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Unraveling the Biomedical Potential of Bacterial Cellulose: A Review of Current Research and Future Directions

Pushpa Reddy[1]*, Soumya Menon[2]*, Umme Javeria[1], Sree Nitya[1], Rajani P.[1]
[1.] Department of Life Sciences-Biochemistry, Indian Academy Degree College-Autonomous, Bangalore 560043, Karnataka, India.
[2.] Department of Chemistry and Biochemistry, School of Sciences, Jain (Deemed-to-be) University, JC Road, Bangalore, Karnataka, India
**Corresponding author email: Email: pushpa.lifesciences@iadc.ac.in; pushpareddymsc@gmail.com*
Email: sweetsou_02@yahoo.com

***Abstract:** Bacterial cellulose (BC) is a type of organic material produced by some bacteria, such as Novacetimonas, Gluconacetobacter, and Komagataeibacter, that is obtained through the process of microbial fermentation. BC has demonstrated itself to be a highly flexible biomaterial with outstanding potential in a range of biomedical applications. Its unique properties, which include high water-holding capacity, biodegradability, mechanical strength, and biocompatibility, make it an appealing choice for a range of applications, such as wound healing, tissue engineering, and drug delivery. This study examines the latest developments in the use of BC in biomedical fields, emphasizing its use in cancer therapies, epithelization, nerve and urethral implants, dermal applications, wound healing, artificial corneas and retinas, drug delivery, anesthesia, and analgesics. In terms of encouraging tissue regeneration, lowering inflammation, and improving general patient outcomes, BC has shown encouraging results. To fully explore its potential and optimize the approaches and strategies for various medical conditions, more clinical research is necessary. To sum up, BC represents a valuable biotechnological response to clinical challenges, and ongoing research holds the promise of expanding its role in improving patient healthcare.*

***Keywords:** Bacterial Cellulose, Biomedical Applications, Wound Healing, Tissue Engineering, Drug Delivery.*

Introduction

As a result of microbial fermentation, bacterial cellulose (BC) finds use in medical supplies, electrical devices, and food additives, among other areas. It can be applied either on its own or in combination with other elements like nanoparticles and biopolymers. This rise in medical engineering products for wound care, organ regeneration, disease diagnosis, and drug delivery has drawn significant attention to biomedical devices in recent years (Mona Moniri et al., 2017). Tissue engineering is an important technique used to reconstruct damaged tissues and organs. In tissue engineering, BC can be presented as a novel and exciting material for use as scaffolds and implants. It is made up of a bacterial-spun mesh of pure cellulose nanofibers. Its strength and capacity for structural and chemical engineering at the nano, micro, and macroscales made an exception. Because of its high water content and purity, the substance can be used in a variety of medicinal applications without harm. It also comprises general details regarding the manufacture of BC by microorganism processes and the development of its nanocomposite (Nathan Petersen and Paul Gatenholm., 2011). The major biomedical applications (Fig. 2) of BC include artificial skin, blood vessels, vascular grafts, scaffold rotation, engineering, and wound dressing. The main methods for creating BC composites are: ex-situ penetration of reinforcing materials into microfibrils or in-situ addition of such components that form a synthetic medium (Nasrullah Shah et al., 2013).In the context of regenerative medicine, BC promotes epithelization and accelerates wound healing by improving cellular adhesion, proliferation, migration, and differentiation.

BC, as a biopolymer, has provided innumerable therapeutic approaches for wound injury management. The studies related to how the mechanisms of these biomaterials affect cell behavior give a better view of how to understand and develop potential repair strategies for various wounds. When BC-based scaffolds were tested on sprague-dawley rats, epithelial regeneration was observed within 14 days, which showed controlled excessive inflammation and a reduction of scavenger receptor-A (SR-A) expression. Furthermore, the BC scaffold is noticed to have stimulated the balance for M1/M2 macrophages that have been reprogrammed for beneficial tissue repair (Cherng et al., 2021). BC is the ideal illustration of a biotechnological solution to a medical issue. It has been very helpful in treating cancer lesions, including skin lesions after radiation and chemotherapy, cell carcinoma, and breast cancer, which is another skin ailment that requires the use of wound dressings. Larger lesions usually have considerable drainage because they are vascularized and necrotized(Cherng et al., 2021). For each of these kinds of skin lesions, the optimum wound dressing needs to protect the wound. In order to absorb wound exudate, accelerate the process of epithelialization for wound closure, lessen discomfort and healing time, and prevent infection, moisture is necessary. However, specialized, targeted therapies that address the needs of each unique lesion are necessary.All of these needs necessitate the use of an innovative, integrative, and adaptable dressing application (Raquel et al., 2019).

