ORIGINAL ARTICLE

Preparation of Novel Arabic Gum-C_6H_9NO Biopolymer as a Bedsore for Wound Care Application

Zahra Doozandeh[1], Saeed Saber-Samandari[2], Amirsalar Khandan[2]

[1] *Department of Nursing Science, Islamic Azad University, Isfahan (Khorasgan) Branch, Esfahan, Iran*

[2] *New Technologies Research Center, Amirkabir University of Technology, Tehran, Iran*

Received: 28 Apr. 2020; Accepted: 11 Nov. 2020

Abstract- The subcutaneous or hypodermic tissue is the innermost layer of the skin, which is essential for adipose tissue. The dermal attachment to the epidermis is a basal layer composed of collagen. This basal layer performs four different functions and acts as a scaffold for soft tissue organization. It is citing for regeneration that has selective permeability for serum filtration. Also, it is a barrier between different cell types, and cite where the epithelium subcutaneous to the cells. Untreated, bedsores can lead to serious complications, one of which is cellulite, a potentially life-threatening bacterial infection. As the bedsore wound spreads to the joints and bones, it may cause bone and joint infections that can damage the cartilage, tissue, and reduce joint function. The bacteria can then enter the bloodstream through wounds, leading to shock and life-threatening conditions. Stage II wounds can heal in one to six weeks, but wounds that lead to stage three or four may last several months or may never heal, especially in children with health problems. The purpose of this study was to design bio-based wounds with gelatin, Gum Arabic, and polyurethane. The wounds were made with different bio composite specimens. The procedure is gelatin, and gum Arabic was combined with certain percentages. The temperature of mixing and solubilization was set at 50°C. After complete fabrication of the material and complete dissolution of the samples in the solvent without any agglomeration, the samples were placed in a low-temperature freezer at -70°C and were placed in a freeze dryer. After the drying process is completed and the pores are ready on the wound heal sample, in the next stages, several tests are carried out to check the suitability of the produced wounds. The SEM analysis was performed on bio-based wounds in which the results showed the suitability and porosity of these wound dress were suitable. The presence of proper porosity and moisture level for wound healing and non-acidity, as well as the use of bed wound healing, have been distinguished from other conventional wound healing products in the market and research domain.

Acta Med Iran 2020;58(10):520-530.

Keywords: Wound; Bed sore; Hospital infectious; Freeze-drying; Soft tissue engineering

Introduction

The focus of studies on the healing and healing of late wounds and superficial and deep infection can cause skin damage or enter the chronic, and the untreatable stage is of great importance. The skin is an important part of protecting the internal organs of the body against external factors and prevents dehydration in them, and skin must be protected against damage. The skin consists of three layers: the epidermis, the dermis, and the hypodermis (1-4). The epidermis is the outermost layer of skin, consisting of adherent epithelial cells and chiefly keratinocytes. Its thickness varies from about 0.1 mm in the eyelids to 1 mm in the palms and feet (5-6). The epidermis consists of four distinct layers, from inside to outside: the stratum germinatum, the stratum granulosum, the Leucojum stratum, and the stratum corneum. There are two other types of cells typically found in the epidermis: Merkel and Langerhans cells. Merkel cells are receptors that transmit stimulation to an axon through a chemical synapse. Langerhans cells play an important role in skin immune reactions. The dermis consists of two layers of papillary and reticular. The papillary layer lies directly below the epidermis and is composed of primary fibroblast cells and has the ability to produce collagen, which is part of the aging tissue. The reticular layer lies

Corresponding Author: A. Khandan* and Z. Doozandeh**
* New Technologies Research Center, Amirkabir University of Technology, Tehran, Iran
Tel: +98 9135719626, Fax: +98 2142910703, E-mail address: amir_salar_khandan@yahoo.com
** Department of Nursing Science, Islamic Azad University, Isfahan (Khorasgan) Branch, Esfahan, Iran
Tel: +98 132372543, Fax: +98 2142910703, E-mail address: Zahra.doozandeh@gmail.com

beneath the papillary layer, producing collagen and elastic tissue, as summarized in Figure 1.

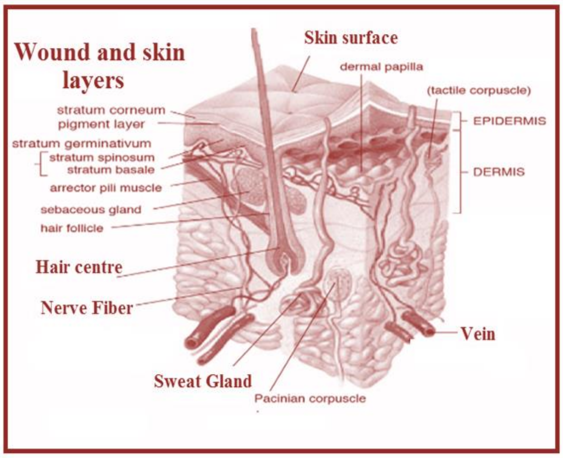

Figure 1. Cross-section of human skin (1).

