Journal of Materials and Electronic Devices 3 (2022) 12-19

JOURNAL OF MATERIALS AND ELECTRONIC DEVICES
FYTRONIX JMED http://dergi-fytronix.com/

Investigation of Morphological and Mechanical Properties of New Anthraquinone Substance Added Polymeric Wound Healers

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Wound is defined as the cessation of the structural and functional function of living tissue as a result of the deterioration of the entire skin for various reasons. Wound treatment started with the history of humanity. The main purpose of wound treatment; It is to restore the deteriorated skin structure and functional properties by providing tissue repair as soon as possible. For this reason, there are many different techniques in wound treatment today. Natural compounds with anthraquinone are used in the fields of medicine, pharmacy, cosmetics, bio and nanomaterials [1]. By attaching bioactive groups to compounds with an anthraquinone skeleton in the laboratory environment, the molecule can be made more active, and thus, targeted, active molecules that can be used in treatments and that have various biological activity properties can be obtained by organic synthesis method. By adding anthraquinone to polyvinyl alcohol (PVA) polymer, nanocomposite mat production will be provided by nanotechnological electrospinning technique. The material properties will be determined by morphological (Scanning Electron Microscopy-SEM) and mechanical (TENSILE) analysis of the produced nanocomposites. It is thought that nanofiber-wound dressing tapes containing original anthraquinone analogues will provide a new perspective for studies in the health sector and biomaterials in the future.

Keywords: *Original anthraquinone analogues, polymer, electrospinning, wound healing tape, nanocomposite.*

Submission Date:13 September 2022
Acceptance Date: 01 October2022

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1. Introduction

The skin is the organ with the largest surface area, which consists of three main components: epidermis, dermis and subcutaneous fat layer, and protects our body against external factors. While the outer epidermis protects the body against damage such as burns and injuries, the inner dermis protects the body against trauma. The main structural component of the underlying dermis is collagen, which is located in fibrils [2,3]. The word wound is defined as the deterioration of the anatomical integrity and function of the tissue or organ due to a pathological event of internal or external origin. Skin injury is an important problem that threatens physical and mental health, and how to support wound healing has become a focus. Developing new dressings is an important strategy in skin regeneration [4]. Skin diseases are one of the fourth-ranked problems worldwide and not only harm the patients' body/mind, but also impose a great economic burden on society [5-8]. Skin injuries are classified as acute and chronic. Acute wounds such as burns, blunt wounds and penetrating wounds may heal quickly, whereas chronic wounds such as diabetic foot ulcers, bedsores and venous leg ulcers are more difficult to heal. These chronic wounds may be prone to infection and inflammation of the skin [9,10]. Wound healing means restoring the integrity of tissue or organ after injury. Injured tissues are partially or completely repaired. In the animal kingdom, we see complete regeneration in worms and salamanders. However, in mammals, complete regeneration is only possible in some tissues. Examples of these tissues in humans are epithelial tissue (epidermis, digestive and respiratory mucosa epithelium), liver parenchyma, bone, smooth muscles and some striated muscles [11].

