Nanomed Res J 9(4):356-372, Autumn 2024

RESEARCH ARTICLE

Development, Characterization and Bioactivity of PVA/VPA/Aloin Nanofibrous Scaffolds for Biomedical Applications

Mona Raei[1], Mohammad Shabani [2,*], Kazem Privar[1], Mohammad Najafi [2], Mahdi Adabi[3]

[1] Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran

[2] Department of Biochemistry, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

[3] Department of Medical Nanotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran

ARTICLE INFO

Article History:
Received 18 Sep 2024
Accepted 15 Oct 2024
Published 01 Dec 2024

Keywords:
Nanofibrous scaffolds
Polyvinyl alcohol
Vinyl phosphonic acid
Aloin
MTT assay

ABSTRACT

Objective(s): Nanofibrous scaffolds have been considered for biomedical applications due to their structural and functional versatility. Polyvinyl alcohol (PVA) is frequently used in electrospinning, and its characteristics can be enhanced by adding substances. This study aimed to produce the fabrication of PVA-based nanofibers functionalized with vinyl phosphonic acid (VPA) and aloin as bioactive agents and evaluate their physicochemical, mechanical, and biological characteristics.

Methods: Nanofibrous scaffolds were produced through electrospinning using optimized conditions of voltage and distance. The scaffolds were analyzed through scanning electron microscopy (SEM), Fourier-transform infrared spectroscopy (FTIR), water contact angle measurements, tensile strength testing, and BET/BJH surface analysis. cell viability was assessed by using MTT assays. The influence of VPA (5%) and different aloin concentrations (3 mg and 6 mg) was systematically evaluated.

Results: SEM analysis confirmed that the optimized PVA/VPA (5%) nanofibers were smooth and bead-free, while the addition of aloin significantly altered fiber diameter. FTIR spectra validated the integration of VPA and aloin into the nanofibers. Measurements of the water contact angle indicated improved hydrophilicity. Mechanical testing revealed that VPA improved tensile strength, while aloin reduced it slightly at higher concentrations. BET/BJH analysis indicated that VPA increased porosity, whereas aloin's incorporation reduced porosity. MTT assays demonstrated enhanced cell viability with optimized aloin concentrations.

Conclusions: The PVA/VPA/Aloin nanofibrous scaffolds demonstrated adaptable properties ideal for biomedical uses, with VPA enhancing morphology, strength, and hydrophilicity, while aloin contributes bioactive effects dependent on its concentration. These scaffolds are promising for nanomedicine, tissue engineering and drug delivery.

How to cite this article
Raei M., Shabani M., Privar K., Najafi M., AdabiM. Development, Characterization and Bioactivity of PVA/VPA/Aloin Nanofibrous Scaffolds for Biomedical Applications. Nanomed Res J, 2024; 9(4): 356-372. DOI: 10.22034/nmrj.2024.04.003

INTRODUCTION

Tissue engineering offers a promising alternative by employing biomaterials, cells, and bioactive substances to repair and regenerate injured skin tissue, providing innovative solutions to overcome the limitations of traditional treatments [1, 2]. Skin tissue traumas, such as burns, wounds, surgical incisions, limb ischemia, and chronic wounds, pose important challenges in clinical practice. Clinical treatments such as skin tissue transplantation create an economic,

* Corresponding Author Email: *shabani.mo@iums.ac.ir*

physiological and psychological burden on patients, as they often face limitations in efficacy due to poor survival rates, especially in extensive wounds that require multiple surgeries [3, 4]. On the other hand, systemic antibiotics cannot provide sufficient local drug concentrations and may cause systemic side effects. In addition, conventional gauze dressings lack essential properties such as gas-liquid exchange, wetting ability, and sustained drug release [5-7]. Hence, finding multifunctional skin substitutes that combine the properties of biocompatibility, biodegradability, breathability, water absorption, antibacterial properties, and resistance to external stimuli, while enabling easy removal without causing tissue damage, is of great importance. It is of great importance. One of the excellent candidates for engineering skin tissue scaffolds to be used for complex drug delivery systems is nanofibers [8].

Nanofibers have beneficial features that make them highly suitable for wound-healing applications. Their framework resembles the natural extracellular matrix (ECM), offering excellent water uptake, interlinked porosity, airflow, and moisture passage, fostering an ideal setting for hemostasis, infection control, cell movement, growth, respiration, and fluid absorption [9-11]. The porous network of nanofibers facilitates oxygen diffusion to the wound site, while their excellent moisture retention ensures a moist wound environment, minimizing adhesion to damaged tissues. Compared to bulk materials like hydrogels, nanofibers' high porosity and large surface area enhance cell activity. In addition, their unique physicochemical properties can make them powerful drug carriers, capable of delivering active substances such as growth factors, cytokines, and antimicrobial agents. These drug-loaded nanofiber scaffolds promote enhance cellular proliferation and migration, hemostasis, stimulate angiogenesis, reduce chronic inflammation, inhibit scar formation, combat bacterial infections, and ultimately accelerate wound healing [12-14].

Natural and synthetic biopolymers are usually used to make electrospinning polymer nanofibers used in biomedicine. Common synthetic biopolymers include PVA, polylactic acid (PLA), polylactic-co-glycolic acid (PLGA), and VPA, while natural compounds such as chitosan, collagen, and cellulose also play significant roles [15]. meanwhile, multicomponent nanofibers, created by blending distinct polymer solutions, provide perfect properties and are fabricated using single-nozzle electrospinning systems. These fibers, such as PVA/hyaluronic acid composites and cellulose/nano-hydroxyapatite scaffolds, are extensively utilized in therapeutic fields, which shows their compatibility and effectiveness in various biomedical applications [16]. PVA is a synthetic, biocompatible polymer with widespread applications in tissue engineering, drug delivery, and regenerative medicine due to its excellent mechanical properties and mimicry of the extracellular matrix (ECM) [17-19]. However, pure PVA nanofiber membranes face challenges such as low strength, limited cell adhesion, and rapid dissolution in aqueous environments, prompting the need for modifications through polymer composites [18-21].

VPA, a phosphonate compound, complements PVA by offering antimicrobial properties, similarity to phosphate groups in hydroxyapatite, and compatibility for bone tissue engineering [15, 22]. VPA and its derivatives have emerged as promising compounds in medical research, particularly due to their significant antiviral characteristics. VPA-based copolymers have demonstrated notable effectiveness against viral infections, such as influenza, with certain derivatives exhibiting potent antiviral efficacy combined with minimal cytotoxicity [23]. VPA copolymers with 4-acryloylmorpholine significantly reduced virus-related mortality in animal studies, highlighting their therapeutic potential. VPA polymers have been widely employed in drug delivery systems and as functional coatings for medical equipment. Their ability to serve as carriers for biologically active molecules enhances drug efficacy and facilitates controlled release mechanisms. Poly (vinylphosphonic acid) also exhibits favorable mechanical strength and film-forming characteristics, making it suitable for hydrogel applications in medical delivery systems. Additionally, in bone and dental medicine, VPA-based bisphosphonates have been employed as coatings to enhance the integration and performance of implants [24, 25].

To further extend the performance of these nanofibers, Aloin, a bioactive compound derived from Aloe vera, was incorporated into the PVA/VPA nanofiber system. Research has shown its anti-inflammatory properties, as it successfully decreased inflammation, supporting its application in the treatment of arthritis and other inflammatory ailments [26]. Moreover, aloin exhibits strong

antimicrobial characteristics, demonstrating effectiveness against multiple pathogens, which supports its role in wound healing and infection prevention [27]. Notably, its anticancer potential has garnered significant interest, with research indicating that aloin can inhibit tumor growth, making it a promising candidate for cancer treatment strategies [28].

The therapeutic potential of aloin is further highlighted by its clinical applications. Its capability to enhance rapid wound healing is linked to its role in stimulating cell proliferation and tissue repair, rendering it essential in injury management [27]. In gastrointestinal health, aloin functions as a laxative and aids in managing digestive disorders, while its role in blood sugar regulation suggests potential benefits for diabetes management [26, 27]. Also, it accelerates fibroblast proliferation and collagen synthesis, making it a valuable addition to tissue engineering [29, 30]. Aloin, has been utilized in various pharmaceutical formulations, with polymer matrices like PVA, alginate, and chitosan demonstrating controlled release capabilities [26, 31, 32]. By integrating aloin into the electrospun PVA/VPA nanofibers, this study aims to develop a multifunctional scaffold combining advanced structural and bioactive features for therapeutic applications.

This study introduces a novel PVA/VPA nanofibrous membrane, that represents the first successful synthesis of VPA nanofibers. On the other hand, this study also shows the first application of VPA in the medical field. Combining the strengths of both polymers, the research explores the enhanced properties of these hybrid membranes. Also, different gelatins of aloin extract were loaded in various matrices produced by electrospinning solutions containing PVA and VPA polymer compounds. The aim of this study is to characterize several electrospun nanofiber membranes based on PVA and VPA loaded with aloin. Types of electrospun VPA/PVA nanofiber membranes and types of electrospun VPA/PVA nanofiber membranes containing aloin in laboratory conditions by SEM, FTIR, Contact Angel, Tensile Strength, Brunauer–Emmett–Teller (BET) are characterized. Finally, MTT was performed using Rat L-929 cells to investigate the application potential of synthesized nanofibers in medical settings and tissue engineering.

