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REVIEW

Recent Advances in Whiskers: Properties and Clinical Applications in Dentistry

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Abstract: Whiskers are nanoscale, high-strength fibrous crystals with a wide range of potential applications in dentistry owing to their unique mechanical, thermal, electrical, and biological properties. They possess high strength, a high modulus of elasticity and good biocompatibility. Hence, adding these crystals to dental composites as reinforcement can considerably improve the mechanical properties and durability of restorations. Additionally, whiskers are involved in inducing the value-added differentiation of osteoblasts, odontogenic osteocytes, and pulp stem cells, and promoting the regeneration of alveolar bone, periodontal tissue, and pulp tissue. They can also enhance the mucosal barrier function, inhibit the proliferation of tumor cells, control inflammation, and aid in cancer prevention. This review comprehensively summarizes the classification, properties, growth mechanisms and preparation methods of whiskers and focuses on their application in dentistry. Due to their unique physicochemical properties, excellent biological properties, and nanoscale characteristics, whiskers show great potential for application in bone, periodontal, and pulp tissue regeneration. Additionally, they can be used to prevent and treat oral cancer and improve medical devices, thus making them a promising new material in dentistry.

Keywords: whiskers, dentistry, growth mechanism, biomaterials

Introduction

Whiskers are fibers that form naturally or grow under artificially controlled conditions (predominant form) as single crystals.[1] They have a very small diameter of about 0.1–10 μm, and an aspect ratio of 5–1000.[2] They do not contain defects such as grain boundaries, dislocations, or cavities, that are usually present in other material, and their atomic arrangement is highly ordered. Consequently, their strength is close to the theoretical value of the intact crystals, and their mechanical strength is equal to the inter-atomic forces between neighboring atoms.[3] In addition to high modulus and elongation, the highly oriented structure of whiskers imparts them with superior electrical, optical, magnetic, dielectric, conductive, and superconductive properties. With a nearly complete crystal structure, whiskers have incredible mechanical strength, as plastics, coatings and light brittle class of inorganic and other materials modification additives, showing excellent physicochemical properties and mechanical properties. Thus, they are known as the reinforcing and toughening materials of the 21st century.[4,5]

In 1574, Erker L found a hair or beard-like material on the surface of sulfate ores of copper and silver.[6] Subsequently, Boyle (1661) compared the different forms of growth of silver whiskers on stone and glass.[7] In 1952, the American Bell Telephone Company determined the strength of tin (Sn) whiskers for the first time in the laboratory and found that it was much greater than (close to the theoretical strength) that of the ordinary metal Sn.[8] The earliest industrialized whiskers product appeared in 1962, however, its application was limited by its extremely high price (3000–5000/kg for silicon carbide (SiC) whiskers). Subsequently, a breakthrough in their application occurred in the 1980s, when the cheaper potassium titanate(K_4TiO_4) whiskers were introduced in Japan. Calcium sulfate ($CaSO_4$) and calcium carbonate ($CaCO_3$) whiskers were successfully developed at lower costs. The aluminum borate (H_3AlBO_2) whisker was examined in Japan

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in 1987, followed by small batch production (10 tons per annum [t/a]) in 1991 and a large-scale production (200 t/a) in 1995. In the late 1990s, the study of whiskers became a hot topic in materials science research, resulting in the development of more than 100 different whiskers, to date.[5,9]

Whiskers are used in various applications due to their unique physical and chemical properties.[5,9] Autologous bone grafting is considered the gold standard for bone regeneration in the treatment of bone defect repair.[10] However, autologous bone grafts have drawbacks, such as limited access and donor damage, and allogeneic bone grafts may cause severe immune rejection. The proposal and development of bone tissue engineering (BTE) has led to new ideas for the repair and regeneration of bone defects.[11] The current materials applied to BTE are deficient in biocompatibility, bioactivity, and osteoinductive capacity.[12,13] Some materials may trigger an immune or inflammatory response, leading to tissue damage or dysfunction,[14] while others have limited osteoinductive ability to meet the needs of complex bone defect repair.[15,16] Owing to their unique physicochemical properties and biocompatibility, whiskers can be used as high-performance scaffolding materials and carriers of bioactive factors for BTE, aiding in the effective repair and regeneration of bone defects.[17]

Periodontal and pulpal regeneration involves the repair of damaged periodontal and pulpal tissues, respectively, via biological means, resulting in the restoration of their normal functions.[18] Existing periodontal and pulpal regeneration materials can lead to impaired cellular connectivity, microenvironmental disruption, and impaired cell loss and differentiation.[19–22] Whiskers with high strength and modulus provide stable support structures during regeneration and promote tissue reconstruction and repair.[23] The superior biocompatibility of this material helps reduce irritation and damage to periodontal and pulpal tissues and facilitates cell adhesion and proliferation.[24] In addition, as a nanoscale material, whiskers facilitate close bonding with periodontal and pulpal tissues, promoting cellular exchange and nutrient transfer during regeneration.[25] They offer significant benefits in periodontal and pulpal regeneration applications and are expected to bring significant advances in dentistry.

