Bioinspired Materials Inherited with Antimicrobial Properties for Tissue Engineering

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Abstract

The advancement in the preparation of biomaterials that possess tissue engineering applications has predominantly concerted on developing biomimetic materials inherited with the properties of designing new tissue and very definite in cellular responses. The tissue generation is owed by identifying specific biomolecules which can be influenced by changing the microenvironment. Tissue engineering scaffolds and drug delivery systems are gaining huge interest these days. However, one of the common threats associated with the insertion of an implant is the colonization of pathogenic microbes and the development of bacterial/fungal or mixed biofilms in the implant. Theoretically, biomimetic materials mimic the functions of extracellular matrix (ECM) in tissues; therefore, biomimetic scaffolds can offer biological signals for cell-matrix interactions to promote tissue growth. Various biodegradable polymers are used as a base for

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local drug delivery or temporary sustenance for tissue regeneration. These polymers are disintegrated nonenzymatically through hydrolysis or by particular enzymes. Excellent biocompatibility marks them as competent material for various medical purposes. Nevertheless, the renewal of living tissue and the capability to preclude microbial colonization should be considered while fabricating materials for implant construction. This chapter gives insight into the background and applications of biomaterials with antimicrobial properties and the prospects of bioinspired materials.

Keywords

Antimicrobial activity · Cells · Biomaterials · Tissue engineering · Implants

8.1 Introduction

Nanomaterials possess outstanding properties, such as distinctive optical, magnetic, and electrical characteristics, and these materials have dimensions in the nanoscale (1–100 nm). These nanotextured materials are utilized as healing medicines and for designing devices (Ali et al. 2021). As their dimensions are reduced to the nanoscale, they exhibit plentiful exceptional properties, making these materials distinct from customary macromolecules. Representative characteristics commonly inherited by nanomaterials are high surface-to-volume ratio, enhanced electrical conductivity, superparamagnetic behavior, the spectral shift of optical absorption, and distinctive fluorescence characteristics.

Considering the versatility of nanotextured materials, they have been extensively utilized in the medical field, such as the use of nanomaterials in drug transference, well-ordered discharge systems, etc. Their amplified penetrability permits crossing biological barriers and enhances biocompatibility (Cheng et al. 2021). The interesting topological features and nanorange dimensions of nanomaterials have boosted permeability and retention effects, thus facilitating the achievement of additional entry to the cubicles of cells and tissues. Various parameters such as dimension, morphology, and surface chemistry of nanotextured materials can be automated using physiochemical tools, therefore, can provide exciting features such as the potency of nanomaterials to design many arrangements, including particles, fibers, and porous sponges. These aforementioned nanotextured materials are being utilized as scaffolds for application in medicines and the healthcare system (Zhang and Wang 2019). Furthermore, nanomaterials have been proven to demonstrate auspicious potential in crucial industries, specifically in nanomedicine, pharmacology, and the biomedical field (Albalawi et al. 2021). Profitable funding has been invested in nanotechnology research, and by the year 2024, the global nanotechnology market is expected to surpass USD 124 billion, with ~50% of the market falling in Asia Pacific states (Pinto et al. 2020).

8.2 Outline and Background of Nanomaterials and Nanofibers

Electrospun fibers are frequently described as nanofibers with dimensions roughly as thin as 500 nm. These e-spin nanofibers were primarily employed in the Soviet Union in 1938 to construct air filters to trap aerosol particles. In 1939, this effort managed to project a factory for engineering smoke filters, with nanofiber-based mats as gas masks. Throughout this period, a mechanistic understanding of electrospinning was gradually established. During 1964–1969, Geoffrey Taylor handed out several revolutionary articles, presenting mathematical models that indicate the spherical to conical silhouette alteration of polymer solutions under the impact of a robust electric current (Xue et al. 2019). Precisely, as the strength of the electric field was amplified up to a specific dire limit, the spherical droplet would progressively change into a cone (denoted as Taylor cone) and spring as a liquid jet. Later on, it would take 20 years to develop the electrospinning technique, and during this period, it did not get considerable attention from academia or industry. This inactive period was due to a lack of characterization tools; however, researchers were gifted with tools capable of measuring dimensions down to the submicrometer assortment. However, an assortment of useful applications was projected for e-spin fibers throughout this era, counting their prospective usage as wound dressing materials demonstrated by a patent (filed in 1977). During the initial 1980s period, Donaldson Co. Inc., headquartered in the United States, started to construct and sell filters consisting of e-spin fibers for air filtration. However, the company kept the manufacturing strategy of goods confidential.

