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An Overview on recent trends in Biopolymer Base Composites for Tissue Regeneration

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Abstract. This paper focused on the short review of biopolymer based composite for tissue regeneration. Biopolymers have been slowly introduced into medical applications as a result of their ability to be bio-degradable and to be easily made. By selecting the appropriate biopolymer containing the selected additives to facilitate the polymer-filler interaction, composites with the desired properties can be obtained. Interfacial interactions between biopolymers, and thus Nano-fillers, significantly control the mechanical properties of biopolymer composites and these biopolymer composites such as bone, cartilage, vascular implants, and others.

1 Introduction

Biopolymers are of great interest due to their adaptability and little or no environmental impact, and the fact that they are readily available, environmentally friendly, renewable and lightweight. They have a variety of uses in biomedical engineering, medical research and other disciplines [1]. The fact that biopolymer composites have little or no environmental impact is also the driving force behind their development. On the other hand, developing ways to address architectural design issues requires a trade-off between vision and goals. This often conflicts with unique and challenging biomaterials [2].

These are polymers from natural resources that can be biosynthesized by living organisms (such as plants and bactérie) or chemically synthesized from biological components. It is renewable and biodegradable and is used in a variety of fields such as food, manufacturing,

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packaging and biomedical engineering. Biopolymers are promising due to their unique qualities such as abundant properties [3], biocompatibility and non-toxicity. Monomeric components such as proteins, starches, celluloses, DNA, RNA, lipids, collagens, carbohydrates, peptides, and sugars, amino acids, and nucleotides are examples [4].

1.1 Types of biopolymers

Biopolymers may be classified in a whole lot of ways, which include the aid of using kind, origin, and quantity of monomer units, compatibility, degradability, warmness response, and so on. Some of those training are indexed below [5] :

1. Classification by Types

a. Sugar–based Polymer – A sugar-based polymer is such as glucose. They combine to form starch, glycogen and cellulose.

b. Starch-based polymer Starch is a natural polymer composed of glucose molecules. It is present in plant tissues.

c. Biopolymer from cellulose. This polymer is made from glucose from natural resources such as cotton. Consider cellophane material.

d. Synthetic substances Biodegradable polymers made from petroleum-based plastics.

2. Classification by country of origin

a. Organisms form natural biopolymers.

b. Degradable synthetic biopolymers from renewable raw materials such as polylactic acid. Microorganisms produce biopolymers of micro-organisms.

3. Monomer units are used to classify products. A type of sugar is polysaccharides. These are branched or linear carbohydrate chains (e.g starch, cellulose, etc.). Polymers consisting of amino acids are known as amino acid polymers and examples are collagen and fibrin. c) Polynucleotide Nucleic acid is a long polymer chain consisting of 13 or more monomer units. Examples are DNA, RNA, and other similar molecules.

1.2 Application of polymers

1. **Biomedical Engineering**: Biofilm forming agents are widely used in the field of biomedical engineering as a result of their characteristics such as degradability and non-toxicity, bio-compatibility properties, and so on; they`re used in tissue engineering, the pharmaceutical industry, medicine, drug administration, and so on, and polypeptides are cheap, readily available, and widely used in biomedical materials. Collagen sponges are used to heal burns, while collagen plus chitosan is utilized in tissue engineering. Biofilm-forming agents such as collagen and chitosan are employed as drug delivery systems to target medications and increase drug absorption [6].

2. **Industrial** - Biofilm-forming agents are added to certain materials to improve and improve their quality so that they can be used in more desirable and practical ways. They are used in the automotive industry to manufacture interior and exterior components, electrical components, engines and flywheels. They are added to the cement during the mixing process to give them the required properties. They are used to create upholstery. Chitosan has the ability to remove metals from water, so it can be used in situations where water purification or microbial growth is a problem [7].

3. **Agriculture/fishing is one of the other uses**.

   a. Fishing lines, fertilizers, honeycombs, nets and traps are just a few examples.

   b. Electronic equipment: Audio equipment, circuit boards, insulated wires, cables, and other electronic equipment are all made of electronic equipment.

c. Cosmetics Used in cosmetics such as sunscreens, hair care products and lotions, and used in cleaning, manicure and pedicure.
d. Nano-technology is also used in the manufacture of nanomaterials.