Oral cancer is a major health challenge in today's world. The existing materials face poor carrier selection and release, limited delivery, and significant side effects during the prevention and treatment of this disease.[26] Insufficient targeting performance may lead to phagocytosis, and the mechanisms of action and power sources of these materials need to be clarified.[27] Moreover, drug transportation is limited, and safety is doubtful.[28] Alternatively, the highly targeted positioning of whiskers enables precise action on tumor tissues and reduces damage to normal cells.[29] Furthermore, the biocompatibility of this material can effectively reduce the immune rejection reaction during treatment.[30] The excellent drug-carrying properties of whiskers can aid in transporting large amounts of drugs directly to the lesion, thereby improving the therapeutic effect.[31] The emergence of whiskers provides new and innovative strategies for cancer treatment and opens up new directions for future research and applications.

Oral medical devices have issues related to biocompatibility, corrosion resistance, abrasion resistance, and mechanical properties.[32–35] However, whiskers have high strength, high modulus of elasticity, and low density and can serve as reinforcement and support in medical devices.[36,37] They significantly enhance the mechanical properties of the material through various mechanisms, such as crack bridging, crack deflection, and pullout effect. This improves the toughness, crack extension resistance, and fatigue life of the composite material and enhances the overall performance of the material.[38] Whiskers have good compatibility with human tissues and do not readily cause rejection or inflammatory reactions in the body. They have good chemical stability, which is conducive to maintaining a stable performance of the medical device in the physiological environment.[39] In addition, they have antimicrobial properties, which help prevent medical devices from causing infections during use, thus further improving the safety and reliability of the devices.[40]

Whiskers have been extensively studied in biomedical applications. Some whisker-based materials, such as chitin whiskers (which are used to promote osseointegration between the jawbone and the implant), have reached the clinical trial and translational stage.[41] Chitin whiskers significantly enhance gingival production and angiogenesis.[24] Titanium dioxide (TiO_2) whiskers act as drug carriers to increase the intracellular concentration of the anticancer drug garcinia cambogia and enhance its potential antitumor efficacy.[42] Zinc oxide (ZnO) nanowhiskers significantly mitigate the consequences of *Staphylococcus aureus*-induced dermatitis.[43] However, the use of whiskers in dentistry is in its infancy, and there are many challenges in the clinical application and translation of this material in the dental field. Rigorous regulatory and experimental evaluations and preclinical assessments are required before they can be used in the clinic.[44]

Before the clinical application and translation of whiskers in dentistry, it is important to ensure that they strictly comply with the relevant medical device regulations and undergo the registration and approval process.[45] Thus, whiskers need to undergo rigorous and exhaustive clinical trials to fully validate their effectiveness in diagnosing and treating oral diseases.[46] During clinical application and translation, conducting a thorough safety assessment of whiskers is critical. The assessment includes but is not limited to, in-depth studies of the biocompatibility of whiskers with oral tissues and cells to ensure that the material does not cause adverse reactions or rejection in the oral environment.[47,48] In addition, toxicological testing is required to clarify whether the material has any potential toxic or adverse effects on the human body.[49,50] Therefore, the clinical application of whiskers has a long way to go, and much effort is needed to enhance its clinical breakthrough.

The research and application of whiskers are expanding with the continuous progress of science and technology and the growing demand for applications. Refinements in preparation technologies, improvements in performance regulation strategies, and expansions in the fields of application may bring whiskers to the forefront, resulting in added benefits and contributions to the development and progress of human society.

Classification of Whiskers

Small quantities of natural minerals containing whiskers (eg, suanite) exist in nature. For industrial applications, whiskers are mainly synthesized under artificially controlled conditions. More than 100 materials, mainly metals, oxides, carbides, halides, nitrides, graphite, and polymers, can be used to make whiskers. Whiskers can be divided into two main categories: organic and inorganic.[51,52] Among the organic whiskers, cellulose, poly(butyl acrylate-styrene), and poly (4-hydroxybenzyl ester) whiskers (PHB whiskers), are more commonly used in polymers. Inorganic whiskers mainly include ceramic (such as SiC, K_4TiO_4, and aluminum borate (H_3AlBO_2)), inorganic salt (such as $CaCO_3$ and $CaSO_4$), and metal (such as alumina oxide (Al_2O_3) and ZnO) whiskers.