Many research teams, particularly those led by Darrell Reneker and Gregory Rutledge (early 1990s), rediscovered this technique with the aid of electron microscopes possessing resolving capabilities down to the nanometer range. These scientists established that diverse organic polymers could be electrospun into nanofibers, and the term electrospinning was propagated for unfolding this practice. These investigations conveyed innovative connotations about electrospinning, and this technique ultimately converted into the method of choice for manufacturing extended and incessant fibers having dimensions down to the nanometer range.

Nevertheless, by now the electrospinning has begun to achieve accumulative consideration by designing novel materials and formulations, such as the construction of composite as well as ceramic nanofibers (Larsen et al. 2003). These unique fibers have innovative applications in various fields, such as catalysis, energy harvesting, conversion, and storage, which were previously dominated by nanoparticles. On the other hand, innovative approaches have been established to manage the assembly and arrangement of electrospun nanofibers. Nonetheless, these fascinating nanofibers flagged huge opportunities in energy-related and biomedical applications. A lot of approaches have been made for aligning the nanofibers, such as the possibility of diverse syndicate characteristics originating from size, structure, composition, morphology, porosity, and assembly of nanofibers. At the same period, coaxial electrospinning was settled to harvest continuous core-shell and hollow nanofibers and yarns of electrospun nanofibers. Currently, industrial production of electrospun nanofibers has been implemented by numerous companies throughout

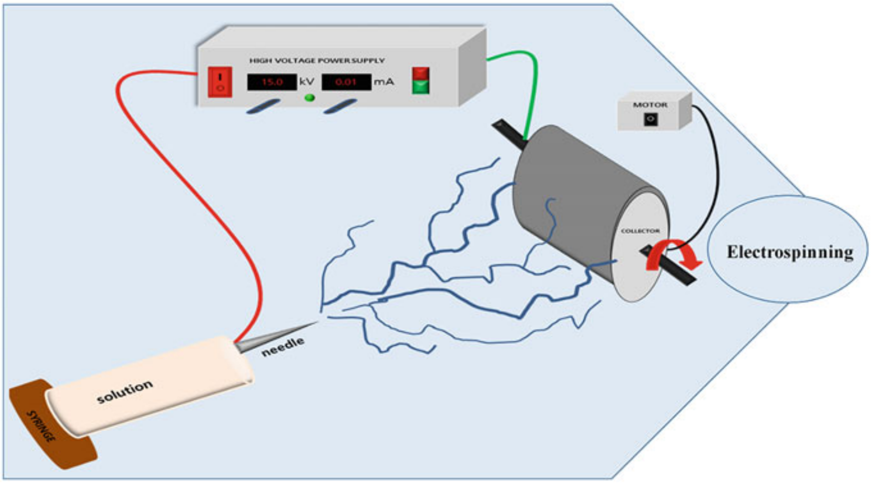

Fig. 8.1 Schematic representation of an electrospinning arrangement for nanofiber fabrication

the globe to produce nanofibers in huge volumes, approving downstream commercial products. Nowadays, these electrospun nanofibers are extensively utilized for water purification, air filtration, wound dressings, implants, etc. (Fig. 8.1). Figure 8.1 demonstrates the basic design of electrospinnig set up.

8.3 Bioinspired Nanomaterials

Nanotextured materials possess essential features, such as reduced size and shape, which are useful in various fields and trades. Nanoparticles and nanomaterials are manufactured on a considerable gauge and are necessary for several industries. This fact has supported research in various disciplines of science such as biochemistry, biophysics, and biochemical engineering and of course, the applications. The combination of nanotechnology and other disciplines has resulted in the fabrication of novel and interesting nanomaterials utilized for diagnostic tools, drug delivery systems, energy storage materials, and conservational and food processing (Barhoum et al. 2022). These nanotextured materials are diverse in size, silhouette, magnitude, configuration, permeability, stage, and consistency. Therefore, various classifications have been utilized to categorize them. Moreover, nanomaterials can be classified as natural, incidental, bioinspired, and engineered, depending on their origin and functionality. Nevertheless, it has been documented that the naturally occurring nanomaterials form all through natural physiological procedures. On the other hand, the incidental nanomaterials, also known as anthropogenic or waste particles, transpire due to simulated industrial procedures. Similarly, engineered nanomaterials are prepared in the laboratory/or in industries to attain materials with definite topography. However, bioinspired materials are nanomaterials that resemble/or imitators of those natural nanomaterials or living stuff. Nowadays engineered and bioinspired nanomaterials are attaining huge consideration compared to natural materials due to variability.