Natural biopolymers produced and used in researches have the ability to absorb water hundred-fold of their original weight. Keeping the wound environment moist to precipitate its healing, investigating discoloration, concentration variation, keeping the wound spot safe from bacteria, contamination, and non-toxicity were among the characteristics of the wounds produced in recent research (4-8). Bed wounds are not only difficult wounds but should be recognized as a method that can lead to very serious systemic complications such as dehydration, electrolytic disorder, bone inflammation, septic infection, and maybe life-threatening in severe cases. Wound healing is a complex process with the purpose of repairing the connectivity of the tissue and the epidermis. Various commercial dressings have been developed and introduced to the market today. However, their diversity makes it difficult for the nurse to choose the right type. Although the most important reason for using a wound dressing is to protect the wound against infection and prevent infection, the main purpose of implementing it is to expedite the wound healing process (9-18). Commercial wounds are presented as hydrogels, hydrocolloids, films, sponges, and nanofibers. Chitosan, Alginate, Arabidopsis, aloe vera, and honey have been identified as the most common polysaccharides in wound dressings and their effect on wound healing. Cleansers that are newly developed and can detect wound infection are delved. There are four mechanisms that contribute to wound healing (19-28). Aloe vera (AV) exists in a variety of forms featuring sugars, enzymes, vitamins, and minerals that show remarkable antibacterial, antioxidant and antiviral activities. Glucomannan, one of the herbal compounds of AV, has a therapeutic influence that eliminates the growth factor of fibroblast, stimulates cell proliferation, and boosts collagen production. Numerous studies have investigated the beneficial effects of AV extract on cell proliferation and wound healing (29-38). The subcutaneous or hypodermic tissue is the innermost layer of the skin, which is fundamental to adipose tissue, causing the skin to move and maintain its body shape and insulation (39-45). The dermal attachment to the epidermis is a basal layer composed of collagen. This basal layer performs four different functions and acts as a scaffold for tissue organization, is a site for regeneration, has selective permeability for serum filtration, is a barrier between different cell types, and is a site that connects the epithelium to the underlying cells (36-45). Untreated bedsores can lead to serious complications; for instance, cellulite, a potentially injurious bacterial infection. If the pressure ulcer spreads to the joints and bones, it can cause bone and joint infections that can damage the cartilage and tissue and reduce joint function. Then the bacteria can penetrate the bloodstream through wounds, leading to shock and detrimental conditions. Stage two wounds can heal within one to six weeks, but wounds that lead to stage three or four may last several months or may never heal, especially in people with health problems. The purpose of this study was to design and produce bio wounds with gelatin, gum Arabic, polyurethane, polyurethane, and polylactic acid. The wounds were made in six different compositions, each with unique materials. In the first sample, gelatin and gum Arabic, the second sample, gelatin, aloe vera, and gum were combined with certain percentages (45-51). In the third sample, gelatin and polypropylene were combined with polypropylene and gum Arabic. In the fifth sample, gelatin, polylactic acid, aloe vera and gum, and sixth and the final sample, gelatin, poly-lactic acid, polyvinylpyrrolidone, aloe vera, and gum were combined. Mixing and solubilization have been done at 50°C. After complete fabrication of the material and complete dissolution of the samples in the solvent without any agglomeration, the samples were placed in a low-temperature freezer, and after a deep-freezing operation, specimens were placed in freeze dryer apparatus. After the drying process completion, proper porosity formation, samples are ready. The next round of tests is carried out to check the suitability of the produced wound dressings. In this research, tests such as scanning electron microscopy (SEM), porosity test, biological analysis, dissolution, toxicity, and antibacterial tests were performed. Finally, the ideal specimen with the best results is presented and suggested as the best wound dresser: proper porosity and moisture level for wound healing and non-acidity. Also, the use of aloe vera and gum Arabic as a bed wound is a distinguishing feature of this wound dressings from other specimens available in the market and research.

Materials and Methods

This study describes the types of materials used in wound dressing preparation, and then the method of preparation of specimens, types of tests, and analyses performed to identify and evaluate properties in different parts of the case. In this study, in order to make a bio-wound, biodegradable, biodegradable gelatin and Arabic gum polymer prepared by Merck German Company with a purity of 98% with biopolymer AV and PVP (C_6H_9NO) as base material was used. It should be noted that the addition of AV powder and PVP to the base of polymeric ameliorate the mechanical and hydrophilic properties of the wound as well as the proliferation of cells. Figure 2 illustrates the process of making and priming multicomponent wound dressing by means of freeze-drying procedure for a variety of wounds.

Figure 2. (a) powders composite, (b) composition of polymers on the magnetic stirrer, and (c) freezing drying technique

Figure 1 shows the powders used, the polymer slurry in the magnetic mixer, and the specimens located in the device. In this study, we have tried to utilize Arabic gum with aloe vera powder plus gelatin powder. The polymeric powders were first distilled in twice-distilled-water, then the polymer solution was placed on a magnetic mixer and dissolved at 50°C. The other powders were then added and poured into a 2% acetone solution for greater solubility in the container. The samples were then placed in the refrigerator at -70°C for 24 hours, according to Figure 2. The specimens were then removed from the refrigerator after 24 hours and placed in a dryer under specific temperature and pressure conditions. After removal of the emulsion from the freezer, the samples were completely frozen, as schematically illustrated, placed into the freeze dryer. Porous wound dressing was made after being in a freeze-drying machine for 48 hours at -45°C and 0.01 bar pressure. After 48 hours, the scaffolds were removed and then prepared for different analyzes. By this method, bio-nanocomposites were made with different percentages of the ceramic-polymer phase. In the first step, gelatin and gum Arabic were combined. In the second stage, gelatin and AV and gum were combined. In the third stage, gelatin and polypropylene were combined with polypropylene and gum. In the fourth stage, gelatin and polypropylene were combined with AV and GA. In the sixth stage, gelatin and polylactic acid and polyvinyl polypropylene, AV and gum were combined. For each step of material production in the solution for two hours, they were placed on a magnetic stirrer at 50°C until the dissolution steps were well performed, and each sample was prepared without dipole flocculation. Freeze at -70°C. In the next step, the specimens were put into the mold, which was a Petri dish in this study, and were labeled on the lid. Subsequently, the dishes were placed in a -70° C freezer for 24 hours prior to the freeze-drying process. The specimens were then placed in a drying apparatus, and the temperature of the apparatus was adjusted to -45°C. The in-device vacuum process was cycled according to the conditions set. After 48 hours, the samples were frozen in a freeze dryer, all liquids and solvents were removed from the solution, and the contents were dried in a Petri dish. The presence of plate-shaped pores and volume after the fluid was removed from the containers, which is characteristic of freeze-drying (FD-DorsaTech), was clearly visible in the samples, and the samples were prepared for further tests and analyzes.

