in the extract.

The percentage inhibition increased with increasing concentration, suggesting that the extract possesses significant radical scavenging potential. The highest antioxidant activity was observed at higher concentrations of the extract, indicating the strong ability of the phytochemicals to donate hydrogen atoms or electrons to neutralize DPPH radicals. This antioxidant activity may be attributed to the presence of phenolic and flavonoid compounds reported in *Biophytum sensitivum*, which are known for their free radical scavenging properties. Antioxidant activity plays an important role in wound healing, particularly under diabetic conditions where excessive oxidative stress delays tissue regeneration.

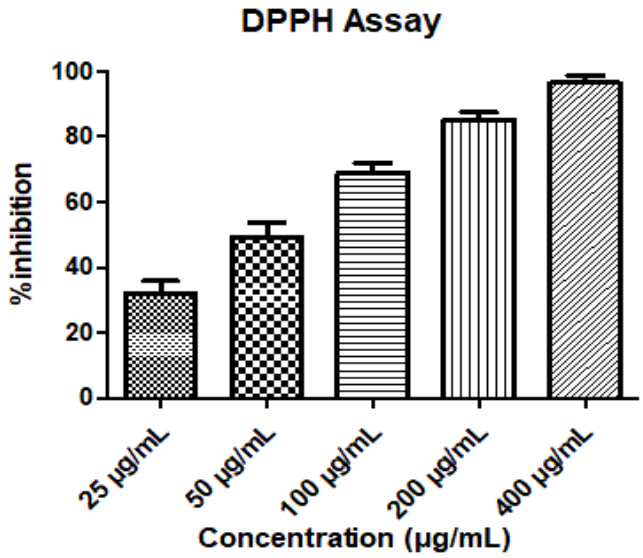

Figure 11. DPPH Assay of the plant extract

Therefore, the observed radical scavenging activity of the extract supports its potential application in the development of plant extract-infused thin films for promoting wound healing in Diabetes mellitus (Figure 11).

3.6 Thickness Measurement

The thickness of the polymeric thin films was measured using a digital micrometer thickness gauge. The CA polymer thin film exhibited a thickness of 0.01 mm, whereas the *Biophytum sensitivum*–incorporated CA film showed an increased thickness of 0.24 mm (Table 12). The notable increase in film thickness after phytochemical incorporation can be attributed to the presence of bioactive compounds within the polymer matrix, which contributes to enhanced solid content and altered polymer chain packing during film formation. This increase in thickness is advantageous for wound dressing applications, as it improves mechanical stability, moisture retention, and sustained release of bioactive constituents. The uniform thickness of the phytochemical-loaded film further indicates good film-forming ability and homogeneous distribution of the plant extract within the polymer matrix. Figure. 12(A) shows the thickness of CA polymer at 0.01mm.

Figure. 12(B) shows the thickness of the phyto compound-infused polymeric thin film, which is about 0.24 mm. The thickness is much higher than CA polymeric film thickness. The thickness of the film normally controls the structure, performance, and biological function. Based on Beer-Lambert's law, the absorbance is directly proportional to thickness, and a thicker film shows increased absorbance. This thickness validates that improvements are due to the incorporation of phytochemicals into the polymer matrix. Thickness ensures the UV blocking of phytochemical-infused polymer film. The thickness governs a moist wound environment and sustained phytochemical release. The thicker film can accommodate more bioactive compounds and enables the prolonged and controlled release. This will enhance the antioxidant and anti-inflammatory properties relevant for diabetic wound healing.

3.7 Swelling Behavior

The swelling behavior of the plant extract-loaded thin film and the control polymeric thin film composed of Cellulose acetate was evaluated to determine their absorption capacity in Phosphate Buffered Saline (PBS, pH 7.4). Both films exhibited a time-dependent increase in swelling, indicating the ability of the polymer matrix to absorb and retain aqueous medium. The control film showed a gradual increase in swelling during the initial time intervals and reached an equilibrium swelling of approximately ~90% at 24 hours. This moderate swelling behavior can be attributed to the semi-hydrophilic nature of cellulose acetate, which allows limited water penetration into the polymer matrix.