Thus expanding the progressive nanofabrication tools, various bioinspired nanomaterials with exact functions can be fabricated by curbing their configurations (Lee et al. 2017). For instance, mechanochromic elastomers have been developed that mimic the photonic structure of chameleon iridophore cells (Rasouli et al. 2018). In these sensors, rigid silica nanocrystals are rooted in an elastomer's background to form non-close-packed crystals. These sensors exhibit a color shift from red to blue during stretching and red to green during compression. Conclusively, biomimetic synthesis is aimed either by mimicking functions of natural materials, structures or the biological processes and are classified as functional biomimetic synthesis and biomimetic process synthesis (Zan and Wu 2016). Up till now, numerous bionanomaterials have been styled (Table 8.1), and many more will be established.

However, despite their particular possessions, only insufficient engineered and bioinspired nanomaterials have been permitted and utilized in the industry due to the limitations of risk assessment practices. In this chapter, our primary focus will be on novel bioinspired materials possessing antimicrobial properties, which are used in tissue engineering and other medical and biomedical fields.

8.4 Overview of Tissue Engineering

Precisely tissue engineering is an up-and-coming biotechnological field that syndicates different features of medicine, cell, and molecular biology, materials science and engineering with the aim of regeneration, restoring and substituting ailing tissues. The term tissue engineering was formally devised by Fung in October 1987 at National Science Foundation Workshop in Washington, D.C. and since the preceding epoch, this field has progressed from scientific narration to science statement possessing research-based acceptance. Tissue engineering necessitates inclusive determinations to conglomerate engineering and physical sciences with life sciences, with the objectives of repairing, interchanging, and refining the functions of impaired tissues and organs (Shafiee and Atala 2017). Tissue and organ failure due to injury or disease has been reflected as the main healthcare trials. Until the second half of the twentieth century, there were no appropriate therapies for patients with dysfunctional organs. However, in 1954, Joseph Murray, Nobel Laureate in Medicine during the 1990s, completed the first successful organ transplant, transferring a healthy kidney donated by Ronald Herrick to his identical twin brother, Richard (Renal homotransplantation in identical twins 2001). The process was guaranteed as risk-free as the donor and recipient were both genetically alike. Later on, almost after 5 years, Murray executed the world's first successful organ transplant among genetically non-identical individuals. Through his pioneering operations, many lives have been saved with organ transplantation. Meanwhile, the high number of people waiting for transplants, the scarcity of organ donors, and the massive aging population demand the progression of innovative approaches

Table 8.1 Summary of some of the recently developed bioinspired-material-based scaffolds and their respective applications published by various researchers

S. No.	Bioinspired scaffolds	Applications	Reference
1.	Pd-Ag-HAP on protruded TiO_2	Dental implant	Jang et al. (2018)
2.	Anodized titanium	Dental implant	Mühl et al. (2022)
3.	Triphasic calcium-based implant (AGNI)	Bone implant	Shaul et al. (2022)
4.	Zirconia-containing biphasic calcium phosphate	Bone implant	Youness et al. (2022)
5.	Poly(L-lactic acid)/mesoporous bioactive glass composite	Bone implant	Pant et al. (2022)
6.	Poly(xylitol-dodecanedioic acid)–co-polylactic acid	Tissue engineering	Sotoudeh et al. (2021)
7.	Hydroxyapatite nanowhisker-reinforced poly (lactic acid) composites	Bone implant	Xu et al. (2022)
8.	Chitosan/gelatin/polycaprolactone	Bone scaffold	Wulin et al. (2022)
9.	Polyurethane (PU)/chitosan (Cs)/carbon nanotubes (CNT)	Cardiac tissue engineering	Ahmadi et al. (2021)
10.	composite alginate-gelatin hydrogels incorporating PRGF	Human dental pulp and cell proliferation	Anitua et al. (2022)
11.	Curcumin-loaded mesoporous silica nanoparticles/nanofiber composites	Stem cell proliferation	Mashayekhi et al. (2020)
12.	Folic acid.MgO:ZnO/chitosan hybrid particles	Fibroblast cell proliferation	Rafie and Meshkini (2021)
13.	Chitosan/aloe vera hydrogel	Wound dressings	Movaffagh et al. (2022)
14.	*Spinacia oleracea* extract incorporated alginate/carboxymethyl cellulose microporous scaffold	Bone tissue engineering	Sharmila et al. (2020)
15.	Cellulose nanofiber scaffold	Bone tissue engineering	Chakraborty et al. (2019)