MATERIALS AND METHODS

I. Material

Aloin AR grade, was purchased from Sigma-Aldrich Chemie GmbH, MO, USA and was used as a model drug. Polyvinyl alcohol, with a molecular weight 72,000 g/mol (99% hydrolyzed), was purchased from Siheung, Republic of Korea. N,N-Dimethylformamide (DMF) and Vinyl phosphonic acid (VPA) (97%) was purchased from TCI Ltd., UK. Deionized and distilled water was purchased from the local market.

II. Preparation of PVA/VPA/Aloin nanofiber

This study focused on the preparation and characterization of PVA, PVA/VPA, and PVA/VPA/Aloin nanofibers, as summarized in Table 1. During the preparation of nanofibers, according to the following instructions, VPA and aloin were added or removed as needed. PVA powder was dissolved in distilled water, while VPA was dissolved in deionized water, resulting in two homogeneous solutions. The PVA concentration was set at 10% w/v, based on prior research, beacuse it provides an optimal viscosity for the electrospinning process and resulting in smooth and bead-free nanofibers [33]. VPA concentrations of 2.5% and 5% w/v were used, marking the initial results of fabricating VPA nanofibers. These concentrations may be optimal for improving mechanical strength or introducing specific functional groups without significantly altering the fiber formation process. Key parameters for the electrospinning process, including a voltage of 10 kV and a nozzle-to-collector distance of 10 cm, were obtained from earlier studies [34].

The prepared PVA and VPA solutions were combined in a 70:30 ratio and stirred thoroughly to achieve a homogeneous polymer blend with appropriate concentration at room temperature. Then, resulting solution was put into a 5 mL syringe with a metallic blunt-ended 18G needle as a nozzle using an electrospinning machine (FANAVARAN NANO MEGHEIAS, Iran), which was connected to a high voltage power supply an optimization process was performed to identify the optimal electrospinning parameters for PVA/VPA nanofiber production. The optimization focused on varying voltage levels (18, 20, and 22 kV) and the distance between the nozzle and collector (8, 10, and 12 cm), as detailed in Table 1. Fibers were generated at a controlled flow rate of 1 mL/h, with

Table 1. Nanofibers synthesis parameters

No.	PVA 10% (ml)	VPA2.5% (ml)	VPA 5% (ml)	aloin (mg)	Voltage (kV)	Distance (cm)	Flow rates(ml/h)
1	7.1	_	_	_	10	10	1
2	5	2.1	_	_	18	8	1
3	5	2.1	_	_	18	10	1
4	5	2.1	_	_	18	12	1
5	5	2.1	_	_	20	8	1
6	5	2.1	_	_	20	10	1
7	5	2.1	_	_	20	12	1
8	5	2.1	_	_	22	8	1
9	5	2.1	_	_	22	10	1
10	5	2.1	_	_	22	12	1
11	5	_	2.1	_	18	8	1
12	5	_	2.1	_	18	10	1
13	5	_	2.1	_	18	12	1
14	5	_	2.1	_	20	8	1
15	5	_	2.1	_	20	10	1
16	5	_	2.1	_	20	12	1
17	5	_	2.1	_	22	8	1
18	5	_	2.1	_	22	10	1
19	5	_	2.1	_	22	12	1
Optimized parameters of nanofiber							
20	5	_	2.1	3	20	10	1
21	5	_	2.1	6	20	10	1

voltage applied to the collector and tip of the device. The nanofibers were collected on the collector of the device under different voltage and distance conditions.

After determining the ideal electrospinning conditions, the model drug aloin was included in the PVA/VPA polymer solution at different concentrations was dissolved in DMF (Table 1). The use of two different concentrations allows for the optimization and comparison of the nanofiber properties such as fiber diameter, while maintaining the structural integrity of the nanofibers. The polymer solution containing aloin was then electrospun under optimized conditions: 20 kV voltage and 10 cm nozzle-to-collector distance. Using the same settings and parameters as electrospinning, PVA/VPA/Aloin fibers were extruded at a flow rate of 1 ml/h and collected on the device's collector. This process ensured the successful fabrication of PVA/VPA/Aloin nanofibers, which were subsequently subjected to further characterization.

III. Tensile strength

The mechanical properties of the fibers were evaluated using a uniaxial tensile strength tester (Shimadzu Co., EZ-LX, Kyoto, Japan) following the ASTM D3822 standard. Each patch was cut with a die of 5 cm length and 1 cm width. The thickness of each nanofiber sample was measured with a digital micrometer (Mitutoyo, Santa Ana, CA, USA). For the test, the sample was secured between two clamps, with one clamp fixed and the other movable, maintaining a 10 mm gauge length. A force of 10 N was applied, and the movable clamp was driven at a constant extension rate (CRE) of 15 mm/min [35, 36].

IV. Contact Angle Measurement

The hydrophilicity of the nanofiber membranes was Measured by the contact angle measurement technique with the non-settling drop method (TGX) at room temperature. Three microliters of distilled deionized water droplets were placed on the surface of nanofiber fragments, and the contact angle was determined with a contact angle meter (Digidrop, GBX, Whitestone Way, France). The water contact angle values were automatically calculated using the software[36, 37].

V. Brunauer-Emmett–T (BET)

In the BET method for physical characterization, adsorption-desorption isotherms are used to measure surface area, pore size distribution, pore volume, pore size and other pore characteristics of nanofiber membranes. In this study, surface

and size analyzer with nitrogen (N2) adsorption-desorption isotherms at 77K under high vacuum (NOVA 3200e, Quantachrome Instruments) was used [35, 38].

VI. Scanning electron microscope (SEM)

The surface morphology of electrospun nanofibers was analyzed by a SEM (JSM-5300, JEOL Ltd., Tokyo, Japan). For this purpose, the nanofibers were first coated with gold for 30 seconds. In all SEM observations, incident electrons from a 10 kV high vacuum electron gun were used in the 800x magnification range. Image J software (National Institutes of Health, USA, version 1.65) was used to determine the average diameter and diameter distribution of nanofibers [35, 39, 40].

VII. Fourier transform infrared spectroscopy (FTIR)

Chemical interactions within PVA, PVA/VPA, and drug-loaded PVA/VPA nanofibers were investigated using Fourier transform infrared spectroscopy (FT-IR, Spectrum GX, PerkinElmer, Inc., Billerica, MA, USA) in transmittance, with a range of 400–4000 cm^{-1} and a resolution of 1 cm^{-1} [35, 38].

VIII. MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide)

MTT test was used to evaluate cell viability in rat fibroblast cell suspension (L929) treated with the nanofibers. The nanofibers were sterilized via UV light exposure for 2 hours. Sterilized samples were placed in 96-well plates, and 100 µL of a cell suspension (3×10^3 cells/well) prepared in cell culture medium (DMEM supplemented with 10% FBS and 100 U/mL penicillin/streptomycin) was seeded onto each well. The samples were incubated at 37°C, 5% CO2 and 95% relative humidity, and the culture medium was changed every 48 hours after incubation for 1, 3 and 7 days. Then, cell viability was measured using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2 H-tetrazolium bromide (MTT) assay after 2 h. The absorbance was measured at 560 nm and the reference wavelength at 630 nm using a microplate reader (BioTek, United States). The control sample consists of wells without nanofibers [41, 42]. This experiment was repeated three times.

RESULTS AND DISCUSSION

A. Characterization of nanofibrous scaffolds

i. SEM

Scanning electron microscopy characterized the prepared fibers' morphology and diameter. The diameters of the nanofibers were recorded and calculated for 100 randomly selected nanofibers from the images using Image J software. In this study, the SEM was performed twice. The first time was done to determine the proper concentration of VPA, the appropriate distance and the proper voltage, and the second time was done to determine the proper concentration of aloin. In the first SEM, it was found that the nanofiber containing 2.5% VPA was not completely smooth and had much more grains than the nanofiber containing 5% VPA. Therefore, the concentration of 5% VPA was chosen. These observations are consistent with reports that the choice of VPA concentration played a critical role in determining the uniformity and smoothness of the nanofibers [43]. In other words, the addition of charged functional groups, such as VPA, improves fiber morphology by enhancing the solution's conductivity and charge density during electrospinning.

PVA/VPA nanofibers (5%) were examined at voltages of 18, 20, and 22 and distances of 8, 10, and 12 in terms of morphology and lack of grain formation in nanofibers, and finally, voltage of 20 and distance of 10 was selected. Similar studies have demonstrated that such parameters critically influence fiber morphology, with inappropriate settings often leading to bead formation or irregular diameters [44].In a comparative analysis of various polymers, Leung, L.M. et al highlight that the geometry of the electrospinning setup, particularly the nozzle-to-collector distance, plays a significant role in fiber formation. Their results corroborate earlier findings by indicating that increased distances can lead to more chaotic fiber deposition and larger fiber diameters, which negatively impacts both aesthetic and mechanical properties[43].Additionally, many studies support the observation that increasing the applied voltage reduces fiber diameter due to enhanced jet elongation and increased drawing forces .This is aligns with the results for fibers produced at 18 kV and 22 kV (panels E and F), where thinner fibers were observed[44]. The optimized conditions in this study further confirm the importance of carefully tuning these parameters to achieve smooth, uniform fibers

PVA(10%)/VPA (5%) /Aloin nanofibers were also made with a voltage of 20 and a distance of 10. All the produced samples were cleaned with Aloin (3mg), Aloin (6mg), PVA and VPA nanofibers. The surface morphology was examined through SEM

analysis of the cleaned samples. Five pictures from various spots of the same sample were analyzed and verified that all fibers were smooth and no beads were present, as shown in Fig 1. According to the obtained results, it seems that both samples containing Aloin (3mg) and Aloin (6mg) are suitable for making PVA/VPA (5%)/Aloin nanofibers. In the rest of the study, wherever VPA is mentioned, it means 5% concentration.