The remarkable physico-chemical and pharmacological properties of the BC, along with its exceptional biological performance, are attributed to its surface charge, topography, and wettability. Applications of BC as a non-caloric material have been researched for almost 20 years due to its smooth texture and water-storing capacity. In addition to absorbing a lot of water, BC can exchange cations. Lipids, blood, and cholesterol do not significantly affect plant-based cellulose. It can be utilized as a food additive in foods low in fat and cholesterol (Soon Mo Choi et al., 2023).

A variety of techniques, such as microbial fermentation, physical modification, chemical modification, and compound modification, have been used to enhance biocompatibility and anti-bacterial activity in BC. In order to guarantee a better application in wound healing, burns, diabetic wounds, infected wounds, and acute traumatic injuries have all been treated using BC-based wound dressings, which have demonstrated exceptional therapeutic efficacy in accelerating wound healing. Additionally, certain commercial dressings based on BC have been used in clinical settings (Mosselhy et al., 2021). The genera of acetic acid bacteria (AAB), rod-shaped, gram-negative, obligate aerobes in the family of acetobacteraceae, are home to some of the most well-known producers of BC. These alpha proteobacteria are very important economically because they can oxidize alcohol, aldehydes, sugars, and sugar alcohol to acetic acid when oxygen is present. This facilitates the production of vinegar, Nata de Coco, kombucha,Kombucha and tea in the food business. They are regarded as a principal commercial bacterium that produces BC because of their high production and quick biosynthesis (Potočnik et al., 2023). *Acetobacter xylinum bacteria* produce BC, a polysaccharide with intriguing characteristics for vascular tissue engineering and arterial grafting. These properties include high water content, high burst pressure, high crystallinity, and an ultra-fine, highly pure fibrous structure that resembles collagen. A thorough analysis of BC shows that mechanical properties are necessary to further support its use in cardiovascular grafting applications, as compliance mismatch is one of the primary causes causing initial hyperplasia in vascular replacement surgeries. A study related to BC's mechanical properties also shows its capacity to hold vascular cells. BC samples were subjected to inflation testing and uniaxial tensile testing in order to accomplish these goals. Further, more dynamic compliance assessments were carried out on BC (Zahedmanesh et al., 2011).

Aerogels are highly porous nanoparticles that are combined with BC to perform an important task: obtaining biocomposites for biomedical applications. Aerogels produced using TEMPO-oxidized BC (OBC) exhibited higher mechanical strength and lower shrinkage than those from native bacterial cellulose (NBC). The aerogels prepared from OBC are more durable and have a lower aerogel shrinkage compared to the aerogels obtained from NBC. Novel biocomposites with high antibiotic action against *Staphylococcus aureus* were created using aerogels based on NBC, OBC, and sodium fusidate. As a result of their anti-bacterial qualities, these aerogels can be employed as functional biomaterials in a variety of applications, including tissue engineering and wound dressing material manufacturing (Revin et al., 2019). Properties of different strains of BC producing bacteria are shown in table 1.

Table 1 Properties of different strains of BC producing bacteria

Bacterial Strain	Carbon source	temperature	Medium	Incubation time	PH	Yield(%/day)
Acetobacter xylinum	glucose	30 °C	Casein hydrolase and peptone medium	14 days	5.50	5.29
Enterobacter sp.	Glucose	30°C	H.S medium	24 days	4-6	0.5
Komagataeibacter	glucose	30 °C	HS-agar medium	7 days	4-5.5	1.88g/100ml
Gluconacetobacter xylinus	xylose	28 °C	Schramm-Hestrin (SH) medium	14 days	4-7	Upto 0.482
Komagataeibacter xylinus B-12068	Maltose, mannitol	30 °C	H.S medium	7 days	3.5	0.071-1.571

Saccharomyces cerevisiae CGMCC1670	glucose	30°C	GYP Medium	22 days	5	~0.118

Biomedical Applications

In many biological applications, including prosthetic cornea and retina, nerve and urethral implants, cutaneous applications, medication transport, anesthesia and analgesics, etc., bacterial cellulose is essential. In summary, BC is a useful biotechnological solution to clinical problems, and further study could increase its contribution to better patient care.