to repair the functions of impaired organs (Atala 2012). According to the US Department of Health and Human Services (https://optn.transplant.hrsa.gov), statistics indicate that in the United States, a new individual is added every 10 min to the National Transplant Waiting List and that 22 individuals pass away every day waiting for a transplant. Indeed, tissue engineering aims to alleviate the life-threatening unavailability of donor organs using in vitro production of biologically functional assemblies. To sum up, in tissue engineering, rudimentary design tactics comprise simply cell assemblies, cells and scaffolds, and solitary scaffolds. Unambiguously, autografts, allografts, and xenografts are biological paradigms constructed from a patient's cells, from other genetically non-identical organisms, as well as even non-human animal species, respectively. Alternatively, the scaffolds are developed from natural (e.g., collagen, decellularized matrices) or synthetic materials and are intended to reproduce a natural three-dimensional (3D) environment, i.e., the extracellular matrix (ECM) in order to make the cells and tissues to flourish and establish into organs that can conserve their specific conformations and topographies. Additionally, these scaffolds should be compatible with the tissue-specific cells and the preferred indigenous atmosphere within the human frame (Langer 2009). Consequently, diverse engineered tissues or/organs require distinctive preparations and constituents. Furthermore, synthetic scaffolds must be synthesized, considering important features such as pore dimension, geometry, penetrability, and spatial dissemination (Khademhosseini et al. 2006). It has been well documented that the bulk and exterior physiognomies of scaffold materials can also influence cellular performance (Khademhosseini et al. 2006). Finally, the degradation of the scaffold must be attuned to the construction of ECM by cells (Fig. 8.2).

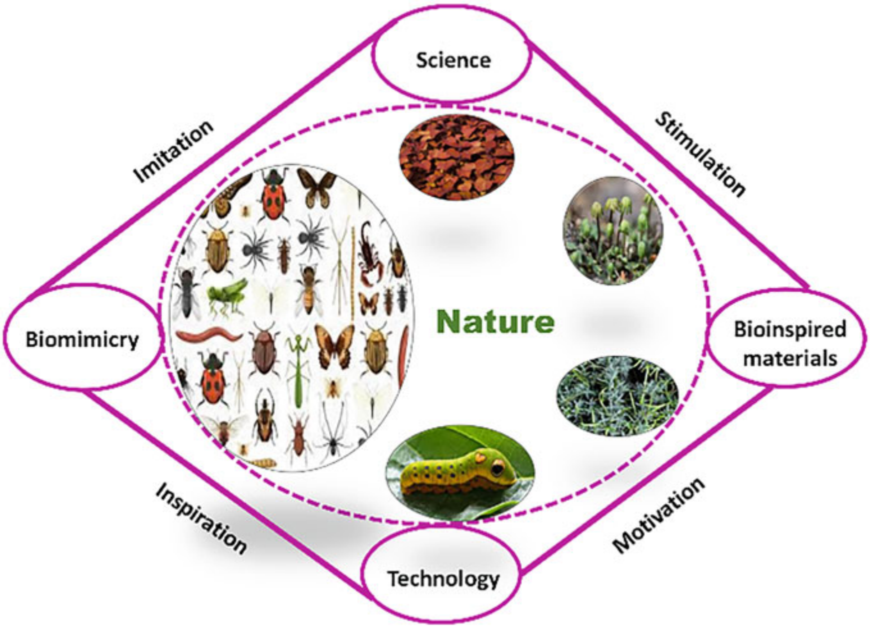

Fig. 8.2 The stepladders and biomimetic/or bioinspired materials in the tissue engineering process. Different levels of processes that can be used for biomimetic synthesis are compiled. The current progress of bioinspired/biomimetic synthesis is systematically summarized according to the following perspectives: motivation, inspiration, stimulation, imitation, and the fusion of science and technology