In contrast, the plant extract-infused thin film demonstrated significantly higher swelling capacity, reaching approximately ~230% swelling at 24 hours. The increased swelling behavior of the test film may be attributed to the incorporation of plant-derived phytochemicals containing hydrophilic functional groups such as hydroxyl and phenolic groups, which enhance water affinity. Additionally, the presence of the plant extract likely disrupts the compact arrangement of the polymer chains, creating additional free volume and micro-porous structures within the film. These structural modifications facilitate greater diffusion of water molecules into the polymer network, resulting in enhanced swelling.

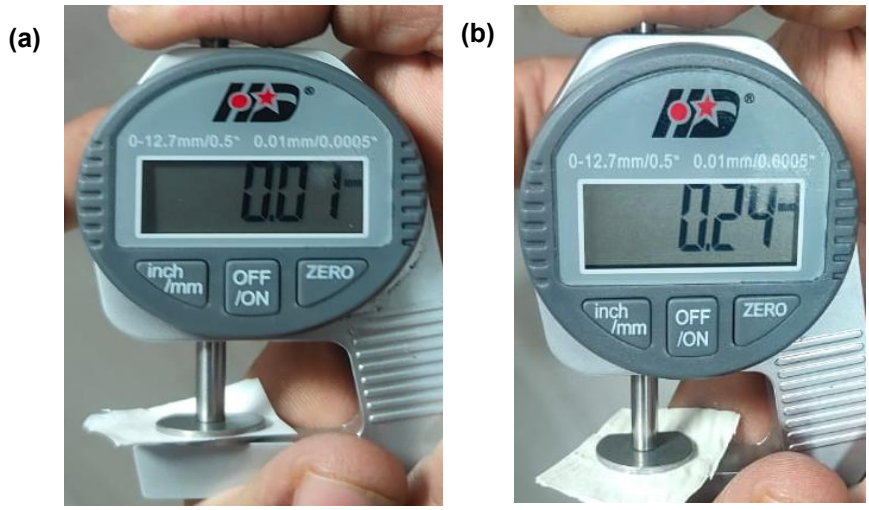

Figure. 12 a) Thickness measurement of Polymeric Thin film and **(b)** Phyto compound infused Polymeric thin films.

Table 3. Thickness measurement of Polymeric Thin film and Phyto compound infused Polymeric thin films

Position	Polymeric Thin film	Phyto compound infused Polymeric thin film
1	0.01	0.22
2	0.01	0.25
3	0.02	0.24
4	0.01	0.25
5	0.01	0.24
mean ± SD (n=5)	0.012 ± 0.0045	0.24 ± 0.012

The swelling profile also indicated a rapid initial uptake of PBS within the first few hours followed by a plateau phase, suggesting that the films gradually approached equilibrium swelling. Such behavior is typical for polymeric wound dressing materials, where the polymer matrix absorbs fluid until osmotic forces are balanced by the elastic resistance of the network.

Overall, the significantly higher swelling observed in the plant extract-loaded film suggests improved fluid absorption capacity, which is a desirable characteristic for wound dressing applications. Enhanced swelling allows the material to effectively absorb wound exudate while maintaining a moist environment that can promote tissue regeneration and accelerate wound healing.

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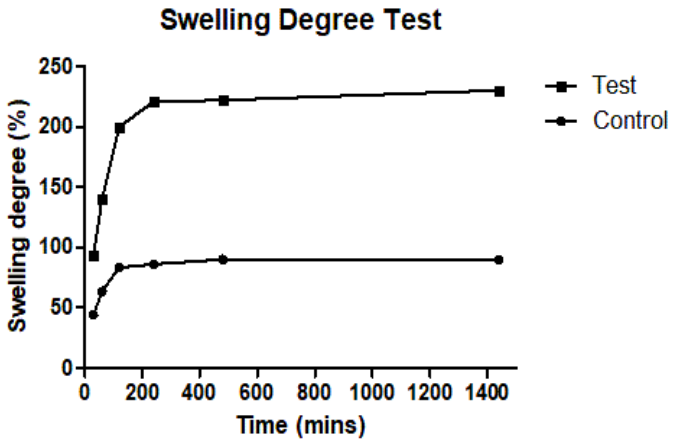

Figure 13. Swelling degree of plant extract-loaded thin film and the control polymeric thin film

Such behavior is typical for polymeric wound dressing materials, where the polymer matrix absorbs fluid until osmotic forces are balanced by the elastic resistance of the network. Overall, the significantly higher swelling observed in the plant extract-loaded film suggests improved fluid absorption capacity, which is a desirable characteristic for wound dressing applications. Enhanced swelling allows the material to effectively absorb wound exudate while maintaining a moist environment that can promote tissue regeneration and accelerate wound healing.