As shown in Fig 1-F, the addition of VPA to PVA increases the diameter of nanofibers, but it is not significant. On the other hand, adding aloin to PVA/VPA significantly increased the diameter of nanofibers. This finding was consistent with Hikmawati D, et al. study conducted in 2018, and the incorporation of aloin in the PVA matrix significantly increased the diameter of nanofibers. [45]. This can be because the addition of some bioactive compounds increases the diameter of the fiber due to the change in the viscosity of the solution. According to previous articles, increasing the amount of aloin reduces the diameter of nanofibers [45], and in our study, the diameter of PVP/VPA/Aloin (6mg) nanofibers was significantly reduced compared to PVP/VPA/Aloin (3mg) nanofibers. In this study, due to the toxicity of aloin, other amounts of aloin were spared. The results indicate that the incorporating aloin into electrospun nanofibers significantly affects the morphology and diameter of the fibers, leading to enhanced functional properties crucial for biomedical applications. However, the dual nature of aloin as both a beneficial and potentially toxic agent underscores the importance of optimizing its concentration for safe use.

ii. FTIR

The FTIR analysis provided insights into the chemical interactions within the nanofiber systems. The result FTIR of PVA, PVA/VPA, PVP/VPA/Aloin (3mg) and PVP/VPA/Aloin (6mg) is shown in Fig 2. PVA is produced from the hydrolysis of poly (vinyl acetate) and is a copolymer of repeating units of vinyl alcohol and vinyl acetate. Although hydrolyzed PVA is used to make nanofibers, some of the unhydrolyzed acetate groups remain in the polymer. In Fig 2-A, the peak at 1728.50 cm^{-1} corresponds to the stretching vibrations of the C=O groups of the remaining vinyl acetate repeat units in PVA. The peak at 2918.42 cm^{-1} corresponds

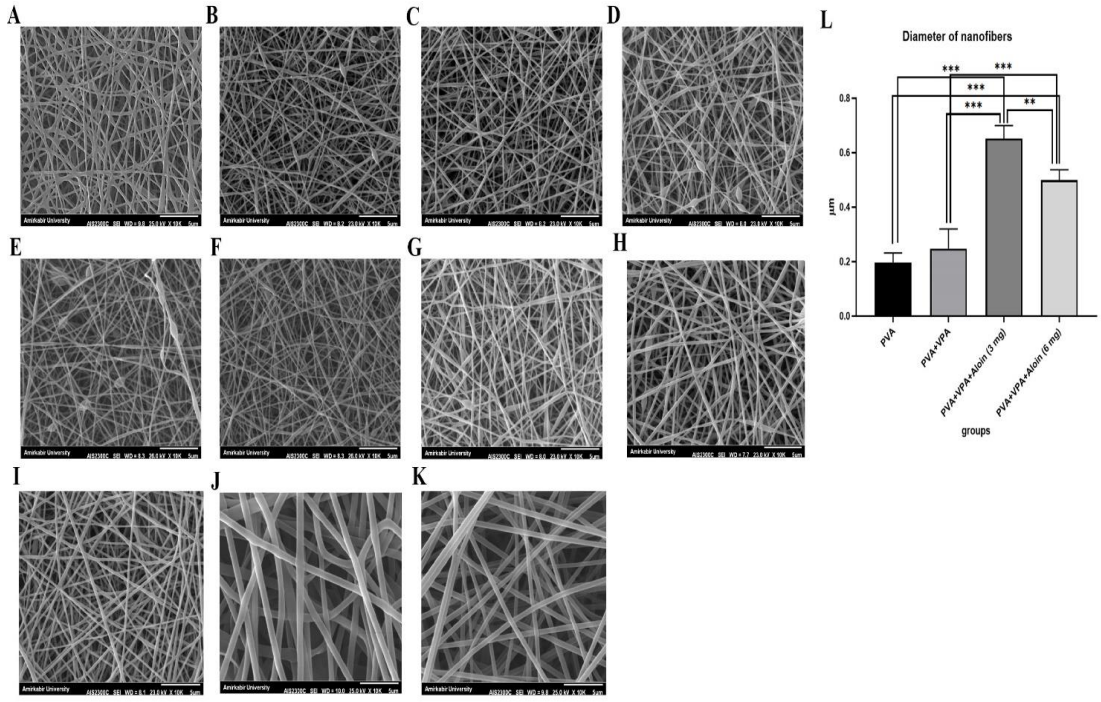

Fig. 1. SEM. A) PVA. B) nanofiber with a distance of 8 cm. C) nanofiber with a distance of 10 cm. D) nanofiber with a distance of 12 cm. E) nanofiber with a voltage of 18 kV. F) nanofiber with a voltage of 20 kV. G) nanofiber with a voltage of 22 kV. H) PVA/VPA (2.5%). I) PVA/VPA (5%). J) PVP/VPA (5%)/Aloin (3mg). K) PVP/VPA (5%)/Aloin (6mg). L) Diameter of nanofibers, Polyvinyl alcohol (PVA), vinyl phosphonic acid (VPA), (n = 5, significance level $*p < 0.5$, $**p < 0.01$, $***p < 0.001$).

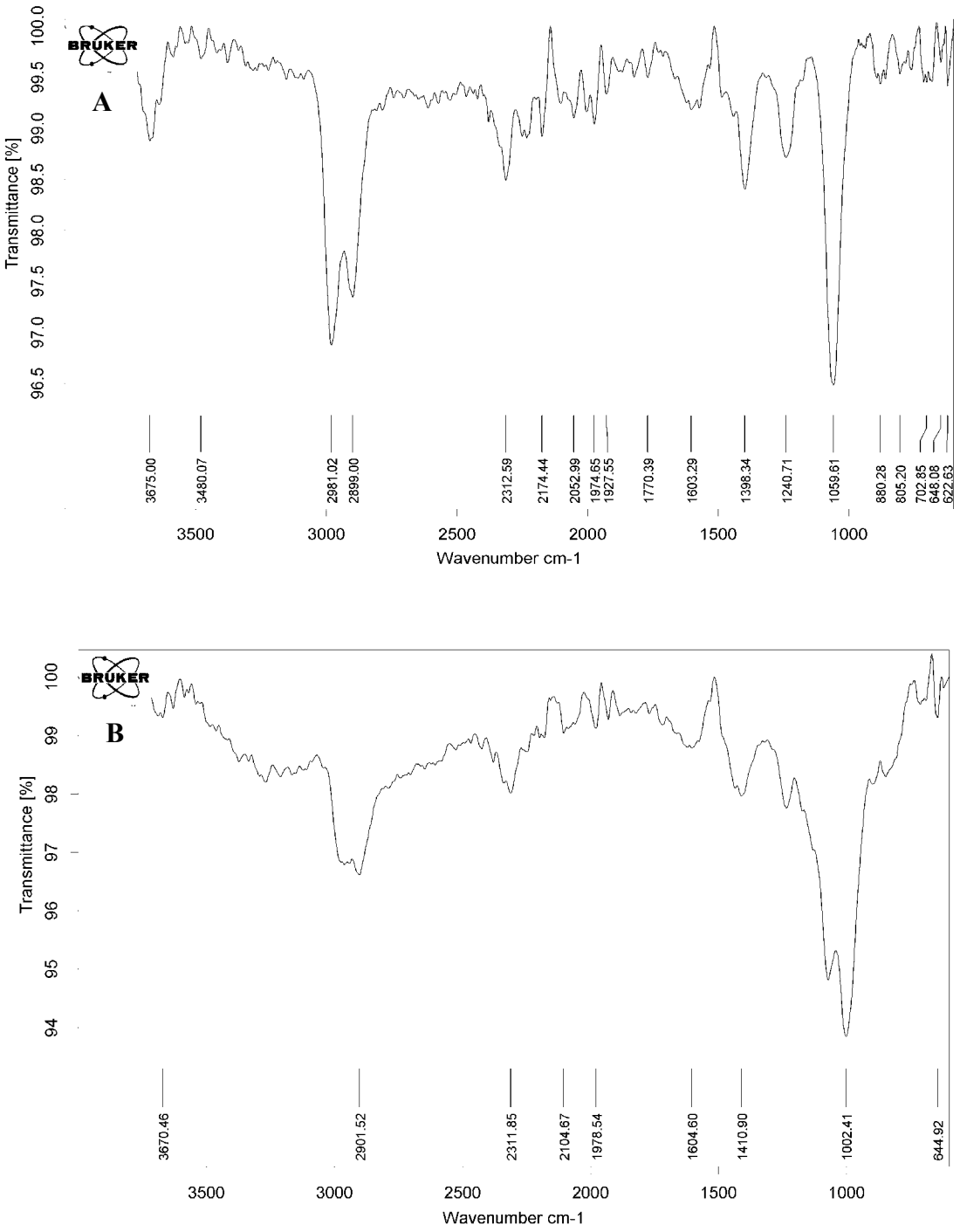

Fig. 2. FTIR spectra of A) PVA. B) PVA/VPA. C) PVP/VPA/Aloin (3mg). D) PVP/VPA/Aloin (6mg).