8.5 Tissue Engineering and Regenerative Medicine

Current progress in scaffold fabrication has boosted the arena of tissue engineering toward sophisticated objectives. A reasonably novel approach in scaffold-free tissue engineering has been presented that allows cells to yield their own ECM and self-assemble to build 3D biological configurations. Tissue engineering is one of the main subjects in regenerative medicine. For instance, the stem cell discipline, gene remedy, soluble molecules, and reprogramming of cell and tissue types are crossing points between tissue engineering and regenerative medicine. During the past 20 years, numerous accomplishments in the assembly of functional tissues and organs have aided in upgrading the quality of life of ailing individuals. The preparation of tissues and organs can be grouped into four main stages. The first and the least complex stage involves flat tissues and organs, such as the skin; the second stage includes the construction of tubular organs, for example, blood vessels and tracheas. Hollow nontubular organ assemblies such as the bladder are the second utmost organs to construct and the most multifarious structures are solid organs, such as the heart, kidney, liver, etc. Several research scientists all over the globe with different disciplines and specialties are occupied to fulfill the projected demands and encounter the challenges in this area. The initial challenge in engineering a tissue/organ is the discovery of suitable cell sources and a sufficient number of cells. The next important step is to provide refined biomaterials and scaffolds to permit all cell types in an organ to make an effort to organize in coordination in order to shape their own ECM (Atala 2009).

Significant progress in stem cell therapies, biomaterials science, and the design of delivery systems able to mimic the production of growth factors will possibly aid treatment breakthroughs for various deadly ailments. Nevertheless, encouraging outcomes of in vitro and in vivo investigations cannot always be of practical use in clinical situations. Consequently, these situations remind us to sidestep the naive interpretations as well as exaggerated optimism concerning innovative technologies (Hassanzadeh et al. 2018). In addition to scaffold and cell-centered approaches, tissue engineering also includes other methodologies to enable the repair of organs and restore their purposes (Naughton 2002). Furthermore, it has also been accredited that the usage of polymer matrix offers stability as well as an organized release profile for proteins as well as for important growth factors (Langer and Moses 1991). Tissue engineering implants are also cherished devices comprising bioactive ingredients (Blanquer et al. 2012). The fabrication of practicable constructs requires the supply of easy-to-harvest cells proficient in differentiation into particular cells which lack immunogenic properties. For instance, the mesenchymal stem cells captured in penetrable biomaterial capsules have revealed anti-osteoarthritis chattels allocated to their regenerative effects (Stock and Vacanti 2001). On the other hand, polymers (e.g., polylactic acid (PLA), polylactic-co-glycolic acid (PLGA), hydrogel, etc.) have already been utilized for the design of 3D tumor models. Meanwhile, the progress of in vitro models proficient to reconstruct the process of tumor progression is a challenging issue in cancer research (Loessner et al. 2010). However, the use of 3D cultures offers the opportunity for improvement in capturing the construction of tumors, cellular imaging as well as high quantity screening.

8.6 Tissue Engineering in Healthcare Systems

As aforementioned, tissue engineering is quickly growing scientific area that utilizes the principles and methods of physical sciences, life sciences, and engineering to apprehend physiological and pathological methods to improve current therapeutic systems. Currently, tissue/organ transplantation, surgical operation, and dialysis are common cures in most countries. But still, limitations associated with these procedures have resulted in amplified awareness in the field of tissue engineering (Lee et al. 2010). In this regard, categories such as autologous or allogeneic cells can be cast off. Alternatively, some other reports have suggested the use of exogenous cell-oriented and endogenous cell approaches (Li et al. 2017), such as the administration of chemokines as signals potentiate cell homing in an anti-inflammatory microenvironment (Aibibu et al. 2016; Andreas et al. 2014). More to the point, cells may be genetically or epigenetically reformed (Sheyn et al. 2010) to augment the efficacy of tissue regeneration. The shortage of in vitro engineered tissues is partly owing to the inability to create engineered blood vessel systems (Lovett et al. 2009). Interestingly, in certain cases, such as in tissues like the skin, cartilage, or cornea, cells can be delivered through diffusion from distant blood vessels. The engagement of endothelial cells for neoangiogenesis and revascularization by biomolecules parenthetically is a common tactic.