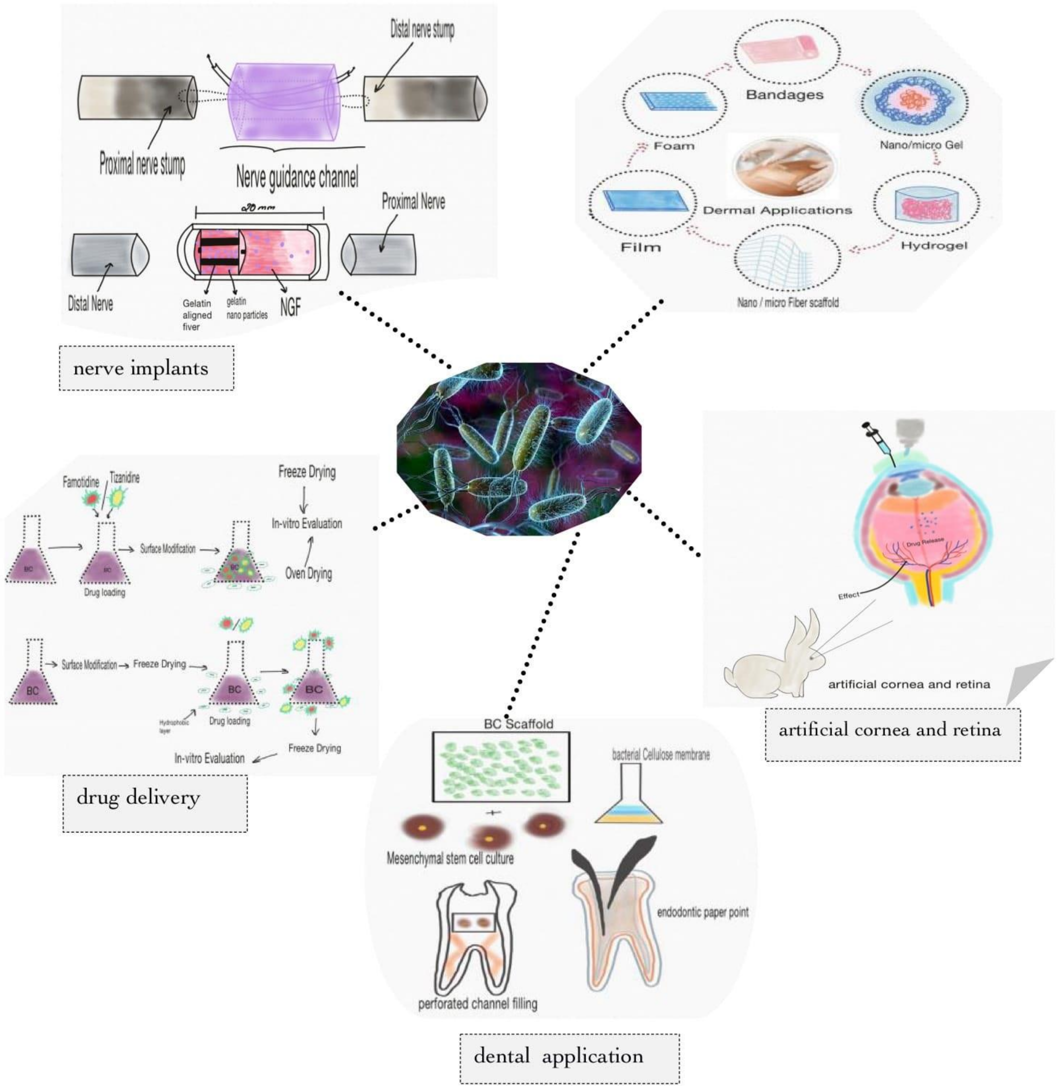

Fig 1: Applications of bacterial cellulose in biomedicine

Artificial Cornea and Retina

Corneal disease is the second-most common cause of blindness. The best treatment option for corneal blindness sufferers is a corneal transplant. Despite corneal transplantation's extensive use and clinical success, some drawbacks include immunological rejection, graft failure, and scarcity of corneal tissue. When considering tissue engineering as an alternative to tissue regeneration, BC has emerged as a promising substrate for the development of corneal stromal cells. There are currently very few instances of corneal regeneration attempts. Selveda et al. (2016) effectively implanted BC and BC-PCL membranes into rabbit corneas. Over the duration of a 45-day follow-up period, the BC and BC-PCL implants maintained their stability in the corneal tissue and safeguarded the ocular surfaces. The findings showed that an inadequate reaction led to a moderate inflammatory response. The findings showed that inadequate epithelialization over the implanted membranes and disordered collagen fibers were the root causes of the mild inflammatory reaction. The biocompatibility evolution of BC scaffolds for corneal stroma TE was examined by Zhang et al. (2019). The biocompatibility of the BC scaffold was evaluated by means of rabbit corneal epithelial and stromal cells. In the BC membrane, a high-transmittance nanofibrous structure was seen. The cornea showed no signs of infiltration under a slit lamp, and the BC insertion was transparent. Seven and thirty days following the procedure, the cornea and BC both appeared transparent. They continued to be translucent for ninety days following the surgery. BC demonstrated strong corneal stromal TE biocompatibility, shown in Fig.1 (Soon Mo Choi et al., 2022.).