Material characterization

To characterize wounds and to relate the physical and chemical properties to the shape and crystallinity of nanomaterials, it is necessary to identify their properties with great accuracy. In this study, scanning electron microscopy (SEM) and X-ray diffraction (XRD) techniques were used to analyze the surface morphology of the samples using a scanning electron microscope (LEO model). In order to increase the electrical conductivity of the specimens and to increase the resolution of the images, a very thin gold coating was applied to the specimens for examination, and then their surface was imaged. This method provides general information about the crystallinity of the sample. Tests performed.

Biological tests

The biological characteristics of the lesions were evaluated by cell culture. MTT salt is used in this method; it is soluble in water and yellow in color and is converted to non-water-soluble purple formazan by the mitochondrial dehydrogenase of living cells. The amount of purple produced is proportional to the number of living cells. In the present study, bioactivity, biodegradability, antibacterial test, and toxicity test (MTT) after 21 and 24 hours, 8 hours were used, respectively. A simulated body solution was used to evaluate the bioactivity of samples in a laboratory environment. This solution has been widely used by researchers to simulate living conditions in the body.

Mechanical tests

Image J software was used to obtain the porosity size using scanning electron microscope results. In order to measure each sample, at least twenty holes were examined in the SEM image. Mechanical Behavior of Boeing Wounds, including Tensile Strength and Elastic Modulus, Using Pressure Strength Test (ASTM-20) with Pressure Device (SANTAM-STM50) at Pressure Rate (0.5 mm/min) at the Institute of New Technology Amirkabir University of Technology was investigated. Mechanical Behavior of Boeing Wounds, including Tensile Strength and Elastic Modulus, Using Pressure Strength Test (ASTM-20) with Pressure Device (SANTAM-STM50) at Pressure Rate (0.5 mm/min) at the Institute of New Technology Amirkabir University of Technology was investigated. The specimens tested in this experiment consisted of six porous bio-wound specimens with cavities of 100-200 µm and a thickness of 1 cm, with four different compositions, such that the weight ratio of the biopolymers was constant and the only additive in each sample was variable. From the data obtained during the tensile test, the strain curve was plotted, and finally, the dip of the diagram was calculated to obtain the elastic modulus, and the maximum point of the curve was considered as the tensile strength.

Results

The SEM analysis was performed on bio-based wounds in which the results showed the suitability and porosity of these wound dress were suitable. The presence of proper porosity and moisture level for wound healing and non-acidity, as well as the use of bed wound healing, have been distinguished from other conventional wound healing products in the market and research domain. Collagen and gelatin have both been widely used as wound dressings and tissue engineering products for human use because of their bleeding properties, excellent biological adaptability, reduced toxicity, low antigenicity, reduced degradability, and ability to stimulate binding and Cellular growth has been used among the more than 3,000 types of wound dressings available on the market, covering all aspects of wound care. Chitosan-based biodegradable composites have been widely used in the field of regenerative medicine for the past several decades. Chitosan composites have been studied to repair damaged tissues and enhance the healing process by enhancing vascularization. Various physicochemical properties, in vitro cytotoxicity studies, and wound healing models have demonstrated the potential efficacy of chitosan composites as skin substitutes for burns and wound healing. Various techniques used for physicochemical modulation and changes in mechanical properties can be concluded by examining the tensile strength results of gum and gelatin-based bio-nano composite coatings, which results in the strength of the specimens shown in Figure 6. In this study, multicellular scabs due to porosity that can contain biocompatible biopolymer for wound healing and control depth, location and extent of scarring, secretion rate, infection, and adhesion of the wound. Traditional wound dressings (for example, cotton and gas bonds) absorb much of the wound's moisture, which is similar to the traditional and modern wound. According to clinical practice, coats are classified as antimicrobial, adsorbent, blockage, adherence, and debridement. Depending on the physical form, the dressing is available. Different types of ointment, film, foam, and gel because of the origin of the material. High water about 40-90 g of water per gram of dressing. Reasons for limiting these types of dressings are high cost and production, difficult to maintain and store. Skin ulcer dressing is usually used to stimulate and strengthen skin tissue repair. Even though ulcers appear to be chronic ulcers with complementary diseases are now a serious challenge in skin tissue engineering for patients. The seemingly simple process of skin repair, the heterogeneous sequence of events, the specific timing, and the high level of organization and coordination between the cell types involved all lead to a scar. It improves a specific process, but we are still unable to fully heal chronic wounds. Reproduction *in vitro* with high fidelity. This review highlights the key features and properties of a natural polymer, widely used as a biological material. Used, i.e., collagen gelatin and its reflected type. The polymer or bioactive compound of an ideal wound dressing should stick to the damaged tissue, maintain a balanced humid environment, allow oxygen to protect and protect against bacterial infection, so an optimal microenvironment can be assured quickly. Provide healing. Temporary dressings and permanent skin engineering alternatives should provide temporary absorption and protection of wound exudates until wound healing, while skin replacements are expected to integrate with the host skin and accelerate the regeneration process. Figure 1 shows the skin is one of the largest organs of the body, with an average surface area of about 2 square meters, as shown in Figure 1. The skin forms a protective barrier between the surrounding world with its muscles, internal organs, blood vessels, and nerves. Figure 2 shows the preparation of the porous bio-nanocomposite dress with a freeze-drying technique. Figure 3 shows the preparation of six samples using the freeze-drying technique. First, the powders were mixed using acetic acid and distilled water for 1 hour on a magnetic stirrer.

Then, the sample was kept in the freezer for 24 h at -70°C and dried for 48 h at -45°C. The prepared sample was selected tensile strength and biological response. Finally, the XRD and SEM analysis were applied to the sample to evaluate the phase and topology characterization. Figure 4 shows the SEM image of sample 3 with agglomeration structure and spherical particles. Figure 5 shows the SEM images of porous bio-nanocomposite wound dress with nanoparticles and biopolymers fabricated by the freeze-drying technique of all six samples.