Inorganic Whiskers

Inorganic whiskers are micron- or nanometer-scale fibers grown by the superposition and polymerization of numerous single crystals with complete and smooth cross-sections. They include ceramic, inorganic salt, and metal whiskers and have a wide range of applications in composites, coatings, batteries, and other products.[53,54] Ceramic and inorganic salt whiskers can be used in ceramic and polymer composites, respectively, whereas metal whiskers are mainly used in metal matrix composites. In addition, inorganic whiskers can be used as fillers, flame retardants, and other products utilized in the production of plastics and rubber to improve the strength, wear resistance, corrosion resistance, and other properties of medical devices.[53,54]

Ceramic Whiskers

Ceramic whiskers are manufactured from special ceramic raw materials, including single-crystal fibers and polycrystalline fibers, and composed of small grains (5×10^{-3}–5×10^{-2} μm). They are characterized by high strength, high modulus of elasticity, low density, and high heat resistance. The whiskers are single-crystal short fibers (1–3 μm in diameter and 20–200 μm in length) grown from composite ceramic materials, such as carbon, silicon, aluminum, and magnesium. They are free of defects found in conventional materials, such as grain boundaries, dislocations, and cavities. The atoms are arranged in a highly ordered manner; hence, the strength of the whiskers is close to that of the theoretical value of the intact crystals. The common ceramic whiskers include Al_2O_3,[55,56] SiC,[57–60] boron carbide(B_4C),[61] zirconium dioxide(ZrO_2),[62,63] aluminum nitride (AlN),[64,65] and silicon nitride (Si_3N_4)[66,67] whiskers. These whiskers are widely used in medical devices due to their light weight, good toughness, high strength, and superior temperature resistance. They can be used as biological scaffolds or enhancement materials in conjunction with stem cells or growth factors during pulp regeneration.[24] Furthermore, ceramic whisker composites with resin or ceramic substrate can improve the mechanical properties and aesthetics of the restorations, reduce the risk of fracture and dislodgement, improve the success rate of the restoration, and extend the service life of the denture.[68,69]

Inorganic Salt Whiskers

Inorganic salt whiskers are composite crystalline materials composed of inorganic salts with specific topological structures and multisystem molecular properties. They can be used to manufacture various types of materials, such as ion exchange resins, activated carbon, molecular sieves, and components used in fine chemicals,[70,71] The adsorption properties, specific surface area, and ionic conductivity of these whiskers can be altered to a certain extent, allowing them to have more functions and applications.[72] Inorganic salt whiskers mainly include $CaSO_4$,[73–75] $CaCO_3$,[76,77] magnesium oxide(MgO),[72,78] zinc sulfide(ZnS),[79] and TiO_2,[80,81] which have a wide range of applications in the industrial field. $CaSO_4$ whiskers are mainly used for reinforcing and toughening polymer materials such as plastics, rubber, and coatings.[82] $CaCO_3$ whiskers are used as reinforcing agents and fillers in plastics,[83] whereas TiO_2 whiskers have photocatalytic and antibacterial properties, which are potentially valuable in the environmental protection and medical fields.[63] In the biomedical field, inorganic salt whiskers are used in the manufacture of medicines, altering their activity and degree of absorption. In dentistry, these whiskers are used as raw materials for oral coatings to improve the hardness and corrosion resistance of the tooth surfaces.[84] In addition, they can be used as drug delivery carriers to improve the therapeutic efficiency of antitumor drugs.[85] Inorganic salt whiskers are used the surface or internal structure of implants, thereby improving the biocompatibility and osseointegration of implants.[86,87]

Metal Whiskers

Metal whiskers are naturally formed on the surfaces of metals or artificially controlled, in the form of single-crystal growths, commonly found in tin Sn,[88,89] Fe,[90] Au,[91] Ag,[92] Cu,[93,94] and other metals with low melting points. The diameter of the metal whiskers is generally between a few nanometers and tens of nanometers, while the length can reach the micron level.[95,96] These whiskers look like animal whiskers with high strength and good elasticity and have electrical, optical, magnetic, dielectric, conductive, and superconductive properties. In the biomedical field, metal whiskers can be used to prepare drug carriers, biosensors, artificial bones, and vascular scaffolds. For example, the excellent conductivity of metal whiskers can be used to prepare wearable medical devices or sensors for monitoring human physiological signals.[97] In addition, they can be used as drug carriers for targeted delivery and controlled release, thereby improving the efficacy of the drugs and reducing side effects.[31] Metal whiskers have antimicrobial properties and can be used to prepare oral care products with antimicrobial functions, such as toothbrushes and toothpastes.[98]