Nerve Implants

This article discusses microbiological cellulose (MBC), which is a biomaterial used in the development of neurointegrated devices and nerve implants. It offers benefits over other synthetic polymers because it is flexible, biocompatible, and has the unique ability to record brain signals. Here, the scientists in question used BC to develop a membrane that heals the body from the various side effects of failed back surgery. The BC nanofibers they developed have lessened inflammation and were well received by animals. This text underlines the use of BC in neuroimplants and mentions that it is good for science. Results: rabbit experiments The BC was electrospun onto the back of the rabbits and the experiment was conducted. "Nerve Implants" has this group of tissue samples from the back of the back of the rabbit. It shows how well the electrospun MBC nanofibers were received by fibroblasts. It also shows how much NIH Image J measured them as having full confluence of growth. That is the official word for perfect biocompatibility. In rabbits, the electrospun MBC showed and improved synthesis of collagen fibers and was less inflammed in the early response than controls. This BC was flexible Once it was electrified, it conformed to the surface of the tissues. The mammal body doesn't have pain transducers at all depths. The fat over muscle will keep you from injuring yourself, but it will not keep you warm. The fat well away from muscle will keep you warm, but it will not keep you from injury. BC would have good pain signal, muscle tension and position feedback at any point of collection if BC was used or would have had feedback at any point. This SCI document suggests BC is compatible with any type of tissue, thereby being compatible with any mammal in the world. Electrospun MBC has complete confluence of well living cells. So it was proven to be biocompatible. The collagen matrix in the rabbits was a significant improvement. Electrospun MBC may be the result of BC never sticking to metal and nerve regrowth over muscles of the back in rats stained for a neurotransmitter. Fig:1(Soon Mo Choi et al., 2022.).

Urethral Implants

In the context of urethral regeneration, decellularized matrixes and synthetic polymer materials have been reported to promote tissue regeneration, restore urethral function.5 These are used as scaffolds to facilitate the proliferation and adhesion of new cells. Decellularized matrixes are derived from natural tissues that have been stripped of their cellular components, much like the small intestine or bladder. These provide a framework for the body's own cells to attach and grow, resulting in the regeneration of the urethral tissue. Furthermore, they retain certain properties of the extracellular matrix, which is critical for tissue regeneration. In contrast, synthetic polymer materials, which include hydrogels and biocompatible polymers, have an advantage because their biodegradation rates and mechanical properties can be regulated. They can be fabricated to mimic the structure.6 Research has shown that the implantation of decellularized matrixes or synthetic polymer materials improves the tissue formation and maturation process,4,7 while urethral repair in animal models has been shown to promote tissue integration and remodeling in the case of decellularized matrixes used as scaffolds. The complexity of the anatomy of urethra is copied by the fabrication of synthetic polymer materials. For example, a bilayer scaffold, that is, a smooth outer shell with a porous sublayer of synthetic polymer materials, is designed to mimic natural tissues. This indicates that effective methods have been developed to treat UBMs, and the latter can assist in the process of tissue repair by implanting urethral matrices. The operable efficacy of urethral matrices and synthetic polymer materials have a considerable influence on the operation of urethral construction as well. Furthermore, with the development of these research areas, more advanced urethral matrices are expected. Lv et al. used a biopolymer PU membrane as a urethral reinforcement, which was composed of a bilayer scaffold, that is, a smooth outer shell with a porous sublayer of PS. The purpose of the researchers in this model was to use a bilayer scaffold to simulate the complex structure of the urethra. The porous sublayer provided a microfibrous structure that resembles native tissue and was created using bacterial cellulose. In contrast, the organ-like outer layer, containing gelatinized potato starch polymers, was smooth and contained no holes. It is important to note that in other studies, bilayer scaffolds have been used for tissue regeneration props, although no such results are available from this study using the bilayer scaffold for urethral reinforcement. In another study, Maia et al. (2018) implanted a bilayer scaffold into the urethra of rabbit models. The findings show that the scaffold underwent changes in the wall thickness after 14 weeks of implantation, indicating tissue remodeling and integration. (Soon Mo Choi et al., 2022.).

