

Effectiveness of using hybrid Biocomposites in regenerative medicine and elimination of Bacterial skin infections

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Abstract

In recent years, the use of natural biomaterials for regenerative medicine has received attention. The use of natural and synthetic polymers alone has not been effective in tissue engineering, but the addition of some reinforcements has led to the production of hybrid biocomposites. The unique properties of these compounds include strong physical structure, adequate strength, biocompatibility, biodegradability, moisture absorption, favorable oxygenation, light weight, uniform drug distribution, and acceptable drug permeability in damaged tissue. In addition, the high effectiveness of hybrid biocomposites in eliminating infectious bacteria is remarkable. Studies show that the presence of reinforced biopolymers in damaged tissues of the human body such as skin wounds and bone tissue can destroy bacteria extensively.

Keywords: Hybrid; Biocomposite; Regenerative medicine; Skin infections

1. Introduction

Understanding skin texture is an introduction to identifying the cause and implementing programs to combat skin diseases and their treatment. The structure of human skin is made up of layers of epidermis and dermis, which are connective tissue layers formed by a special membrane from the same skin base. The stratum corneum, called the stratum corneum, is located in the outermost part of the epidermis [1]. The role of the skin includes protecting the body against ultraviolet light, pathogens, microorganisms, and toxins, and also controlling fluids and immunological surveillance [2]. The above characteristics make the skin susceptible to inflammation and infectious diseases. For this reason, knowledge of the structure and function of the skin can be effective in combating skin-threatening diseases [3].

Scratching the skin allows pathogens to enter and cause infection. Some bacteria, viruses, and fungi are the source of skin infections [4]. With the formation of a wound, complex interactions in the body begin automatically, and a set of body molecules such as platelets and cytokines carry out the wound healing process [5].

2. Materials and methods

2.1. Types of skin wounds

The skin is the body's first line of defense against external threats. When the skin is attacked, its defense system is automatically activated. This attack is carried out by foreign bacteria or the skin's natural microbiome [6]. Bacterial infection enters the body through any opening in the skin, which can be caused by injury such as surgery, burns, scratches, or insect bites [7]. The presence of infection may cause blood clotting, and subsequently, with a lack of blood,

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skin cells are destroyed. Since the body's defense system reaches the site of infection through the bloodstream, when a lack of blood occurs, the body's defense cells are stopped and infectious agents spread rapidly and become difficult to control [8].

As mentioned, wounds are formed when biological tissue of the skin is damaged [9]. Depending on environmental factors and external symptoms, wounds are classified as follows:

- Class 1: Wounds are clean, not infected, and have no signs of inflammation [9].
- Class 2: Wounds are clean-contaminated and have little contamination on the skin surface. These wounds must be carefully monitored [9].
- Class 3: Wounds are contaminated and the cause of their occurrence is the failure to observe sterile principles during dressing [9].
- Class 4: Wounds are completely infected, the main cause of which is the lack of proper treatment and usually occur during heavy physical activities such as surgery [9].

2.2. Wound healing process

The process of skin wound healing occurs in four stages: homeostasis, inflammation, proliferation, and regeneration. If the infection is caused by bacteria, the type of disorders is complex. The main goals during wound healing are to eliminate invading bacteria and cleanse the wound of damaged cells. In fact, if the damaged skin cells at the wound site are unable to regenerate, they are unable to perform the protective function properly and must be isolated [10]. Due to the presence of appropriate temperature, sufficient humidity, and the presence of nutrients, the growth of microorganisms at the wound site is intensified, so performing open wound healing with the help of bioactive dressings is very effective [10].

2.3. Types of skin bacterial infections

The bacteria that invade and grow in skin wounds are very diverse, and the physiological conditions at the wound site, while intensifying their activity, also help the natural flora of the wound to spread rapidly in these conditions, and therefore slow down the healing process of the wound (10). Specialists are able to determine to some extent the type of bacteria present and measure the level of infection of the site by considering the external signs and events that have occurred on the wound surface (10). The most important bacterial infections of skin wounds are (11):

- Impetigo
- MRSA infections
- Furuncles
- Carbuncles
- Ecthyma
- Erythrasma
- Bacterial Folliculitis
- Hot Tub Folliculitis
- Erysipelas
- Hansen's Disease (Leprosy)

2.4. Types of wound dressings

Types of wound dressings and their characteristics are as follows (12):

- Sterile gauze: This method is cheap and available to the general public. This dressing does not retain moisture and must be changed several times a day, and the wound can easily become infected with bacteria. B) Films: This type of dressing is transparent and retains moisture. It is flexible and non-absorbent. It is used for shallow wounds.
- Foams: This dressing has more than one layer and is made of polyurethane or silicone and is able to absorb exudate. It is used for chronic and pressure wounds and must be changed several times a day.
- Hydrogels: Starch polymers are hydrophilic and moisturize the environment and keep the wound cool. This dressing is not suitable for exuding wounds, but is used for surgical wounds.
- Hydrocolloids: These are natural-based hydrophilic polymers that are impermeable but gradually absorb water and reduce the pH of the wound. Although they reduce bacteria, they are not suitable for infected wounds.