3.8 Antimicrobial Susceptibility Test

The antibacterial activity assay for both the cellulose acetate polymer thin film and the phytochemical-infused cellulose acetate polymer matrix is considered crucial. These films have direct and prolonged contact with the surrounding environment, where microbial contamination is inevitable. Normally the thin film-based wound dressing provides more surface area, and these surfaces should have antimicrobial properties; without that, these surfaces become the breeding grounds for most microorganisms. The attachment of microorganisms may result in the formation of biofilm and delay the wound healing. Validating the antibacterial activity for the thin film confirms the functionally protective biological condition. The current study compares the antibacterial property of CA polymer thin film with phytochemical-infused CA polymer thin film. The antibacterial activity in the present study was evaluated using the disc diffusion method, which is a qualitative screening technique and does not allow direct quantification of antibacterial kinetics, as the size of the inhibition zone is strongly influenced by multiple experimental parameters, including agar thickness, diffusion rate, and local concentration gradients of the antibacterial agent. Therefore, this method primarily enables qualitative assessment of antibacterial efficacy rather than quantitative analysis or kinetic evaluation. The organism preferred for the study was a common skin-affecting pathogen of Gram-positive (*Staphylococcus aureus) and* Gram-negative bacteria (*Pseudomonas aeruginosa and*

Escherichia coli). *Staphylococcus aureus*, a gram-positive bacterium, is a major cause of skin infection found at surgical sites and affects the wound environment. *Escherichia coli*, a gram-negative bacterium, is the opportunistic infection associated with wound contamination, and *Pseudomonas aeruginosa*, a gram-negative bacterium, is a highly virulent and antibiotic-resistant pathogen frequently observed in diabetic wounds.

From Figure. 14, the positive control antibiotic (gentamicin) exhibits a distinct and well-defined zone of inhibition around the disc in all three organisms. Both the plant extract disc and the plant extract-infused cellulose acetate thin film disc produced a measurable zone of inhibition towards all three organisms, showing that the antibacterial activity was induced in the film after the infusion of the extract into the CA polymer matrix. In contrast, the negative control, a CA polymer thin film, does not show any antibacterial zone around the disc, reflecting that the base polymer CA is inert and does not have any antibacterial activity. Among the three organisms, the *Staphylococcus aureus* shows a large and clear inhibition zone, which may be due to a simple cell wall structure that is easily susceptible to antibacterial activity induced by film and extract. Moderate inhibition shown in *E. coli* and *P. aeruginosa* may be due to the complex outer membrane. This lower noticeable sensitivity is consistent with known intrinsic resistance. The findings confirm that the cellulose acetate film infused with *Biophytum sensitivum* extract exhibits antimicrobial efficacy derived from the plant extract that was incorporated into the film. Additionally, the cellulose acetate functions as an efficient carrier, allowing for localized antibacterial action without intrinsic antibacterial interference.

Table 4, 5, 6 shows the Zone of inhibition (ZOI) measurements for the antibacterial property of thin film in *S. aureus, E. coli, p.aeruginosa.*