The inference from the aforementioned reports is that tissue engineering has the prospective future to transform approaches of health care systems to mend for the excellence of life. Additionally, it will deliver an economical and long-lasting solution to numerous age-related illnesses. Moreover, the engineered tissues may lessen the requirement for an organ transplant (Fig. 8.3).

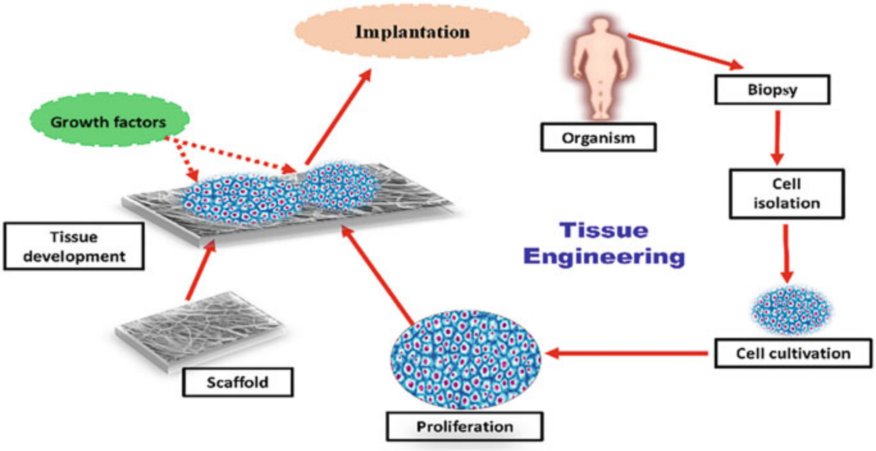

Fig. 8.3 The schematic illustration of probable steps of the tissue engineering procedure

8.7 Antimicrobial Bioinspired Materials

Undeniably a significant number of novel biomaterials and scaffolding structures are designed to exploit them in medical and biomedical areas possessing augmented healthiness potency (Spałek et al. 2022). These biomaterials are being utilized in implantable procedures or drug delivery systems that have noteworthy influences on the quality of life of diseased individuals. Conversely, their continuing exploitation and usage can cause invasion and multiplication of microbes, which may result in biofilms and consequential elicit cytotoxic reactions. These pathogenic microbial infections ultimately result in the failure of implants. Furthermore, they can hamper the distribution of drugs, thus rendering them ineffective. Numerous substitutes have been suggested over the years to avoid such complications, such as the practice of disinfectants, and antibiotics as well as the amendment of posturing lines of biomaterial, amalgamation of biomolecules. In this regard, various stimulating functionalization and alteration procedures have been engaged to encounter opportunist as well as pathogenic microbes (Spałek et al. 2022; Teixeira et al. 2021, 2022; Felgueiras 2021, 2022; Felgueiras et al. 2021; Miranda et al. 2020). Similarly, a report has been published in which collagen-constructed biomaterials fixed with nano clay depicted excellent antimicrobial potential and has been utilized for skin rejuvenation applications (Marin et al. 2021). Likewise, well-characterized skin derivative human defensins antimicrobial peptides have been investigated and their impact on the oozing of angiogenin, (a persuasive angiogenic factor) has been depicted. They discovered that numerous human defensins could arouse the delivery of angiogenin despite sustaining their antimicrobial and other immunomodulatory features (Umehara et al. 2022). Conclusively, it has been comprehended those various strategies, such as understanding of the antimicrobial activity of specific biomaterials and introduction of novel surface amendments, incorporation of bioactive molecules, formation of organic-inorganic composites, etc., can be adapted for the control and complete elimination of microbial infections from the designed implants for successful operations and functionality. Figure 8.4 depicts the schematic illustration of probable steps of the tissue engineering procedure.