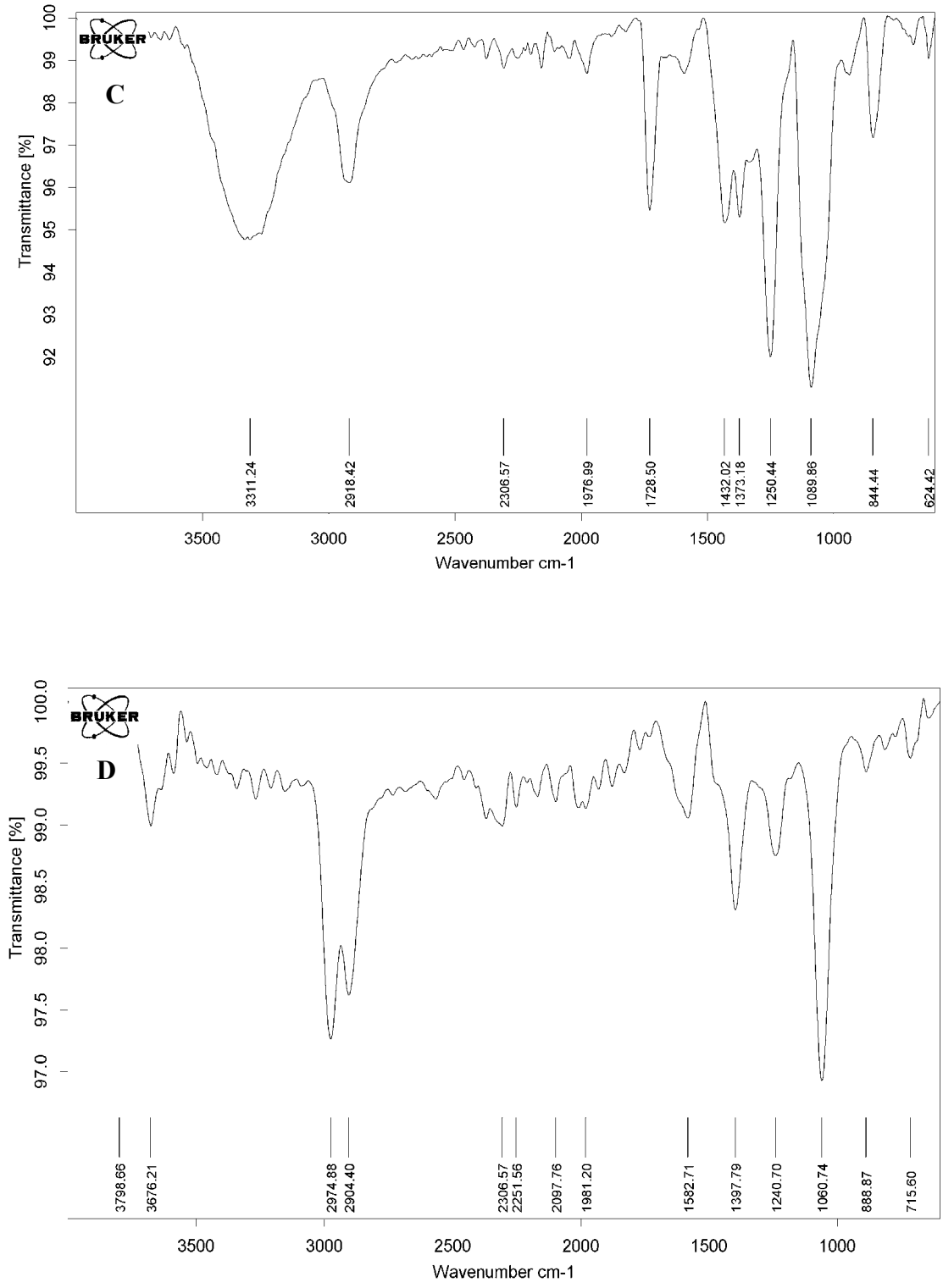

Fig. 2. FTIR spectra of A) PVA. B) PVA/VPA. C) PVP/VPA/Aloin (3mg). D) PVP/VPA/Aloin (6mg).

to the antisymmetric stretch of CH_2 in the PVA sample [46]. In the region of 3500-2750 cm-1, both samples with aloin exhibit a significant band linked to hydroxyl groups found in phenolic substances like anthraquinones [45, 47]. It can be seen that there are characteristic signals between 2800 and 2400 cm^{-1} in all nanofibers containing VPA, which indicates the presence of phosphonic acid. C-H stretching and bending signals are observed at 3000-2800 and 1500-1375 cm-1, respectively [48].

In the figure 2-C, the intensity of the -OH peak has increased in the region of 3400 cm^{-1}, which confirms the presence of Aloin in the nanofiber [49]. This can be ascribed to the establishment of hydrogen bonds among the elements, and when compared to the hydrogen bond in the same polymer, two distinct macromolecules will generate more robust hydrogen bonds. Our results show that the compounds used in the fabrication of nanofibers are well integrated into the structure of nanofibers.

Moreover, the interaction between aloin and the polymer matrix may lead to improved mechanical properties and biocompatibility of the nanofibers. These findings underscore the role of aloin not only as a functional additive in the nanofiber fabrication process but also as a crucial factor in modifying the molecular interactions within the material, resulting in enhanced properties useful in various biomedical applications. Overall, the incorporation of aloin into PVA-based nanofibers demonstrates its capacity to influence the chemical structure and improve the interactions within the polymer matrix, as visualized through FTIR spectroscopy. This insight is essential for optimizing the design and functionality of biomaterials employed in tissue engineering and drug delivery systems [50].

iii. Tensile strength

The tensile properties of the nanofiber were evaluated using a uniaxial tensile strength tester, and the stress-strain behavior is presented in Fig 3. Samples included pure PVA, PVA+VPA, and PVA+VPA with Aloin at two concentrations (3 mg and 6 mg). The stress-strain curves demonstrated significant differences in the mechanical behavior of the various formulations. Pure PVA showed a gradual increase in stress with strain, reaching a maximum stress of approximately 6 MPa at a strain of around 25%. This behavior reflects the elastic and ductile nature of PVA which can be attributed to the polymer ‘s molecular structure and alignment of polymer chains during the electrospinning process. Koski, A., et al reported that electrospun pure PVA nanofiber exhibited high elongation at break along with moderate tensile strength [51]

The addition of VPA significantly increased the mechanical properties. The PVA+VPA sample

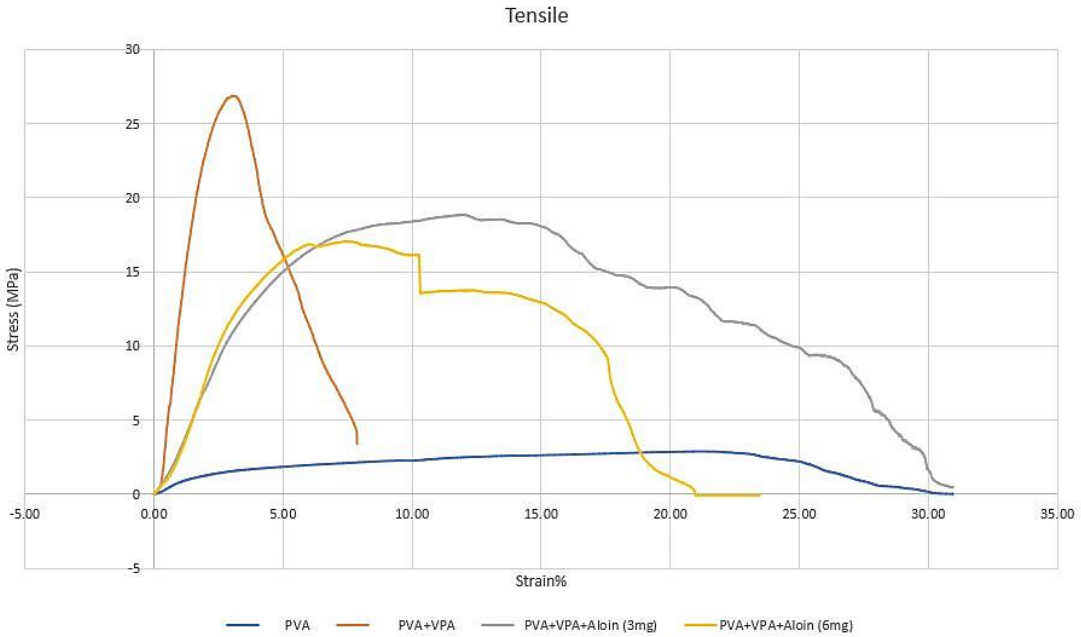

Fig. 3. Tensile strength curves of nanofiber: PVA, PVA/VPA, and PVA/VPA/ Aloin (3 mg) and (6 mg).

reached a peak stress of approximately 28 MPa at a lower strain (~6%), followed by a rapid decrease in stress, indicating brittle behavior compared to pure PVA. This brittleness increases with the addition of VPA, contrasting with the ductility of pure PVA. Additionally VPA might be acting as a reinforcing agent, enhancing strength. This phenomenon can be explained by formation of hydrogen bonds between the phosphonic acid groups of VPA and the hydroxyl groups of PVA. Similar effects have been observed in other studies involving acid-modified PVA nanofibers. Ding ,B,. et al found that incorporating phosphonic acid into PVA nanofibers enhanced their mechanical strength due to increased intermolecular interactions [52].