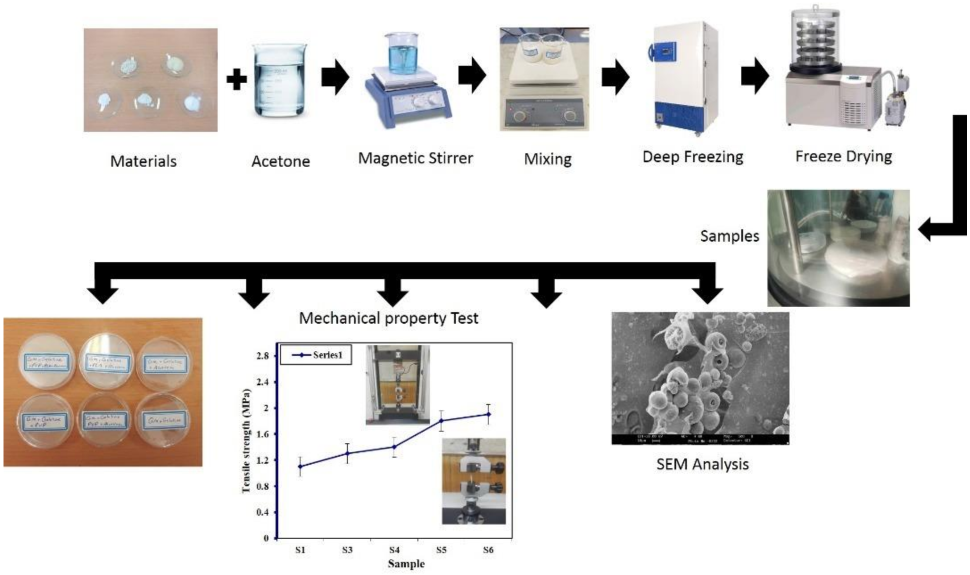

Figure 3. Schematic of the process of making new wound dressings for freezing drying

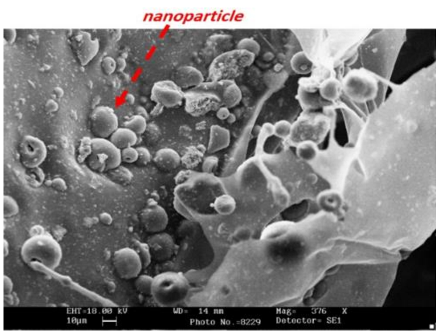

Figure 4. SEM image of bio-nanocomposite wound synthesized by freeze-drying technique

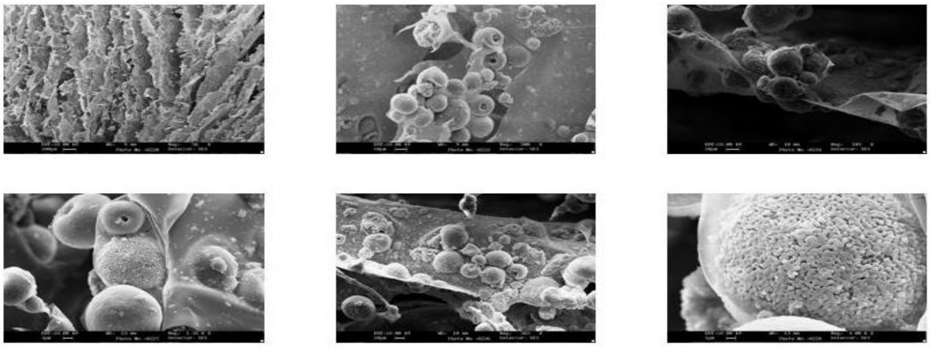

Figure 5. Porous bio-nanocomposite wound dress with nanoparticles and biopolymers fabricated by a freeze-drying technique

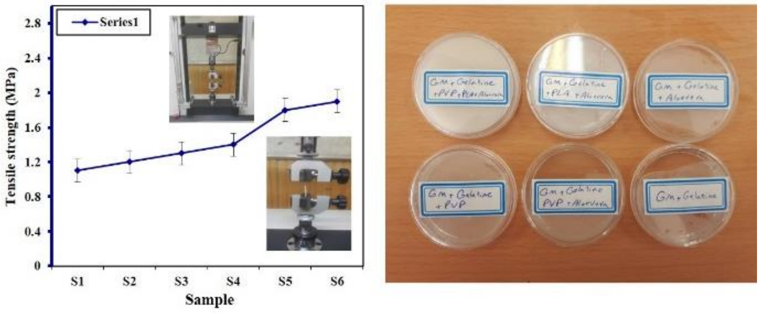

Figure 6. Mechanical strength results of bio-nanocomposite synthesized by freeze-drying with nanoparticles

Figure 7 shows the dissolution results of bio-nanocomposite synthesized by freeze-drying with nanoparticles after seven days in the phosphate buffer saline (PBS).

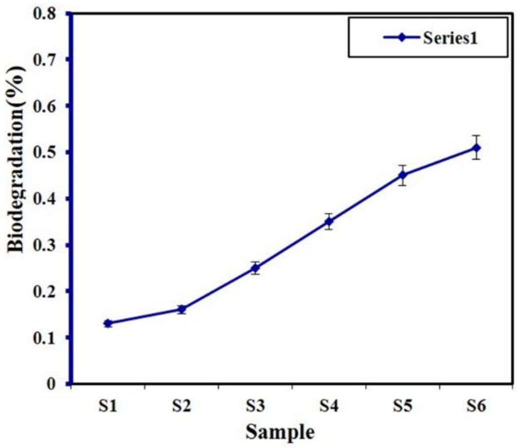

Figure 7. Dissolution results of bio-nanocomposite synthesized by freeze-drying with nanoparticles

Figure 7 shows an upward trend in which samples 4, 5, and 6 have the highest degradation rate compare to the first three samples. Figure 8 shows the porosity value of the sample 1 to 6 obtained from the Image -J software and SEM images.