1.3 Biocomposites

Bio-composites are materials made from natural fibers that are woven together and reinforced. They are composed of a wide range of constituents including polymers, carbohydrates, proteins, sugars, ceramics, metals, nano carbons, films, membranes, molded parts, coatings, other particles, fibers, and foams. In continuation, some research is being done to produce environmentally friendly composites and biomedical materials for use in tissue engineering, implants, scaffolding and other areas [8].

1.4 Biopolymeric composite materials

Arabinoxylan, chitosan, guar gum, xyloglucan, and biomedical polysaccharides are effective polymeric biomaterials and composites that have become perfect candidates for multifunctional, mechanical biocompatible roles, stable, environmentally friendly, and biodegradable for the integration of intermixture that provides curing ability and rational drug discharge suitable for many biomedical operations including wound healing and tissue control and manipulation [9-10].

1.5 Tissue engineering

Tissue engineering involves creating scaffolding from biomaterials for the re-making or regeneration of impaired tissue (see Figure1). Promoting the growth of living tissue requires composition, desirable technical properties, and acceptable physicochemical behavior. & It is generally only effective for some or all tissues (e.g., bones, bladder, skin, cartilage, blood vessels, muscles, etc.). Textiles often require accurate architectural, morphological, and mechanical properties for them to function properly. Tissue Re-modelling can hence be sub-divided into [11-12] :

1. Tissue (Bone) Engineering (BTE) is a quick and easy way to make a three-dimensional bone scaffold. It focuses on skeletal structures, increasing cognition, bone mechanics for tissue regeneration, and clinical therapy options for skeletal and segmental abnormalities, and it contains live cells and bioactive chemicals.

2. Skin tissue engineering: The epidermis, dermis, and subcutaneous tissue are part of layers of skin. The epidermis is the outer waterproof part that regulates body temperature and water, acting as a protective barrier against illness and other substances. 90% of epidermal cells make up of keratinocytes. Langerhans cells, melanocytes, and Merkel cells make up the majority of the epidermal cell population. The dermis makes up about 90% of the weight of the skin and serves as the basis. Skin tissue engineering is used to reconstruct the basic scarring and handle wounds better.

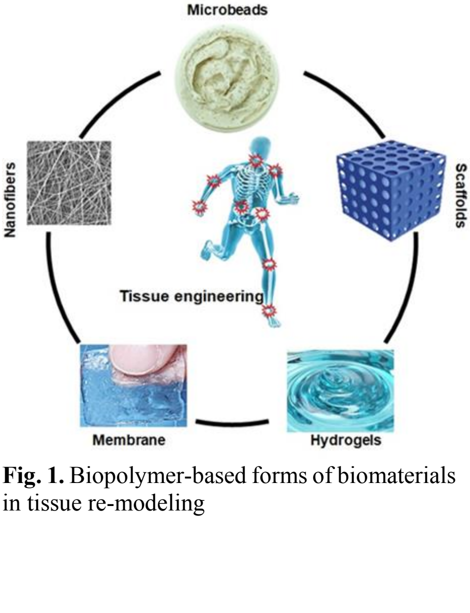

Fig. 1. Biopolymer-based forms of biomaterials in tissue re-modeling

1.6 Hydrogels

In biomedical studies as well as medical fields, hydrogels are employed in the transport of peptides, controlled administration of medications, regeneration therapy, and the development of tissues. It is possible to alter the rate of cross-linking in order to influence the loading and subsequent release of bioactive molecules on the hydrogel. This allows for the development of effective treatments or the synthesis of bioactive chemicals for hydrogel release [13]. For example, dynamics can be sometimes used. This leads to scientific control options. Chemotherapy Chemicals can be delivered to the local environment via hydrogels, supporting systemic delivery. Hydrogels are biocompatible and suited for vital therapeutic applications due to their high water content and physicochemical and biological similarities to the natural extracellular environment [14]. Hydrogels conform to the geometry of the application site, making the synthesis of loaded hydrogels in biomedical applications considerably more practical-intense physiologically. Hydrogels mostly made of poly (ethylene glycol) (PEG) are extremely biocompatible. PEG-based hydrogels, let fibroblasts develop faster. PEG's excellent systemic biocompatibility and the usage of ECM-derived nanomaterials increase cell growth dispersion. As a result, PEG-based cross-linked hydrogels have developed as multifunctional materials for wound healing procedures that rely on low-cost components including cells, peptides and medicines [15].