Organic Whisker

Organic whiskers are high-performance, fibrous materials that utilize natural or synthetic materials. They have an acicular or fibrous appearance, a highly oriented and long-range ordered structure, and are usually made of polymer compounds. The manufacturing methods of organic whiskers mainly include solution spinning, melt spinning, and emulsion spinning. The properties such as high strength, high modulus of elasticity, high temperature resistance, and chemical corrosion resistance make organic whiskers an important raw material in several products, including composite materials, reinforcing materials, sealing materials, and thermal insulation materials.[99,100]

Cellulose Whiskers

Cellulose whiskers are nanomaterials obtained by the modification of natural plant cellulose, They consist of nano-sized cellulose fiber particles with high degrees of crystallinity and orientation. The fiber diameter of cellulose whiskers is usually between 4–10 nm, and the length is between 100–500 nm.[101] Cellulose whiskers have excellent physical properties, their strength is close to the theoretical value of intact crystals and much higher than those of other short-cut fibers.[102,103] In addition, cellulose whiskers have good thermal and chemical stability. After modification treatment, these whiskers can have different functional groups and reactivity, enabling them to chemically bond to various substrates. Cellulose whiskers can form strong hydrogen bonds, which help to control drug release and provide good strength for drug carriers.[104] They enhance the toughness and rigidity of composites, reduce brittleness, and enhance the range of applications for dental composites.[105] Furthermore, they can be used to synthesize silver and other metal nanoparticles with controlled morphology and antimicrobial properties to enhance the antimicrobial effect. These whiskers can be used as wound dressing for skin repair.[106]

Poly (Butyl Acrylate-Styrene) Whiskers

Poly (butyl acrylate-styrene) whisker is a new type of functional composite synthesized using a specific technology. The two different polymer chains (poly(butyl acrylate) and styrene) in the whisker growth process aid in realizing the co-crystallization and co-orientation, the unique structure of the whisker to show a high degree of mechanical strength and toughness.[107] The diameter of this whisker is generally between a few to tens of nanometers, while the length can reach the micron level. This nano-size effect provides the whisker with a large specific surface area and good interfacial interactions, which is conducive to improving the mechanical properties and thermal stability of composites.[108] Poly (butyl acrylate-styrene) whiskers grow in a specific direction to form a highly oriented structure, increasing their tensile strength, modulus of elasticity, and toughness. It is possible to prepare poly (butyl acrylate-styrene) whiskers with different morphologies and properties by adjusting the synthesis conditions and formulations; this will enable their use for different applications in the biomedical, aerospace, automotive, and construction fields. The excellent heat and low-temperature resistance, the high strength and stiffness, and the good impact and abrasion resistance of these whiskers make them useful in dental restorations and tooth fabrications.[109] The properties aid in reducing the brittleness of restorative materials, increasing the strength and wear resistance of restorations, resisting the complexity of the oral environment, and extending the service life of restorations.

Poly (4-Hydroxybenzyl Ester) Whiskers (PHB Whiskers)

The PHB whisker is a linear polymer with unique structure and properties and is prepared by microbial fermentation. They contain many benzene rings in the molecular chain linked together by ester bonds.[110,111] The special arrangement of the benzene rings and ester bonds in the molecular chain provides these whiskers with a high degree of crystallinity and rigidity, resulting in good mechanical properties and stability. PHB whiskers are biodegradable and biocompatible and have a wide range of medical, environmental, and agricultural applications. In dentistry, they are used to prepare surgical sutures, drug carriers, and tissue engineering scaffolds. The nanostructure of these whiskers helps to promote cell adhesion and proliferation, accelerating the bonding of the implant to the surrounding bone tissue and improving its stability and success.[112]

Characterization of Whiskers

Mechanical Properties

Whiskers are micro- and nano-sized short fibers grown from high-purity single crystals. The mechanical strength of the crystal is equal to that generated by the force between neighboring atoms, moreover, the highly ordered atomic structure results in whiskers with high strength, modulus of elasticity, and elongation.[2,113] The typical whisker elongation is comparable to that of glass fibers, while the tensile modulus is comparable to that of boron fibers, combining the best of both worlds. Whiskers, as fine single crystals with a complete internal structure, are at least one order of magnitude stronger than the corresponding common materials.[114,115] They can elastically withstand large strains without permanent deformation. Whiskers are not permanently deformed by a strain of 4%, whereas bulk crystals elastically deform in a range of less than 0.1%. The excellent mechanical properties enable their use as reinforcing materials that can significantly improve the mechanical properties of the composites. Wang et al[116] prepared isotactic polypropylene (PP)/titanate whiskers composites (PP/whiskers) by melt blending with 3-aminopropyl triethoxysilane as surface modification of titanate whiskers and maleic anhydride grafted PP (PP-g-MAH) as a capacitance enhancer (Figure 1). The notched impact strength of the PP/whiskers composite was increased to 7.4 ± 0.1 kJ/m^2, which was 140% higher than that of pure PP, while the tensile and flexural strengths were improved to different degrees. Whiskers are an ideal reinforcing and restorative material in dentistry due to their excellent mechanical properties.[117] They can be used as reinforcing agents for dental composites and introduced into matrix materials, such as resins and ceramics, which can effectively improve the strength and toughness of the restorations and increase their abrasion and fracture resistance. This is of great significance for improving the service life of restorations and reducing the risk of restoration failure.[118,119] Whiskers can be used as a coating or modifying material on the implant surface, increasing the bonding strength between the implant and the surrounding bone tissue and improving the stability of the implant.[120,121] The excellent mechanical properties also minimize problems such as loosening or fracture of the implant during use.[122] Despite the complexity and

