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Applications of piezoelectric biomaterials in dental treatments: A review of recent advancements and future prospects

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ABSTRACT

Piezoelectric biomaterials have attracted considerable attention in dental medicine due to their unique ability to convert mechanical force into electricity and catalyze reactions. These materials demonstrate biocompatibility, high bioactivity, and stability, making them suitable for applications such as tissue regeneration, caries prevention, and periodontal disease treatment. Despite their significant potential, the clinical application of these materials in treating oral diseases remains limited, facing numerous challenges in clinical translation. Therefore, further research and data are crucial to advance their application in dentistry. The review emphasizes the transformative impact of multifunctional piezoelectric biomaterials on enhancing dental therapies and outlines future directions for their integration into oral healthcare practices.

1. Introduction

The concept of biomaterials, first introduced by Joseph W. Lechter in 1970, encompasses natural or synthetic materials designed to interact with biological systems, with diverse applications in medicine and biotechnology. With in-depth research in materials science and significant advances in modern materials technology, especially nanotechnology, the innovation of biomaterials has been greatly propelled [1,2], opening new opportunities for applications in the medical field [3–5]. Piezoelectric biomaterials are a distinct class capable of converting mechanical energy into electrical energy and vice versa without requiring an external voltage. In 1880, physicists P. Curie and J. Curie discovered the piezoelectric effect in tourmaline, and the following year, they confirmed the inverse piezoelectric effect [6]. The piezoelectric effect is reversible. When mechanical stress is applied to deform a dielectric material, it causes a transfer of positive and negative charge centers within the material, resulting in electrical polarization. This phenomenon is known as the direct piezoelectric effect. Applying an electric field to a dielectric material causes the relative displacement of positive and negative charge centers within the material, leading to its mechanical deformation. This is known as the converse piezoelectric effect [7,8]. In inorganic materials, piezoelectricity is caused by the displacement of ions within crystals. In contrast, piezoelectricity in organic materials arises from the reorientation of molecular dipoles within the polymer, achieved through the application of a high electric field or mechanical stretching [9]. In a physiological environment, piezoelectricity is generated due to structural anisotropy or temporary deformations, resulting in a net dipole moment greater than zero [10].

Bioelectricity refers to electrical phenomena generated by cells or applied to cells to influence their phenotype [11]. In living organisms, endogenous electrical, mechanical, and biochemical signals are integrated to drive cell migration, localization, adhesion, proliferation, and differentiation, collectively forming tissues and organs [12–16]. Given the importance of bioelectricity, electrical stimulation has been developed in dentistry for various purposes, including assessing pulp status [17], locating the root apex [18], improving dental material performance [19], alleviating temporomandibular joint (TMJ) pain [20], modifying neuromuscular dysfunction [21], assisting with distraction osteogenesis [22], enhancing implant osseointegration [23], accelerating orthodontic tooth movement [24], and treating oral and maxillofacial malignancies [25]. However, conventional external electrical stimulation devices have clinical drawbacks, including potential pain, infection, and other complications [26]. In contrast, piezoelectric biomaterials, with their unique force-to-electricity conversion capability,

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offer a new strategy for electrical stimulation in dentistry. Although traditional biomaterials can suppress inflammation and promote tissue repair, the complex environment within the host poses significant challenges to their design [27,28]. Piezoelectric biomaterials provide several benefits compared to conventional biomaterials. They can respond to cell migration, body movements, or external stimuli by producing electrical signals that directly act on biological tissues. Additionally, they can regulate cell behavior indirectly by generating free radicals through catalytic reactions [29].

Biomaterials developed for piezoelectric applications to date include PZT, ZnO, HA, PLLA, PVDF, P(VDF-TrFE), and boron nitride (BN), among others [30–35]. Piezoelectric biomaterials are widely recognized for their applications in biomedical fields, such as sensing, actuation, energy conversion, catalytic processes, and therapeutic applications [29]. PZT, PVDF and its copolymers, lithium niobate ($LiNbO_3$), and bismuth tantalate (BiT) are well-known materials with high piezoelectric response. Additionally, two-dimensional materials such as MXenes and graphene have garnered significant attention due to their exceptional specific surface area, superior electrical properties, and excellent biocompatibility. Given their inherent ability to generate electrical charges, piezoelectric biomaterials are particularly suited for guided cell regeneration and wireless manipulation, especially in the treatment of oral diseases. As therapeutic materials, they offer several advantages, including the restoration of damaged tissues via self-powered electrical stimulation during human movement, low cytotoxicity, minimal physiological effects, and high spatiotemporal precision [36,37]. Studies have shown that piezoelectric stimulation modulates the conversion of macrophages from a pro-inflammatory phenotype to an anti-inflammatory phenotype, resulting in a modest immune response that keeps the foreign body reaction at an appropriate level [38–40]. This not only helps to reduce adverse effects, but may also lead to positive biological effects. However, these materials also have certain drawbacks, such as insufficient mechanical strength, poor stability, and a lack of standardized fabrication processes [41,42].

Despite the numerous excellent properties of piezoelectric materials, a thorough review of their potential medical applications has yet to be conducted. Such a review would not only deepen existing research but also uncover important directions that may have been overlooked, thereby driving the development of innovative therapeutic approaches and devices, particularly by utilizing the unique properties of piezoelectric biomaterials through the activation of the adaptive immune system [43,44]. Therefore, this review examines recent advances in the use of piezoelectric biomaterials in dental medicine. Specifically, we focus on their applications in tissue regeneration, antimicrobial treatments, and inflammatory therapies to enhance osseointegration. Initially, we will provide a brief introduction to piezoelectric biomaterials and the concept of bioelectricity. Following this, we will categorize piezoelectric biomaterials for dental applications into inorganic piezoelectric materials, organic polymers, and piezoelectric composites. We will then summarize the latest applications of piezoelectric biomaterials in tissue engineering, the prevention and treatment of oral diseases, and the development of prosthetic devices (Fig. 1). Finally, we will discuss the main challenges and potential prospects for the future use of piezoelectric biomaterials in dental applications, aiming to provide insights into new manufacturing methods and therapies.

2. Fabrication techniques of piezoelectric biomaterials

There are numerous methods for fabricating piezoelectric materials, several of which are briefly discussed in this review.

The fundamental principle of electrostatic spinning involves stretching the polymer solution using Coulombic forces [45]. In this process, spinning polymer droplets, influenced by Coulombic and gravitational forces that exceed surface tension, gradually transition from hemispherical to conical shapes. As the solvent rapidly evaporates, fine fibers are formed on the receiver plate. Ultimately, nanofibrous membranes are created. The electrostatic spinning technique is widely employed for producing piezoelectric materials, including PVDF, P

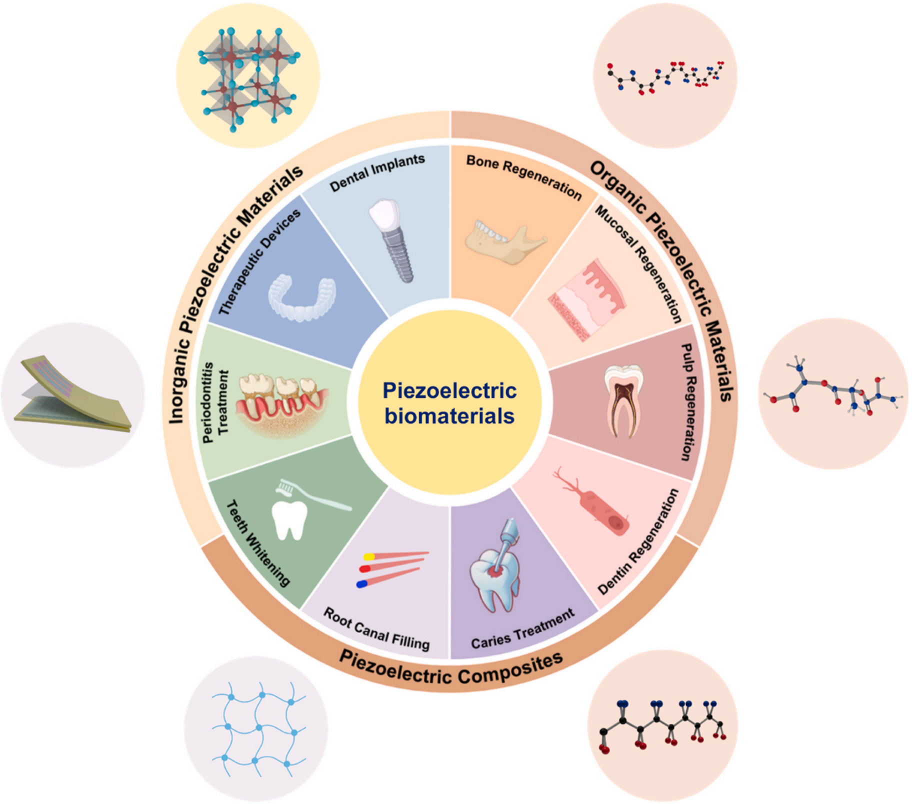

Fig. 1. Schematic illustration of piezoelectric biomaterials for preventing and treating oral diseases.

(VDF-TrFE), PLLA, and PHB, rendering polymer scaffolds highly attractive for tissue engineering applications [46]. The user-friendly nature of electrostatic spinning techniques is attributed to their biomimetic structure, resembling fibrous proteins found in the extracellular matrix (ECM) [47]. The outer layer of PCL/PLA (PP) was optimized using electrostatic spinning to replicate an epidermis that is both waterproof and resistant to bacterial penetration, achieving a tensile modulus of 19.69 ± 0.66 MPa [48]. Nonetheless, the electrostatic spinning method has certain limitations, including low productivity and the potential risk of residual toxic chemicals [49].

Solvent casting is a simple fabrication technique commonly used to prepare piezoelectric polymers and composite piezoelectric materials. Its drawbacks include poor dispersion and agglomeration of nanoparticles in solution [50], brittleness, opaque appearance, and high porosity of the structure. The above factors affect the piezoelectric and dielectric properties of the materials and their strength.

Magnetron sputtering process is a commonly used thin film deposition technique that utilizes plasma energy to sputter atoms or molecules from a target onto a substrate, thereby forming thin films. It is commonly used to prepare thin films of piezoelectric ceramics (e.g., PZT, $BaTiO_3$, and KNN). This process features a high deposition rate [51], is temperature-sensitive [52], produces good film adhesion, is easy to operate, and is suitable for large-area film formation.

3D printing is a technology that creates three-dimensional objects by stacking materials layer by layer [53]. It is commonly used to prepare piezoelectric polymer materials (e.g., PVDF and its copolymers) and piezoelectric composites. Compared with traditional preparation methods, 3D printing technology has the advantages of high efficiency, personalization, controllable size and environmental protection [54]. Fused deposition modeling (FDM) is the most prevalent among 3D printing methods; however, it is primarily suited for polymer-based materials [55]. In contrast, powder-based technologies such as selective laser sintering (SLS) face multiple challenges, including powder transportation and storage.

Hydrothermal method refers to the synthesis of materials by a process of dissolution and precipitation under hydrothermal conditions at high temperature and pressure [56]. This method exhibits several advantages, including simplicity, energy efficiency, and cost-effectiveness. It is a prevalent technique for the preparation of inorganic piezoelectric materials, including $BaTiO_3$, PZT, KNN, and $LiNbO_3$. The tetragonal phase KN nanowires (23.5 pm V^{-1}) prepared using the hydrothermal method at lower temperatures exhibit higher piezoelectric constants compared to orthorhombic phase KN nanowires (11.6 pm V^{-1}) [57]. Additionally, high-quality particle crystallinity was achieved after pretreating $BiFeO_3$ ultrafine particles via the hydrothermal method, which enabled the KNNS-based lead-free piezoelectric ceramics to exhibit

Table 1
Classification and properties of various piezoelectric biomaterials for dental medicine.

Classification	Piezoelectric biomaterials	Structural characteristics	Properties	Ref.
Inorganic Piezoelectric Materials	$BaTiO_3$ (BT/BTO)	High crystallinity Nanostructure	Excellent piezoelectricity Good biocompatibility	[63,64,65–68]
	BWO	High crystallinity	Antibacterial properties Biocompatibility Enhanced piezo-photocatalytic activity	[69]
	KNN	Good crystallinity	Enhanced piezoelectricity Biocompatibility	[70,71]
Organic Piezoelectric Materials	PVDF	\	Piezoelectricity Biocompatibility	[72,73]
	P(VDF-TrFE)	Enhanced crystallinity	Good biocompatibility Mechanical properties Enhanced piezoelectricity	[74]
	VDF-TeFE	\	Antibacterial Properties Piezoelectricity Biocompatibility	[75]
	PTFE	\	Chemical Stability Antibacterial Properties Piezoelectricity Cytocompatibility	[76]
	PLA	Interlocking crystalline	Mechanical deformability Piezoelectricity Catalytic properties Good biosafety	[77]
	Nylon-11	High crystal orientation and crystallinity	Cytocompatibility Piezoelectricity	[78]
Piezoelectric composites	Inorganic piezoelectric materials/organic piezoelectric polymers	Uniform distribution of nanoparticles High crystal orientation and crystallinity	Enhanced piezoelectricity Biocompatibility	[79–82]
	Inorganic piezoelectric materials/organic polymers	Distribution of nanoparticles	Piezoelectricity Biocompatibility	[83–85]
	Inorganic piezoelectric materials/biodegradable polymers	Uniform distribution of nanoparticles High crystal orientation and crystallinity Porosity	Piezoelectricity Bioactivity Biodegradability	[64,86]
	Piezoelectric hydrogel	Uniform distribution of nanoparticles High crystal orientation and crystallinity Porosity Flexibility	Mechanical strength Biocompatibility	[87,88]
	Inorganic piezoelectric materials/metals	High porosity	Piezoelectricity Biocompatibility Hydrophilicity	[89]

excellent electrical properties [58].