Dermal Applications

Fu et al. (2012) also provided evidence of these positive effects of BC-based materials in an animal investigation. They found that dressings based on BC slowed down the inflammatory process and hastened wound healing and regeneration. In a different investigation, Fu et al. (2012) employed BC instead of gauze bandages to repair skin tissues in vivo. From a pathological standpoint, differences in the wound healing process were observed depending on how BC was applied. When BC is placed in a thicker layer, it has been demonstrated to have faster effects on inflammation reduction and healing than when BC is applied in a thinner layer. Biofill was the first dressing substance based on BC to be sold commercially. It can be utilized as a temporary skin replacement or as a biological dressing due to its extremely thin layer of 8.5% water content. The low flexibility of this product, which was noticed when the dressing was put in places with considerable mobility, is its lone drawback. Quick pain alleviation, ease of dressing removal, quick healing, tight adhesion to the lesion's surface, and affordability are some of the benefits of the Biofill product. In light of the aforementioned, materials based on BC do not prevent wound infection when it comes to the production of materials containing antimicrobial compounds. BC-based materials are made using physical or chemical processes in conjunction with antimicrobial chemicals to offer defense against the growth of germs. The two types of BC-based materials are those included with inorganic materials (such as Ag, ZnO, and CuO particles and their derivatives) and those incorporated with organic antimicrobial agents (such as lysozyme), depending on the antimicrobial agents employed. Fig:1(Soon Mo Choi et al., 2022.).

Drug Delivery

Lidocaine hydrochloride and ibuprofen were the subjects of an in vitro penetration investigation to assess the therapeutic efficacy of BC membranes. The diffusion cell technique was used to examine the two medicines' diffusion. The two compounds' releases from the BC compounds were examined in relation to three additional standard formulations: ibuprofen gel, lidocaine hydrochloride gel, and PEG400 solution. It was discovered that, in comparison to traditional preparations, the penetration rate of BC compounds was reduced when lidocaine hydrochloride was used. The outcomes are also a result of the materials made of BC having more porosity.

When employing BC nano-composites combined with zinc oxide nanoparticles, a different team of researchers saw strong antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and Citrobacter freundii.* On animal models, the surface of a burn wound was coated with BC/ZnO nanocomposites. Compared to BC, which had a cure rate of 50.5% after 15 days, nano-composites containing BC/ZnO demonstrated a cure rate of 66%.

Khalid et al. (2017) showed good results related to the incorporation of TiO2 in BC-based materials. Additionally, they studied the rate at which burn wounds recover in vivo using human epidermis. When comparing BC/TiO2 to BC, the nanocomposite's antibacterial activity was significantly higher.

Müller et al. (2013) provided evidence in their study regarding the effectiveness of utilizing BC-based materials when administering serum albumin proteins. When compared to the regular BC materials, it was discovered that the freeze-dried BC materials had a lower protein loading. To enable a drug's gradual release, other research teams have experimented with integrating drug molecules into the BC material. Fig:1 (Soon Mo Choi et al., 2022.).

Anaesthesia and Analgesics

Topical anesthetics, like lidocaine, and non-steroidal anti-inflammatory medications, like ibuprofen and diclofenac, can also be mixed with bacterial cellulose because of its opposite hydrophilicity, which offers an alternative foundation for a water-based wound dressing. First, a 5% lidocaine solution was used to soak the bacterial cellulose. Following diffusion assays, ibuprofen was released three times as quickly as commercial dressings with comparable concentrations of the drug lidocaine, but the former was released at a low, steady rate. Diclofenac was loaded onto the bacterial cellulose by soaking it in glycerol containing 5% of it; this caused the cellulose to swell six times more than it would have if it had been pure bacterial cellulose. The release of diclofenac from loaded BC increased by 9%, indicating that bacterial cellulose loaded with non-steroidal anti-inflammatory medication is a better option than transdermal dressings. (Sam Swingler et al., 2021).

Epithelization

After assessing a crystalline fibrillar scaffold's (BC) biocompatibility with human adipose tissue (hASCs) for seven days, the study discovered that BC enhanced cell proliferation and survival. Because of their wide surface area, BC scaffolds promote cell attachment and trigger cytoskeletal protein mediation. The research additionally discovered that BC is capable of preserving stem function, an essential component for tissue regeneration following damage. Additionally, BC can promote keratinocyte differentiation, vital for maintaining the skin epidermis by Cherng et al. (2021). Furthermore, the immunoregulation of a bone marrow (BC) scaffold on macrophages allows us to understand their M1/M2 behavior. The researchers hypothesized that BC could stimulate the balance of M1/M2 macrophage reprogramming, which is essential for cell proliferation and tissue repair. The results showed that BC scaffolds significantly enhanced the expression of iNOS and Arg-1, indicating that BC can control inflammation and function in M1/M2 polarization. The study also found that SR-A, a key inflammatory cytokine, is associated with phagocytosis and waste product uptake. This suggests that BC can control inflammation and promote cell proliferation and tissue repair (Cherng et al., 2021).