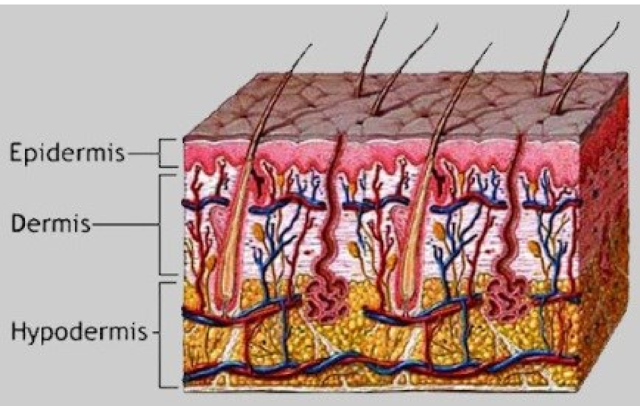

Figure 1.1. *The skin layer on our body [11]*

Figure 1.2. *Wound formation in skin tissue [11]*

Figure 1.3. *Diabetic patients'* wounds that are more difficult to heal *[11]*

Wound repair is provided by a process that we call wound healing in other tissues of our body, consisting of intertwined, successive stages and resulting in a nonspecific connective tissue called scar. Scar tissue provides tissue integrity, but its tensile strength and energy absorption capacity are less than intact tissue. While there are chronic wounds such as venous ulcers, pressure sores, diabetic wounds, there are also temporary wounds that occur in situations such as falling and hitting. With the regeneration of the upper and inner layers of the skin, healing is observed in skin wounds. But especially chronic wounds are extremely difficult to heal. It is very important to produce wound healing tapes that allow wounds to heal faster, release medication, absorb pus, provide tissue regeneration, and prevent the entry of bacteria and viruses. It is also known that breathable plasters support the healing process [12]. For all these purposes, nanotechnological band-aids with large surface area have replaced other bands. The term nanotechnology was first used by Professor Norio Taniguchi from Tokyo University of Science in 1974, and he stated that "nanotechnology generally consists of the processes of separating, combining and decomposing materials atom by atom or molecule by molecule". With the start of the nanotechnology revolution, it has been determined that materials show unique properties at the nanoscale. In the following years, nanotechnology has attracted great interest due to the discovery of the molecule called fullerene and the synthesis of carbon nanotubes, due to the high strength and other unique properties of these materials. This multidisciplinary science covers many fields such as materials science, optics, electronics, biology, chemistry, medicine, pharmacy, cosmetics, textile, space and aircraft industries [13]. The electrospinning method is a technique that attracts worldwide attention because it has simple and easy adaptability features as a technical setup while creating fine filamentous structures using electrostatic forces. In principle, electrospinning is the phenomenon of thinning and elongation of the polymer solution exposed to a high field, forming continuous and solid fibers as a result of phase separation. Flow rate, electrical voltage, polymer concentration, solvent conductivity, relative humidity of the air etc., which are important in electrospinning studies. parameters affect the resulting fiber quality.

Figure 1.4. *Electrospinning device*

Electrospinning method; It attracts attention due to its various advantages such as allowing the production of fibrous nano-sized porous materials and working in a wide range of materials, not requiring expensive equipment and low operating costs [14]. During the preparation of nanofibers, biodegradable and biocompatible polymers (Polylactic acid (PLA), Polyvinyl alcohol, Polylactic-co-glycolic acid (PLGA), PCL etc.) are used. Cell scaffolds created with these polymers are durable and give good results. Besides synthetic biocompatible polymers, alginate, collagen, chitosan etc. Naturally biocompatible polymers are also used. Although natural polymers have disadvantages compared to synthetic polymers, the structure has biodegradability and biocompatibility, there may be problems in meeting the mechanical strength of the product. Anthraquinone molecules are found in nature in St. John's Wort and Aloe Vera plants. St. John's Wort (*Hypericum perforatum*) plant oil is known to have a strong antibacterial effect. The active ingredient of the plant, arachidonic acid, can suppress the production of leukotrienes, thus preventing the reduction of inflammation and the reduction of inflammation of white blood cells and the infiltration of white blood cells into the area of inflammation. St John's Wort is generally used in the treatment of burns and minor skin wounds due to these effects. The aloe vera plant has been used for years in the treatment of skin diseases and is considered a medicinal plant. In recent years, the medicinal healing properties of Aloe Vera have attracted the attention of scientists and have been added to wound dressing materials in dressings to improve the therapeutic effect [15]. Emodin, an anthraquinone derivative found in the Aloe Vera plant and sold commercially as a chemotherapy drug, shows anti-cancer and anti-inflammatory properties. Amino quinizarins obtained from the reaction of 1,4-Dihydroxy anthraquinones with amine derivatives, whose specific name is quinizarin, show dyestuff properties and these dyestuffs have been included in patent studies with many properties. In the literature, it has been stated that anthraquinones inhibit tumor cell divisions by reducing the activity of telomerase enzyme in cancer cells. A practical, economical and one-step original synthesis methodology was created and patented by our team for the synthesis of amino and thioanthraquinone derivatives [16]. Synthesis of some anthraquinone derivatives in the literature, cesium carbonate etc. expensive and hard-to-find chemicals; It is carried out in an inert gas environment with carcinogenic and difficult to remove organic solvents such as toluene, dimethyl formamide and tetrahydrofuran. This situation makes the sustainability of the reactions difficult. In our study, ethylene glycol is used as organic solvent. Since the reactions take place in the heat environment, the fact that ethylene glycol is a non-volatile, easily available and low-cost solvent makes the synthesis methodology unique. Since it is known that the chlorine atom in chloro anthraquinones is more reactive than the hydroxyl groups found in hydroxy anthraquinones, chloro anthraquinones, which have easier placement with active substituents, were chosen for the synthesis in our proposed study.