8.8 Future of Bioinspired Materials

From the aforementioned discussions and literature scan, it has been agreed and implied that bioinspired nanomaterials are novel choices for various diseases, such as cardiovascular ailment (Bose et al. 2021). Subsequently, Bountiful research conducted during the decades have resulted in the outcomes in which it looks like numerous materials are overcoming their performance limits (Wegst et al. 2015). The fusion of 2D nanotextured materials and the idea of bioinspiration has stimulated the establishment of innovative materials and techniques (Zhang et al. 2020). Contrariwise, there are up now loads of trials and challenges to be resolved that bound the progress of bioinspired nanomaterials/technologies beyond 2D

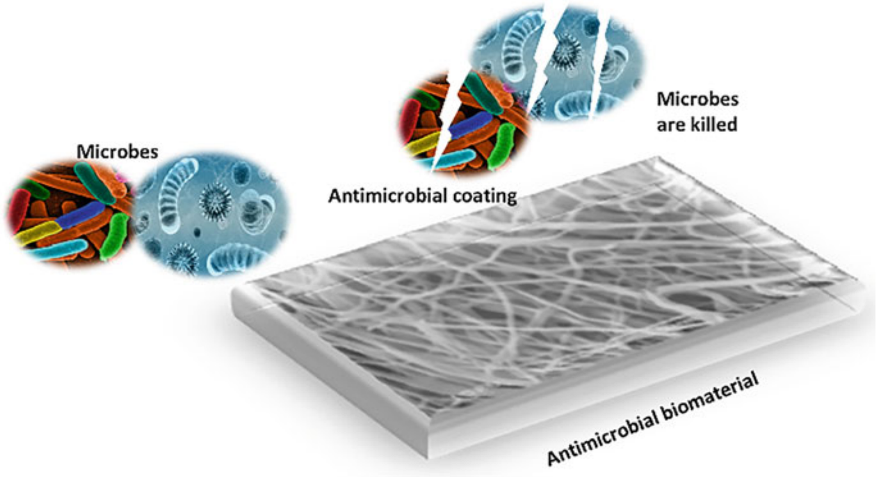

Fig. 8.4 Diagrammatic representation of antimicrobial scaffolds and bactericidal activity

bioinspired materials. Yearly, lots of investigations are being conducted to achieve success in clinical applications, and development is continuous, with the nice cooperation between researchers, clinicians, scientists, as well as engineers (Langer and Vacanti 2016). Nevertheless, bio-artificial tissue engineering has emerged as an indispensable trial. A variety of cells, growth factors, scaffolds, and stratagems are accessible and the amalgamation of these factors under in vitro and in vivo conditions is producing fruitful results. Additionally, the assortment of suitable approaches for cell stimulation, scaffold synthesis, and tissue transplantation performs a conclusive role in efficacious tissue engineering (Bakhshandeh et al. 2017). Interestingly, stem cell co-culture arrangements are remarkable and prevailing tools owing to their exceptional properties. On top, the feedback opinions and outcomes have revealed upshots success in engineering tissues (Paschos et al. 2015). However, scientists and researchers with different specializations ought to coordinate together to encourage the development of tissue engineering and regenerative medicine for practical uses.

8.9 Conclusion

The objective of tissue engineering is to generate functional and patient-specific tissues for transplantation. Diverse scientific disciplines, such as molecular biology, microbiology, cell biology, engineering, pharmacology, and medicine, as well as cellular and developmental biology, etc., have come together to work on engineering tissues with the aim of implant preparation. Virtually, almost all tissues of the human body have been investigated for the likelihood of replacement with living tissues and engineered structures. However, suitable resources of cells for tissue engineering are prerequisites and must be inevitability recognized. Additionally, several stimulating functionalization and alteration procedures are being adopted to control the growth and expansion of opportunist as well as pathogenic microbes. Screening of appropriate scaffolds for ECMs is indeed a huge and far-reaching task. Nevertheless, the optimization of delivery time and the total price of laboratory-cultivated organs are other big tasks to be considered in recruiting a marketplace for engineered organs. Currently, under in vitro conditions, engineered tissues such as skin and cartilage are being utilized in clinics in various countries. Nevertheless, tissue engineering has emerged as a swiftly growing interdisciplinary area, in which practitioners attempt to fix organ failure by implanting natural, synthetic, or semi-synthetic tissues/organs that mimic the original one.

Although tissue engineering has delivered prospective ways to overcome inadequate conventional transplantation methods, the future goal is to fabricate individual organs.

Accordingly, the progress in this auspicious field crests an innovative arrangement for the improvement of the healthcare system of the present society.

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