3. Piezoelectric biomaterials for dentistry: general classification

Currently, piezoelectric biomaterials utilized in dentistry are broadly classified into three types (Table 1): inorganic piezoelectric materials (including piezoelectric crystals and ceramics), organic piezoelectric materials, and piezoelectric composites. Organic piezoelectric materials are mainly defined as piezoelectric polymers. Piezoelectric composites are composite materials that exhibit a piezoelectric effect, consisting of a combination of piezoelectric and non-piezoelectric phases. The preparation techniques for these materials are diverse and include sol-gel process, electrospinning, hydrothermal method, hot pressing process, and 3D bioprinting [59–62].

3.1. Inorganic piezoelectric materials

Inorganic piezoelectric materials include piezoelectric single crystals and piezoelectric ceramics. Piezoelectric crystals generally refer to piezoelectric single crystals, while piezoelectric ceramics refer to piezoelectric polycrystals. The development of their properties can be divided into two stages: single-component (e.g., $BaTiO_3$, $PbTiO_3$) and morphotropic phase boundary (e.g., lead zirconate titanate (PZT), (1-x) $Pb(Mg_{1/3}Nb_{2/3})O_3$-x$PbTiO_3$ (PMN-PT), and $Ba(Zr_{0.2}Ti_{0.8})O_3$-x $(Ba_{0.7}Ca_{0.3})TiO_3$ (BCT-BZT)) [90]. The development of new single-crystal or polycrystalline materials, such as piezoelectric ceramics doped with heterovalent ions, represents a crucial step in advancing the performance of inorganic piezoelectric materials [91].

The chemical formula for perovskite structure is ABO_3, where A represents a lanthanide or alkaline earth metal and B represents a transition metal [92]. One of the earliest piezoelectric materials was PZT; however, it was unsuitable for biological applications due to its cytotoxic nature. Compared to conventional piezoelectric ceramics containing toxic lead components, environmentally friendly lead-free piezoelectric ceramics have a wide range of applications (such as energy converters, wearable biosensors, tissue engineering and biomedical devices) [93]. Barium titanate ($BaTiO_3$), abbreviated as BT or BTO, is a typical chalcogenide-based bio-piezoelectric material with good biocompatibility and electromechanical coupling. It has been demonstrated for therapeutic applications in dental medicine [63]. BT has a non-centrosymmetric tetragonal crystal structure [94,95]. Due to the spontaneous polarization inherent in this structure, BT exhibits significant ferroelectric, piezoelectric, and thermoelectric properties [96,97]. The excellent piezoelectric properties of BT nanoparticles enable their use in biocatalytic and antimicrobial therapeutic applications [98]. In addition to BT, potassium sodium niobate (KNN), a new lead-free ferroelectric ceramic, exhibits high piezoelectric coefficients, temperature stability, and mechanical strength [99]. Additionally, Bi_2WO_6 (BWO) has a chalcogenide structure and represents a novel approach to piezoelectric catalysis as a catalyst driven by mechanical energy [100]. It has been demonstrated that BWO and its composites are not only expected to serve as antimicrobial agents to prevent bacterial biofilm formation, but they may also exhibit promising anticancer properties [101]. Although piezoelectric ceramics offer several advantages, such as strong piezoelectricity, high sensitivity, stability, lower manufacturing energy costs, and high economic benefits, they still have certain limitations, including temperature dependence, brittleness, and frequency dependence, prompting researchers to explore organic piezoelectric materials [102–104].

3.2. Organic piezoelectric materials

In recent years, organic piezoelectric materials have attracted considerable interest in biomedical applications due to their biocompatibility, processability, flexibility, and stability [105–108]. However, piezoelectric polymers also have some inevitable drawbacks, such as typically lower piezoelectric coefficients and susceptibility to deformation [108–110]. Poly(vinylidene fluoride) (PVDF) is a classical bio-piezoelectric polymer and its monomeric unit has a directionality of CH_2 (head)-CF_2 [111]. PVDF can exist in five distinct crystalline phases: α, β, γ, δ, and ε. The C-F bond is polar, and when all dipoles of the polymer are aligned in the same direction, the highest recorded dipole moment is 2.1D, corresponding to the β phase of the polymer [112]. As one of the PVDF copolymers, poly(vinylidene fluoride-trifluoroethylene) (P(VDF-TrFE)) has gained widespread application in flexible sensors as well as in tissue healing and regeneration [113,114]. Wang et al. demonstrated that P(VDF-TrFE) nanofiber nanogenerators can be used to achieve precise electrical stimulation, which resulted in a significant proliferation of preosteoblasts *in vitro* [35]. Furthermore, Ico et al. proposed that the piezoelectric performance of P(VDF-TrFE) could be enhanced by regulating fiber size through electrospinning [115].

In addition to classical piezoelectric polymers, a number of organic polymers can be prepared to be piezoelectrically active and to generate an electric charge upon application of mechanical stress. This can be achieved through specific processes, such as polarization. Permanent charges are introduced into poly(tetrafluoroethylene) (PTFE) via high-voltage polarization, forming a piezoelectric electret that is capable of generating a charge response, i.e., piezoelectric properties, when subjected to a mechanical force [116,117]. Additionally, PTFE has the capacity to generate ROS through its intrinsic piezoelectric effect, making it a valuable material for chemical degradation. The nylon-11 nanoparticles prepared by the antisolvent method are distinguished by their high crystallinity, which implies that the internal dipole arrangement of the material is highly ordered, the energy is concentrated, and the mechanical properties are stable [78]. Polylactide (PLA) is a piezoelectric polymer approved by the FDA, known for its biodegradability, biocompatibility, and piezoelectric characteristics. While PLA demonstrates piezoelectricity in both crystalline and amorphous forms, its piezoelectric coefficient remains lower compared to conventional piezoelectric polymers [118]. The piezoelectric mechanism of PLA is attributed to its chirality, which forms a helical chain with a $-CO-O$ polar group bonded to an asymmetric carbon atom. When PLA chains are aligned and placed close together, shearing the helix-shaped molecules along the chain c axis causes a slight rotation of the $C=O$ dipoles, altering the chain's polarization. This induces a polarization perpendicular to the shear plane of the chains, generating an electrical potential. Schönlein et al. reported that enhancing optical purity and using post-stretch annealing processes can further improve the piezoelectric coefficient of PLA [119]. PLLA, a specific type of PLA, refers to PLA containing only L stereoisomers. Chernozem et al. found that the crystallinity and molecular structure of the polymer affect the piezoelectric response of PLLA [120]. Poly(3-hydroxybutyrate) (PHB), a key representative of the polyhydroxyalkanoate (PHA) family [121], is a widely utilized biodegradable piezoelectric polymer in biomedical engineering. Vatlin et al. demonstrated that PHB films exhibit piezoresponse and inhibit bacterial growth under mechanical stimulation simulated by ultrasound [122]. Furthermore, a study has demonstrated that chitosan (CS)-PHB composites exhibit enhanced electrostriction effect, leading to a higher apparent piezoelectric response [123]. Compared to pure PHB materials, CS-PHB blend films show significantly improved biocompatibility and piezoelectric properties, making them a promising candidate for applications in tissue engineering.

3.3. Piezoelectric composites

While piezoelectric ceramics or polymers typically possess a single functionality, multi-functionalized piezoelectric composites not only exhibit the core properties of piezoelectric materials but also address the limitations of their constituents (e.g., the brittleness of inorganic bio-piezoelectric materials). As a result, they exhibit higher piezoelectric coefficients and mechanical stability, greater flexibility, and improved biocompatibility [124,125]. Additionally, piezoelectric composites can be prepared as fibers, films, and hydrogels. Although piezoelectric composites hold significant promise for various applications, they are still constrained by limitations such as complex preparation processes, challenges in balancing mechanical and piezoelectric properties, and suboptimal interfacial bonding [126–129]. Piezoelectric composites for dental applications are broadly categorized into seven groups based on their composition: inorganic piezoelectric materials/organic piezoelectric polymers, inorganic piezoelectric materials/organic polymers, inorganic piezoelectric materials/biodegradable polymers, piezoelectric hydrogels, metal/inorganic piezoelectric materials, and multiphase composites. For example, combining BTO nanoparticles with P (VDF-TrFE) imparts excellent piezoelectric properties to composites for bone tissue engineering [130–133]. Composites of inorganic piezoelectric materials and organic piezoelectric polymers typically employ $BaTiO_3$ or zinc oxide (ZnO) for the inorganic component, and P (VDF-TrFE) or PVDF for the polymer component [134]. The dispersion and interfacial bonding of the two materials must be considered in the preparation process. Composites consisting of inorganic piezoelectric materials and organic polymers are relatively simple to prepare; the inorganic materials provide the piezoelectric effect, while the organic polymers mainly offer mechanical support [135,136]. Additionally, the properties of composites are influenced by factors such as filler, polarization, and the brittleness of the inorganic components [137–139]. Biodegradable polymers, as alternatives to traditional polymers, can be naturally degraded by microorganisms to produce environmentally friendly materials such as CO_2 and CH_4 [140]. Therefore, composites made with biodegradable polymers and inorganic piezoelectric materials are characterized by biocompatibility, non-toxicity of degradation products, and antimicrobial properties [64,86]. Inorganic piezoelectric materials can also be combined with metals to enhance material performance in composites. Hydrogels have a wide range of applications as dressings in wound management [141]. Notably, the antimicrobial, anticancer, and antioxidant activities of composite hydrogels hold great promise as therapeutic tools for wound healing and cancer treatment [142]. Conventional hydrogel encapsulation systems present significant challenges, such as the controlled release of drugs from the hydrogel matrix and the diffusion of hydrogels *in vivo* [143]. As a novel non-surgical therapeutic strategy, piezoelectric hydrogels achieve bioactive effects through a self-powered mechanism, thus avoiding the development of drug resistance [87].

Piezoelectric composites, such as hybrid composites based on polyhydroxyalkanoates (PHA) and hybrid lead-free PVDF- or PVDF-TrFE-based materials [121,144], exhibit the high-voltage electrical characteristics of bio-piezoelectric ceramics, along with the biocompatibility and mechanical flexibility of piezoelectric polymers. These advantages render piezoelectric composites promising candidates for the treatment of dental diseases.

4. Application of piezoelectric biomaterials in oral diseases

4.1. Tissue regeneration

Electric fields play a crucial role in mediating numerous human physiological processes, thereby influencing tissue development and regeneration. Piezoelectric biomaterials generate electric fields when mechanically deformed and can also be deformed by electric fields. Since electrical phenomena can enhance cellular behavior and promote tissue differentiation, piezoelectric biomaterials are widely used in tissue engineering and regenerative medicine (TERM).

Endogenous electric field (EnEF) is a naturally occurring electric field in tissues and organs. EnEF mediates various physiological processes and influences the development and regeneration of tissues (such as nerves, bones, skin, and muscles) [145]. Bio-piezoelectricity, a subclass of EnEF, usually originates from the non-central symmetry of biological macromolecules [146]. Piezoelectric materials generate electric fields in response to external physical stress or electric fields, modulating cellular behavior and indirectly mimicking the role of EnEF in biological processes [147]. Regenerative dentistry has become a prominent area of research in recent decades. Thus, we summarize the use of piezoelectric biomaterials for regenerating dentition and related tissues.

4.1.1. Bone regeneration

Bone and cartilage exhibit piezoelectricity, derived from their building blocks such as collagen and hydroxyapatite (HA) [148,149]. In 1892, Julius Wolff discovered that changes in the forces acting on bone resulted in corresponding changes in bone density. This phenomenon, known as Wolff's law, suggests that the piezoelectric properties of bone and cartilage can promote bone formation [150]. The shear piezoelectric coefficient of bone (d_{14}) is 0.2 pC/N [151]. Under physiological compressive loading, the charge density generated in the bone is approximately 7×10^{-11} $\mu C/cm^2$, and the piezoelectric potential is negative [145]. Osteogenesis is the result of a combination of effective mechanical strain stimulation and endogenous electrical currents [152]. Numerous studies have demonstrated that electrical signals can promote cell proliferation, differentiation, and tissue regeneration [86,89]. Piezoelectric materials can generate electric fields under stress and deliver electrical stimulation through the extracellular matrix (ECM), thereby regulating cell activity [153]. Thus, piezoelectric biomaterials serve as suitable bone substitutes to fill bone defects and as electrical stimulators to aid bone and cartilage formation, leading to their widespread use in regenerative medicine.