The PVA+VPA+Aloin (3 mg) sample showed peak stress of ~18 MPa at ~9% strain, followed by gradual stress relaxation. In contrast, the PVA+VPA+Aloin (6 mg) sample showed a peak stress of ~15 MPa at ~6% strain but displayed a sharp decline in post-peak stress, indicating higher aloin content reduces mechanical stability. The result demonstrates that the increased aloin concentrations may lead to reduced tensile strength, likely due to the combined effects of plasticizing and possible disruption of intermolecular interactions within the polymer matrix [53]

This is well consistent with the behavior reported in the study of Sosiati H, et al. they have stated that PVA nanofibers with optimal aloe vera concentration (4%) show the highest strength and tensile modulus, while at higher concentrations (6%) these properties decrease [54]. These findings emphasize that choosing the appropriate concentration of additives can be very important to achieve optimal mechanical properties. Also, Jegina S, et al and Kakroodi S, et al confirmed that adding compounds such as aloe vera can increase the tensile strength and elongation at break of PVA nanofibers [53, 55]. However, the Aloin-containing samples maintained reasonable mechanical properties, with the 3 mg formulation demonstrating a balanced combination of strength and elongation.The observed mechanical behavior can be explained by the interactions between aloin and the PVA/VPA matrix. At lower concentrations, aloin may enhance the fiber's ductility and flexibility, contributing to improved tensile properties. However, at higher concentrations, the potential cytotoxic effects of aloin and its influence on the viscosity of the electrospinning solution may lead to reduced fiber uniformity and increased brittleness [56].

iv. Contact angles

The water contact angle measurements demonstrate that combining PVA with VPA and aloin significantly enhances hydrophilicity in the synthesized nanofibers. The reduction in contact angle, from 54.8° for pure PVA to 39.7° for PVA/VPA nanofibers, highlights the hydrophilic nature of VPA (Fig 4 A, B). It can be seen that combining PVA with VPA can increase the amount of hydrophilicity. This improvement can be attributed to the presence of phosphonic acid groups within VPA, which are known for their ability to form strong hydrogen bonds with water molecules, thus facilitating enhanced wetting and absorption [57]. Also, additional decrease in water contact angle for PVA/VPA/Aloin nanofibers (47.6° for 3 mg and 44.3° for 6 mg) indicates that aloin further enhances hydrophilic properties. This observation is consistent with previous research showing that aloe vera-derived extracts, such as aloin, contribute phenolic hydroxyl groups that improve surface wettability[58].

The results of water contact angle measurements showed that PVP/VPA/Aloin (6 mg) is more hydrophilic than the other synthesized nanofibers, producing a fiber surface that optimized water interaction. The increased wettability can facilitate better cellular interactions and tissue integration, thereby enhancing the overall effectiveness of biomaterials in medical applications. Previous studies have demonstrated that increased wettability not only enhances cell adhesion but also promotes nutrient and oxygen diffusion, which are critical for tissue regeneration and healing [59,60]. Thus, the development of PVA/VPA/Aloin nanofibers holds significant promise for advancing the field of biomaterials, where surface properties play a critical role in determining the performance and efficacy of the materials used.

v. BET Surface Area and Pore Characteristics

The surface area and pore characteristics of the nanofiber membranes were analyzed using nitrogen (N2) adsorption-desorption isotherms at 77 K, as shown in Fig. 5. The isotherms for all groups demonstrated Type IV behavior, typical of mesoporous materials, with a pronounced hysteresis loop, indicating capillary condensation within the pores. This observation announced that the nanofiber membranes contain interconnected

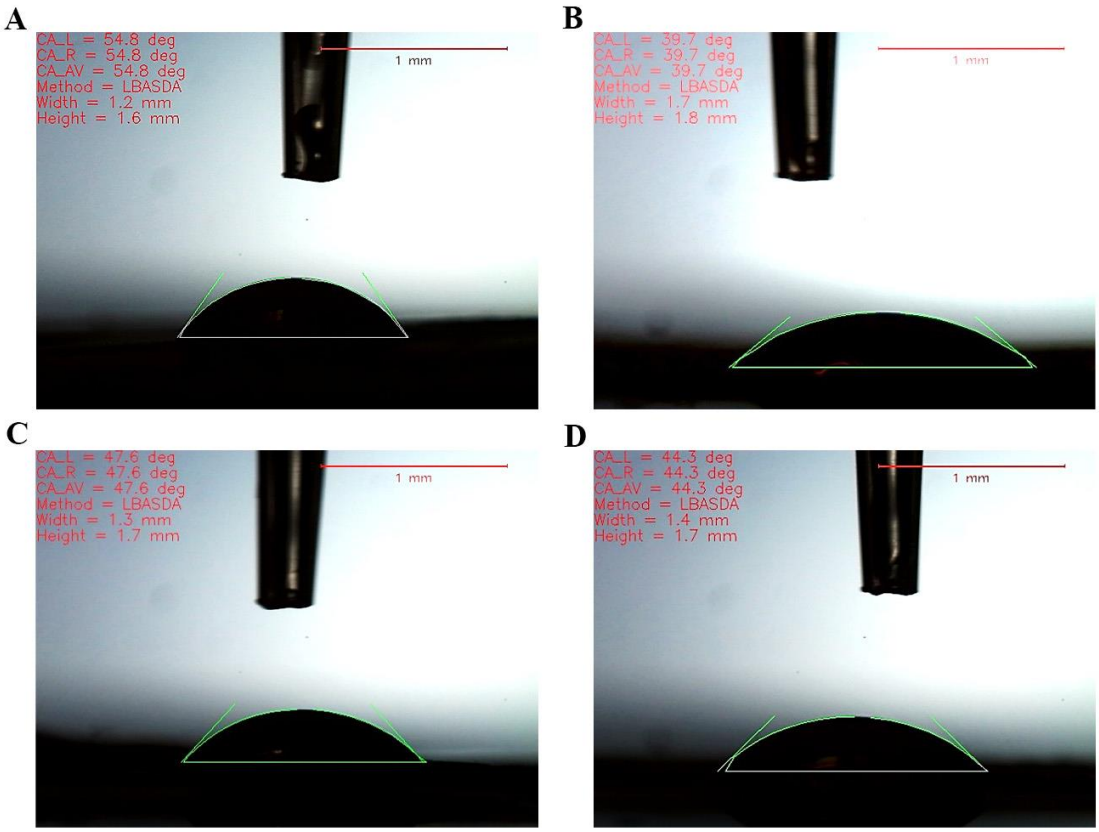

Fig. 4. Contact angles. A) PVA. B) PVA/VPA. C) PVP/VPA/Aloin (3 mg). D) PVP/VPA/Aloin (6 mg).

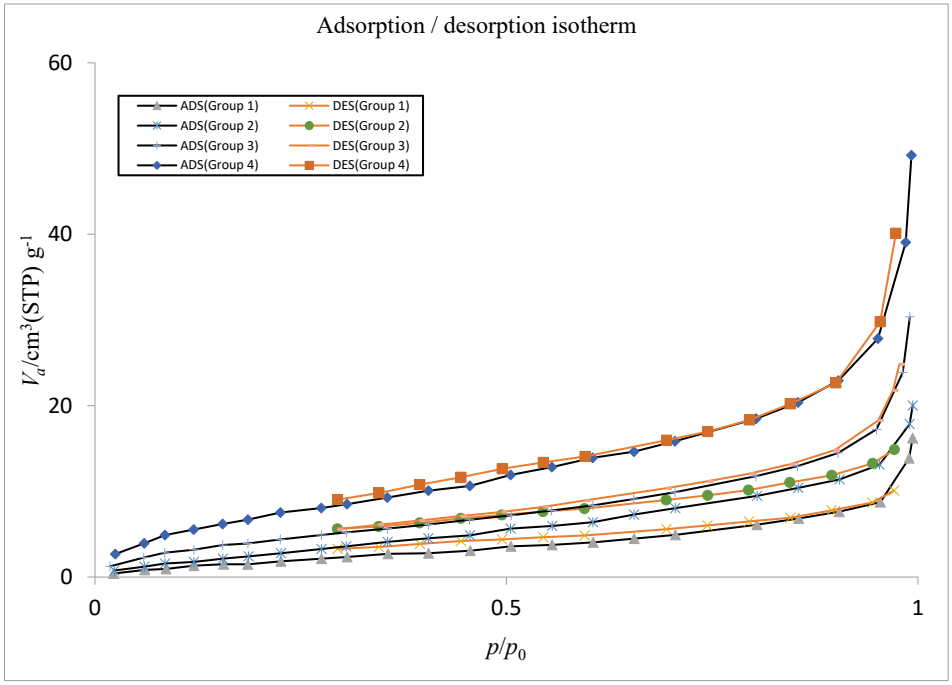

Fig. 5. BET Adsorption/desorption of Group 1) PVA , Group 2) PVA /VPA , Group 3: PVA / VPA / Aloin (3 mg), Group 4: PVA / VPA / Aloin (6mg)

Table 2. The result of BET analysis

	a_s BET	*c*	Total pore volume	V_p	r_P	a_p
PVA	8/5043	9/26	0/022042	0/023389	1/85	10/78
PVA/VPA	13/703	7/8257	0/027723	0/030593	1/85	18/231
PVA/VPA/Aloin (3mg)	17/351	19/18	0/046778	0/047785	1/21	19/644
PVA/VPA/Aloin (6mg)	27/006	32/564	0/07145	0/072358	1/85	30/776

porous structures Table 2. In group 1 with PVA 10%, the baseline membrane showed the lowest surface area and pore volume among the groups, consistent with the absence of VPA or Aloin, which can influence the polymer structure and porosity. In group 2 with PVA 10% / VPA 5%, the addition of VPA resulted in a noticeable increase in surface area and pore volume, attributed to its role as a crosslinking agent, which enhances the porosity of the membrane. For Group 3 by PVA 10% /VPA 5% / Aloin 3 mg, the incorporation of 3 mg of Aloin slightly reduced the surface area and pore volume compared to Group 2, which indicated a partial blockage of pores or structural compaction due to the incorporation of aloin in the polymer matrix. And Group 4 with PVA 10% / VPA 5% /Aloin 6 mg showed at higher Aloin concentration (6 mg), a further reduction in surface area and pore volume was observed, likely due to excessive incorporation of Aloin, which disrupts the porous structure and decreases the overall void space.