- Alginate: This dressing is produced from a polysaccharide based on seaweed and results in the formation of a gel that is porous. Since it sticks to the wound and creates an unpleasant odor, it is not suitable for dressing infected wounds.
- Antimicrobial: This dressing uses a combination of silver and iodine. Despite its antimicrobial effect, it may contaminate the wound due to the silver composition. They are used for very infected wounds.
- Nanofibrous wound dressing: This dressing is porous and permeable to water and oxygen. They have good adaptability to the wound. They provide adequate coverage and are a good protection against infection [18].

2.5. New wound dressings with a combined biological base

In fact, wounds are the entry routes for bacteria into the human body. The wound healing process is carried out with the aim of preventing the entry and development of infection. As mentioned, wound dressing operations are carried out with the aim of preventing bleeding and infection, treating inflammation, accelerating the wound healing process and skin regeneration. In the past, the use of chemical drugs was common, which increased the resistance of microorganisms and weakened the body's immune system, but new methods relying on the use of combined composite materials and also nanocomposites with antibacterial materials have shown interesting results in wound healing [13].

2.6. Introduction to composites

A composite is a material which consists of two or more individual materials blended together or joined together to form a newer material which is meant for their improved properties [14]. Important properties of composites include corrosion resistance, design flexibility, strength, light weight, and durability [15]. The composite material consists of two parts, which include the matrix and the filler. The filler component has reinforcing properties, and the matrix component connects the filler parts together and gives the composite a suitable shape [14].

2.7. Composites are divided into two categories: synthetic and natural

Natural composites are made from materials that have a biological structure, which is why they are called "green composites" [14]. Most of the research conducted shows that green composites or biocomposites are polymers with natural fibers that improve the thermal, physical, mechanical and rheological properties of these compounds. Extensive operations have been carried out on biocomposites, which leads to their stability [16].

Synthetic composites are made from polymers made with chemicals, such as petrochemical compounds, and have a stronger texture and the same properties [14]. This group of composites is made from various raw materials that have special properties through chemical and physical reactions. Synthetic composites are used in various industries such as automotive and medical [17].

2.8. Structure of biocomposites

Biocomposites are formed as a result of synergy of natural polymer compounds such as alginate and chitosan and reinforcing materials such as cellulose and nanofibers [18]. One of the most important applications of biocomposites is in tissue engineering and regenerative medicine. These compounds develop extracellular matrix scaffolds and facilitate cell growth. In addition, biocomposites are used in the manufacture of implantable medical devices [18]. Based on the research conducted, biocomposites are classified into three main categories [19]:

- Hybrid biocomposites
- Natural fiber reinforced biocomposites
- Synthetic fiber reinforced biocomposites

2.9. Types of biocomposites in medical applications

Biocomposites are used in a wide range of medical applications, including hardware and software. These synthetic and natural fiber composites are used in the production of living tissue. They are also widely used in the production of medical devices such as biosensors, artificial hearts, and pacemakers [20]. In recent years, the application of biocomposites and functional polymers has played a prominent role in medical services due to their distinctive physicochemical properties and flexibility in biological activities [21]. Figure 1 shows the application of polymer biocomposites in skin wound healing and tissue engineering.



Figure 1 Application of polymer biocomposites in skin wound healing and tissue engineering [22]

2.10. Structure of hybrid biocomposites

The focus of the biocomposites industry has slowly shifted from traditional forms to hybrid biocomposites due to their diverse applications. The new strategy is based on overcoming the limitations of traditional biocomposites. These limitations include the physical, strength, and mechanical properties of the structure of these compounds [23]. Hybrid composites are micro-compounds of organic and inorganic materials that have diverse physical and mechanical properties [24]. The hybridization property in composites is related to the presence of two or more reinforcing elements that enhance the performance of the composite [24]. Natural reinforcers are of organic and plant origin, while mineral reinforcers are of gypsum, asbestos, talc, etc [24]. Synthetic reinforcements are of interest in composites due to their mechanical and strengthening properties, but limitations such as environmental sustainability, energy consumption, high weight, and recycling problems have led to the introduction of natural reinforcements as alternative compounds [25].

In view of the above, biocomposites have significant effectiveness in living tissue, including their role in medical services including bone regeneration, orthopedic implants, wound healing, and tissue engineering [26].

2.11. Application of hybrid biocomposites in the medical services

Hybrid biocomposites are derived from biopolymers, and studies show that their mechanical properties, with the help of plant (such as hemp and bamboo), animal (such as silk and wool), and mineral (such as basalt and asbestos) reinforcements, have led to improved performance in various applications, including tissue engineering, biomedical sciences, regenerative medicine, and pharmaceuticals [25].

As mentioned, one of the most important reinforcements used in biocomposites is plant-based biological materials that improve the functional properties of biocomposites, such as durability and tensile strength, which are used in medical services such as tissue engineering, surgical dressings, and prosthetics [26]. Some applications of hybrid biocomposites in medical science are presented in Table 1.