The osteogenesis-inducing mechanisms of piezoelectric biomaterials include: (1) promotion of osteogenic differentiation, (2) promotion of vascularization, (3) modulation of osteoclasts, and (4) regulation of the immune microenvironment and antimicrobial activity. These mechanisms have been demonstrated in both *in vitro* and *in vivo* studies on bone repair effectiveness. Piezoelectric materials generate electric fields and promote the aggregation of charged macromolecules [154]. For example, Xu et al. prepared KNN lead-free piezoelectric ceramics using the solid-phase sintering method [70]. They found that KNN piezoelectric ceramics (Fig. 2A) after corona discharge poling, favor protein adsorption and cell adhesion. Additionally, polarized KNN ceramics (P-KNN) were observed to regulate the expression of osteogenic genes, thereby promoting the proliferation and osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs). In another study, Sun et al. verified that during the fabrication of $BaTiO_3$-$SrZrTiO_3$ (BTO-SZTO) piezoelectric coatings, variations in substrate temperature affect grain size, crystal interface morphology, and lattice defects, thus influencing the piezoelectric properties [155]. Enhanced electrical properties (piezoelectric constant and surface potential) of the coating film positively affect osteoblast activity maintenance, differentiation maturation, and gene expression [65]. An electropositive $BiFeO_3$ (BFO+) nanofilm was designed to match endogenous electrical signals. A built-in electric field was formed between the BFO + nanofilm (+75 mV) and the negatively charged bone defect wall (−52 to −87 mV). The attraction between positive and negative charges produced a clustering effect, leading to more negative fibronectin (FN) being adsorbed onto the BFO + surface. This process provided more cell-binding sites, enhanced cell adhesion and spreading, and significantly increased the rate of implant osseointegration in animal models [156]. Besides the strength of the surface potential, the integrin status at the cell-material interface is also crucial for osteogenic differentiation. Zhang et al. created an asymmetric arrangement of integrins α5β1 and αvβ3 by altering the heterogeneous potential gradient on the $CoFe_2O_4$/P (VDF-TrFE) (CFO/P(VDF-TrFE)) membrane, leading to cytoskeletal rearrangements and inducing a signaling cascade response. The potential gradient (Δ_ζ) of piezoelectric polymer films determines their electroactivity and osteogenic properties. However, both excessively low and high potential gradients negatively impact cellular osteogenic differentiation. In *in vitro* and *in vivo* experiments, films with a Δ_ζ of 0.672

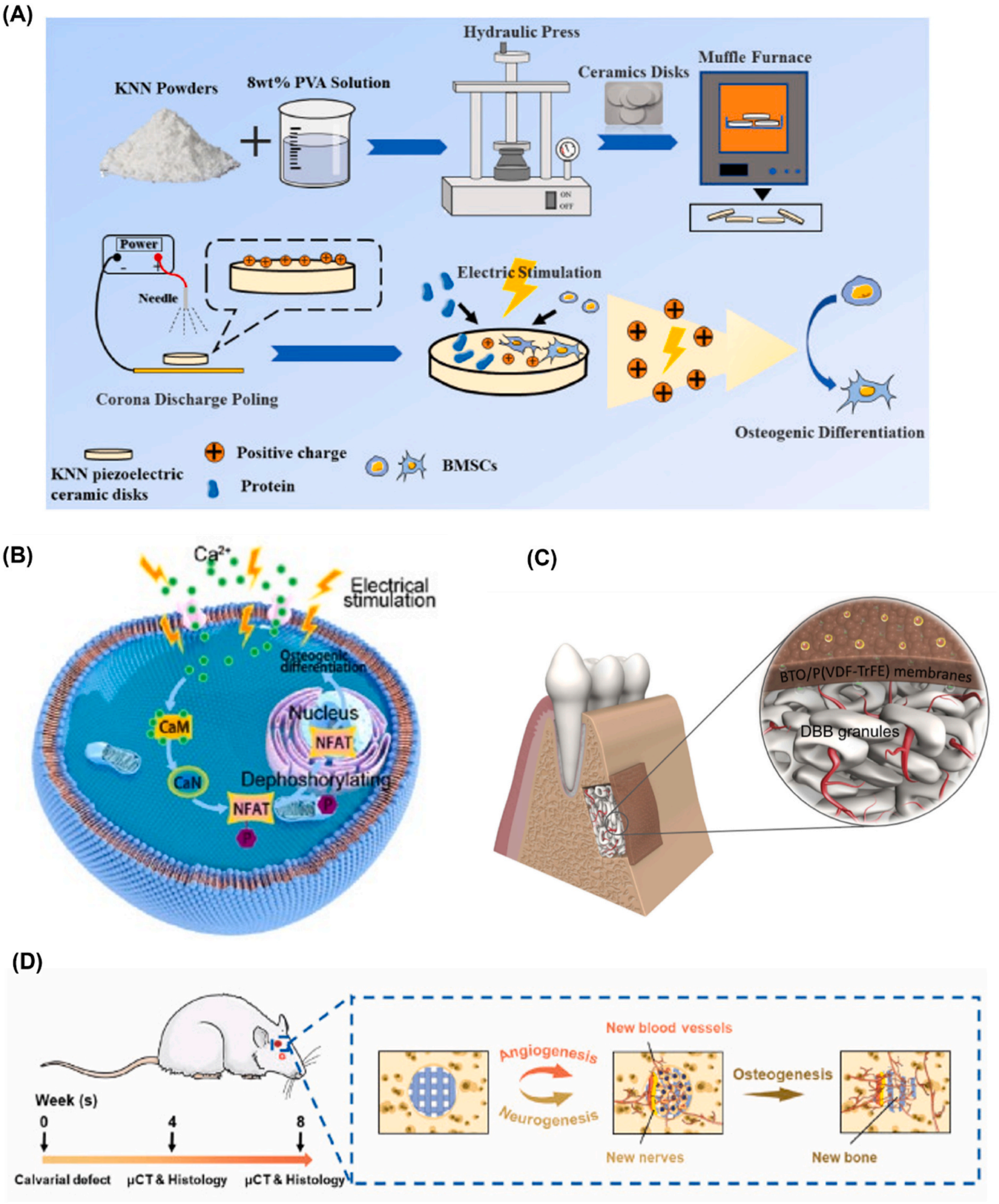

Fig. 2. (A) Schematics of the potassium sodium niobate (KNN) lead-free piezoelectric ceramics. Reproduced with permission from Ref. [70]. Copyright 2023 Elsevier. (B) Schematic illustration of pathways induced by electrical microenvironment. Reproduced with permission from Ref. [158]. Copyright 2023 Elsevier. (C) Illustration of the synergistic effects of combining piezoelectric BTO/P(VDF-TrFE) nanocomposite membranes with xenogenic DBB grafts on the repair of critical-sized bone defects. Reproduced with permission from Ref. [80]. Copyright 2019 Taylor & Francis. (D) A schematic showing the establishment of 5-mm skull defect model of SD rats and the mechanism for enhanced bone regeneration via the promoted neurogenesis and angiogenesis. Reproduced with permission from Ref. [86]. Copyright 2022 Elsevier.

p.m./(V*μm) demonstrated optimal osteogenic differentiation, enhancing the expression of *Runx2* and *ALP* genes, as well as *ALP* and *OCN* proteins [74]. Moreover, ultrasound-activated piezoelectric nylon-11 nanoparticles (nylon-11 NPs) can also non-invasively promote the osteogenic differentiation of dental pulp stem cells (DPSCs) [78]. Compared to the poor bone regeneration ability of solitary piezoelectric polymers, composite piezoelectric materials exhibit good bioactivity and osteointegration, making them highly promising for bone repair applications. Creating a sustainably maintained artificial microenvironment to mimic physiological bioelectricity offers a promising strategy for facilitating the bone repair process. The composite membrane of 5 vol% PDA@BTO NPs/P(VDF-TrFE) was corona-polarized to a surface potential of −76.8 mV, which falls within the range of natural endogenous biopotentials. The nanomembrane exhibited high stability, and the sustained electrical microenvironment promoted rapid bone regeneration [130]. Tang et al. developed a polydimethylsiloxane (PDMS)/aluminum nitride (AlN) film that creates a cell electrical microenvironment under mechanical vibration [84]. This promoted the adhesion and proliferation of MC3T3-E1 osteoblasts. Interestingly, piezoelectric nanoscaffolds composed of ZnO@PCL/PVDF showed similar *in vitro* phenomena, and *in vivo* experiments demonstrated that piezoelectric actuation effectively accelerated the repair of mandibular defects in rats [82]. PVDF and its composites are commonly used piezoelectric biomaterials for bone regeneration. Bagherzadeh et al. reported that the piezoelectric behavior of PVDF composite scaffolds promotes the differentiation of stem cells into osteoblasts [157]. Liu et al. fabricated a piezoelectric PVDF composite fiber membrane via electrospinning [72]. The researchers incorporated TiO_2 nanoparticles into PVDF to enhance its piezoelectric properties. The resulting TiO_2@PVDF piezoelectric composite fiber membranes provide a suitable electrical microenvironment for osteogenesis, generating piezoelectric signals. These signals accelerate the osteogenic differentiation of BMSCs by modulating Ca^{2+} transport-related signaling pathways. Chen et al. further explored the mechanism by which electrical stimulation promotes the osteogenic effects of mesenchymal stem cells [158]. Fluorescence staining and Western blotting results showed that electrical stimulation increased intracellular Ca^{2+} concentration and promoted the relative protein expression of calmodulin (CaM), calmodulin neurophosphatase (CaN), and nuclear factor of activated T cells (NFAT), thereby enhancing osteogenic differentiation (Fig. 2B). Zheng et al. combined poly(L-lactic acid) (PLLA) with calcium/manganese co-doped $BaTiO_3$ (CMBT) nanofibers to prepare PLLA/CMBT composites using solution casting and thermally induced phase separation (TIPS) techniques [79]. The polarized PLLA/CMBT composites greatly enhanced osteogenic activity *in vitro* and *in vivo*, while demonstrating potent antibacterial and anti-inflammatory properties, positioning them as superior candidates for bone regeneration.

Bone is a highly vascularized tissue, making angiogenesis critical to the success of bone tissue engineering [159]. Electrical signals have been shown to stimulate angiogenesis. In addition, a recent study has proposed that wireless electrical stimulation can be used for tumor vascular normalization [160]. Since piezoelectric biomaterials can provide stable radio stimulation, they present a new strategy for the clinical treatment of bone defect repair. Li et al. created a piezoelectric bioactive glass composite (P-KNN/BG) incorporating polarized potassium sodium niobate to improve angiogenic properties [161]. Wireless electrical stimulation-induced cell membrane hyperpolarization enhances the influx of active ions into cells, thereby promoting endothelial cell adhesion, migration, and differentiation. Additionally, P-KNN/BG can upregulate the expression of angiogenesis-related growth factors and activate the eNOS/NO signaling pathway. Early vascularization of a composite in a bone defect is a prerequisite for the ingrowth of osteogenic reparative cells to regenerate bone. This is because a lack of vessels cannot ensure sufficient nutritional support for the bone graft [162]. Bai et al. created a biomimetic piezoelectric nanocomposite membrane consisting of $BaTiO_3$ nanoparticles (BTO NPs) and P(VDF-TrFE) to improve the outcome of guided bone regeneration [80]. It acted as a barrier membrane to induce early neovascularization in a rabbit mandible defect model (Fig. 2C). Vascular endothelial growth factor (VEGF) is not only a key regulator in angiogenesis but also indirectly promotes osteogenesis [163]. The dual ability of VEGF, particularly its family member VEGF-A, has been demonstrated in increasing alkaline phosphatase (ALP) and mineralization. Liu et al. fabricated a Ti6Al4V scaffold coated with piezoelectric $BaTiO_3$ for repairing bone defects [89]. The researchers showed that the polarized scaffold significantly enhanced VEGF and PDGF-BB secretion by human umbilical vein endothelial cells (HUVECs), as observed on day 5 in the pTi/$BaTiO_3$ (poled) group in *in vitro* experiments. Native bone is a neuro-vascular tissue, so the process of osteogenesis is closely related not only to the degree of angiogenesis but also to neurogenesis. It has been demonstrated that magnesium ions (Mg^{2+}) promote the expression of angiogenesis-related genes [76]. Wang et al. designed a versatile biomimetic composite scaffold incorporating piezoelectric whitlockite (PWH), emulating the composition and piezoelectricity of the bone [86]. The PWH composite scaffold enhances the regeneration of neurovascularized bone tissue through the synergistic effect of sustained Mg^{2+} release and piezoelectricity, simultaneously promoting neuron and blood vessel formation (Fig. 2D). Fracture healing is a multicellular, complex, and continuous process. Revascularization supports the influx of immune and progenitor cells from circulation and initiates the process of bone tissue repair [164]. Recently, Chen et al. developed a piezoelectric foam nanogenerator composed of PVDF/ZIF-8 [73]. It can upregulate the expression of angiocrine factors (such as FGF-1 and TGFβ), form new capillaries, and recruit more osteoprogenitor cells, thus accelerating the coupling of angiogenesis and osteogenesis.

Inhibiting bone resorption is a key factor affecting osteogenesis and development. Wang et al. reported that piezoelectric PWH scaffolds can inhibit osteoclast activation [86]. The efficacy of the PWH scaffold was confirmed by *in vitro* RAW246.7 macrophage culture and qPCR was used to detect the relative expression of osteoclast-related genes (TRAP, MMP9, and cathepsin K). Similarly, Jeong et al. prepared a piezoelectric porous composite nanofiber comprising PVDF and a polyhedral oligomeric silsesquioxane-epigallocatechin gallate (POSS-EGCG) conjugate [165]. *In vitro* experiments showed that as the content of POSS-EGCG conjugate in the composite nanofibers increased, the decrease in the expression level of osteoclastogenic factor IL-6 was more significant, especially at 6 wt% (PE06). In addition, the PE06 group formed the most bone-like calcium deposits in all time periods. The metallic element strontium (Sr), used as a coating material for implants, enhances osteoblast activity and inhibits osteoclast activity to support bone regeneration. Swain et al. developed a novel piezoelectric composite for medical implants that mimics bioelectric modulation of osteoblasts to accelerate bone repair and exhibits good antimicrobial properties [166].