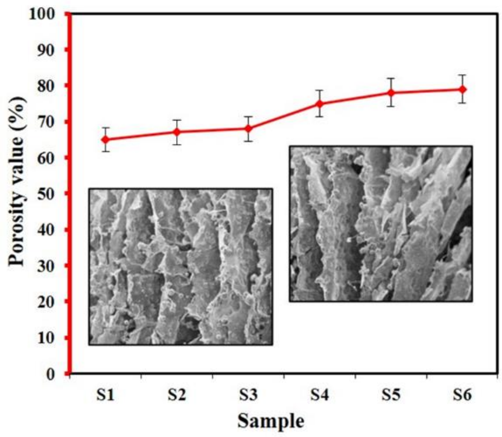

Figure 8. Porosity results of bio-nanocomposite wound dressings synthesized by freeze-drying method containing different biopolymer

The SEM images and obtained results from the sample for porosity value shows an increasing trend with a 0.07 rate. Figure 9 shows the antibacterial behavior (%) of the sample compared with the roughness value (micron) in which the results show an upward trend. The wettability of the sample was researched using a CCD camera on samples 1 to 6.

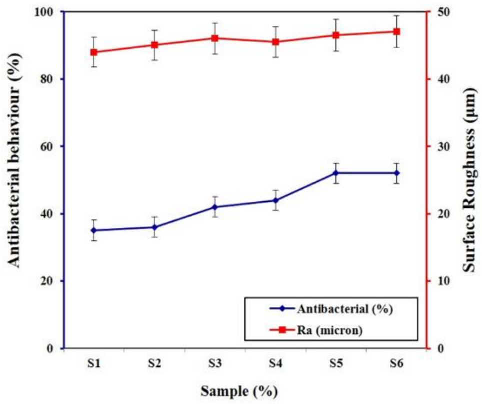

Figure 9. Antibacterial response vs. roughness results of nano-biocomposite wound dressings synthesized by freeze-drying method containing different biopolymer

The wetting features shows that the sample S3, S4, S5, and S6 present similar wettability properties while sampling 1 and 2 present weak wetting response lower than 70° as shown in Figure 10.

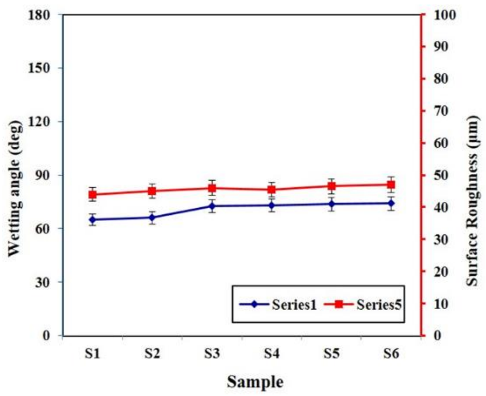

Figure 10. Wettability and surface roughness results of nano-biocomposite wound dressings synthesized by freeze-drying method containing different biopolymer

Also, the roughness parameter was measured using a roughness testing machine, which shows the Ra value 40-50 micron. Figure 11 shows the cell behavior and toxicity of bio-nanocomposite wound dress synthesized using a freeze-drying technique containing different biopolymer content after seven days. The best sample incubated in the MTT assay was sample 3 regarding the results presented in Figure 11 compared with the control specimen. Figure 8 shows that with the addition of polyvinyl pyridine and Alvera, porosity has increased, which is clearly evident in the scanning electron microscope images.

Discussion

Gelatin-Alvera-Arabidopsis gelatin-polyurethane-polyurethane-polyvinyl pyridine (PVP) bio-wound wounds were synthesized by constant weight percentages by the freeze-drying method, as shown in the schematic form. In the next section, after the wound healing, the porosity was measured and scanned by scanning electron microscopy and x-ray diffraction and fuzzy identification. On the other hand, water absorption was measured by swelling and immersion tests. Then, the compressive strength of the scaffolds was by a determined compressive test. Finally, scaffolds made for animal testing on rats were tested. Wound healing is a complex and continuous process that is affected by a variety of factors, which require an appropriate environment for rapid healing. The process of wound healing absorbs three different stages: inflammation, proliferation, and puberty. Due to different types of wounds as well as advances in medical technology, different products have been developed to repair different skin lesions. The precise definition of a wound is to disrupt the immune function of the skin. Loss of epithelial cohesion with or without loss of primary connective tissue resulting from direct thermal or physical damage to the skin. It is divided into acute and chronic according to the process and duration of the wound healing. Acute ulcers are the result of unexpected events. On the other hand, chronic burns, decubitus, leg ulcers that do not heal within a specified time. The largest part of the human body is about 2 square meters in area. A barrier that protects internal organs from microbial invasion and ultraviolet radiation and regulates body temperature. In addition, the skin helps the immune system and the body's sense-making process. Louis Pasteur and Joseph Lister have pioneered work in identifying the causes of infection and ways to prevent it. Pasteur said the bacteria enter the wound through an external source. Eliminate pathogenic bacteria through aseptic techniques. Wound healing varies in thickness and intensity. To this end, wound healing involves three continuous stages of inflammation, proliferation, and puberty. The process of wound healing is influenced by local and systemic factors. On the one hand, local factors directly affect the wound, including radiation, hypothermia, infection, tissue oxygenation, tension, and pain. On the other hand, systemic factors are related to the level of health that affects one's ability. In addition to poor nutrition, protein vitamins, minerals deficiency, and age are other factors that can extend the recovery time. The skin plays a key role in maintaining the physiological homeostasis of the human body. Wounds can be classified according to various criteria such as appearance, duration of the repair, and the area affected.