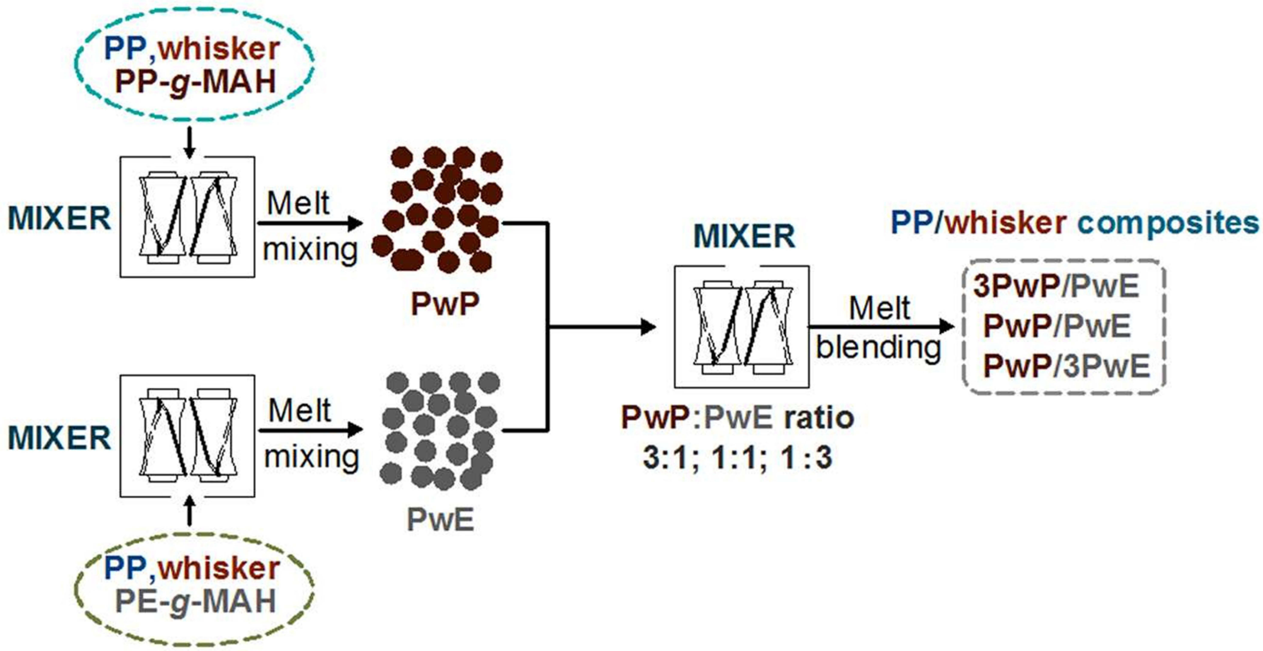

Figure 1 The mechanical properties of titanate whisker reinforced isotactic polypropylene.
Note: Reprinted from *Composites Science and Technology*, Vol 164, Wang X, Song R, Chen Y, Zhao Y, Zhu K, Yuan X, Mechanical properties of polypropylene by diversely compatibilizing with titanate whiskers in composites, 103–109, Copyright © 2018, with permission from Elsevier.[116]

variability of the oral environment, the high temperature stability of whiskers allows them to maintain stable performance in the oral environment.[123] Thus, the superior mechanical properties of whiskers bring new possibilities for development in the field of dentistry. Through further research and application, whiskers are expected to provide more reliable and effective solutions for dental restoration, regeneration, and implantation.