The immune system regulates the inflammatory response and bone repair [167]. Bacterial infection or inflammation can lead to gingivitis, periodontitis, and pathological resorption of the alveolar bone [168]. However, the participation of immune cells in the regulation of the bone healing process also results in the triggering of inflammatory responses of varying degrees. Macrophages are a significant cell population in the immune response, secreting cytokines that influence the onset of inflammation [169]. Electrical stimulation has been shown to inhibit M1 polarization of macrophages, affect the secretion of pro-inflammatory cytokines, and ultimately promote osteogenic differentiation [79]. Consequently, piezoelectric materials act as immunomodulators, facilitating the transition of macrophages from a pro-inflammatory M1 phenotype to an anti-inflammatory M2 phenotype. Another strategy to modulate the immune response is through the scavenging effect of reactive oxygen species (ROS). ROS refers to oxygen radicals (such as superoxide anion radicals and hydroxyl radicals) and non-radical oxidants (such as hydrogen peroxide and singlet oxygen) [170]. The superoxide radical ($O_2^{\cdot -}$) is the most reactive and toxic form of ROS, with a relatively short half-life and limited diffusion from its production site [171]. The lattice structure of the piezoelectric material $BaTiO_3$ generates an internal electric field during mechanical deformation. Driven by this electric field, the enriched electrons react with surface O_2 to generate superoxide anion radicals ($\cdot O_2^-$), while the holes migrate and interact with H_2O to form hydroxyl radicals (·OH). Sun et al. discovered that following ultrasonic irradiation, ROS were produced, initiating a chain reaction whereby NO released from ROS decomposition prompted macrophages to polarize to the M1 type [67]. Furthermore, Mao et al. developed a piezoelectric $BaTiO_3$/β-TCP (BTCP) ceramic using a two-step sintering method [65]. This ceramic offers dual benefits: regulating bone's immunomodulatory properties and attenuating local inflammatory responses, while simultaneously forming an immune microenvironment conducive to osteogenesis.

4.1.2. *Oral mucosal regeneration*

Soft tissues, including the oral mucosa, periodontal tissues, nerves, and tongue, are crucial for normal oral functions. Due to its sensitive, fragile, and mucus-secreting characteristics, the oral mucosa is difficult to repair once damaged, which weakens its protective, sensory, and absorptive functions. The primary repair mechanism of mucosal regeneration is neoangiogenesis [172]. In recent years, numerous studies have used ex vivo-engineered alternatives to aid in the healing of intraoral wound defects. A piezoelectric polymer membrane with good biocompatibility can effectively restore the fibrous component of the oral mucosa and reduce the inflammatory response during the healing process [173]. Badaraev et al. obtained non-woven piezoelectric polymer membranes of vinylidene fluoride and tetrafluoroethylene copolymer using the electrospinning technique [75]. *In vivo* experiments showed that modified non-woven VDF-TeFE membranes outperformed the original ones as dressings, resulting in faster soft tissue formation and more rapid wound repair within 7 days. Additionally, the piezoelectric polymer membrane with a copper coating via magnetron sputtering is endowed with high antibacterial activity and significantly accelerates the tissue regeneration process of oral mucosa. Under external stimuli, the VDF-TeFE-based electrospinning non-woven membrane produces a piezoelectric effect, promoting fibroblast migration, adhesion, and related cytokine secretion, thereby contributing to wound healing.

The intensity of neoangiogenesis in oral mucosal wound defects coated with piezoelectric polymer membranes has been evaluated [173]. Furthermore, Chernova et al. found that piezoelectric VDF-TeFE membranes strongly promote oral mucosal regeneration compared to PTFE membranes, which exhibit dielectric behavior [174]. The experimental group with wound defects covered by a VDF-TeFE membrane showed high-quality fibrous connective tissue healing and less pronounced scar formation compared to the group with open wound defects (Fig. 3A). In addition, Koniaeva et al. used a protective piezoelectric polymer membrane on oral mucosal wound defects in rats and observed changes in cellular composition at various stages [175]. On day 12 of implantation, the piezoelectric polymer membrane significantly reduced inflammation and promoted fibroblast proliferation. In another study, the same group found that piezoelectric polymer membranes based on vinylidene fluoride and tetrafluoroethylene showed impressive results in closing oral mucosal wounds [176]. Microscopic examination showed that the piezoelectric polymer membrane restored hemodynamic parameters at the injury site and significantly increased VEGF expression to promote neoangiogenesis. These studies show great promise for the treatment of oral mucosal injuries, suggesting that the selection of appropriate piezoelectric composites may reduce the risk of postoperative complications and improve treatment outcomes. Yang et al. developed flexible nano-piezoelectric membranes and found that the electric field generated by their deformation promotes wound healing [177].

4.1.3. *Tooth tissue regeneration*

Tooth loss is a public health problem. Partial or total loss of dental tissues due to bacterial, traumatic, congenital, environmental, or other factors not only prevents normal mastication and affects facial aesthetics but also leads to various mental health problems [178]. Dental tissues include enamel, dentin, pulp, and cementum, which are different yet interconnected in terms of tissue structure and physiological function. Current treatment strategies are limited to preventing disease progression and cannot regenerate lost tissues. The current treatment method involves using materials to repair missing tooth tissue. If the lesion affects the pulp and causes irreversible inflammation or necrosis, root canal therapy is required to remove the contents and prevent or heal periapical lesions [179]. The enamel surface lacks cells after eruption, preventing regeneration after injury. Various biomaterials are widely

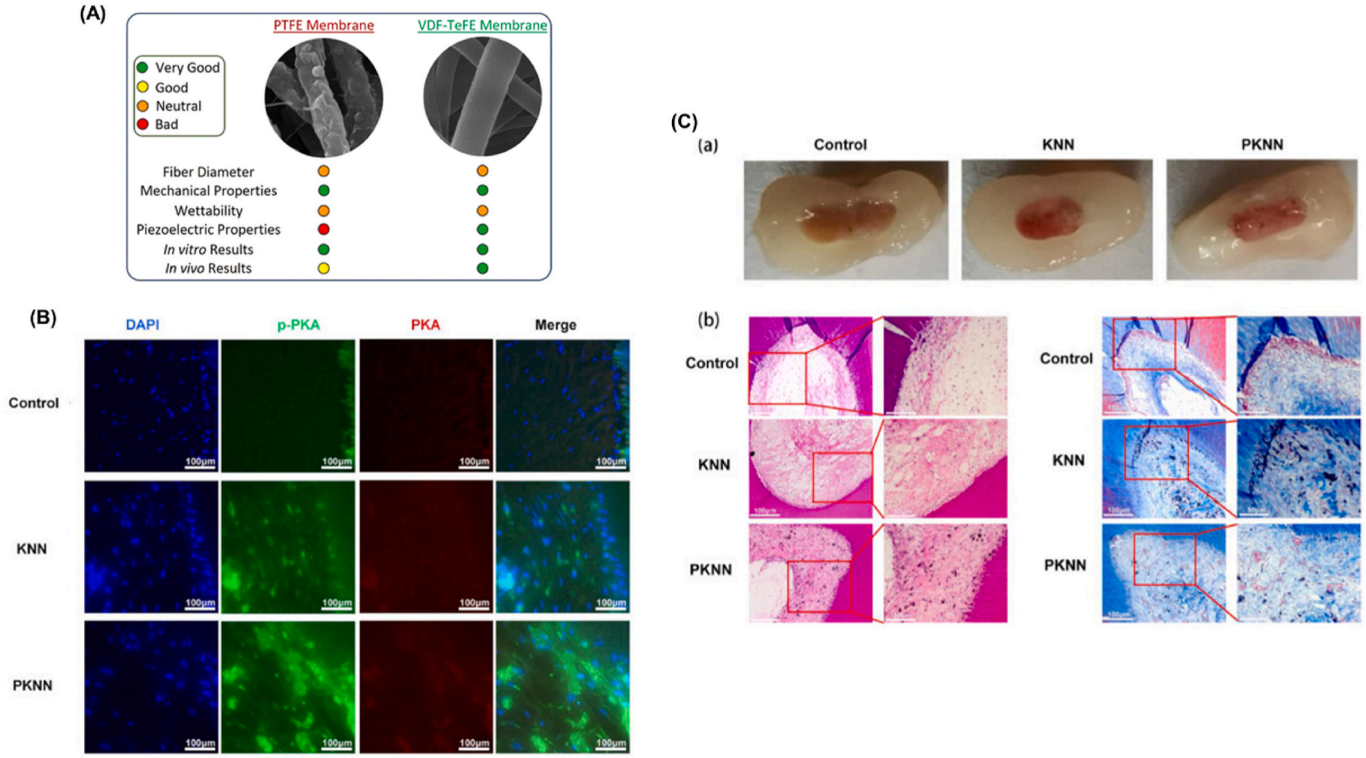

Fig. 3. (A) Schematic overview of the study results for the investigated membrane made of PTFE and VDF-TeFE. Reproduced with permission from Ref. [174]. Copyright 2024 ACS Publications. (B) Immunofluorescence result of *in vivo* pulp regeneration section. (C) PKNN induced odontogenic differentiation of DPSCs *in vivo*. Reproduced with permission from Ref. [71]. Copyright 2023 Elsevier.

used in dentin-pulp tissue engineering, but they have limitations such as poor predictability, safety, feasibility, and effectiveness [180,181]. Piezoelectric biomaterials, as a new type of material, are promising bio-composites found to promote stem cell differentiation and produce antimicrobial effects due to their bioactive properties. Therefore, the interaction between piezoelectric biomaterials and the dentin-pulp complex for repair and regeneration represents an important area for future research.

In classical tissue engineering, regenerative endodontic procedures (REP) rely on stem cells, cytokines, and scaffold materials to regenerate damaged dental pulp through techniques such as pulp revascularization, autologous pulp stem cell replantation, or cell homing [182–184]. As a unique method, the scaffold-free approach uses cell sheets, spheroids, or tissue strands as building blocks to secrete ECM and fuse into larger tissue structures, cooperating with scaffold-based systems to regenerate dental pulp [185]. Zheng and colleagues developed piezoelectric nanoparticles that wirelessly induce intracellular electrical effects, stimulating mitochondrial calcium levels, activating the cAMP/PKA signaling pathway, and inducing odontogenic differentiation of DPSCs [71]. *In vivo* experiments showed that pulp-like tissue regeneration was observed in the KNN and PKNN groups after 8 weeks (Fig. 3B, C).

Strontium (Sr) is an essential trace element for the human body and is widely used in dental restorative materials [186]. Sr is known to stimulate osteoblast differentiation and enhance bone regeneration. Odontogenic differentiation of human dental pulp stem cells (HDPSCs) is crucial for successful dental pulp regeneration. Reports indicate that Sr promotes pulp-dentin complex regeneration by activating the mitogen-activated protein kinase (MAPK) signaling pathway, enhancing ALP activity, DPSC differentiation, and promoting gene expression of dentin sialophosphoprotein (DSPP), dentine matrix protein 1 (DMP-1), and KDR [187–190]. Additionally, piezoelectric materials can stimulate cells to produce physiological electrical effects, thereby regulating cell behavior. So far, few studies have examined the effect of combining metal strontium and piezoelectric materials on dentin regeneration. Recently, Li et al. creatively added strontium to the P(VDF-TrFE) biofilm, characterized by high elasticity, good biocompatibility, and a high piezoelectric coefficient [191]. *In vitro* studies confirmed that the 2 wt% $SrCl_2$-added P(VDF-TrFE) (SP) film induced the targeted differentiation of DPSCs into odontoblast cells by constructing a weak electric field as well as releasing Sr^{2+} ions. Researchers utilized microcurrents generated by piezoelectric films to promote new dentin formation and mineralization, showing promising results in a canine pulp capping model (Fig. 4). Biophysical and biochemical cues from biomaterials can modulate the behavior of DPSCs. Compared to the surface potential of unpolarized films (−52.9 mV), P(VDF-TrFE) films treated with positive and negative polarization exhibited significantly increased surface potentials (+902.4 and −502.2 mV) and promoted cell adhesion [192]. *In vivo* studies demonstrated that the polarized P(VDF-TrFE) film induced odontogenic differentiation of DPSCs and accelerated restorative dentin formation, suggesting its potential as a direct pulp-capping agent for restorative dentin formation.

Many types of biocomposites have been widely studied and applied in dental pulp tissue engineering. However, candidates with ideal properties are yet to be identified. Future work will focus on studying the effect of piezoelectric biomaterials on the expression of genes related to the odontogenic differentiation of HDPSCs and their potential to regulate cell physiological activities.