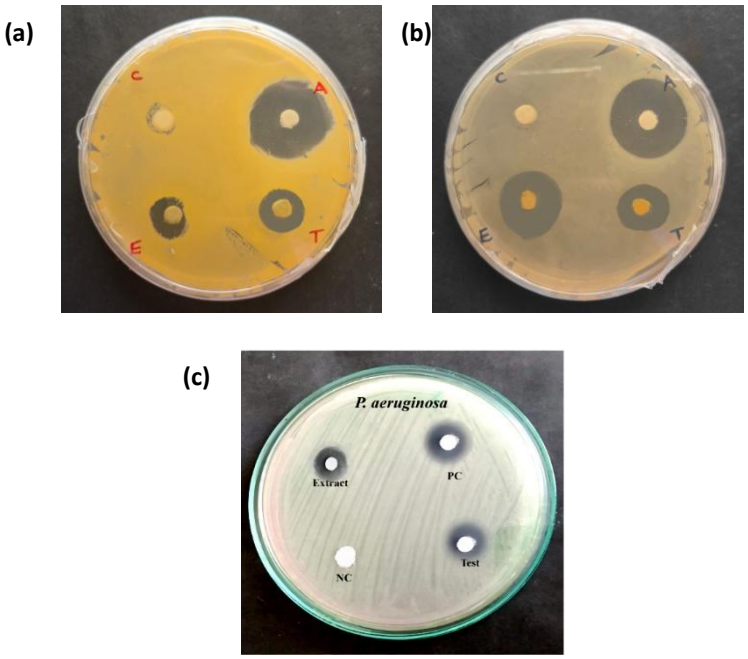

Figure 14. Antibacterial Property of Thin film towards **(a)** S. aureus, **(b)** E. coli and **(c)** P.aeruginosa (PC -Positive control have the antibiotic (gentamicin), Test - Biophytum sensitivum incorporated CA film, NC-Negative control has CA film, Extract - Biophytum sensitivum plant extract)

Table 4. Zone of inhibition (ZOI) for the antibacterial property of thin film in S. aureus

Sample	Trial 1 (mm)	Trial 2 (mm)	Trial 3 (mm)	Mean ± SD (mm)
Antibiotic (A)	13	15	11	13.0 ± 2.0
Test Film (T)	8	7	8	7.7 ± 0.6
Extract (E)	10	10	9	9.7 ± 0.6
Control (C)	-	-	-	

Table 5. Zone of inhibition (ZOI) for the antibacterial property of thin film in E. coli

Sample	Trial 1 (mm)	Trial 2 (mm)	Trial 3 (mm)	Mean ± SD (mm)
Antibiotic (A)	14	13	12	13.0 ± 1.0
Test Film (T)	9	8	7	8.0 ± 1.0
Extract (E)	11	10	12	11.0 ± 1.0
Control (C)	-	-	-	

Table 6. Zone of inhibition (ZOI) for the antibacterial property of thin film in p.aeruginosa

Sample	Trial 1 (mm)	Trial 2 (mm)	Trial 3 (mm)	Mean ± SD (mm)
Antibiotic (A)	14	13	12	13.0 ± 1.0
Test Film (T)	7	8	7	7.33 ± 0.58
Extract (E)	8	10	9	9.00 ± 1.00
Control (C)	-	-	-	

3.9 In vitro cytocompatibility assessment (MTT assay)

The in vitro cytocompatibility of the plant extract and the extract-loaded cellulose acetate thin film was systematically evaluated using the MTT assay on 3T3 mouse fibroblast cell lines, which are key contributors to wound healing and tissue regeneration. The untreated control group exhibited nearly 100% cell viability, confirming that the experimental conditions supported normal cell growth and metabolic activity. Upon exposure to the plant extract, a clear concentration-dependent decrease in cell viability was observed, with values of approximately 80% at 25 µg/mL, 72% at 50 µg/mL, and 63% at 100 µg/mL (Figure 15). This trend suggests that while the extract contains beneficial bioactive phytoconstituents, higher concentrations may exert mild cytotoxic effects, likely due to increased cellular stress or membrane interaction caused by phenolics, flavonoids, or other secondary metabolites. Nevertheless, the fact that cell viability remained above 60% even at the highest concentration indicates that the extract retains an overall acceptable safety profile within the tested range.

In contrast, the plant extract-loaded thin film demonstrated significantly improved cytocompatibility, maintaining cell viability in the range of 78%, which is notably higher than that of the highest extract concentration and comparable to lower, safer doses. This enhancement in cell viability can be attributed to the incorporation of the extract within the cellulose acetate matrix, which acts as a controlled delivery system. The polymer network likely facilitates a sustained and gradual release of phytochemicals, thereby minimizing direct exposure of cells to high local concentrations and preventing burst release–induced toxicity. Additionally, the homogeneous dispersion of the extract within the film, as evidenced by SEM analysis, may contribute to uniform bioactive release and reduced localized stress on cells. The polymer itself also provides a protective microenvironment that can buffer potentially reactive compounds, further enhancing cellular compatibility.