Wound Healing Properties

BC has a complicated chemical structure that is held together by hydrogen bonding between water molecules. BC fibers are made up of linear chains of glucan units connected by -1,4 glycosidic linkages. The glucan chains are connected by inter- and intramolecular hydrogen bonds, allowing BC to be mechanically strong while remaining pliable. The free water (unbonded) that can access and exit the BC molecular structure oversees maintaining the hydration level, which is critical for wound dressing application. The BC water holding capacity (WHC) is proportional to the available pore volume and surface area. WHC values are lower in a more compact BC structure with denser fibril configurations and lower pore volume and surface area by Wang et al. (2012). The available space and number of trapping sites to collect water molecules are reduced in such fibril formations. Denser microfibrils result in more water being retained in the system due to the creation of hydrogen bonds and less free bulk water,preventing water evaporation (Gelin et al., 2007).

Aerogels

The oxidation of carbon (BC) has improved the process of obtaining aerogels from OBC, resulting in reduced shrinkage and increased strength. This is beneficial for applications like thermal insulation and medical composite materials. However, the strength of BC aerogels decreases with lower density, making it necessary to maintain high strength at low density. Divalent metal ions were used to create cross-links between two carboxyl groups, resulting in a four- to five-fold increase in strength. This method is simple and does not require further modification of BC. The aerogels can be used as heat-insulating or sound-insulating materials due to their low thermal conductivity. However, heavy metals may be advisable for medical materials due to their antimicrobial properties. The inclusion of Mg2+ in the aerogel composition led to a more uniform microporous structure, resulting in a decrease in thermal conductivity coefficient (Revin et al., 2019).

Cancer applications

In cancer therapies including nano therapies paired withcancer therapies including Nano therapies paired with stimuli-activated agents have emerged as viable alternatives to standard chemotherapy. Primarily coated with hydrogels followed by the loading of a monomethyl ether like hematoporphyrin and doxorubicin made up the core of Fe_3O_4 nanoparticles. Laser-sensitized magnetic nanoparticles (LMNs) were prepared by grafting folic acid on the surface for the constituents which were then put into the BC membrane.

Post the 14th day of targeted treatment the tumor growth inhibition (TGI) was estimated at 80.38% . This newly modified BC/LMNs have been observed to provide a variety of satisfactory answers to the challenges faced by enhancing transdermal drug administration that are either guided by a magnetic field or laser ,including low penetration depth by intervening with the stratum corneum barrier (Ling-Kun Zhang et al., 2019).

Photo Dynamic Therapy of Skin Cancer

Since the majority of photo-sensitizer chemicals are hydrophobic, it is becoming more and more crucial to design drug delivery methods for photodynamic therapy (PDT). A high loading capacity and huge surface area make bacterial cellulose (BC), a very pure cellulose produced by bacteria, ideal for use in drug delivery systems. BC membranes encapsulating photo-sensitizer chloroaluminum phthalocyanine (ClAlPc) were studied with the goal of using them as a medication delivery system for PDT skin cancer procedures. The thickness and optical transmission of BC membranes were tuned throughout the manufacturing process. Thinner membranes result in greater relative incorporation efficiency. Pig's ears were used as a skin model for in vitro skin permeation and retention studies. ClAlPc was found in the stratum corneum and epidermis/dermis, indicating that it has appropriate characteristics for topical delivery by Peres et al. (2016). The work demonstrated the viability of employing BC as a matrix for photo-sensitizer inclusion and controlled release. By altering the bacterial strains and production durations, varied characteristics of BC membranes were achieved. FTIR spectra confirmed the interaction of the BC with ClAlPc. The findings revealed that the structural features of membranes (such as thickness, number of fibers, and surface area) are related to drug incorporation efficiency. The permeation and retention profiles found for BC-ClAlPc support the use of this system in topical delivery throughout the PDT procedure. ClAlPc's photophysical characteristics are unaffected by its inclusion in BC membranes. Furthermore, these membranes showed no in vitro cytotoxicity, indicating their potential for safe biological usage (Peres et al., 2016).

Artificial Blood Vessels

Cardiovascular diseases (CVDs) are the leading cause of death or impaired quality of life for individuals worldwide. Although progress has been made in preventing and treating CVDs, the global spread of smoking, increased cases of diabetes, and a growing aging population have elevated the incidence of CVDs by Lee et al. (2017). Bacterial synthesized cellulose (BASYC) has been utilized successfully in rats and pigs for carotid artery implantation and long-term maintenance. Other tests of BASYC tube prostheses for rat blood vessels have revealed that the implanted BASYC tube becomes completely merged with the carotid artery and the aorta. Recently, in vivo biocompatibility has been discovered. The endothelialization of BC tubes was found to be complete, with a confluent endothelial layer and no macroscopic evidence of inflammation around the implants. Scherner et al. (2015) demonstrated that BC grafts serve as a scaffold for cell ingrowth and neoformation of a three-layered vascular wall, indicating that BC is a potential biomaterial. Furthermore, a study investigating the relationship between leukocytes and prosthetic BC in the presence of vascular inflammation demonstrated no toxicity or immunoreactivity. An innovative strategy for scaffold preparation was to include a co-former in a culture of *G. xylinus*. The BC-GO composite made by adding graphene oxide demonstrated improved biocompatibility, cell stimulation, and proliferation. Similarly, Andrade et al. (2015) demonstrated that endothelial cell adhesion was improved by modified BC and angiogenesis was stimulated. As a result, advancements in the usage of BC composites have a significant potential for use in implants of artificial blood vessels (Lee et al., 2017).