4.2. *Treatment of dental and endodontic diseases*

4.2.1. *Caries treatment*

The primary treatment principles for caries are to prevent further development, protect the dental pulp, and restore the function and shape of teeth [193]. Glass ionomer, light-cured composite resin, and root canal sealing materials are often used to terminate or eliminate lesions and promote remineralization of demineralized tissues. Filler is a

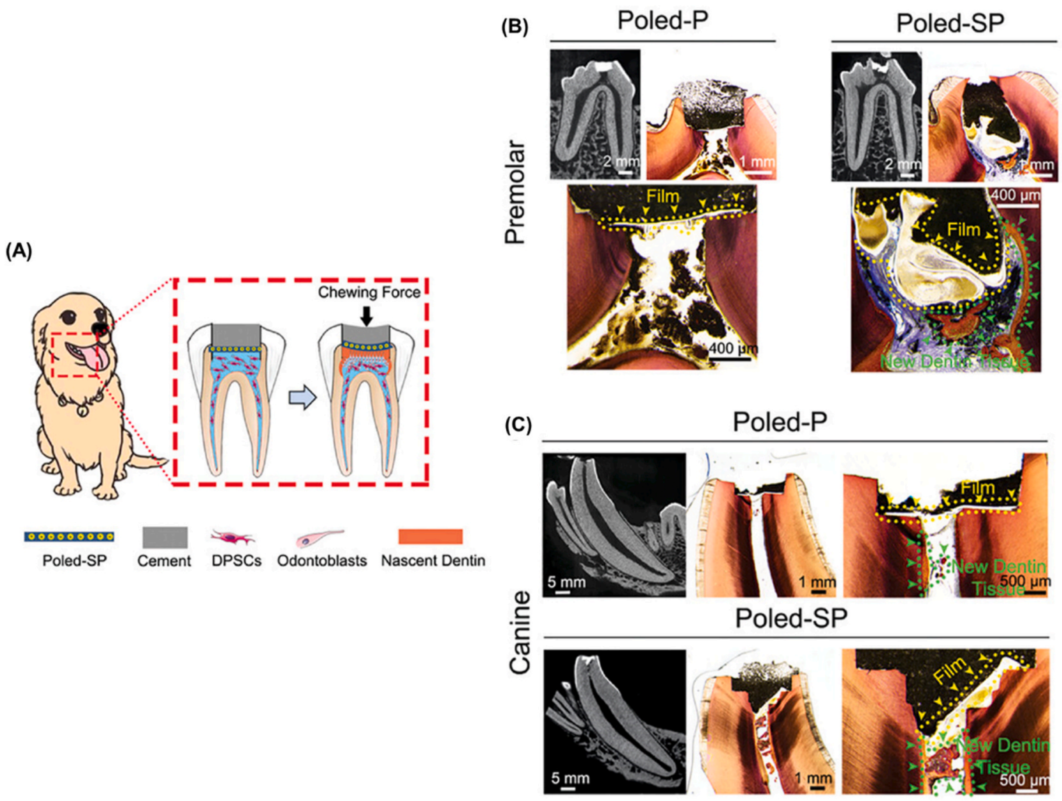

Fig. 4. (A) Schematic illustration of dentin tissue regeneration *in situ*. (B), (C) X-ray images and Van Gieson stain of the two groups at 3 month timepoint. Reproduced with permission from Ref. [191]. Copyright 2023 Wiley.

key factor affecting the performance of dental resin composites (DRCs) [194]. Its size, diameter, and quantity determine the mechanical and aesthetic properties of the resin [195]. Therefore, introducing fillers with different functions is a method researchers use to optimize the comprehensive performance of DRCs. Bai et al. studied the application of Zn-doped mesoporous silica nanoparticles (Zn-MSNs) in dentistry and their effect on the physical and mechanical properties of composite resins [196]. The mechanical properties of the materials were significantly improved after the introduction of Zn-MSNs. With the increase in its content and soaking time, the cumulative release of Zn^{2+} gradually increased, positively affecting the inhibition of dental caries formation. Wang et al. synthesized a bioactive dental composite resin containing MgO nanoparticles with broad-spectrum antibacterial effects. The degradation product, magnesium ion, can be effectively metabolized in the human body [197]. Besides, Childs et al. developed an antimicrobial dental composite using methyl methacrylate (K18-MMA) and glass filler (K18-Filler), with good antibacterial activity against *Streptococcus mutans*(*S. mutans*), *Streptococcus sanguis*, and *Candida albicans* [198]. In addition to antibacterial activity, the resin's mineralization ability should also be improved. Nano-hydroxyapatite (nano-HA) mimics the composition of bone inorganic substances and is considered a novel dental repair material [199]. Zhao et al. demonstrated that DRCs containing nano-hydroxyapatite (n-HA) can form a precipitated apatite layer after immersion in artificial saliva (SBF) [200]. However, existing DRC methods have limitations such as uncontrolled release, potential toxic effects, and limited ability to penetrate bacterial cell membranes. In addition, avoiding the triggering of bacterial drug resistance is an important consideration. Therefore, incorporating piezoelectric particles into resins to form novel and more targeted materials is ideal for improving the success of clinical treatments. The electrostatic effect of piezoelectric charge can prevent bacterial adhesion and ultimately inhibit biofilm growth. Additionally, piezoelectric resin can provide a continuous remineralization effect. Montoya et al. studied the influence of piezoelectric charge and materials on antibacterial activity and mineralization in dental treatment (Fig. 5 A-C), preparing piezoelectric resin composites by combining piezoelectric nanoparticles ($BaTiO_3$) with dental resin for the first time [63]. Researchers found that in an *in vitro* model of single-species biofilms, the antibacterial effect was the best (up to 90%) when the piezoelectric composite had a low amount of barium titanate (BTO) (<10%) and a small amount of charge (<3.2 pC/cm^2). In the mineralization model, a charge density of 3.2 pC/cm^2 produces a calcium phosphate mineral layer with a thickness of 23.1 ± 3.7 μm on a 60%BTO piezoelectric composite. Although exciting results have been achieved, refining the bond strength of materials remains a challenge. Additionally, the effect of piezoelectric charge on cell processes remains to be studied.

4.2.2. *Root canal filling*

High-quality root canal filling is crucial for ensuring the long-term success of root canal treatment. In most cases, root canal reinfection is caused by the failure of the gutta-percha point (GP) to tightly fill the canal, leading to leakage and bacterial regeneration [202]. Studies have shown that *Enterococcus faecalis* (*E. faecalis*) is the most frequently isolated bacterium from reinfected root canals and is highly resistant to conventional antimicrobial agents like sodium hypochlorite, chlorhexidine, and calcium hydroxide [203]. Therefore, controlling the growth and reproduction of *E. faecalis* is a key research priority to prevent the failure of endodontic treatment [204]. Eliminating persistent intracanal infections requires not only existing mechanical instruments and antibacterial irrigants but also more advanced techniques and strategies for complete disinfection. Sonodynamic therapy (SDT) is an emerging therapeutic approach that uses ultrasound (US) to generate highly cytotoxic ROS, achieving non-antibiotic-mediated bactericidal effects [205]. Xu et al. developed a piezoelectric GP (piezoGP) with BTO@Au nanoparticles on its surface (Fig. 5D) [201]. After US treatment (1 W cm^{-2}, 5 min), the piezoGP reduced the number of *E. faecalis* by up to 95% (Fig. 5E). Even in cases of root canal reinfection, the infection can be cleared by non-invasive means.

4.2.3. *Teeth whitening*

The emergence of cosmetic dentistry has led to rapid development in teeth whitening techniques. Tooth discoloration has many causes,

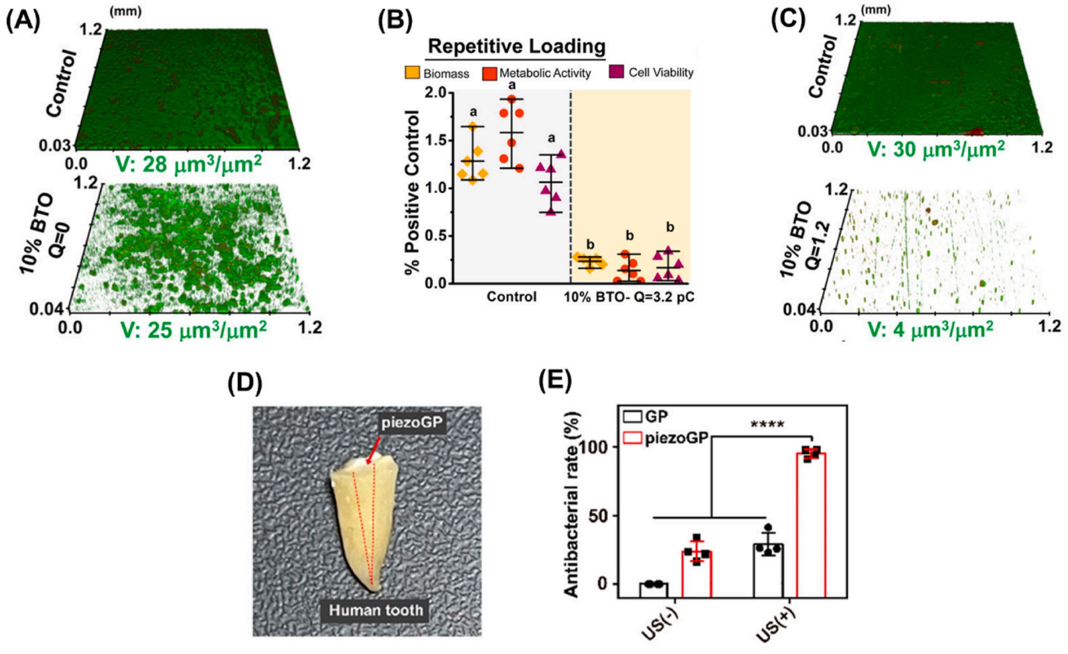

Fig. 5. (A) Representative CLSM images of *S. mutans biofilms on control and piezoelectric composites with 10% filler content without repetitive loading.* (B) Biofilm–biomaterial evaluations for the control and piezoelectric composites with 10% filler content under repetitive loading. (C) Representative CLSM images of *S. mutans* biofilms on control and piezoelectric composites with 10% filler content and under repetitive loading. Reproduced with permission from Ref. [63]. Copyright 2021 ACS Publications. (D) Digital image of piezoGP implanted in ex vivo human teeth. (E) antibacterial rates of GP and piezoGP in infected ex vivo human teeth after ultrasonic stimulation (1 W cm^{-2}, 5 min). Reproduced with permission from Ref. [201]. Copyright 2023 ACS Publications.

mainly exogenous factors (e.g., pigment-producing bacteria, foods, drugs, beverages) and endogenous factors (e.g., systemic diseases, dental diseases, tetracyclines, fluoride, restorative dental materials) [206]. Endogenous discoloration is associated with morphological or structural changes in tooth development or the penetration of pigment into the tooth. Exogenous discoloration is usually caused by pigmentation on the tooth surface. Tooth staining and discoloration greatly affect appearance, leading to the development of various treatments such as sandblasting and polishing, laser whitening, tooth bleaching, and covering with veneer or crown prosthesis. Hydrogen peroxide, commonly used as a whitening agent in tooth bleaching, decomposes into free radicals via redox reactions and may cause side effects such as tooth sensitivity, enamel demineralization, or pulp cytotoxicity [207].

Recently, non-destructive, efficient, and time-saving strategies based on the piezo-catalytic effect have been investigated for tooth whitening (Fig. 6A). Importantly, piezo-catalytic treatment not only ensures the safety of the whitening material but also generates ROS, contributing to the elimination of bacterial biofilms. Wang et al. synthesized BTO nanoparticles using the hydrothermal method to replace conventional toothpaste abrasives [66]. They demonstrated that the nano-sized BTO remained structurally stable after three recycling processes. Furthermore, they showed that the solution containing poled BTO nanoparticles achieved complete tooth whitening after prolonged treatment (over 10 hours) and continuous vibration (Fig. 6B). Besides, through the