In this study, chloroanthraquinone doped PVA nanofiber membranes were produced by electrospinning technique. The produced membranes were characterized. It is aimed to use the obtained composite membranes as a wound dressing that will provide ideal properties.

2. Material and Method

2.1. Material

In this study, 85,000-124,000 g/mol Sigma/Aldrich (Germany) brand PVA was used. Greaseproof paper was preferred in the electrospinning stage.

2.2. Method

2.2.1. Purification of original analogs

Synthesized original amino and thio anthraquinone compounds will be purified by chromatography methods. The stationary phase filler to be used for purification in glass chromatography columns is silicagel. The determination of how the pure separation of the products obtained as a result of the reaction will be done in column chromatography is determined by thin layer chromatography. According to the separation of rf values determined in thin layer chromatography, a single organic solvent or organic solvent mixtures suitable for column chromatography are determined. In this way, the unique anthraquinone analogs in the reaction are obtained separately, by taking advantage of the different Rf values of the substances.

2.2.2. Preparation of original anthraquinone derivative added polymer solutions

Wound healing solutions were prepared by supplementing the original anthraquinone derivatives with various polymers at the values in Table 2.1.

Table 2.1. Preparation parameters of original anthraquinone derivative doped polymer solutions

Polymer / Additive	**Solvent**	**Mixture Temperature (˚C)**	**Mixture Time (Minute)**
10% PVA	Distile Water	60	60
10% PVA-1% Unique anthraquinone derivative	Distile Water	60	60
10% PVA-3% Unique anthraquinone derivative	Distile Water	65	60
10% PVA-5% Unique anthraquinone derivative	Distile Water	65	65
10% PVA-8% Unique anthraquinone derivative	Distile Water	70	65

2.2.3. Production of wound healing nanofiber membranes by electrospinning method

The electrospinning parameters required for the fabrication of wound healing nanofiber membrane are shown in Table 2.2.

Table 2.2. Electrospinning parameters required for fabrication of wound-healing nanofiber membranes

Polymer / Additive	Working Distance (cm)	Flowrate (ml/hour)	Voltage (kV)
10% PVA	15	2.5	31
10% PVA-1% Unique anthraquinone derivative	15	3.0	30
10% PVA-3% Unique anthraquinone derivative	15	3.0	32
10% PVA-5% Unique anthraquinone derivative	15	3.5	32
10% PVA-8% Unique anthraquinone derivative	15	3.5	32

The nanofiber membranes to be obtained will be placed in a vacuum oven and dried at 50 ˚C for one day. The schematic representation of the production of anthraquinone-doped nanotechnological wound dressing tape by electrospinning is given in Figure 2.1.

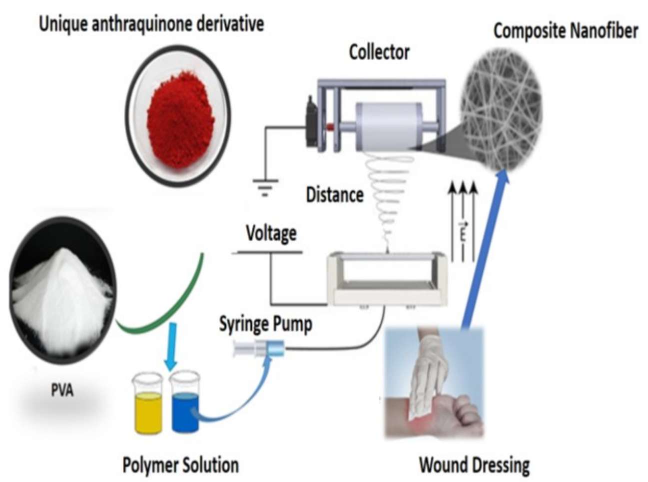

Figure 2.1. *Schematic representation of the production of anthraquinone-doped nanotechnological wound dressing tape by electrospinning method*

2.2.4. Characterization studies of nanocomposite mats

Morphological Analysis

Field Emission Gun Scanning Electron Microscopy (FEGSEM)

Nanofiber composites will be coated with gold-palladium material under argon gas for 40 seconds. After the coating process, the samples will be viewed with high and low vacuum detectors on the Quanta brand FEI FEG450 model FESGEM device at x12000 magnification.