Magnetic and Electrical Properties

Whiskers are ideal for studying the magnetic domains of ferromagnetic substances because of their small size, internal structure, and perfect shape. Whiskers with small diameters are single magnetic domains, those with large diameters also have relatively simple structures. Similar to the mechanical properties, the coercivity of whiskers is also three orders of magnitude higher than that of the common material (close to the theoretically calculated value). The coercivity increases with the increase in the diameter of the whisker and is greatly improved when the whisker diameter is with 1 μm. The electrical properties of whiskers are sensitive to changes in size, on the one hand, they are influenced by the high degree of integrity of their internal structure, while on the other hand, they are affected by the strong interaction of the interfaces (the whisker surfaces and grain boundaries).[60] The resistance of the whisker is significantly reduced by the structural integrity of its internal structure, alternatively, the presence of the interface increases the diffraction of electrons, reduces the mean free range of the electrons, and raises the resistance.[124,125] The magnetic and electrical properties of whiskers are still in the exploratory stage for applications in dentistry, but have shown potential applications. Magnetic properties of whiskers used to design novel magnetic dental restorative materials.[126] Magnetically responsive restorations are prepared by introducing magnetic whiskers into dental composites. The whiskers are precisely positioned and fixed by an external magnetic field, improving the precision and stability of the restoration. In addition, magnetic fields can affect cell growth and differentiation, and magnetic whiskers are used as a novel biomaterial for the construction of oral therapeutic devices capable of generating localized magnetic fields to promote the regeneration and repair of oral tissues.[127,128] Meanwhile, whiskers with electrical properties are used to construct electrical stimulation therapy devices to promote healing and regeneration of oral tissues by applying appropriate electrical stimulation.[129,130]

Biosafety

Whiskers are fibrous single crystals with an aspect ratio greater than 10:1. They are highly pure, ultrafine synthetic inorganic non-metallic materials, that are biologically safe for the following reasons: good biocompatibility, compatibility with human tissues, and do not produce rejection reactions.[131] Whiskers are chemically stable and will not cause harm to the human body.[43] The mechanical properties of whiskers are excellent, they can withstand tremendous pressure and bending, cannot be easily broken, and can maintain their performance for a long time.[132] The mature preparation process of whiskers makes it possible to control their shape, size, and performance and ensure their stability and reliability.[39] Whiskers degrade slowly in the human body and can maintain their functionality for a long time. The excellent Biosafety of whiskers allows them to integrate well with oral tissues when used as enhancers or bioactive coatings, reducing inflammatory reactions and rejection caused by implants or restorative materials.[120,133] In addition, whiskers with excellent biosafety can be used as scaffold materials or cell culture substrates to provide strong support for tooth tissue regeneration.[23] Combining whiskers with growth factors and cells makes it possible to construct a biologically active tooth regeneration system that promotes the regeneration and repair of tooth tissue.[24] Similarly, by combining whiskers with antimicrobial drugs or agents, oral restorative materials or oral care products with highly effective antimicrobial properties can be prepared to effectively prevent and treat oral infections.[134,135]

Growth Mechanism of Whiskers

Whisker growth is a complex process influenced by multiple factors, including the temperature, pressure, melting and solidification processes, structure and orientation of the crystals, impurities and defects, and various growth kinetic processes. The growth of whiskers mainly depends on the diffusion and dislocation motion mechanisms.[136] In the diffusion mechanism, the reverse surface tension generated by the surface oxidation process that diffuses into the neighboring region of the whisker, is the source of whisker growth; it reduces the surface free energy and provides the driving force for whisker growth. The dislocation motion mechanism drives whisker growth through the motion of dislocations, which are linear defects that occur in crystals and can be eliminated or created through motion.[137] The position and motion of dislocations can significantly influence the direction and morphology of the whisker growth. Additionally, specific conditions, such as surface projections and specific atmospheres, can also affect the motion of dislocations and, consequently, the whisker growth.

The whisker growth process involves specific growth stages and mechanisms and can be divided into the following phases: nucleus formation, primary growth phase, secondary growth phase, and end growth phase.[138] Among them, the main growth phase has a selective orientation growth characteristic, where rapid directional growth occurs along a certain direction of the crystal structure. The secondary growth or overgrowth phase occurs mainly at the top of the whisker. In the whisker growth stage, the crystal mainly undergoes a one-dimensional directional growth, the growth rate of the edge surface is generally slow, and almost no growth occurs relative to the axial growth rate. Once the difference between the anisotropic growth rates of the crystals is small, the crystals grow uniformly in all directions along the three dimensions, forming a normal crystal.

Considerable research has been done on the whisker growth mechanism since the discovery of helical dislocations in metallic Sn whiskers by Frank in 1958.[139,140] Whiskers can be square, rectangular, hexagonal, triangular, or circular in cross-section. Depending on the growth process, the growth rates vary from 0.1 nm/s for spontaneous growth to several mm/s for some chemical and solution pathways. The five mechanisms proposed for whisker growth are as follows:[141] (1) the presence of axial helical dislocations, which applies to both vapor-phase growth and liquid–phase growth; (2) the vapor–liquid–solid (VLS) mechanism, which applies only to vapor–phase growth; (3) anisotropic growth of the structure; (4) toxicoplasmic-induced growth; and (5) restricted diffusion growth.