According to ISO 10993-5 guidelines, materials exhibiting greater than 70% cell viability are classified as non-cytotoxic. Based on this criterion, the thin film and the lower extract concentration (25 µg/mL) can be confidently considered biocompatible, while the intermediate concentration shows borderline acceptability and the highest concentration indicates mild cytotoxicity. Importantly, the improved viability observed in the thin film highlights the advantage of formulating plant extracts into a polymeric system rather than applying them in free form, especially for biomedical applications requiring prolonged contact with living tissues.Overall, the MTT assay results demonstrate that the plant extract-loaded cellulose acetate thin film achieves an optimal balance between therapeutic efficacy and cellular safety. The formulation not only reduces the cytotoxic effects associated with higher concentrations of the free extract but also maintains a favorable environment for fibroblast survival. These findings strongly support the potential application of the developed thin film as a biocompatible and effective wound dressing material, warranting further investigation through advanced in vitro models and in vivo studies to fully validate its clinical relevance in diabetic wound healing.

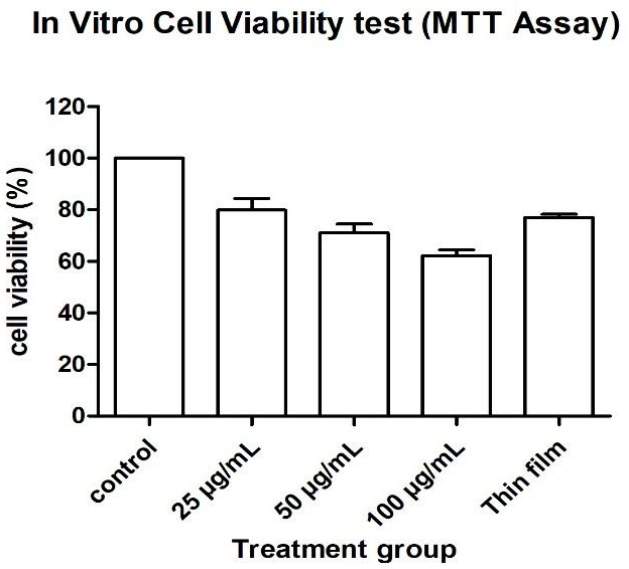

Figure 15. In vitro cell viability test (MTT Assay) of the plant extract loaded thin film and different concentration of plant extract (25, 50, 100µg/mL).

4. Conclusion

The present study reports the development and preliminary evaluation of a *Biophytum sensitivum*-incorporated cellulose acetate thin film as a potential multifunctional wound dressing system. Physicochemical characterization using FTIR, XRD, SEM, and UV–Vis analyses confirmed the successful incorporation of the plant extract within the polymer matrix and indicated structural modifications that may influence functional performance. The developed film exhibited appreciable swelling behavior, suggesting its capacity for wound exudate absorption and maintenance of a moist environment. Antimicrobial activity against common wound pathogens and antioxidant potential of the plant extract further support the therapeutic relevance of the system. In addition, cytocompatibility assessment using fibroblast cells demonstrated that the film is non-toxic and suitable for skin-contact applications.

Overall, these findings indicate that the formulated film possesses a combination of properties relevant to wound management at an in vitro level. However, the current study is limited to preliminary material characterization and biological screening. Further investigations involving wound-specific functional parameters such as water vapor transmission,

degradation behavior, extract release kinetics, surface wettability, and in vivo validation are necessary to establish its suitability for diabetic wound healing applications. Nonetheless, this work provides a promising foundation for future development of plant-based multifunctional wound dressing systems.

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M.P. Mahamahima: Conceptualization, Methodology, Formal analysis, Writing original draft. S. Anu: Validation, Data curation, Writing - Review & Editing. K. Kala Conceptualization, supervision, Writing review and Editing. All the authors read and approved the final version of the manuscript.

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Data Availability

The data supporting the findings of this study can be obtained from the corresponding author upon reasonable request.

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