Mechanical Analysis

Tensile Test

Tensile testing of nanofiber composites in accordance with ASTM D882-10 standards will be carried out in a DEVOTRANS brand DVT UZM K3 model tensile-compression test device. 5 mm^2/min. to the samples under 500 N load. The mechanical properties will be determined by adjusting the pulling speed and 10 mm jaw spacing.

3. Result and Discussion

Morphological (SEM) analysis

Nanofiber formation was observed in all samples. As the anthraquinone analog is added, the fibers are more tightly packed. While the orientation of the fibers occurred more, the highest strength in the study was realized in 10% PVA-8% Unique anthraquinone derivative sample [17,18]. SEM images of nanofiber membranes are shown in Figure 3.1., Figure 3.2., Figure 3.3., Figure 3.4., Figure 3.5. Nanofiber size distribution range of nanofiber membranes is shown in Table 3.1.

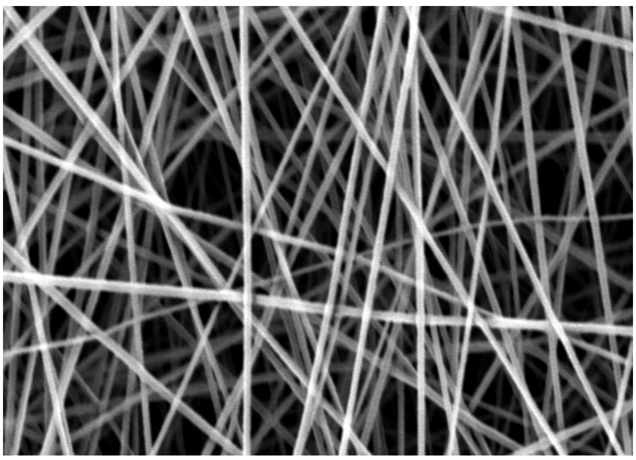

Figure 3.1. *Image of 10% PVA x12000 SEM*

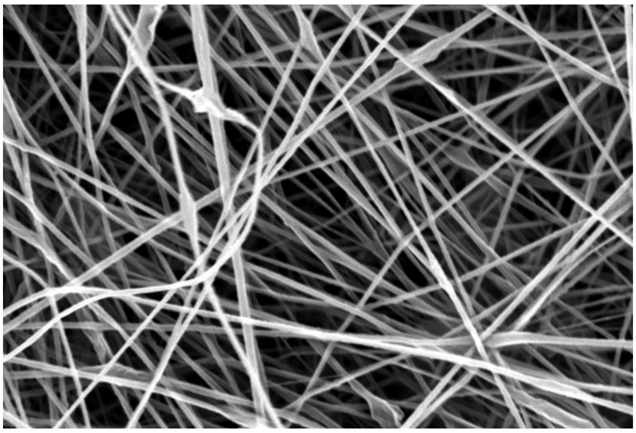

Figure 3.2. *Image of 10% PVA-1%* Unique anthraquinone derivative *x12000 SEM*

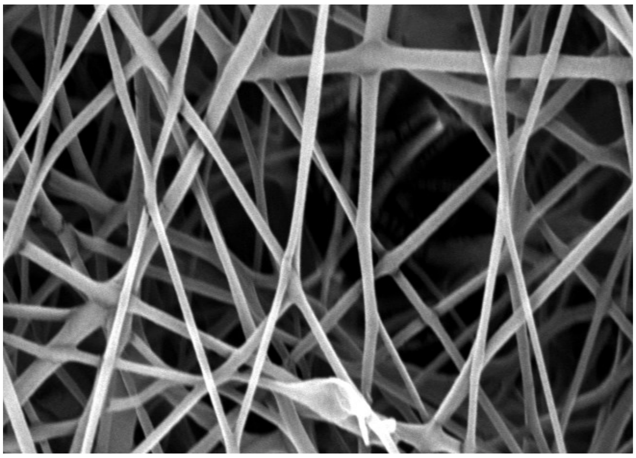

Figure 3.3. *Image of 10% PVA-3%* Unique anthraquinone derivative *x12000 SEM*

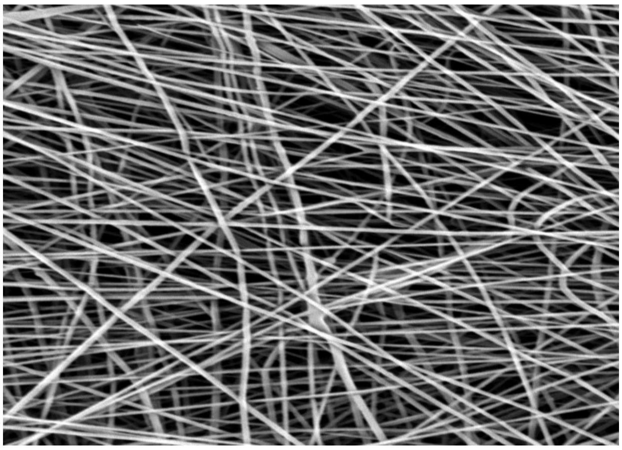

Figure 3.4. *Image of 10% PVA-5%* Unique anthraquinone derivative *x12000 SEM*

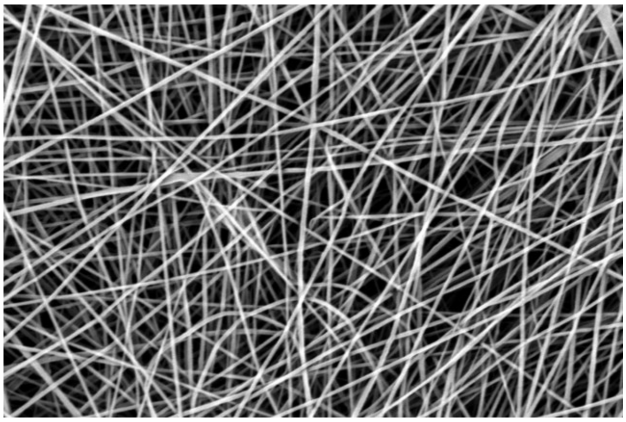

Figure 3.5. *Image of 10% PVA-8%* Unique anthraquinone derivative *x12000 SEM*

Table 3.1: Nanofiber size distribution range of nanofiber membranes

Sample Name	Nanofiber avarage size (nm)
10% PVA	180-350
10% PVA-1% Unique anthraquinone derivative	240-460
10% PVA-3% Unique anthraquinone derivative	220-430
10% PVA-5% Unique anthraquinone derivative	170-300
10% PVA-8% Unique anthraquinone derivative	150-280

Mechanical (Tensile) analysis