VLS Growth Mechanism

The VLS growth mechanism was proposed by Wagner and Ellis in 1964 during their study on silicon whisker growth, which is the important theoretical basis for the preparation of the vast majority of commercial whiskers.[142,143] The V in VLS stands for feedstock vapor, S stands for liquid catalyst, and L stands for solid whisker. The main theory of this mechanism is the existence of catalytic droplets between the gas-phase environment and the reactants. Droplets are formed by the fusion of impurities and other components, and the gas-phase feedstock enters the catalytic droplets through the gas-wave interface. The liquid phase molecules can form whiskers after a supersaturation level for whisker growth is reached. The whiskers grow as the gas-phase feedstock continues to enter the catalytic droplet through the gas-wave interface by crystallizing at the interface between the liquid and solid whisker products. The droplet is lifted as the whisker grows gradually and eventually remains at the top of the whisker. This constitutes the whisker morphology characteristic of the VLS growth mechanism, which is applicable to the growth of whiskers in the gas phase.[144,145]

Vapor-Solid (VS) Growth Mechanism

The VS growth mechanism is derived from the dislocation theory proposed by Frank in his study of the growth mechanism of Sn whiskers.[146] Stresses on Sn whiskers due to surface oxidation allow them to grow continuous metal fibers in the bulk metal, where the screw-type dislocation structure creates conditions for their continuous movement around the whisker roots. The reduced surface free energy of the whisker surfaces due to oxidation improves the driving force for whisker growth. The degree of supersaturation of the gas-phase reactants in the VS growth mechanism greatly influences whisker growth.[147] As shown in Figure 2, CO_2 whiskers were formed at low temperatures (−70 °C to −65 °C) and moderate pressures (4.4–1.0 bar), revealing the VS growth mechanism of CO_2 whiskers in the supersaturated state (Figure 3). Whiskers are easily formed when

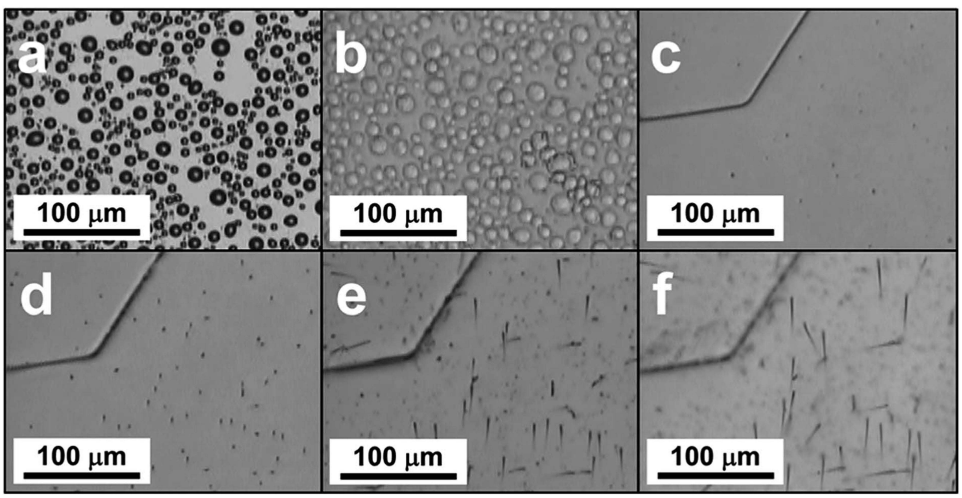

Figure 2 Chronological illustrations of the growth process of CO_2 whiskers.
Notes: (**a**) Condensation of water vapor into droplets. (**b**) Freezing of water droplets into ice crystals. (**c**) Formation of the solid CO_2 layer over the ice crystals. (**d**) Formation of nuclei on the solid CO_2 layer upon gradual depressurization of the stage. (**e**) Initial growth of CO_2 rod-like structures. (**f**) Growth of CO_2 whiskers. Used with permission of Royal Society of Chemistry from *RSC Advances*, Growth of carbon dioxide whiskers, Both AK, Cheung CL, Vol 9(41), 23780–23784, Copyright © 2019; permission conveyed through Copyright Clearance Center, Inc.[149]