Among natural macromolecules, collagen, and its denatured form, gelatin is the most appropriate building block for the development of wound dressing and biomimetic biological materials to human skin.

Table 1. Mechanical and biological property of the fabricate wound dress using a freeze-drying technique

Sample	Tensile strength (MPa)	Porosity (%)
Sample 1	1.1	65
Sample 2	1.2	67
Sample 3	1.3	68
Sample 4	1.4	75
Sample 5	1.8	78
Sample 6	1.9	79

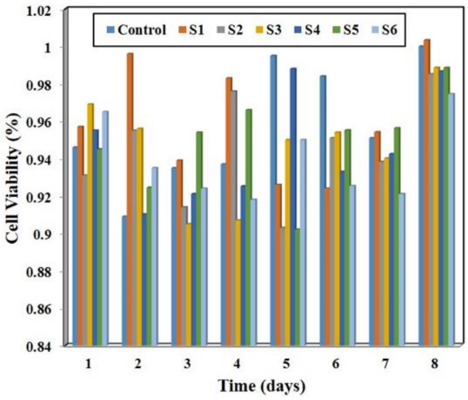

Figure 11. Cell behavior and toxicity of nano-biocomposite wound dressings synthesized by freeze-drying method containing different biopolymer

The increase in porosity is due to the biopolymer base. Porous wound dress can dry and control the surface of the wound because they permit oxygen to pass through the wound surface, resulting in increased healing speed and reduced pain in the dressing. A wide variety of polymers have been produced in the form of films, foams, and gels that can provide optimal wound healing. Depending on the depth of the wound surface, the exudate surface, and the characteristics of the wound bed, the existing dressings can be used in the wound healing process. Again, epithelialization is hampered by slow vascularization and optimization of several properties of biological materials used, such as porosity, density, fluid uptake, thickness, and morphology. Therefore, temporary dressings include bioactive compounds (33-43). Growth factors or microbial growth factors are important for improving skin porosity and biodegradability. Therefore, new epidermal methods are used to achieve suitable wound healing for better cell migration, adhesion, and cell proliferation (36-50). Types of synthetic and natural polymers were used for wound dressing applications, but synthetic polymers are only suitable for superficial wounds and reduce some dressing defects such as low adhesion, absorption, and permeability. Natural biopolymers such as alginate, silk, fibrin, creatine have been widely used in skin tissue engineering because of their good biocompatibility, degradability, easy adsorption, and capacity to repair or repair damaged tissue (15-16). Synthesis of synthetic/natural polymers is very effective for prolonging the degradation time until the recovery process. Biocompatible materials are used to control the moisture content of the wound volume to increase mechanical properties and control the permeability of gas and water vapor. Products degraded in herbal compounds with natural polymers in the new dressing react in the next stage of wound care (35-42). Compounds containing herbs transmit antioxidant and antimicrobial activities to wound dressings, and help wound contraction, vessels, and epithelization. By making composites with suitable additives such as collagen, gelatin, etc., one can reduce the inherent disadvantages of the materials such as gelatin used in this research, such as their biomechanical and flexible properties. Gelatin-based composites are emerging as potential candidates and have a very promising future (39-49).

Proper porosity and moisture level for wound healing and non-acidity. Also, the use of aloe vera and Arabic gum as a bed wound is a distinguishing feature of this wound with other specimens available in the market and research. Porous sores can dry and control the surface of the wound because they can transmit oxygen to the wound surface, resulting in an increase in the rate of healing and pain reduction in the dressing, which the biopolymers used in this study perform well. Bed wounds are damage to the tissues (skin and underlying tissue) caused by abnormal blood flow to the capillary vessels due to prolonged pressure on the skin and underlying tissue. Stress reduces cellular metabolism and results in a lack of oxygen and malnutrition, resulting in local necrosis. In this study, suitable biopolymer wounds were fabricated. The results showed that aloe vera and other polymeric bases increased the tensile strength and relative porosity of the wounds. The results also showed that the addition of these biopolymers is effective in the rate of solubilization of the wound, which is effective in controlling solubility and wound moisture.

References

1. Raisi A, Asefnejad A, Shahali M, Doozandeh Z, Kamyab

Moghadas B, et al. A soft tissue fabricated using freeze-drying technique with carboxymethyl chitosan and nanoparticles for promoting effects on wound healing. J Nanoanalysis 2020 (Articles in Press).