Table 1 Some applications of hybrid biocomposites in medical science

Hybrid composites	Name of Tissue	Reference number
poly(lactide-co-caprolactone) poly(p-dioxanone) poly(lactide-co-caprolactone)	Tendon tissue repair	27
Polymer composite based on epoxy resin with calcium carbonate and hybrid filler in the form of a mixture of silica and perlite	Implants with natural bone properties for use in orthopedics and veterinary medicine	28
hybrid bio polymer matrix composites using high density poly ethylene with Titanium Oxide (TiO ₂) particles and Alumina (Al ₂ O ₃) particles	orthopaedic applications, particularly in bone fixation plates, hip joint replacement, bone cement and bone graft	29
(BNC and TiO ₂) hybrids	cell-compatible cell carriers	29

Antimicrobial porous hybrids with BNC and silver nanoparticles	Wound dressing	29
Electrochemical biosensor based on reduced graphene oxide and TEMPO nanocellulose	detection of Mycobacterium tuberculosis	29
Gelatin-hydroxyapatite (HAp)-based scaffolds	bone tissue engineering applications	30
hybrid bionanocomposites composed of poly(3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) combined with zinc oxide (ZnO) and silicon-doped hydroxyapatite (SiHAP) nanocrystals.	bone tissue disorders removal	31
polyhydroxyalkanoate-based (PHA)	bone, cartilage, nerve and skin tissue engineering	32

2.12. Application of hybrid biocomposites in the production of wound dressings

The common structure of wound dressings is based on polymers. When natural and synthetic polymers are combined with specific biomaterials, they become hybrid biocomposites that are defined as ideal dressings. The most important features of these wound dressings are preventing bacterial invasion, reducing odor, absorbing secretions, ease of use, preventing further skin tearing, creating a moist, soothing environment, and being permeable to gases [33]. The most important natural polymers used in the structure of hybrid composites and which eliminate bacteria from skin wounds are shown in Table 2.

Table 2 Natural polymers effective in eliminating common bacteria in skin wounds [34]

Natural polymer	Bacterial inhibited	applications
cellulose	<i>E. faecalis</i> <i>P. aeruginosa</i> <i>E. coli</i>	Wound infections
		Wound dressing
collagen	<i>Candida albicans</i> , <i>P. aeruginosa</i> , <i>S. epidermidis</i> , <i>B. cereus</i> , <i>C. Lusitaniae</i> , <i>B. subtilis</i>	Wound dressing
Gelatin	<i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. aureus</i>	Wound dressing
Alginate	<i>E. coli</i> , <i>S. aureus</i> , <i>P. aeruginosa</i>	Wound dressing
Fibrin	<i>E. coli</i> <i>S. aureus</i>	Wound healing

The presence of hydrogel materials and other natural polymers and reinforcing materials in the structure of hybrid biocomposites has led to their widespread use in regenerative medicine, along with their biocompatibility and excellent cell adhesion properties. Their most important applications are in bone regeneration, dental implants, wound healing, and tissue engineering [39]. Table 3 lists a group of biocomposites that are effective in eliminating infectious skin diseases.

Table 3 Some hybrid biocomposites with a polymer structure for the treatment of a group of skin diseases

Disease name	Pathogenic agent	Hybrid biocomposite name	Reference number
Impetigo	Staph aureus, Strep pyogenes	Pectin-ZnO bionanocomposite based on Annona muricata	35
MRSA infection	Staph aureus	injectable self-healing bioactive nanoglass hydrogel	36
furuncles and carbuncles	Staph aureus	(Various natural polymers, such as chitosan, collagen, and alginate) (Bacterial cellulose)-(polymeric films) low-molecular-weight hydrogel (LMWG)	37
erythrasma	Corynebacterium minutissimum	metal oxide nanoparticles (MONPs)zinc oxide impregnated mesoporous silica carboxymethyl cellulose zinc oxide nanoparticles cerium oxide (CeO ₂) nanoparticles into poly (ε-caprolactone) cerium oxide (CeO ₂) and peppermint oil (PM oil) on polyethylene oxide (PEO)/ graphene oxide (GO) polymeric	38

3. Results and Discussion

- The continued presence of biocomposites in the human body requires further studies to accurately assess their potential side effects and toxicity [40].
- The use of biopolymers is effective in wound healing, but due to their poor mechanical properties, they require reinforcements to produce hybrid polymers that can be effective in dressing infected wounds by creating resistant scaffolds [40].
- Antimicrobial biocomposites with bacterial cellulose structure are able to easily heal infected wounds [41].
- When biopolymers are combined with selected biological enhancers and compounds, they produce biocomposites that become highly effective hybrid dressings [42].
- Biocomposite materials play an important role in wound dressing repair due to their biocompatibility and biodegradability [43].

4. Conclusion

Based on the research conducted, it seems that when biological materials are produced with natural and synthetic polymer structures, they have the appropriate physical structure and strength. These compounds, along with biological enhancers, lead to the creation of hybrid biocomposites that play a great role in regenerative medicine. The mechanism of these materials is to eliminate bacterial infectious agents by creating hybrid scaffolds that, with the addition of some chemical compounds in their structure, provide a good effect in wound healing and regeneration of damaged tissue. It should be noted that further research is absolutely necessary to know the exact side effects of these compounds in the human body.

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