Dental Implants

As a biomaterial for dental and oral applications, bacterial cellulose exhibits considerable promise. It has mostly been applied to the healing of oral mucosal surgical wounds, periodontal regeneration, and dental pulp tissue regeneration. Furthermore, the use of bacterial cellulose in dental root canal therapy has been investigated as a way to completely eliminate residue and dry the canal. This study details several studies on bacterial cellulose that are targeted at these uses, along with benefits, drawbacks, and significant findings from assessments conducted both in vitro and in vivo, taking into account the anatomical and physiological elements of the specific tissue. Additionally, in comparison to other biomaterials, this work describes the characteristics and benefits of bacterial cellulose in dental and oral applications.Lastly, composite materials based on bacterial cellulose and inspired by biological tissue are suggested for alveolar bone regeneration in the new era of biomaterials (Cañas-Gutiérrez et al., 2020).

One of the main issues with dental implants is their absorption into the surrounding tissue. Furthermore, for bone regeneration to occur, total osseointegration between the implant and bone is required. Due to BC's excellent mechanical strength, superior volume retention, and strong absorptive capacity, it may be a viable option for commercial dentistry applications. Compared to other paper point materials, BC offers biological properties, tensile strength expansion, and absorption, which have been demonstrated in a few studies as dental canal therapy or oral field applications. Under damp conditions, the BC retains good mechanical qualities and an excellent capacity for absorption and expansion (Choi et al., 2022).

BC membranes were created by An et al. for directed bone regeneration. To break BC's glucose bonds, electron beam irradiation was used. The EI-BC was evaluated in vitro to determine NIH3T3 cells' cytocompatibility. The EI-BC membrane's in vivo biodegradability and bone regeneration outcomes after 4 and 8 weeks in rat calvarial models demonstrated its ability to effectively connect with cells and stimulate bone regeneration. In a similar vein, we created a promising BC-Hap composite coupled with osteogenic-generated peptide (OGP) for the regeneration of critical-size calvarial lesions in mice. At 60 and 90 days, the incorporation of OGP increased the gene expression of bone biomarkers including Tnfrsf11b, Alpl, and Spp, suggesting that composites may be useful for bone regeneration in mice with critical-sized calvarial lesions (Choi et al., 2022).

The alveolar process's height presents challenges for dental implant insertion in the posterior maxillary region. BMP-2-loaded BC was created by Koike et al. (2019) to enable efficient alveolar bone augmentation; BC preserved the graft area and continuously delivered BMP-2 to encourage the best possible bone development. In the maxillary sinus, the combination of BC and BMP-2 may improve bone regeneration and be helpful for clinical pre-dental implant-bone augmentation (Choi et al., 2022).

However, surgical lesions to the oral mucosa provide significant challenges in the field of dentistry. Moderate lesions can be treated with split or full-thickness grafts, whereas small flaws typically heal mostly on closure. When a defect affects the majority of the buccal mucosa, another surgical site must be used. Chiaoprakobji et al. (2022) created a unique three-dimensional composite made of BC-SA (BCA) for this purpose. HaCatcells, a keratinocyte cell line, were seeded on the BC and BCA scaffolds in this investigation. The findings indicate that the BCA scaffold exhibits promising potential for covering surgical wounds in the oral cavity. Similar to this, Jinga et al. (2021) employed commercial mineral trioxide aggregate as a reinforcing material along with cellulose whiskers. According to the study, BC reduced the proportion of calcium hydroxide crystals and quickened the mineral trioxide aggregate cement's hardening process. Fig:1 (Choi et al., 2022).