The mechanical properties of the produced membranes were repeated three times and their arithmetic averages were taken. The average tensile strength value of the PVA membrane was 22.22 MPa. As a result of the addition of Unique anthraquinone derivative to PVA, a linear tensile strength has been achieved. When the tensile strength values of all samples are examined, 10% PVA-8% Unique anthraquinone derivative membrane has the highest value with a tensile strength value of 51.25 MPa. The reason for this is that the reinforced Unique anthraquinone derivative additive wraps around the PVA membranes homogeneously, thinning the PVA nanofibers and making them a more tightly packed structure [19]. The tensile strength values of composite membranes are given in Table 3.2.

Table 3.2: Tensile strength values of composite mats

Sample Name	Mat Thickness (mm)	Tensile Strength (MPa)
10% PVA	0.18	22.22
10% PVA-1% Unique anthraquinone derivative	0.19	26.50
10% PVA-3% Unique anthraquinone derivative	0.24	42.45
10% PVA-5% Unique anthraquinone derivative	0.28	49.09
10% PVA-8% Unique anthraquinone derivative	0.28	51.25

4. Conclusion

In this study, anthraquinone-doped PVA nanofiber membranes were produced by electrospinning technique. According to the characterization studies, the fiber diameters are in the range of 170-230 nm according to their morphological characterization, and they have the thinnest fibers in this study. It was determined that the thinnest fibers belonged to 10% PVA-8% Anthraquinone compound. In terms of mechanical properties, the active ingredient thinned the PVA fibers. The strongest material in the study belongs to 10% PVA-8% Anthraquinone compound. It is aimed that the obtained composites will be an ideal band-aid.

Acknowledgements

This work was financially supported by the Scientific Research Projects Coordination Unit of Istanbul University-Cerrahpasa (Project number: BEK-2017-26753) for supplying the equipment and material. We would like to thank ArelPOTKAM for his contributions to the determination of the mechanical properties of nanofiber membranes in production and material supply.