2. Literature review

By providing the ideal conditions for cell division and growth, biopolymer composites assist in the three-dimensional formation of new tissues. likewise research into tissue engineering. It is therefore essential in tissue engineering. Natural macromolecules are abundant and have minimal immunogenicity, among other advantages [9, 15].

Bone - Bone is a mineral mixture of organic and inorganic components. Low mechanical strength and dimensional fracture are two major problems in polymer scaffolding for bone tissue formation. Composite polymer / bioactive ceramic has been created for bone tissue engineering. The bioactivity and flexibility of these scaffolds are extraordinary. Its fine structure adapts to bone defects, has excellent mechanical properties, and has bone conductivity [15-16]. The inorganic phase's micro or nanoscale particles can be incorporated into various polymer matrices. Solvent casting could be used to produce bioactive glass composites from PHBs and nanoparticles. The inclusion of nanoparticles in the composite module provided a significant healing effect. With the addition of nanoparticles, the modulus increased 1.5-fold. Our findings indicate that phosphorylation efficiently induces the production of hydroxyapatite (HAp) on BC [17]. Bone tissue was formed on a scaffold that grew with cells. It was discovered using in vitro microcomputer tomography and an in vivo skull defect model.

The inclusion of HAp or bioglass particles on the scaffold surface is another two technique for improving the compressive strength [18].

Alginate-based stuff is used in orthopaedic studies to enhance bone formation and help in the delivery of cells. [19-21].

Skin - The integrated multicellular response to tissue healing and damage is unique to wound dressings and enables cell colonization and array remodeling (Figure 2). As a result, healing requires angiogenesis and inflammation [10]. Common features of wound dressings come into direct contact with the wound site and an outer elastic secures the device [11]. It is based on the properties of bears, etc. There is a development of a chitin / AgNP composite framework with improved blood coagulation capacity for use in wound dressings [12,19].

Antibacterial and anti-inflammatory properties are also evident in alginate-based sponges containing AgNP. To also add, the combination of chitosan and zinc enhanced fungi activity [13,20]. Nina et al. Investigated the effects of pectin, carboxymethyl cellulose, and micro fibrillated cellulose scaffolds on the development of NIH3T3 and found that the calcium content in the material had a significant effect on cell survival [14, 21]. Metal is needed for healing, but the toxicity of scaffolds containing metal.

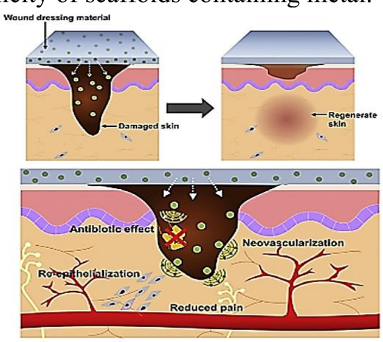

Fig 2. Biopolymer composites for injury dressing

Vascular graft- New blood vessel formation is necessary for the treatment of numerous vascular diseases and tissue engineering procedures. Recently, biopolymers have been employed to disperse growth stimulants and tiny molecules inside of living things. In a rat model, a section of the carotid artery was replaced with a Kremgroup BC tube (0.7 mm wall thickness, 1 mm diameter, and 5 mm length). After 4 weeks, connective tissue had grown over the BC/carotid complex, suggesting that BC might be used as a vascular replacement (see Figure 3) [17, 22–24]. The tubules, which are created from a combination of BC and fibroin that has undergone glutaraldehyde treatment, more nearly match the mechanical properties of actual, small blood arteries because they crosslink the polymer [25]. Vasculature made on BC-based vessels (BASYC®) is believed to be reliable and biocompatible. Morphological investigations revealed structural abnormalities at the interface between BC-based vessels and the surrounding medium. Fibroblasts' presence in this region indicated that integration was occurring without degradation (activation) [17, 25–26].