These findings showed that the addition of VPA significantly enhances the surface area and pore characteristics of the membranes, while the inclusion of Aloin results in a trade-off between functional modification and porosity [38]. In a study by Saravanan, A., et al. it was stated that adding natural biomaterials can change the surface topography in PVA nanofibers. They acknowledged the addition of 5-Fluorouracil increased the specific surface, but the addition of composite biomaterials decreased the specific surface [61]. This behavior is similar to the decrease of the specific surface due to the addition of Aloin, which can be related to the compaction of the structure. The results show that the samples of groups 1 and 2, which are basic polymers, are mesoporous and heterogeneous, and after adding 3 mg and 6 mg of aloin, the specific surface area increased and changed from mesoporous to microporous. Almeida, V., et al. discovered that the manipulation of additive concentrations in polymer matrices could indeed lead to transformations in pore size distributions, directly correlating with increased functionality while altering the pore characteristics, thereby transitioning between mesoporous and microporous structures, as observed in their PVA-alumina composite studies [62].

The pore size distribution of the nanofiber membranes was evaluated using the BJH method, which analyzes desorption data from nitrogen (N_2) isotherms at 77 K. Fig 6 shows the BJH pore size distribution curves for the four groups. In Group 1 with PVA10%, The baseline membrane demonstrated a relatively broad distribution of pore sizes focused on smaller diameters. This indicates an irregular porous structure due to the lack of additives like VPA or Aloin that could modify the pore network. In Group 2 with a PVA 10% / VPA 5%, the incorporation of VPA resulted in a noticeable shift in the distribution toward more defined mesopores. The pore network became more organized, featuring a greater pore volume and an enhanced peak in the mesopore range (2–50 nm). This behavior can be attributed to the crosslinking action of VPA, which improves the interconnected porous structure. in Group 3 with PVA 10% /VPA 5% / Aloin 3 mg, With the addition of 3 mg of Aloin, the pore size distribution became narrower, and the peak shifted slightly toward smaller pore sizes. This indicates that there may be some pore obstruction or increased density resulting from the integration of Aloin molecules into the pore structure. And Group 4 containing PVA 10% / VPA 5% / Aloin 6 mg, showed an additional decrease in both pore volume and size at the concentration of 6 mg Aloin.

The distribution curve shows diminished mesoporosity, likely due to excessive Aloin incorporation, which disrupts the porous matrix and leads to a denser, less porous structure. in this study, the BJH analysis complements the BET results, demonstrating the dual role of VPA and Aloin in modifying the nanofiber membranes. While VPA enhances mesoporosity through crosslinking, Aloin's influence depends on its concentration, balancing functional modification and structural densification. The maximum pore

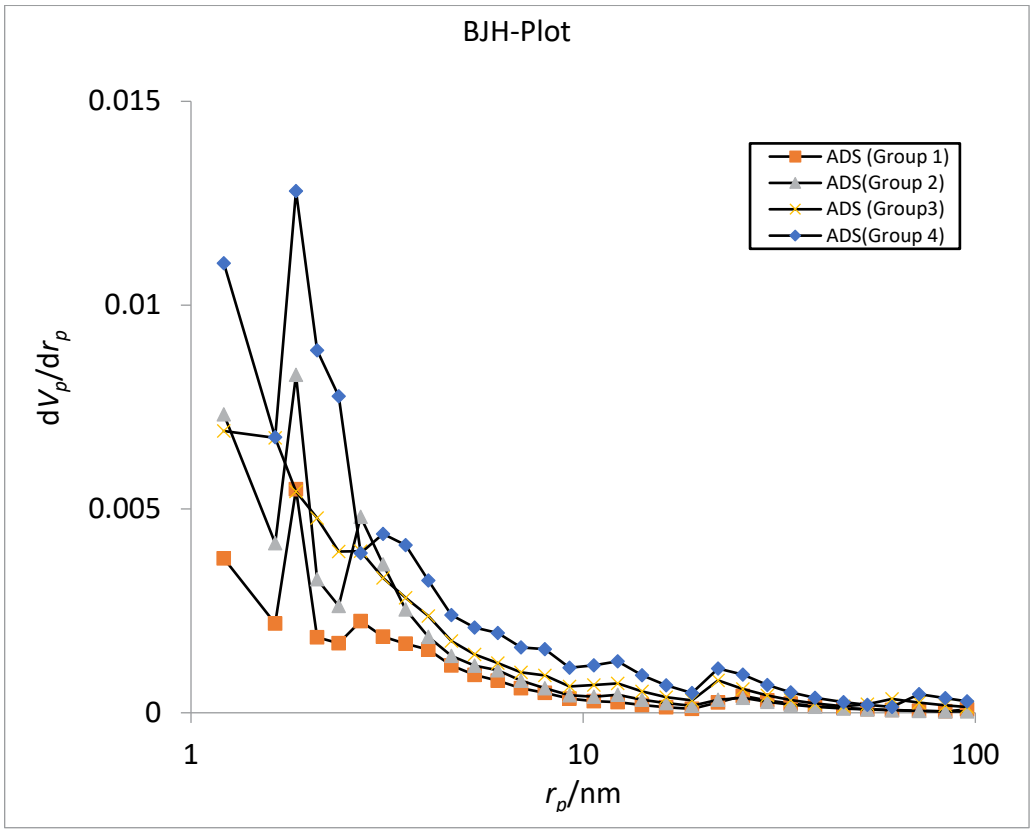

Fig. 6. BJH pore size distribution curves. Group 1)PVA , Group 2) PVA / VPA , Group 3) PVA / VPA / Aloin (3 mg), and Group 4) PVA / VPA / Aloin (6 mg).

dimensions and their distributions validate the existence of mesoporous characteristics across all groups, consistent with Type IV isotherms. Also, another study conducted by Bozorgi M, et al, which was conducted on PVA/Chitosan nanofibers with different contents of ZnO-NH2 nanoparticles, showed that the surface area and cavity volume increased with the addition of ZnO-NH2 nanoparticles up to a concentration of 10% by weight [63]. The nanometer dimensions of these particles and the improvement of porosity were attributed. However, at concentrations higher than 10% by weight, the surface area decreased, which was caused by the accumulation of ZnO-NH2 nanoparticles and the decrease in the availability of active sites, which led to the compaction of the structure. Also, the addition of ZnO-NH2 nanoparticles initially increased the mesopores.

However, at higher concentrations, the porosity decreased due to particles' accumulation in the present study, VPA improved the mesopores (type IV isotherm) with a prominent hysteresis loop. At the same time, the addition of aloin in high concentrations caused a change in micropores. Also, the size distribution of the pores changed with the addition of ZnO-NH2, and initially, larger pores were observed, and high concentrations of nanoparticles caused an irregular pore structure due to the accumulation of particles [63]. However, in the present study, BJH analysis showed that VPA caused a more regular pore network with mesopores, while Aloin caused a narrower distribution and reduced pore size due to partial blockage or condensation.

vi. MTT

In this study, the cell viability in the 3D environment of PVA/VPA nanofibers was investigated as the control group, PVP/VPA/Aloin (3 mg) and PVP/VPA/Aloin (6 mg). According to Fig 7-A. On the 6h, PVP/VPA/Aloin (3 mg) nanofibers showed improved cell viability compared to PVA/VPA nanofibers, likely due to the bioactive properties of aloin, which promote