References

[1] Karade, V. C., Patil, R. B., Parit, S. B., Kim, J. H., Chougale, A. D., & Dawkar, V. V. Insights into Shape-Based Silver Nanoparticles: A Weapon to Cope with Pathogenic Attacks. ACS Sustainable Chemistry & Engineering. 2021, 9(37), 12476-12507.

[2] Lee, K.H., Tissue-engineered human living skin substitutes: Development and clinical application, Yonsei Medical Journal, 2000, 41, 6, 774-779.

[3] Kazaroğlu, N.M. Yara örtüleri için alternatif doku iskeleleri: in vitro çalışmalar. 2009

[4] Jiaheng Liang, Longlong Cui, Jiankang Li, Shuaimeng Guan, Kun Zhang and Jingan Li. Aloe vera: A Medicinal Plant Used in Skin Wound Healing. TISSUE ENGINEERING: Part B. 2021, 27, 5.

[5] Zhang, X.J., Wang, A.P., Shi, T.Y., et al. The psychosocial adaptation of patients with skin disease: a scoping review. BMC Public Health. 2019, 19, 1404.

[6] Verhoeven, E.W., Kraaimaat, F.W., van de Kerkhof, P.C., et al. Psychosocial well-being of patients with skin diseases in general practice. J Eur Acad Dermatol Venereol. 2007, 21, 662.

[7] Karimkhani, C., Dellavalle, R.P., Coffeng, L.E., et al. Global skin disease morbidity and mortality: an update from the global burden of disease study. JAMA Dermatol. 2013, 153, 406, 2017.

[8] Lim, H.W., Collins, S., Resneck, J.S., Jr., et al. The burden of skin disease in the United States. J Am Acad Dermatol. 2017, 76, 958.

[9] Kathawala, M.H., Ng, W.L., Liu, D., et al. Healing of chronic wounds: an update of recent developments and future possibilities. Tissue Eng Part B Rev. 2019, 25, 429.

[10] Johnson, T.R., Go´mez, B.I., McIntyre, M.K., et al. The cutaneous microbiome and wounds: new molecular targets to promote wound healing. Int J Mol Sci. 2018, 19, 2699.

[11] Topalan, M., & Aktaş, Ş. (2010). Güncel Yönleriyle Kronik Yara.

[12] Buluş, E., Buluş, G. S., & Şahin, Y. M. (2020). Production and Characterization of Nanotechnological Tape for Wounds Caused by Diabetes. JOURNAL OF MATERIALS AND ELECTRONIC DEVICES, 5(1), 20-24.

[13] Cakmakci, E. Elektrospinning yöntemi ile yeni polimerik malzemelerin sentezi ve karakterizasyonu. 2009.

[14] Taygun, M.E., Hatinoğlu, G., Öztürk, P., Yerli, N., Küçükbayrak, S. Characterization of the rheology of polymer/bioactive glass solutions and fabrication of nanocomposite materials. Eurasian J. Bio. Chem. Sci. 2018, 1(1): 1-6.

[15] Salehi, B., Albayrak, S., Antolak, H., et al. Aloe genus plants: from farm to food applications and phytopharma cotherapy. Int J Mol Sci. 2018, 19, 2843.

[16] Ozkok, F., Sahin, Y.M. Biyoaktif Antrakinon Analogları ve Bunların Sentezine Yönelik Metot. TR2016/19610.

[17] Buluş, E., Buluş, G. S., Akkaş, M., Cetin, T., Yaman, E., & Altındal, T. (2020). Nanotechnological Wound Healing Bandage Production from Polymer Solutions Containing Tea Tree Oil, Echinacea, Spider Web and Aloe Vera. JOURNAL OF MATERIALS AND ELECTRONIC DEVICES, 6(1), 19-23.

[18] Buluş, E., Buluş, G. S., Akkaş, M., Cetin, T., Yaman, E., & Altındal, T. (2020). Production and Characterization of Natural Sourced Hydroxyapatite Added Polystyrene Tissue Scaffolds by Electrospinning. JOURNAL OF MATERIALS AND ELECTRONIC DEVICES, 6(1), 12-18.

[19] Buluş, E., Buluş, G. S., & Akkaş, M. (2021). Investigation of the Effects of Working Parameters in Electrospinning Technology on Morphology of Polymeric Nanofiber Membranes Using Reference Polymers. JOURNAL OF MATERIALS AND ELECTRONIC DEVICES, 2(1), 6-11.