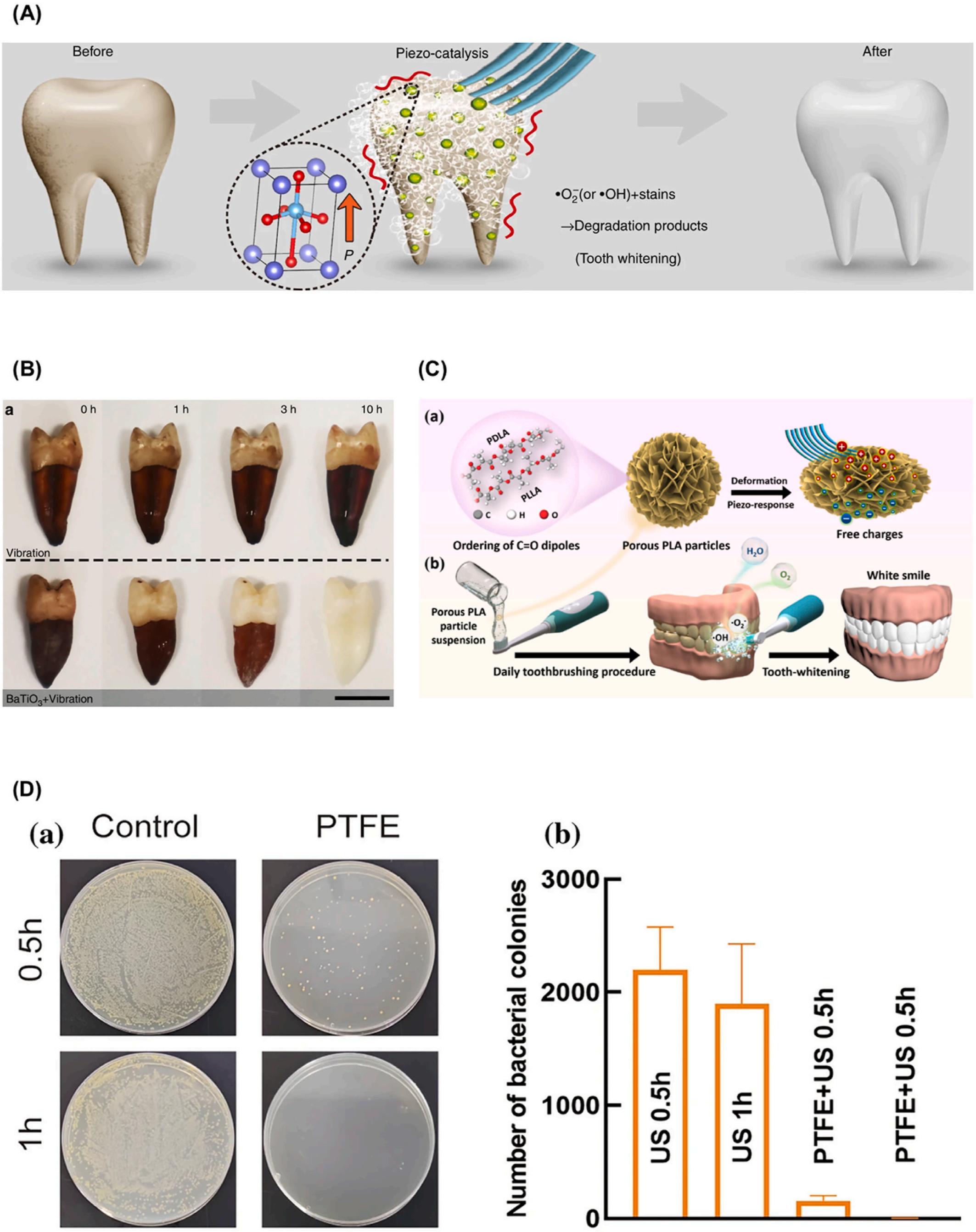

Fig. 6. (A) The proposed piezo-catalysis effect-based tooth whitening method. (B) Photographs of teeth under treatment of vibration in (top) pure deionized water and (bottom) turbid liquid of BTO nanoparticles for 0, 1, 3, and 10 h, respectively. Reproduced with permission from Ref. [66]. Copyright 2020 Nature Communications. (C) Schematic illustrating the piezocatalytic effect. Reproduced with permission from Ref. [77]. Copyright 2023 ACS Publications. (D) Antibacterial activity of PTFE. Reproduced with permission from Ref. [76]. Copyright 2024 SpringerLink.

microscopic morphology and structural hardness evaluation, the enamel of the treated teeth was not damaged. The experimental results indicate that BTO nanoparticles have a whitening effect with good stability and biocompatibility.

However, the mechanical stresses from oral physiological movements and daily activities (e.g., toothbrush vibration) may not be sufficient to stimulate the electric field required for teeth whitening. Therefore, the piezoelectric potential and localized electric field can be generated by altering the mechanical properties of the material or through ultrasonic stimulation [208]. Deng et al. studied the piezoelectricity of porous polylactide (PLA) particles in terms of structural stability and porosity [77]. Hierarchically designed biodegradable PLA particles exhibit stronger piezoresponse under weak mechanical stimuli. Porous PLA particles with piezoelectric output up to 18.8 V were prepared by controlling the chain conformation of interlocking crystalline lamellae and the porosity of the lamellar network. Their stronger piezoelectric response to weak mechanical stimulation by an electric toothbrush triggered ROS, whitening teeth without damaging the enamel (Fig. 6C).

Compared to tooth discoloration, bacterial tooth disease presents a more serious challenge. Bacteria adhere to biofilm on the surface of teeth and produce acidic and toxic substances that damage tooth health. Therefore, in addition to removing tooth stains, tooth whitening methods that maximize the removal of biofilms are the focus of future research. Sharma et al. synthesized $NaNbO_3/ZnO$ binary nanocomposites with p-n heterojunction using hydrothermal method [209]. The heterojunction architecture can establish internal electric fields on both sides, improving the separation of electron-hole pairs and promoting the generation of ROS. Additionally, the composite demonstrated enhanced antimicrobial activity due to the synergistic effects of ZnO and ROS. On agar medium, the number of *Escherichia coli* (*E. coli*) colonies decreased with increasing vibration time of the material, resulting in a 21 mm zone of inhibition. Recently, He et al. prepared direct Z-scheme-g-C_3N_{4-x}/Bi_2O_{3-y} (CNB) heterostructures [210]. The g-C_3N_{4-x}/Bi_2O_{3-y} heterostructure exhibited the highest piezoelectric photocatalytic degradation efficiency (97.6%), which was much higher than that of single photocatalytic or piezoelectric treatment methods. The antimicrobial test showed that the CNB heterostructure had significant bactericidal effects on both planktonic *S. mutans* and *S. mutans* in biofilms. Oxygen vacancies (OVs) result from the detachment of lattice oxygen from metal oxides in specific environments. OVs regulate piezoelectric catalysis by affecting material structure and carrier dynamics [211]. Previous studies have shown that introducing heterometals to promote the generation of surface OVs is a promising way [212]. Liu et al. uniformly doped Cu element into Bi_2WO_6 substrate to study the role of Cu-doped Bi_2WO_6 (CBWO)-based three-in-one synergistic therapy in dental care [69]. The teeth whitening test showed that all samples doped with copper ions exhibited higher degradation efficiency than pure Bi_2WO_6, with 0.5CBWO had the best piezoelectric photodynamic degradation ability (99.7%). Therefore, the strategy of synergistic therapy (photodynamic, sonodynamic, and chemo-dynamic therapy) holds great potential in future oral health care.

While most existing studies focused on toothpaste or preparations for teeth whitening, Ma et al. developed a PTFE electret with a piezoelectric catalytic effect, exhibiting excellent whitening and antimicrobial abilities [76]. After ultrasonic treatment, PTFE exhibited high-voltage electrocatalytic efficiency. During low-frequency ultrasonic vibration, deformation induced by external force generated piezoelectric potential energy and formed a large amount of ROS in the aqueous solution, which effectively degraded the edible pigment. Additionally, they were able to achieve a bacterial inhibition rate of more than 80% (Fig. 6D). These studies provide a promising strategy for developing dental cleaning tools (e.g., toothbrushes) with good biocompatibility.

4.3. Periodontitis treatment

Periodontal diseases, including gingival diseases and periodontitis, are the most common inflammatory lesions in oral health [213]. These conditions can affect general health and are closely related to systemic diseases. Infection and inflammation are the main characteristics of periodontal disease, leading to the destruction of periodontal attachment structures, loss of affected teeth, and associated lesions. Other lesions associated with periodontitis (such as combined periodontal-endodontic lesions, furcation involvement, periodontal abscess, gingival recession, root sensitivity, and breath malodor) add to the complexity of diagnosis and treatment. Plaque control is key to periodontal disease treatment, leading to the development of numerous biomaterials and biotechnologies [214]. Among these, piezoelectric biomaterials with higher success rates and fewer side effects have played an indispensable role. Montoya et al. investigated the interaction of periodontitis-derived subgingival microorganisms with various biomaterials [68]. Among these, antimicrobial piezoelectric composites (BTO) were subjected to cyclic loading, where the generated charge activated the antimicrobial effect, controlling the viability of the microbiome. However, it did not significantly affect the microbiome composition and abundance, thereby preventing species imbalance.

The concept of non-surgical periodontal therapy (NSPT) was introduced in the 1980s. Previous studies have shown that bacteria and their products are the primary initiating factors of periodontal disease. Understanding the etiology and risk factors of periodontal disease enables the use of new equipment and methods to eliminate pathogenic factors or halt the progression of the disease, thereby achieving effective treatment [215].

Roldan et al. developed an injectable piezoelectric hydrogel (PiezoGEL) using 200 mg/mL gelatin methacryloyl (GelMA) and 9 mg/mL silanized particles BTO (Fig. 7A) [88]. The cyclic PiezoGEL altered the adhesion potential on biomaterial surfaces, thereby downregulating the expression of *porP* and *fimA*. The piezoelectric charge triggered the antibacterial mechanism of ROS, significantly upregulating *OxyR* in the cyclic PiezoGEL group. In addition, PiezoGEL upregulated the expression of *RUNX2* (initiating osteogenic differentiation), *COL1A1* (mediating bone matrix synthesis), and *ALP*, thereby promoting osteogenic differentiation. Finally, piezoelectric charge stimulation triggered alveolar bone regeneration in the mouse periodontitis model injected with PiezoGEL hydrogel. After one month of treatment, PiezoGEL reduced periodontal pocket depth (Fig. 7B).

Liu et al. constructed a piezoelectric hydrogel made from piezoelectric tetragonal $BaTiO_3$ nanoparticles (t-BTO NPs) and tilapia fish gelatin hydrogel [87]. This innovative system effectively generated electric signals under external stimulation, modulating immunomodulation and osteogenesis to treat periodontitis. Piezoelectric hydrogel-generated piezoelectric stimulation significantly increased the mitochondrial membrane potential of damaged PDLSCs, thereby energising the osteogenic differentiation of damaged PDLSCs. Additionally, piezoelectric stimulation induced M2 polarization of macrophages. This stimulation promoted osteogenic differentiation and bone regeneration in periodontitis both *in vivo* and *in vitro*. The biocompatible piezoelectric hydrogel used in the study exhibited excellent piezoelectric properties. The effectiveness of the piezoelectric hydrogel was confirmed by *in vitro* culture of periodontal ligament stem cells (PDLSCs) and *in vivo* experiments using a rat periodontitis bone defect model. The results showed that the output voltage measured by the GelMA + t-BTO hydrogel was 40 mV under US stimulation. *In vivo* experiments, involving the injection of piezoelectric hydrogel into rat periodontal tissues followed by physiological activities like chewing, demonstrated enhanced bone regeneration in periodontal defects associated with periodontitis. This improvement was particularly evident in the group that received both exercise and piezoelectric hydrogel 12 weeks post-injection.

Guided tissue regeneration (GTR) barrier membranes are widely used clinically in periodontitis treatment to guide the adhesion and

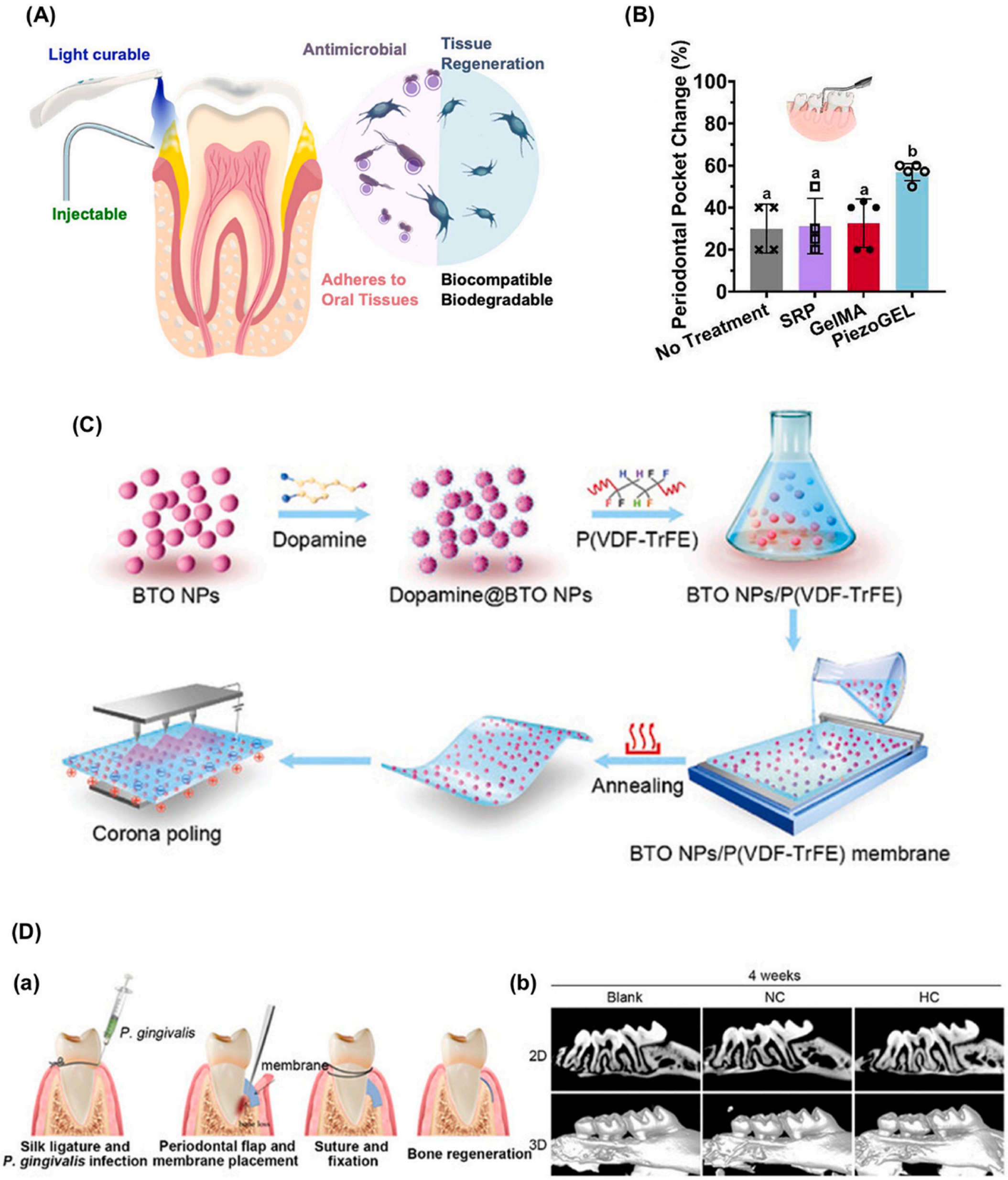

Fig. 7. (A) Schematics of the injectable piezoelectric hydrogel for periodontal disease treatment. (B) Change of periodontal pocket depth. Reproduced with permission from Ref. [88]. Copyright 2023 ACS Publications. (C) Schematic diagram of the fabrication process of BTO NP/P(VDF-TrFE) EMs with varying surface electrical potentials. (D) (a) Graphical depiction of the establishment of the *P. gingivalis*-induced periodontitis model and therapeutic mechanisms of the electroactive nanocomposite membrane. (b) After implantation of the different EMs for 4 weeks, representative micro-CT sagittal and 3-D Isosurface images of maxillary alveolar bone surrounding the second molar. Reproduced with permission from Ref. [81]. Copyright 2024 Wiley.