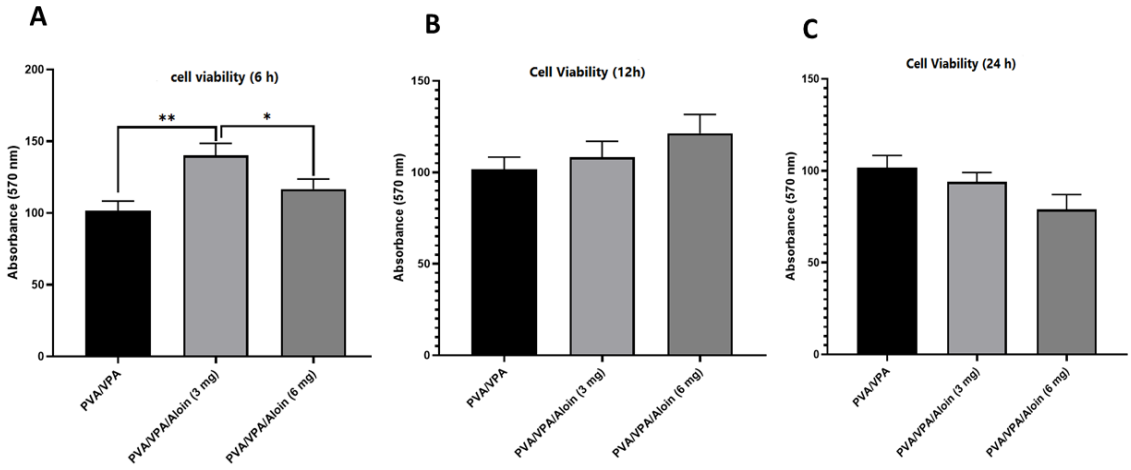

Fig. 7. Cell viability. A) 1th. B) 3th. C) 5th. PVA 10%, VPA 5%, PVA 10%, VPA 5%, Aloin (3 mg), PVA 10%, VPA 5%, Aloin (6 mg). (n = 5, significance level $*p < 0.5$, $**p < 0.01$, $***p < 0.001$).

initial cell proliferation. This observation aligns with previous research highlighting aloin's role in enhancing cellular activity in low concentrations [64, 65]. Also, in a study conducted by Ghosh, T., et al. different concentrations of aloe vera were used in PVA nanofibers, and the cytotoxicity examination of these nanofibers did not show any toxicity for HDF cells [66]. In a study conducted by Rafieian, S., et al. they used aloe vera, chitosan, and electrospun PVA nanofibers for wound dressing applications. They acknowledged that all concentrations used in the study were nontoxic to fibroblasts. And in most cases, they caused little cell proliferation. Although chitosan is non-toxic, it cannot significantly increase cell activity, while the presence of aloe vera can improve this activity to some extent [29] and This can be consistent with the results of our study.

However, the 24h results reveal a nonsignificant decline in cell viability in PVP/VPA/Aloin (6 mg) nanofibers, which can be attributed to aloin's cytotoxic effects at higher concentrations. This is consistent with studies by Rajashekar, C.B., et al. 2023, showing that elevated levels of phenolic compounds can induce oxidative stress and cytotoxicity in cell cultures [67]. The slight decline in cell viability in PVP/VPA/Aloin (3 mg) nanofibers on 24h, though not statistically significant, suggests that even moderate aloin concentrations may exert cumulative effects over time. The underlying mechanisms by which aloin enhances cell viability may be attributed to its antioxidant properties, which help reduce oxidative stress in cells. This is particularly important in the context of cytotoxicity, where reactive oxygen species (ROS) can negatively impact cell viability[68]. By scavenging these free radicals, aloin can protect cells and promote a more favorable environment for growth. These findings highlight the need to carefully balance aloin concentrations in nanofiber formulations to harness its bioactive benefits while minimizing cytotoxic risks.

CONCLUSION

This study effectively showed the fabrication and enhancement of nanofibrous scaffolds containing PVA, VPA, and aloin, attaining a balance among structural, mechanical, and biological characteristics. The addition of VPA significantly improved fiber morphology, mechanical strength and hydrophilicity. While aloin offered bioactive features with concentration-dependent effects on fiber diameter, porosity, and biocompatibility. Significantly, the addition of aloin enhanced initial cell viability but required careful concentration control to reduce cytotoxic effects. These nanofibrous scaffolds offer promising potential for applications in wound healing, tissue engineering, and controlled drug delivery systems. Future studies should further explore the long-term in vivo effectiveness and adjustment of aloin levels to maximize therapeutic efficacy and safety.

ABBREVIATIONS

PVA: Polyvinyl alcohol
VPA: vinyl phosphonic acid

SEM: scanning electron microscopy
FTIR: Fourier-transform infrared spectroscopy
ECM: Extracellular matrix
PLA: Polylactic acid
PLGA: Polylactic-co-glycolic acid
BET: Brunauer–Emmett–Teller
DMF: N, N-Dimethylformamide

ACKNOWLEDGMENTS

Research team is grateful to the Dr. Ghazaleh Chizari Fard and S. Ahmad Dehdast for advice and support in conducting the research.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

REFERENCES

1. Sahoo DR, Biswal T. Alginate and its application to tissue engineering. SN Appl Sci. 2021;3(1):30. https://doi.org/10.1007/s42452-020-04096-w
2. Wang Y, Wang Z, Dong Y. Collagen-based biomaterials for tissue engineering. ACS Biomater Sci Eng. 2023;9(3):1132-50. https://doi.org/10.1021/acsbiomaterials.2c00730
3. Chen J, et al. Designing biomimetic scaffolds for skin tissue engineering. Biomater Sci. 2023;11(9):3051-76. https://doi.org/10.1039/D3BM00046J
4. Golder HJ, Papalois V. Enhanced recovery after surgery: history, key advancements and developments in transplant surgery. J Clin Med. 2021;10(8):1634. https://doi.org/10.3390/jcm10081634
5. Son YJ, et al. Biomaterials and controlled release strategy for epithelial wound healing. Biomater Sci. 2019;7(11):4444-71. https://doi.org/10.1039/C9BM00456D
6. Dreyfuss I, et al. Review of the current antibiotic guidelines used in dermatologic surgery. Dermatol Ther. 2022;35(7):e15557. https://doi.org/10.1111/dth.15557
7. Sheshala R, et al. In vitro drug dissolution/permeation testing of nanocarriers for skin application: A comprehensive review. AAPS PharmSciTech. 2019;20:1-28. https://doi.org/10.1208/s12249-019-1362-7
8. Chappidi S, et al. Recent trends in diabetic wound healing with nanofibrous scaffolds. Eur J Pharmacol. 2023;945:175617. https://doi.org/10.1016/j.ejphar.2023.175617
9. Sharma A, et al. Phytoconstituent-loaded nanofibrous meshes as wound dressings: a concise review. Pharmaceutics. 2023;15(4):1058. https://doi.org/10.3390/pharmaceutics15041058
10. Khalil HA, et al. A review on micro-to nanocellulose biopolymer scaffold forming for tissue engineering applications. Polymers. 2020;12(9):2043. https://doi.org/10.3390/polym12092043
11. Serrano-Aroca Á, et al. Scaffolds in the microbial resistant era: Fabrication, materials, properties and tissue engineering applications. Mater Today Bio. 2022;16:100412. https://doi.org/10.1016/j.mtbio.2022.100412
12. Parvinzadeh Gashti M, Dehdast SA, et al. PDDA/Honey Antibacterial Nanofiber Composites for Diabetic Wound-Healing: Preparation, Characterization, and In Vivo Studies. Gels. 2023;9:173. https://doi.org/10.3390/gels9030173
13. Yao T, Baker MB, Moroni L. Strategies to improve nanofibrous scaffolds for vascular tissue engineering. Nanomaterials. 2020;10(5):887. https://doi.org/10.3390/nano10050887
14. Chen S, et al. Electrospinning: An enabling nanotechnology platform for drug delivery and regenerative medicine. Adv Drug Deliv Rev. 2018;132:188-213. https://doi.org/10.1016/j.addr.2018.05.001
15. Sengel SB, Sahiner N. Poly (vinyl phosphonic acid) nanogels with tailored properties and their use for biomedical and environmental applications. Eur Polym J. 2016;75:264-75. https://doi.org/10.1016/j.eurpolymj.2016.01.007
16. Baghersad S, et al. Optimal Aloe vera encapsulated PCL/Gel nanofiber design for skin substitute application and the evaluation of its in vivo implantation. J Drug Deliv Sci Technol. 2022;74:103536. https://doi.org/10.1016/j.jddst.2022.103536
17. Türkoğlu GC, et al. PVA-Based Electrospun Materials-A Promising Route to Designing Nanofiber Mats with Desired Morphological Shape-A Review. Int J Mol Sci. 2024;25(3):1668. https://doi.org/10.3390/ijms25031668
18. Park JC, et al. Electrospun poly (vinyl alcohol) nanofibers: effects of degree of hydrolysis and enhanced water stability. Polym J. 2010;42(3):273-6. https://doi.org/10.1038/pj.2009.340
19. Ji X, et al. Preparation of electrospun polyvinyl alcohol/nanocellulose composite film and evaluation of its biomedical performance. Gels. 2021;7(4):223. https://doi.org/10.3390/gels7040223
20. Almasian A, et al. Polyurethane/carboxymethylcellulose nanofibers containing Malva sylvestris extract for healing diabetic wounds: Preparation, characterization, in vitro and in vivo studies. Mater Sci Eng C. 2020;114:111039. https://doi.org/10.1016/j.msec.2020.111039
21. Franco RA, Sadiasa A, Lee BT. Utilization of PVPA and its effect on the material properties and biocompatibility of PVA electrospun membrane. Polym Adv Technol. 2014;25(1):55-65. https://doi.org/10.1002/pat.3205
22. Nazarova O, et al. New Copolymers of Vinylphosphonic Acid with Hydrophilic Monomers and Their Eu3+ Complexes. Polymers. 2022;14(3):590. https://doi.org/10.3390/polym14030590
23. Zarubaev V, et al. Synthesis and anti-influenza activity of vinylphosphonic acid (co)polymers. Dokl Biochem Biophys. 2022;506(1):183-5. https://doi.org/10.1134/S1607672922050155
24. Margel S, et al. Bisphosphonates vinylic monomers and polymers and uses thereof. US Patent. 2018.
25. Macarie L, Ilia G. Poly(vinylphosphonic acid) and its derivatives. Prog Polym Sci. 2010;35(8):1078-92. https://doi.org/10.1016/j.progpolymsci.2010.04.001