2. Hashemi SA, Esmaeili S, Ghadirinejad M, Saber-Samandari S, Sheikhbahaei E, Kordjamshidi et al. Micro-Finite Element Model to Investigate the Mechanical Stimuli in Scaffolds Fabricated via Space Holder Technique for Cancellous Bone. ADMT J 2020;13:51-8.
3. Esmaeili S, Aghdam HA, Motififard M, Saber-Samandari S, Montazeran AH, Bigonah M, et al. A porous polymeric–hydroxyapatite scaffold used for femur fractures treatment: fabrication, analysis, and simulation. Eur J Orthop Surg Traumatol 2020;30:123-31.
4. Kordjamshidi A, Saber-Samandari S, Nejad MG, Khandan A. Preparation of novel porous calcium silicate scaffold loaded by celecoxib drug using freeze drying technique: Fabrication, characterization and simulation. Ceram Int 2019;45:14126-35.
5. Doillon CJ, Silver FH. Collagen-based wound dressing: Effects of hyaluronic acid and firponectin on wound healing. Biomaterials 1986;7:3-8.
6. Foroutan S, Hashemian M, Khandan A. A novel porous graphene scaffold prepared using Freeze-drying technique for orthopedic approaches: Fabrication and buckling simulation using GDQ method. Iran J Mater Sci Eng 2020;17.
7. Maghsoudlou MA, Nassireslami E, Saber-Samandari S, Khandan A. Bone regeneration using bio-nanocomposite tissue reinforced with bioactive nanoparticles for femoral defect applications in medicine. Avicenna J Med Biotechnol 2020;12:68.
8. Farazin A, Aghadavoudi F, Motififard M, Saber-Samandari S, Khandan A. Nanostructure, molecular dynamics simulation and mechanical performance of PCL membranes reinforced with antibacterial nanoparticles. J Appl Comput Mech 2020 (Articles in Press).
9. Khandan A, Saber-Samandari S, Telloo M, Kazeroni ZS, Esmaeili S, Sheikhbahaei E, et al. A mitral heart valve prototype using sustainable polyurethane polymer: fabricated by 3D bioprinter, tested by molecular dynamics simulation. AUT J Mech Eng 2020 (Articles in Press) .
10. Farazin A, Aghdam HA, Motififard M, Aghadavoudi F, Kordjamshidi A, Saber-Samandari S, et al. A polycaprolactone bio-nanocomposite bone substitute fabricated for femoral fracture approaches: Molecular dynamic and micro-mechanical Investigation. J Nanoanalysis 2019;6.
11. Bagherifard A, Joneidi Yekta H, Akbari Aghdam H, Motififard M, Sanatizadeh E, Ghadiri Nejad M, et al. Improvement in osseointegration of tricalcium phosphate-zircon for orthopedic applications: an in vitro and in vivo evaluation. Med Biol Eng Comput 2020;58:1681-93.
12. Moghadas BK, Safekordi AA, Honarvar B, Kaljahi JF, Yazdi SA. Experimental Study of Dorema aucheri Extraction with Supercritical Carbon Dioxide. Asian J Org Chem 2012;24:3691-4.
13. Moghadas BK, Akbarzadeh A, Azadi M, Aghili A, Rad AS, Hallajian S. The morphological properties and biocompatibility studies of synthesized nanocomposite foam from modified polyethersulfone/graphene oxide using supercritical CO2. J Macromol Sci 2020;57:451-60.
14. Shirani K, Sheikhbahaei E, Torkpour Z, Nejad MG, Moghadas BK, Ghasemi M, et al. A narrative review of COVID-19: the new pandemic disease. Iran J Med Sci 2020;45:233.
15. Aghdam HA, Sanatizadeh E, Motififard M, Aghadavoudi F, Saber-Samandari S, Esmaeili S, et al. Effect of calcium silicate nanoparticle on surface feature of calcium phosphates hybrid bio-nanocomposite using for bone substitute application. Powder Technol 2020;361:917-29.
16. Tahririan MA, Motififard M, Omidian A, Aghdam HA, Esmaeali A. Relationship between bone mineral density and serum vitamin D with low energy hip and distal radius fractures: A case-control study. Arch Bone Jt Surg 2017;5:22-7.
17. Aghdam HA, Sheikhbahaei E, Hajihashemi H, Kazemi D, Andalib A. The impacts of internal versus external fixation for tibial fractures with simultaneous acute compartment syndrome. Eur J Orthop Surg Traumatol 2019;29:183-7.
18. Biazar E, Beitollahi A, Rezayat SM, Forati T, Asefnejad A, Rahimi M, Zeinali R, Ardeshir M, Hatamjafari F, Sahebalzamani A, Heidari M. Effect of the mechanical activation on size reduction of crystalline acetaminophen drug particles. Inter J Nanomedi 2009;4:283.
19. Salmani MM, Hashemian M, Yekta HJ, Nejad MG, Saber-Samandari S, Khandan A. Synergic Effects of Magnetic Nanoparticles on Hyperthermia-Based Therapy and Controlled Drug Delivery for Bone Substitute Application. J Supercond Nov Magn 2020;33:2809-20.
20. Saber-Samandari S, Yekta H, Saber-Samandari S. Effect of iron substitution in hydroxyapatite matrix on swelling properties of composite bead. JOM 2015;9:19-25.
21. Saber-Samandari S, Yekta H, Ahmadi S, Alamara K. The role of titanium dioxide on the morphology, microstructure, and bioactivity of grafted cellulose/hydroxyapatite nanocomposites for a potential application in bone repair. Int J Biol Macromol 2018;106:481-8.
22. Joneidi Yekta H, Shahali M, Khorshidi S, Rezaei S, Montazeran AH, Samandari SS, et al. Mathematically and experimentally defined porous bone scaffold produced for bone substitute application. Nanomed J 2018;5:227-34.
23. Ghasemi M, Nejad MG, Aghaei I. Knowledge management orientation and operational performance