BC is coated with tripeptide RGD, which causes endothelialization and increases BC's blood compatibility, according to Andrade et al. They discovered that when human microvascular endothelial cells are grown on RGD-coated BC, they create a confluent layer that inhibits platelet adhesion [27-28]. The in vivo data validation test for alginate was used to construct the 3D alginate-based cardiac patch.

However, produced 3D alginate-based cardiac patches have not yet been evaluated in clinical settings [29], despite the availability of encouraging in vitro results. Clinical experiments are actively looking into gelatin-based films for the creation of autologous human cardiac stem cells (ALCADIA) and cardiac patches. Additionally, considerable in vitro testing has been done on new composites created by the methacrylization of biopolymers like Gel MA (methacrylate gelatin) and MeTro (methacrylate tropoelastin) [30].

In vitro, hydrogels made of polysaccharides and carbon nanotubes have been utilized to enhance the electrical connections between neighboring heart cells. Angiogenesis is crucial to the success of cardiac structures, just like it is for all significant-sized structures [31].

One strategy for increasing host infiltration is to introduce growth factors that induce angiogenesis into the matrix. After myocardial infarction, the left ventricle was reconstructed using a polymer composite containing single-walled carbon nanotubes (SWNTs). Increased expression of intercellular and electrochemical compounds in rats undergoing SWNT-based transplantation shortens in vivo engraftment of these devices compared to the untreated heart. Both ejection fraction and speed have increased dramatically. On the other hand, the long-term biocompatibility of SWNTs in vivo poses challenges in moving these scaffolds to human clinical trials [32].

Cartilage – Due to the highly hydrated ECM content and structure. Polymer scaffolds are made of flexible biomaterials that resist compression while providing a favorable environment. Collagen and HA, natural components of being combined with endogenous cartilage materials, are the most commonly used polymer scaffolds currently used in clinical trials of cartilage re-making. Several studies were conducted on alginate as a scaffold. Alginate implants promote chondrocyte viability and have produced cartilage-like ECM 4 weeks after transplantation. Alginate implants, on the other hand, do not possess the proper mechanical characteristics compared to natural cartilage tissue [17, 22, 33].

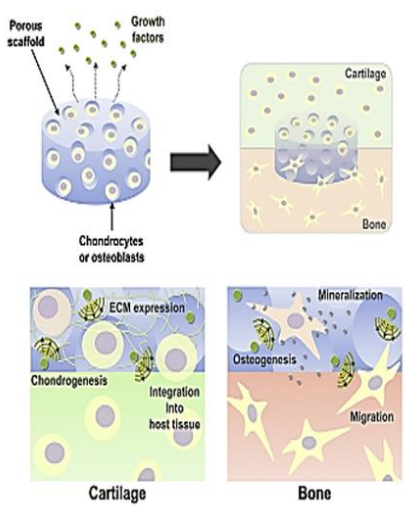

Fig 3. Bone and cartilage regeneration using biopolymer composites

Collagen has been studied and preliminary in vivo studies suggest that conducting transplantation of subcultured chondrocytes seeded on collagen scaffolds enhances cartilage repair in canine models. Notwithstanding, the regenerated articular cartilage's mechanical strength still needs to be examined. While atelocollagen scaffolds provide in vitro cartilage development with sufficient elasticity and rigidity for in vivo use, prematurely degraded collagen scaffolds do not deliver the building character required for ECM deposits in chondrocyte cultures [23-24, 34].

BC composites are effective cartilage substitutes according to some studies. It has identical spontaneous characteristics as natural cartilage and, according to researchers, can meet the criteria for artificial cartilage. Unconstrained compression tests have shown that BC/poly (vinyl alcohol) composites exhibit Young's modulus data identical to real articular cartilage. Though, no in vivo research has been carried out to prove the biocompatibility of BC-based cartilage substitutes [17, 35].