26. Yang Y, et al. Can aloin develop to medicines or healthcare products? Biomed Pharmacother. 2022;153:113421. https://doi.org/10.1016/j.biopha.2022.113421
27. Song X, Chen X. Advances in the research of promotion effect of Aloe vera on wound healing and its clinical use. Zhonghua Shao Shang Za Zhi. 2016;32(10):634-7.
28. Xiao J, et al. The potential health benefits of aloin from genus Aloe. Phytother Res. 2022;36(2):873-90. https://doi.org/10.1002/ptr.7371
29. Rafieian S, Mahdavi H, Masoumi ME. Improved mechanical, physical and biological properties of chitosan films using Aloe vera and electrospun PVA nanofibers for wound dressing applications. J Ind Text. 2021;50(9):1456-74. https://doi.org/10.1177/1528083719866932
30. Chakraborty T, et al. Wound healing potential of insulin-loaded nanoemulsion with Aloe vera gel in diabetic rats. J Drug Deliv Sci Technol. 2021;64:102601. https://doi.org/10.1016/j.jddst.2021.102601
31. Matharasi DSP, et al. Synthesis and antibacterial activity of aloin Schiff's bases. Eur J Sci Res. 2010;43(3):297-306.
32. Lima LL, Bierhalz ACK, Moraes ÂM. Influence of the chemical composition and structure design of electrospun matrices on the release kinetics of Aloe vera extract rich in aloin. Polym Degrad Stab. 2020;179:109233. https://doi.org/10.1016/j.polymdegradstab.2020.109233
33. Ullah S, et al. Stabilized nanofibers of polyvinyl alcohol (PVA) crosslinked by a unique method for efficient removal of heavy metal ions. J Water Process Eng. 2020;33:101111. https://doi.org/10.1016/j.jwpe.2019.101111
34. Alwan T, et al. Preparation and characterization of the PVA nanofibers produced by electrospinning. Madridge J Nanotechnol Nanosci. 2016;1(1):1-3. https://doi.org/10.18689/mjnn-1000101
35. Afzal A, et al. Development and characterization of drug-loaded PVA/PCL fibres for wound dressing applications. Polymers. 2023;15(6):1355. https://doi.org/10.3390/polym15061355
36. Ulag S, et al. Propolis-based nanofiber patches to repair corneal microbial keratitis. Molecules. 2021;26(9):2577. https://doi.org/10.3390/molecules26092577
37. Khan MQ, et al. Preparation and characterizations of multifunctional PVA/ZnO nanofibers composite membranes for surgical gown application. J Mater Res Technol. 2019;8(1):1328-34. https://doi.org/10.1016/j.jmrt.2018.08.013
38. Ge JC, et al. Study on the preparation and lipophilic properties of polyvinyl alcohol (PVA) nanofiber membranes via green electrospinning. Nanomaterials. 2021;11(10):2514. https://doi.org/10.3390/nano11102514
39. Çerçi A, et al. Preparation and Characterization of Amoxicillin-Loaded Polyvinyl Alcohol/Sodium Alginate Nanofibrous Mat: Drug Release Properties, Antibacterial Activity, and Cytotoxicity. Arab J Sci Eng. 2024. https://doi.org/10.1007/s13369-024-09075-6
40. Khanzada H, et al. Fabrication of promising antimicrobial aloe vera/PVA electrospun nanofibers for protective clothing. Materials. 2020;13(17):3884. https://doi.org/10.3390/ma13173884
41. Nezari S, et al. Investigating the effect of poly(ε-caprolactone) nanofibers scaffolds with random, unidirectionally, and radially aligned morphologies on the fibroblast cell's attachment and growth behavior. Turk J Chem. 2023;47(1):54-62. https://doi.org/10.55730/1300-0527.3516
42. Zarrinnahad H, Dehdast SA, Fard GC, et al. The effect of biosynthesized zinc oxide nanoparticles on gene expression and apoptosis in triple-negative breast cancer cells. DARU J Pharm Sci. 2025;33:10. https://doi.org/10.1007/s40199-024-00553-8
43. Leung LM, Lee SH, Shon HK. The influence of electrospinning parameters on the morphology of polymer fibers. Polymer. 2016;98:529-38.
44. Khan Y, Sulaiman AA, Hussain A. Effect of applied voltage on the diameter of electrospun nanofibers. J Appl Polym Sci. 2018;135(16):46106.
45. Hikmawati D, et al. The effect of aloe vera extract variation in electrospun polyvinyl alcohol (PVA)-Aloe vera-based nanofiber membrane. J Phys Conf Ser. 2018; [Conference paper]. https://doi.org/10.1088/1742-6596/1120/1/012096
46. Koosha M, Mirzadeh H. Electrospinning, mechanical properties, and cell behavior study of chitosan/PVA nanofibers. J Biomed Mater Res A. 2015;103(9):3081-93. https://doi.org/10.1002/jbm.a.35443
47. Gutiérrez Rafael BJ, et al. Study of the Incorporation of Gel and Aloe vera Peel Extract in a Polymer Matrix Based on Polyvinylpyrrolidone. Polymers. 2024;16(14):1998. https://doi.org/10.3390/polym16141998
48. Jaafar H, et al. Aloin: A potential natural additive for biomedical applications. J Ethnopharmacol. 2018;220:101-14.
49. Koski A, Kostiainen J, Laaksonen P. Mechanical properties of electrospun poly(vinyl alcohol) nanofibers. Eur Polym J. 2004;40(3):575-80.
50. Ding B, et al. Mechanical properties of phosphonic acid-modified PVA nanofibers. Mater Sci Eng C. 2014;34:201-7.
51. Kakroodi AR, et al. Development of nanofibers with enhanced mechanical properties through the incorporation of metal oxides. Mater Sci Eng B. 2018;233:134-41.
52. Sosiati H, Widodo AN, Nugroho AW. The influence of ALOEVERA concentration on morphology and tensile properties of electrospun ALOEVERA-PVA NANOFIBER. J Sains Mater Indones. 2018;19(4):157-62. https://doi.org/10.17146/jsmi.2018.19.4.4965
55. Jegina S, Kukle S, Gravitis J. Evaluation of aloe vera extract loaded polyvinyl alcohol nanofiber webs obtained via needleless electrospinning. IOP Conf Ser Mater Sci Eng. 2018. [Conference paper]. https://doi.org/10.1088/1757-899X/459/1/012016
56. Gutiérrez Rafael D, Cortés C, García M, Pérez M. The role of aloin in modifying the mechanical properties of polylactic acid nanofibers. Compos Sci Technol. 2024;206:108672.
57. Yang L, Zhang H, Liu Z, Huang Y. Hydrophilicity and

antifouling properties of modified polyvinyl alcohol membranes. J Membr Sci. 2021;619:118831.
58. Ranjbar-Mohammadi M. Characteristics of aloe vera incorporated poly(ε-caprolactone)/gum tragacanth nanofibers as dressings for wound care. J Ind Text. 2018;47(7):1464-77. https://doi.org/10.1177/1528083717692595
59. Zhang L, Chen H. Hydrophilicity implications of nanofibers in biomedical applications. Adv Healthc Mater. 2023;12(4):2201876.
60. Singh T, Gupta R. The importance of wettability in biomaterials for wound healing applications. J Biomed Mater Res A. 2022;110(5):1011-25.
61. Saravanan A, et al. Synthesis and characterization of natural biomaterial composite nanofibers for ocular drug delivery systems. OpenNano. 2023;10:100122. https://doi.org/10.1016/j.onano.2023.100122
62. Almeida V, Santos M. Pore structure manipulation in cellulose and PVA composites for improved adsorption in gas-phase applications. Polym Bull. 2020;78(11):5895-908.
63. Bozorgi M, et al. Performance of synthesized cast and electrospun PVA/chitosan/ZnO-NH2 nano-adsorbents in single and simultaneous adsorption of cadmium and nickel ions from wastewater. Environ Sci Pollut Res Int. 2018;25:17457-72. https://doi.org/10.1007/s11356-018-1936-z
64. Ali F, et al. Oral administration of aloe vera ameliorates wound healing through improved angiogenesis and chemotaxis in sprague dawley rats. Curr Pharm Biotechnol. 2021;22(8):1122-8. https://doi.org/10.2174/1389201021999201001204345
65. Hormozi M, Assaei R, Boroujeni MB. The effect of aloe vera on the expression of wound healing factors (TGFβ1 and bFGF) in mouse embryonic fibroblast cell: In vitro study. Biomed Pharmacother. 2017;88:610-6. https://doi.org/10.1016/j.biopha.2017.01.095
66. Ghosh T. Fabrication of a Novel Aloe Vera (AV) and Polyvinyl Alcohol (PVA) as Dressing for Facial Abrasion. Oncosurgery. [In press].
67. Rajashekar CB. Dual role of plant phenolic compounds as antioxidants and prooxidants. Am J Plant Sci. 2023;14(1):15-28. https://doi.org/10.4236/ajps.2023.141002
68. Gupta S, Ali A. The role of natural products in biomedical applications: Aloe vera extracts. J Biomater Res. 2022;114(4):567-80.