relationship in medical tourism (overview of the model performance in the COVID-19 pandemic and post-pandemic era). Health Serv Manage Res 2020;0951484820971438.
24. Ghasemi M, Nejad MG, Bagzibagli K. Knowledge management orientation: an innovative perspective to hospital management. Iran J Public Health 2017;46:1639-45.
25. Malekzadeh R, Abedi G, Abedini E, Haghgoshayie E, Hasanpoor E, Ghasemi M. Ethical predictability of patient safety in Iranian hospitals. Int J Risk Saf Med 2020 (Online ahead of print).
26. Ghadirinejad M, Atasoylu E, Izbirak G, Gha-Semi M. A stochastic model for the ethanol pharmacokinetics. Iran J Public Health 2016;45:1170-8.
27. Mohammadzadeh Rad M, Saber-Samandari S, Sadighi M, Tayebi L, Mohammadi Aghdam M, Khandan A. Macro- and micromechanical modelling of HA-Elastin scaffold fabricated using freeze drying technique. J Nanoanalysis. 2020 (Articles in Press).
28. Khandan A, Nassireslami E, Saber-Samandari S, Arabi N. Fabrication and Characterization of Porous Bioceramic-Magnetite Biocomposite for Maxillofacial Fractures Application. Dent Hypotheses 2020;11:74-85.
29. Morteza PH, Reza FM, Nasrin S, Ehsan N, Ali RS, Amini M. Deterioration of parabens in preserved magnesium hydroxide oral suspensions. J Appl Sci 2007;7:3322-5.
30. Nassireslami E, Nikbin P, Amini E, Payandemehr B, Shaerzadeh F, Khodagholi F, et al. How sodium arsenite improve amyloid β-induced memory deficit? Physiol Behav 2016;163:97-106.
31. Chamanara M, Abdollahi A, Rezayat SM, Ghazi-Khansari M, Dehpour A, Nassireslami E, et al. Thymol reduces acetic acid-induced inflammatory response through inhibition of NF-kB signaling pathway in rat colon tissue. Inflammopharmacology 2019;27:1275-83.
32. Seyedi SY, Salehi F, Payandemehr B, Hossein S, Hosseini-Zare MS, Nassireslami E, et al. Dual effect of cAMP agonist on ameliorative function of PKA inhibitor in morphine-dependent mice. Fundam Clin Pharmacol 2014;28:445-54.
33. Amini E, Nassireslami E, Payandemehr B, Khodagholi F, Foolad F, Khalaj S, Hamedani MP, et al. Paradoxical role of PKA inhibitor on amyloidβ-induced memory deficit. Physiol Behav 2015;149:76-85.
34. Razmjooee K, Saber-Samandari S, Keshvari H, Ahmadi S. Improving anti thrombogenicity of nanofibrous polycaprolactone through surface modification. J Biomater Appl 2019;34:408-18.
35. Razmjooee K, Nassireslami E, Dadpay M, Chehri H, Golaghei A. Chitosan physical hydrogel for diabetic wound treatment. Paramed Sci Mil Health 2018;13:11-20.
36. Moeini M, Barbaz Isfahani R, Saber-Samandari S, Aghdam MM. Molecular dynamics simulations of the effect of temperature and strain rate on mechanical properties of graphene–epoxy nanocomposites. Mol Simul 2020;46:476-86.
37. Barbaz-I R. Experimental determining of the elastic modulus and strength of composites reinforced with two nanoparticles [dissertation]. Tehran: Iran University of Science and Technology, 2014.
38. Malekzadeh M, Abbasi-Rad S, Shahgholi M, Naghdi P, Hoseini MS, Yazdi NA, Shiran MB, et al. Design and validation of synchronous QCT calibration phantom: practical methodology. J Med Imaging Radiat Sci 2019;50:157-62.
39. Abbasi-Rad S, Akbari A, Malekzadeh M, Shahgholi M, Arabalibeik H, Rad HS. Quantifying cortical bone free water using short echo time (STE-MRI) at 1.5 T. Magn Reson Imaging 2020;71:17-24.
40. Karimipour A, Malekahmadi O, Shahgholi M, Li Z. Thermal conductivity enhancement via synthesis produces a new hybrid mixture composed of copper oxide and multi-walled carbon nanotube dispersed in water: experimental characterization and artificial neural network modeling. Int J Thermophys 2020;41:1-27.
41. Shahgholi M, Oliviero S, Baino F, Vitale-Brovarone C, Gastaldi D, Vena P. Mechanical characterization of glass-ceramic scaffolds at multiple characteristic lengths through nanoindentation. J Eur Ceram Soc 2016;36:2403-9.
42. Takzaree N, Hadjiakhondi A, Hassanzadeh G, Rouini MR, Manayi A. Synergistic effect of honey and propolis on cutaneous wound healing in rats. Acta Med Iran 2016;54:233-9.
43. Fayazzadeh E, Rahimpour S, Ahmadi SM, Farzampour S, Anvari MS, Boroumand MA, et al. Acceleration of skin wound healing with tragacanth (Astragalus) preparation: an experimental pilot study in rats. Acta Med Iran 2014;52:3-8.
44. Bidgoli SA, Mahdavi M, Rezayat SM, Korani M, Amani A, Ziarati P. Toxicity assessment of nanosilver wound dressing in Wistar rat. Acta Med Iran 2013;51:203-8.
45. Vahedian-Ardakani J, Baghai-Wadji M, Nazerani S, Keramati MR, Mirshekari TR, Ansari K. Impact of morphine dependency on secondary intention wound healing in rat. Acta Med Iran 2012;50:380-7.
46. Talebi-Ardakani MR, Torshabi M, Karami E, Arbabi E, Esfahrood ZR. In vitro study of Er: YAG and Er, Cr: YSGG laser irradiation on human gingival fibroblast cell line. Acta Med Iran 2016;54:251-5.
47. Biazar E, Rezayat SM, Montazeri N, Pourshamsian K, Zeinali R, Asefnejad A, et al. The effect of acetaminophen

nanoparticles on liver toxicity in a rat model. Int J Nanomedicine 2010;5:197-201.

48. Shojaie S, Rostamian M, Samadi A, Alvani MA, Khonakdar HA, Goodarzi V, et al. Electrospun electroactive nanofibers of gelatin-oligoaniline/Poly (vinyl alcohol) templates for architecting of cardiac tissue with on-demand drug release. Polym Adv Technol 2019;30:1473-83.
49. Seyfi J, Panahi-Sarmad M, Oraei Ghodousi A, Goodarzi V, Khonakdar HA, Asefnejad A, et al. Antibacterial superhydrophobic polyvinyl chloride surfaces via the improved phase separation process using silver phosphate nanoparticles. Colloids Surf B Biointerfaces 2019;183:110438.
50. Biazar E, Beitollahi A, Rezayat SM, Forati T, Asefnejad A, Rahimi M, et al. Effect of the mechanical activation on size reduction of crystalline acetaminophen drug particles. Int J Nanomedicine 2009;4:283-7.
51. Panahi-Sarmad M, Goodarzi V, Amirkiai A, Noroozi M, Abrisham M, Dehghan P, et al. Programing polyurethane with systematic presence of graphene-oxide (GO) and reduced graphene-oxide (rGO) platelets for adjusting of heat-actuated shape memory properties. Eur Polym J 2019;118:619-32.