proliferation of periodontal ligament cells. Collagen is among the most commonly used natural polymers for producing biodegradable membranes [216]. However, these polymers have drawbacks, including rapid degradation, weak mechanical strength, and poor cell adhesion. Chitosan possesses biological properties such as controlled biodegradability, effective antimicrobial activity, and the ability to induce tissue regeneration, making it useful in bone tissue engineering [217]. Houshyar et al. fabricated chitosan/$BaTiO_3$ composite membranes using the solvent casting method [64]. The membranes' high intrinsic conductivity enhanced the adhesion and proliferation of periodontal cells in damaged areas exposed to alternating electric current, while their high dielectric constant promoted apatite formation. The results of the electrical properties study indicated that the film containing 6% $BaTiO_3$ was more suitable for the treatment of periodontitis. Besides, Song et al. designed a flexible $BaTiO_3$/P(VDF-TrFE) electroactive nanocomposite membrane (EM) (Fig. 7C), which exhibited excellent mechanical strength [81]. For periodontal inflammation, the surface electrical potential of the flexible electroactive nanocomposite membranes (EMs) suppressed the proliferation of *Porphyromonas gingivalis* (*P. gingivalis*), as well as reduced localized inflammation. Applying EMs to alveolar bone defects in mice increased bone mineral density (BMD) and reduced bone loss after 4 or 8 weeks of implantation (Fig. 7D).

4.4. Therapeutic devices

Tooth loss resulting in dentition defects and edentulism poses significant health risks [218]. The demand for dental restoration is rising due to both younger and aging populations experiencing tooth loss [219]. Removable dentures, consisting of a base plate, artificial teeth, connectors, and retainers, are a common method for dental prosthesis.

The base plate material is closely linked to the incidence of denture stomatitis. Poly(methyl methacrylate) (PMMA) is widely used for manufacturing denture bases in dental restorative treatments [220]. However, pure PMMA resin has several shortcomings, including low bacterial resistance, significant shrinkage, and ease of wear [221–223]. Candida-associated denture stomatitis is a common clinical issue in patients with removable dentures, primarily caused by *Candida albicans* (*C. albicans*). Montoya et al. discovered that cyclic deformation of the PMMA surface triggers the transition from normal flora to pathogenic yeast [85]. Consequently, they loaded $BaTiO_3$ piezoelectric nanoparticles instead of antifungal agents into PMMA (Fig. 8A). The piezoelectric fillers generated charges on the composite surface, inhibiting the morphological transition of *C. albicans* from yeast to hyphae, thereby inducing fungal cell death and producing antifungal effects (Fig. 8B). These results offer new opportunities for designing antifungal dentures.

Piezoelectric materials exhibit a unique mechanical-electrical coupling effect; they generate an electric field when subjected to mechanical deformation and can be mechanically deformed by an electric field. They have been used as biosensors and smart devices, with broad development potential in occlusion analysis, diagnosis, and orthodontic treatment [224,225]. Compared to conventional invisible appliances, those made of biological piezoelectric material offer many advantages. Shi et al. developed polyethylene terephthalate glycol-modified (PETG) composites containing piezoelectric $BaTiO_3$ nanoparticles ($BaTiO_3$NPs) (Fig. 8C) [83]. The PETG/$BaTiO_3$NPs nanocomposite diaphragm does not require external device assistance. Small mechanical stimuli from daily oral activities generate an electrical charge on the material's surface, leading to spontaneous antimicrobial activity. This ensures the appliance can be used for an extended period. Furthermore, the antimicrobial rate of the invisible aligners reached 41.65 ± 2.34%, 63.15 ± 4.98%, and 67.39 ± 5.35%, respectively, with increasing polarization and nanoparticle content.

4.5. *Dental implants*

Over the years, dental implants have become the mainstream treatment for restoring missing teeth. Due to their high long-term survival rate, predictability, stability, and good patient satisfaction, dental implants are often the preferred treatment choice [226,227]. The key to successful implantation is achieving rapid osteogenic differentiation of bone cells on the implant while simultaneously preventing bacterial infection [228]. Plaque is the primary cause of peri-implantitis [229]. Due to anatomical differences between implants and natural teeth, bacterial colonization and inflammation are more likely to occur. However, the materials used for existing artificial roots, such as titanium and its alloys, have several disadvantages for biomedical applications, including corrosion tendency, low wear resistance, and high Young's modulus [230]. Therefore, it is necessary to find alternative materials

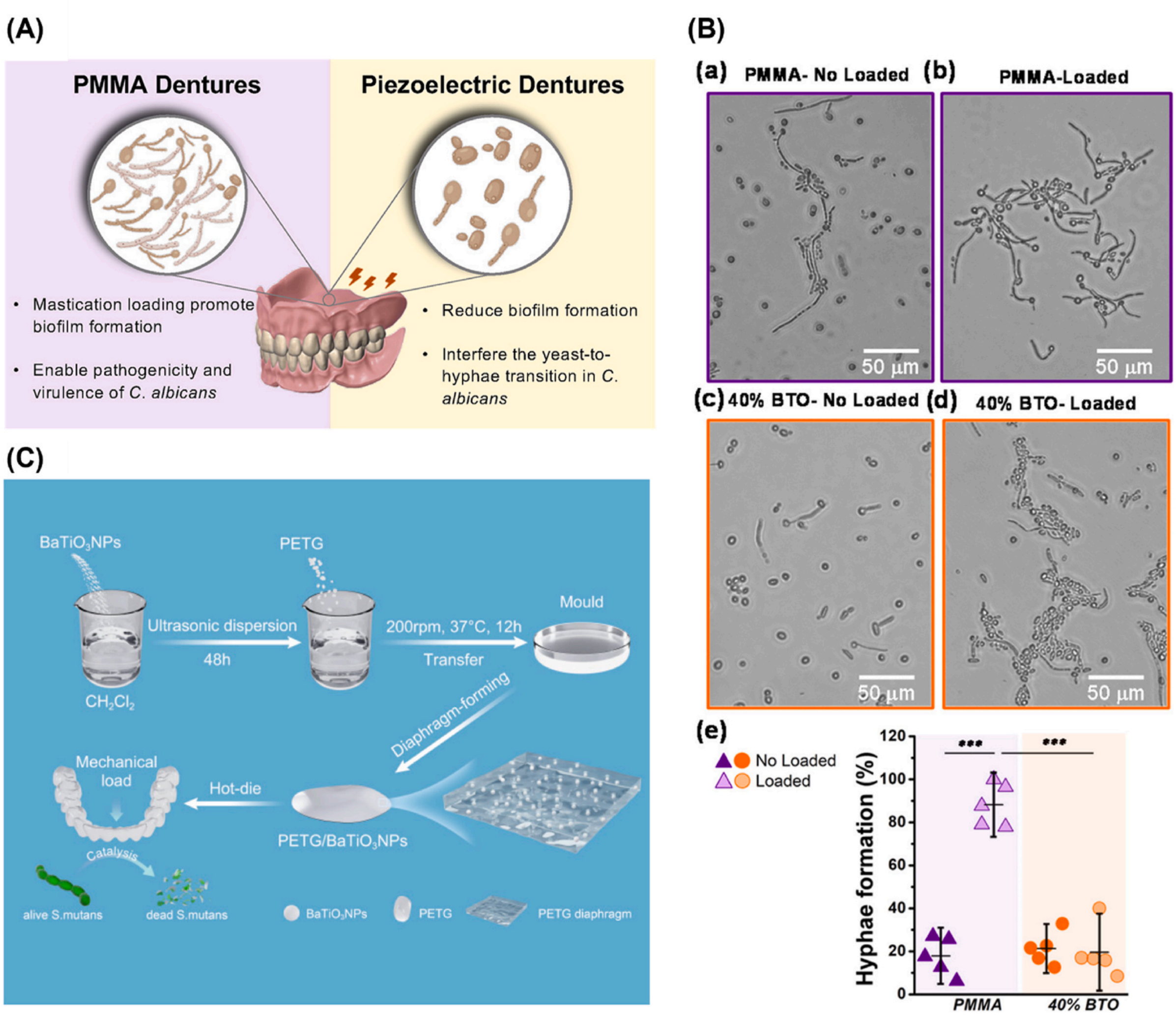

Fig. 8. (A) Comparison between poly(methyl methacrylate) (PMMA) dentures and piezoelectric dentures. (B) Yeast-to-hyphae transition. Reproduced with permission from Ref. [85]. Copyright 2021 ACS Publications. (C) Schematic diagram of synthesis of PETG/$BaTiO_3$NPs. Reproduced with permission from Ref. [83]. Copyright 2023 MDPI Open Access Journals.

with more suitable properties than titanium, such as piezoelectric ceramics. Fernandes et al. discovered that zirconia composites with added piezoelectric $BaTiO_3$ promote osteoblast differentiation, thereby contributing to peri-implant bone healing [231].

Furthermore, it is crucial to employ safe, antibiotic-free antibacterial technologies to prevent implant surface infections and promote bone integration. Several studies have observed that ultrasound can excite the piezoelectric effect, achieving a response similar to normal mechanical motion stimulation [208]. US-driven piezoelectric coating materials offer a novel option in terms of dental restoration. Wu et al. prepared $Ba_{0.85}Ca_{0.15}Zr_{0.1}Ti_{0.9}O_3$(BCZT)/$TiO_2$ biological piezoelectric coatings for implant surfaces using an in-situ reaction method [232]. Notably, the surface ion exchange and piezoelectric properties of the biomaterials synergistically promoted apatite deposition after 14 days of low-frequency ultrasound stimulation. The cavitation effect on the cell membrane, combined with piezoelectric catalysis, produces reactive oxygen species (ROS) that destroy the cell structure of microorganisms under ultrasound activation. For example, Li et al. focused on the application of piezoelectric nanostructures in mediating immune regulation and antimicrobial activity [233]. Researchers constructed a piezoelectric BTO surface on BTNPs Ti implants and subsequently deposited gold nanoparticles as co-catalysts to prepare piezotronic Ti (piezoTi) (Fig. 9A). *In vivo* model test, piezoTi with ultrasound radiation eliminated 99.5% of free *Staphylococcus aureus* (*S. aureus*) and reduced biofilm formation by 98.0% due to *in situ* ROS. Meanwhile, piezoTi activated the PI3K-AKT pathway to promote phagocytosis of immune cells. Sun et al. reported a US-responsive one-dimensional oxygen-deficient $BaTiO_3$ and l-arginine ($BaTiO_{3\text{-}x}$/LA) nanorod array exhibiting antibacterial activity after generating ROS, NO and $ONOO^-$ under ultrasound irradiation [67]. $BaTiO_{3\text{-}x}$/LA modulated macrophage M1 polarization in the early stage of infection, exerting a synergistic antimicrobial effect. In the late stage of implantation, $BaTiO_{3\text{-}x}$/LA promoted macrophage M2 polarization, which was beneficial to the bone formation of Ti implants. Metal/piezoelectric nanostructures embedded on implant surfaces can inhibit bacterial activity by activating oxidative stress, enhancing their performance in the anti-infection applications of SDT (Table 2). Xu et al. demonstrated this concept by constructing piezo PCL based on polycaprolactone (PCL) [201]. Under ultrasound infection (1 W cm^{-2}, 50% duty cycle, 1 MHz), piezo PCL significantly controlled *S. aureus* infection and alleviated inflammation in the tissue around the implant, thereby improving the efficiency of SDT (Fig. 9B, C).

5. Conclusion

Piezoelectric biomaterials represent a promising tool capable of providing stable electrical stimulation [234]. This paper reviews the classification of piezoelectric biomaterials in dental medicine and briefly compares the characteristics of inorganic and organic piezoelectric materials. The advantages of different materials guide their selective use for medical purposes. This paper summarizes the latest applications of piezoelectric biomaterials in endodontics, periodontics, prosthetics and implants, and orthodontics. However, further extensive exploration of new materials and optimization of existing piezoelectric materials are still needed.