Critical Analysis

BC is considered one of the best materials to fit the newest trend because of its unique and inherent qualities, which include low viscosity, high water holding capacity, tolerance to acid, salt, and ethanol, as well as biocompatibility, non-toxicity, biodegradability, gas permeability, suspension stability, and low viscosity. Additionally, they are recyclable and eco-friendly, which could provide components that aren't derived from petroleum (Choi et al., 2022). A variety of techniques, such as microbial fermentation, physical modification, chemical modification, and compound modification, have been used to enhance the biocompatibility and anti-microbial activity of BC in order to guarantee a better application in wound healing. Burns, diabetic wounds, infected wounds, and acute traumatic injuries have all been treated using BC-based wound dressings, which have demonstrated exceptional therapeutic efficacy in accelerating wound healing. Additionally, certain commercial dressings based on BC have been used in clinical settings (Mosselhy et al., 2021).

The aforementioned study highlights the numerous developments in the use of BC as a biopolymer for a range of biomedical applications, such as the treatment and repair of wounds. It shortens the time needed for the damage to recover and has been shown to be very effective. Comparatively speaking, the adverse effects are smaller than those of other conservative therapy modalities. Due to its many qualities, such as its strong tensile strength and ability to hold water, BC helps to properly close wounds by covering the affected region more extensively. However, as we correctly said, there are some drawbacks to BC's way of repair, which might differ from person to person depending on their underlying diseases as well as the methodologies and strategies involved. In addition, additional clinical trials need to be considered in order to maximize outcomes.

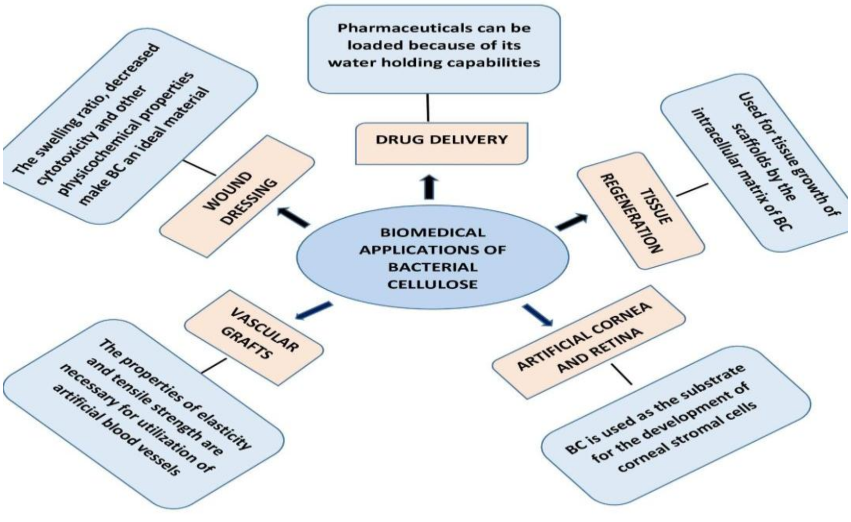

Fig 2: Biomedical applications of bacterial cellulose

Conclusion

In conclusion, bacterial cellulose (BC) stands out as a versatile and safe biomaterial for various therapeutic applications. Its unique properties, such as high tensile strength, porosity, and antimicrobial efficacy, make it ideal for wound dressings, dental grafts, and antibiofilm treatments. While BC shows great promise, efforts to scale up production are essential. Creating new fermenters and utilizing advanced biotechnological techniques can help reduce production costs and make BC more accessible for future biomedical devices. BC is positioned to make a big contribution to the field of biomedicine because of its potential and adaptability. In the realm of corneal disease, BC scaffolds offer a beacon of hope for patients suffering from blindness, mitigating the drawbacks of traditional transplantation through enhanced biocompatibility and tissue regeneration. Similarly, in nerve implantation, BC's flexibility and biocompatibility pave the way for improved outcomes in neurointegrated devices, heralding a new era in neural engineering.

Urethral regeneration and dermal applications further underscore BC's versatility, offering solutions to complex challenges in tissue repair and wound healing. Through decellularized matrices and drug delivery systems, BC demonstrates its prowess in promoting tissue integration and therapeutic efficacy, offering novel avenues for clinical intervention.

In cancer therapy and cardiovascular applications, BC-based nanocomposites and artificial blood vessels present groundbreaking approaches to disease management and tissue engineering, highlighting BC's potential to revolutionize treatment modalities and patient outcomes.

In the realm of dental and oral healthcare, BC emerges as a formidable candidate for tissue regeneration and implantology, offering superior mechanical properties and biocompatibility for enhanced therapeutic interventions.

As we navigate the frontier of BC research and innovation, collaboration between scientists, clinicians, and industry stakeholders becomes paramount. By harnessing BC's unique properties and advancing novel techniques, we can unlock its full potential to address unmet clinical needs and improve patient care.

The journey of bacterial cellulose in biomedicine represents a testament to human ingenuity and scientific advancement. As we continue to explore its applications and refine its functionalities, BC stands poised to revolutionize the landscape of regenerative medicine, offering hope and healing to millions worldwide.

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