Other organ - One of the body's biggest internal organs, the liver has a complicated structure made up of numerous types of tissues. Toxins can be extracted from the bloodstream and broken down or metabolized by the liver. Toxins, pathogenic microorganisms, and tissue loss due to surgical resection can all cause the liver to self-repair. Liver repositioning is now part of the few treatments for liver illness. One of the most crucial aspects of liver regeneration is the preservation of hepatic function. Hepatocytes cultured on 3D scaffolds had better shape and function than those cultured on 2D scaffolds [36].

Hepatocyte culture has traditionally used type I collagen as the standard material as depicted in Table 1. Chitosan was found to be a better hepatocyte culture scaffold than collagen. Chitosan scaffolds induced more urea production and rounder cell shape in vivo than collagen scaffolds [37]. For Kundu and his colleague's liver tissue engineering, he produced a macropolar scriogel from silk gland fibroin, which may have a naturally occurring RGD sequence. Cliogel, a waterabsorbent material resists mechanical compression without deformation. In addition, the resulting cryogel maintains the survival of human liver cancer cells while preventing aggregation. The equilibrium between cell adhesion and cell contraction controls the shape of hepatocyte aggregates. Cell morphogenesis of human hepatocellular carcinoma cells was controlled in this work by merely modifying the pore shape at different gelation températures (20 and 80 ° C). We tested a cell-free microporous alginate scaffold as a biocompatible matrix that facilitates liver regeneration, according to Synteyer et al. Alginate scaffolds provide a surrogate environment for the surviving hepatocytes, minimizing cell necrosis, improving liver production, and boosting regeneration [38].

Table 1. Some biopolymeric materials which are used as potential biomaterials in wound healing.

S/N	POLYMERS	SALIENTS FEATURES
1	Silk sericin/keratin/fucoidan	Anti-viral, anticoagulant, antithrombic, anti-inflammatory, antitumor
2	Agar/Acetobacter xylinum/Bovine serum	Anti-bacterial, bioactive, cyto-compatible, cell proliferation, biocompatible, cell adherence
3	Arabinoxylan/guar gum/gelatin/collagen	Biocompatible, anti-bacterial, bioactive cytpcompatible, cell proliferation, cell adherence, biodegradable.
4	Hyaluronic acid/Alginate/ xyloglucan / fibrinogen	Anti-bacterial, biocompatible, fibrous protein, fibrous, cell proliferation, adherence,
5	Chitosan/ Beta-glucan	Bioactive, biocompatible, adherence, bioactive molecules release, cell proliferation, antibacterial
6	Petin/ Bacterial cellulose/ carrageenan	Cell adherence, cyto-compatible, anti-bacterial, bioactive, cell proliferation, biocompatible.

Discussions

Numerous research teams engaged in the development of biopolymer-based composites have shown that these materials are a prime possibility for application in tissue regeneration. When creating tissue engineering scaffolds, biological polymers have various advantages over commonly utilized synthetic polymers. Despite recent advancements in the mechanical characteristics, porosity, and bioactivity of scaffolds, additional research is still required to address numerous unresolved issues in the production of scaffolds [39]. To increase their cell-adhesive properties or to actively drive cell migration, proliferation, and differentiation, polymeric medical devices are typically changed by immobilizing growth factor or cell-adhesive binding moieties. The downsides of naturally occurring biomaterials include chemical heterogeneity and high disparity, which affect local degradation rates as well as mechanical characteristics [40], framework, and functionality. Notwithstanding these drawbacks, biopolymers scaffolds have been used satisfactorily in clinical settings to heal human organs, bone, cartilage, skin, and vascular grafts [41–42].

Conclusion

This study examines the use of biopolymers, biocomposite materials, wound healing, tissue remodeling, and advanced operational biomaterials. The mechanical properties of biopolymers, such as their tremendous impact strength, tensile strength, flexural strength, and thermal stability, make them the best alternatives to synthetic polymers manufactured from petroleum. The innovations, improvements, and blending methods that have been employed in the past were discussed. Some biopolymeric materials which are used as potential biomaterials in wound healing were highlighted..

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