6. Outlook

1) The release of piezoelectric particles and metal ions from piezoelectric materials may pose potential risks to human health [235]. For example, cations such as Sr^{2+}, Pb^{2+}, and Ba^{2+} may displace Ca^{2+} ions (both Ca(I) and Ca(II)) in the structure of hydroxyapatite (HAP) [236], leading to the incorporation of heavy metals into dental tissues. Therefore, controlling the release of ions is essential to ensure the safety of piezoelectric materials. This can be achieved through material selection and modification, designing slow-release systems, or using surface coating techniques [237–239]. However, these approaches have limitations, including insufficient material biocompatibility, issues with coating adhesion and durability, and challenges related to the complexity and regulation of slow-release systems.
2) Most piezoelectric biomaterials are currently in the *in vitro* experimental stage and face significant challenges in clinical application and translation. These challenges include a lack of supporting clinical data and absence of relevant biological evaluation guidelines [240–242].
3) Despite the development of various inorganic and organic piezoelectric materials, their applications in treating oral diseases remain

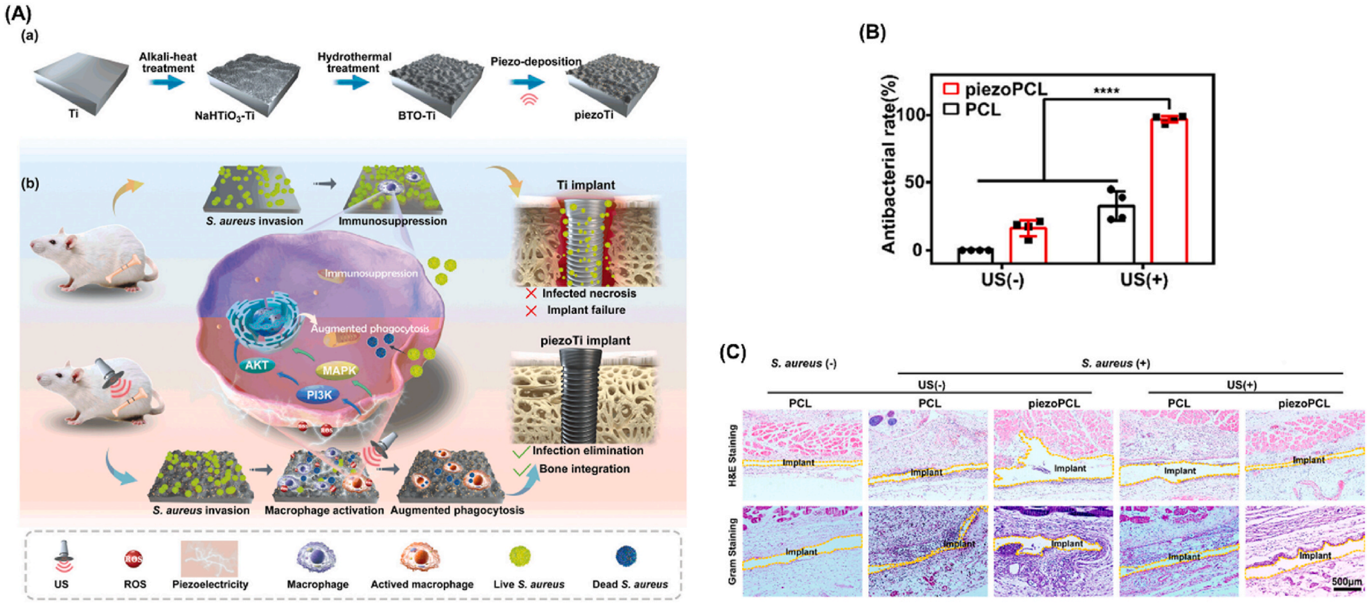

Fig. 9. (A) Schematic illustration of synthetic processes and working mechanisms of piezoTi. Reproduced with permission from Ref. [233]. Copyright 2023 Wiley. (B) Antibacterial rates against *S. aureus* of different samples. (C) H&E and Gram staining images after 1 day of treatment with different samples. Reproduced with permission from Ref. [201]. Copyright 2023 ACS Publications.

Table 2
Recent applications of piezoelectric biomaterials for oral prevention and treatment.

Application	Material/Scaffold	Fabrication technique	Specific purpose	Advantages	Ref.
Bone tissue regeneration	$BaTiO_3$–$SrZrTiO_3$	Magnetron sputtering	Promoting bone formation	Extend piezoelectric effect and improve hydrophilicity	[155]
	$CoFe_2O_4$/P(VDF-TrFE)	Solvent casting and thermal treatment	Accelerate the differentiation of BMSCs	Provide a heterogeneous electric potential gradient	[74]
	Nylon-11	Solvent casting	Promote the osteogenic differentiation of dental pulp stem cells (DPSCs)	High cytocompatibility and image DPSCs	[78]
	PDMS/AlN	Physical vapor deposition	Promoting bone formation	Flexibility, biocompatibility and osteoconductive ability	[84]
	ZnO@PCL/PVDF	Electrospinning	Promoting bone formation	Dual piezoelectric structure, combine antibacterial and immunomodulatory effects	[82]
	TiO_2 @PVDF	Electrospinning	Promoting bone formation	Enhanced electrical microenvironment	[72]
	PLLA/Ca/Mn co-doped $BaTiO_3$ (CMBT) scaffolds	Solvent casting	Promoting bone formation	Antimicrobial, anti-inflammatory, and biodegradable	[79]
	P-KNN/BG	Solid-state synthetic method	Promoting bone formation and vascularization	Enhance the differentiation and proliferation of endothelial cells, and release active ions continuously	[161]
	BTO/P(VDF-TrFE) nanocomposite membranes	Solvent casting	Promoting bone formation and vascularization	High-efficient and flexible	[80]
	Porous Ti6Al4V scaffold coated with $BaTiO_3$	Electron beam melting and hydrothermal treatment	Promoting bone formation and vascularization	Stimulate secretion of angiogenic factors	[89]
	PCL/PWH scaffold	3D printing	Promoting bone formation and vascularization	Biocompatibility and Degradability	[86]
	PVDF/ZIF-8 foam	Solid-state shearing milling	Promoting bone formation and vascularization	Stable voltage output and antibacterial effect	[73]
	PVDF/POSS–EGCG nanofibers	Electrospinning	Promoting bone regeneration and inhibiting bone resorption	Reduce oxidative stress and the expression of inflammatory cytokines	[165]
	$BaTiO_3$ nanorod arrays and l-arginine ($BaTiO_3$/LA)	Hydrothermal treatment and oxygen vacancies	Promoting bone formation and immunomodulation	High antimicrobial efficacy, enhanced piezoelectric response and acoustic dynamic synergy therapy	[67]
	$BaTiO_3$/β-TCP (BTCP)	Two-step sintering	Promoting bone regeneration and modulating cellular immunity	Create a favorable immune microenvironment	[65]
Oral mucosal regeneration	VDF-TeFE membrane with a copper coating	Magnetron sputtering	Promoting oral mucosa regeneration	Protect wounds, reducing infection, and antibacterial effect	[75]
	VDF-TeFE	Electrospinning	Promoting oral mucosa regeneration	High specific surface area, greater elongation, and prevent adhesion to wounds	[174]
	VDF-TrFE membrane modified with copper	\	Promoting oral mucosa regeneration	Enhancement of fibroblast activity, reducing inflammation, and reduction of complications	[175]
	VDF-TrFE membrane		Promoting oral mucosa regeneration	Promote blood vessel formation and reducing inflammation	[176]
Dental tissue regeneration	PKNN	Solvothermal process	Promoting dental pulp tissue regeneration	A wireless and direct method for chairside therapy	[71]
	Strontium-containing P(VDF-TrFE) film	Solvent casting	Promoting dentin tissue regeneration	Induce the odonto-differentiation of DPSC, and good biosafety	[191]
Endodontic diseases	$BaTiO_3$ nanoparticles		Treatment for caries	Good antibacterial Effects, mineralization, and mechanical properties	[197]
	BTO@Au nanoparticles	Solvent casting with piezo-deposition	Root canal therapy	Antimicrobial, non-invasive, efficient, simplified, biocompatible and safe	[201]
	$BaTiO_3$	Hydrothermal method	Tooth whitening	Non-destructive, biocompatible and effective	[66]
	PLA	Low-temperature melt-processing method	Tooth whitening	Non-destructive, convenient and safe	[77]
	$NaNbO_3$/ZnO	Hydrothermal method	Tooth whitening	High catalytic efficiency and inhibition of bacterial growth	[209]
	g-C_3N_{4-x}/Bi_2O_{3-y} heterostructure	Thermal condensation	Tooth whitening	Adsorption of bacteria and biofilm eradication	[210]
	Cu-doped Bi_2WO_6	Hydrothermal method	Tooth whitening	The three-in-one synergistic treatment	[69]
	PTFE electret	Ultrasonic treatment	Tooth whitening	High-efficient degradation of pigments and antibacterial properties	[76]
Periodontitis	BTO	\	Treatment for periodontitis	Reduction of microbial population and inhibition of biofilm formation	[68]
	GelMA/BTO hydrogel	Mixing, photopolymerization, and curing	Treatment for periodontitis	Easy handling and delivery into periodontal pockets, mechanical stability, and minimally invasive	[88]
	GelMA + t-BTO hydrogel	Thermal calcination	Treatment for periodontitis	Promote conversion of macrophages from M1 to M2 phenotype	[87]
	Chitosan/$BaTiO_3$ composite membranes	\	Treatment for periodontitis	Biodegradability and antimicrobial activity against periodontal pathogens	[64]

(*continued on next page*)

Table 2 (*continued*)

Application	Material/Scaffold	Fabrication technique	Specific purpose	Advantages	Ref.
	BTO NP/P(VDF-TrFE) membranes	Solution casting	Treatment for periodontitis	Broad-spectrum antibacterial effects, promotion of tissue regeneration, biocompatibility	[81]
Therapeutic Devices	$BaTiO_3$ nanoparticles		Denture restoration	Continuous antifungal effect, long-term stability and avoidance of drug resistance	[85]
	PETG/$BaTiO_3$NPs	Solution blending	Orthodontic treatment	No need for external energy and self-powering antibacterial properties	[83]
Dental implants	$BaTiO_3$	Press-and-sintering technique	Dental implants	Catalyzing antimicrobial efficacy and improving long-term success of implantation procedures	[231]
	$Ba_{0.85}Ca_{0.15}Zr_{0.1}Ti_{0.9}O_3$(BCZT)/$TiO_2$ coating	Hydrothermal reaction	Dental implants	Non-toxic and promoting calcium deposition	[232]
	BTO-Ti	Hydrothermal method	Dental implants	Noninvasive, antibiotic-free, and efficient strategy for implant infection	[233]
	$BaTiO_{3-x}$/LA nanorod array	Hydrothermal method	Implant infection treatment	Synergistic effects of acoustic therapy and immunomodulation	[67]
	PiezoPCL film embedded BTO@Au NPs	Hydrothermal method	Implant infection treatment	Anti-biofilm formation, anti-reinfection and good biocompatibility	[201]

limited. To expand future options, bio-piezoelectric materials with excellent properties must be developed using new technologies and efficient synthesis methods to overcome limitations such as poor stability and unpredictable therapeutic efficacy.

4) The production of lead-free piezoelectric ceramics involves significant energy consumption during the sintering process [243]. Therefore, more efficient and environmentally friendly manufacturing processes must be developed to reduce energy waste, increase resource efficiency, and enhance environmental sustainability.
5) The key factors for successful pulp regeneration include stem cells, biomaterial scaffolds, and growth factors. Biomaterials not only provide space for cell growth but also regulate cellular functions [244]. It has been shown that nanofibrous PLLA scaffolds can promote the odontogenic differentiation of dental pulp stem cells, providing a favorable environment for the formation of the pulp-dentin complex [245]. Additionally, hydrogels demonstrate great potential in pulp regeneration. Vascular reconstruction is a critical step in pulp regeneration [246]. Given the piezoelectric properties retained by blood vessels, piezoelectric nanoparticles that provide electrical stimulation signals [247], in combination with other materials, can be used to guide tissue revascularization in a biomimetic manner. Considering the unique structure of the pulp chamber and root canal, the application of nanotechnology [248, 249] and the design of material pore sizes [250] are also important factors to take into account.
6) Joint regeneration and repair have long been challenging for both physicians and patients. A study on biodegradable piezoelectric scaffolds as joint implants demonstrated cartilage regeneration in rabbit femoral joints [251]. While most joint surfaces are covered with hyaline cartilage, the temporomandibular joint (TMJ) is covered with fibrocartilage, differing significantly in structure and repair mechanism. To our knowledge, no studies have explored the use of piezoelectric biomaterials as TMJ implant materials.

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CRediT authorship contribution statement

Kaichen Zeng: Writing – original draft, Software, Resources, Formal analysis, Data curation, Conceptualization. **Yifan Lin:** Validation, Supervision. **Shirong Liu:** Visualization, Investigation. **Ziyan Wang:** Methodology, Data curation. **Lvhua Guo:** Writing – review & editing, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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