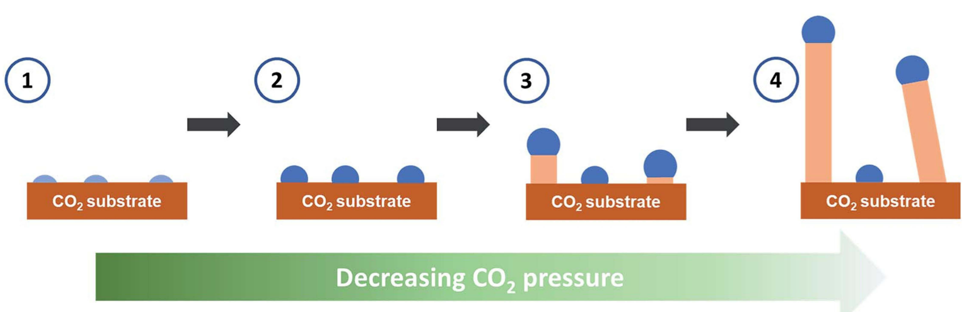

Figure 3 Schematics for the growth mechanism of CO_2 whiskers.
Notes: Light blue, nuclei containing water saturated with CO_2; blue, particles supersaturated with CO_2; beige, solid CO_2. Used with permission of Royal Society of Chemistry from *RSC Advances*, Growth of carbon dioxide whiskers, Both AK, Cheung CL, Vol 9(41), 23780–23784, Copyright © 2019; permission conveyed through Copyright Clearance Center, Inc.[149]

the degree of supersaturation of the gas-phase material is low. Medium supersaturation results in the formation of flakes, dendrites, or a mixture of whiskers and crystals. At high supersaturation, the gas-phase reactants will no longer form whiskers and will form granular products instead. This mechanism applies to the vapor-phase environment at high temperatures, where, after nucleation, the reactive components are transferred through the vapor phase, and VS reactions occur, causing the crystals to grow in a fixed direction to form whiskers.[148]

Liquid-Solid (LS) Growth Mechanism

As a special case of single crystal growth, whiskers may also exist in two stages: nucleation and growth. Whisker growth requires a substrate with helical dislocations and a supply of raw materials for the mass transfer process. The co-solvent acts as a high-quality carrier to continuously transport the liquid reactants to the substrate, and as the temperature rises and the thermostatic time is prolonged, the nucleus is formed first and then grows, which leads to the proposed four-step growth model - the formation of the reaction microregion, the formation of the nucleus, the growth of the nucleus, and the formation of whiskers.[150] This mechanism is mainly used for the growth of whiskers via the hydrothermal method. It is easy to prepare various shapes of whisker materials by changing the composition of the system and the process conditions.

Preparation Methods of Whiskers

There are many ways to prepare whiskers. Different whiskers can be prepared using different methods, and even the same kind of whiskers can be prepared using various methods. A whisker is a special form of single crystal, and the methods of crystal growth applicable to the preparation of whisker materials include the following,: vapor-phase,[3] liquid-phase,[151–153] solid-phase,[154] and electrolytic methods[155] (Table 1).

Vapor Phase Method

Whisker preparation using the vapor-phase method involves heating and gasifying the raw material, followed by crystal nucleation and growth in the low-temperature region. This preparation method has the advantages of simple operation and high controllability.[3] The commonly used vapor-phase whisker preparation methods include chemical vapor deposition (CVD)[172,173] and physical vapor deposition (PVD).[174,175] CVD is a chemical reaction of vapor-phase feedstocks where the reaction products grow into whiskers in a region of lower temperature. This method is commonly used to prepare oxides, nitrides, carbides, and other ceramic whiskers (Figure 4). PVD is a physical method used to vaporize

Table 1 Methods and Conditions for the Preparation of Whiskers

Whiskers	Preparation Methods	Raw Materials	Temperature (°C)	Catalyst
SnO_2[156]	Vapor-phase transfer method	Sn; SnO; O_2	400–1300	SN/Al;Fe/K/Ca
Si_3N_4[30,157]	Chemical vapor deposition	Si_2Cl_6; NH_3; H_2	1200	Fe
β-Si3N4[57,158]	Chemical vapor deposition	Si_2Cl_6; NH_3	1200	Cr
MgO[159]	Liquid-phase method	MgCl; H_20	700–900	KCl
Si[160]	Vapor-phase transfer method	Si; I_2	800–1100	Ni
$CaSO_4$[75,161]	Hydrothermal method	$CaSO_4$; H_2O	110–160	-
Mullite[162–164]	Vapor-phase method	Al_2O_3; AlF_3	1150–1700	-
AlN[165,166]	Carbothermic method	Al_2O_3; C; N_2	1800	-
TiO_2[42,167,168]	Chemical vapor deposition	Na_2TiF_6	700–1300	-
Sn[160,169]	Spontaneous reaction	Sn	Indoor temperature	-
Al_2O_3[170,171]	Liquid-phase method	AlF_3; H_2O	1400	-
SiC[60,99]	Chemical vapor deposition	$SiCl_4$; CCL_4; H_2	1300–1450	-

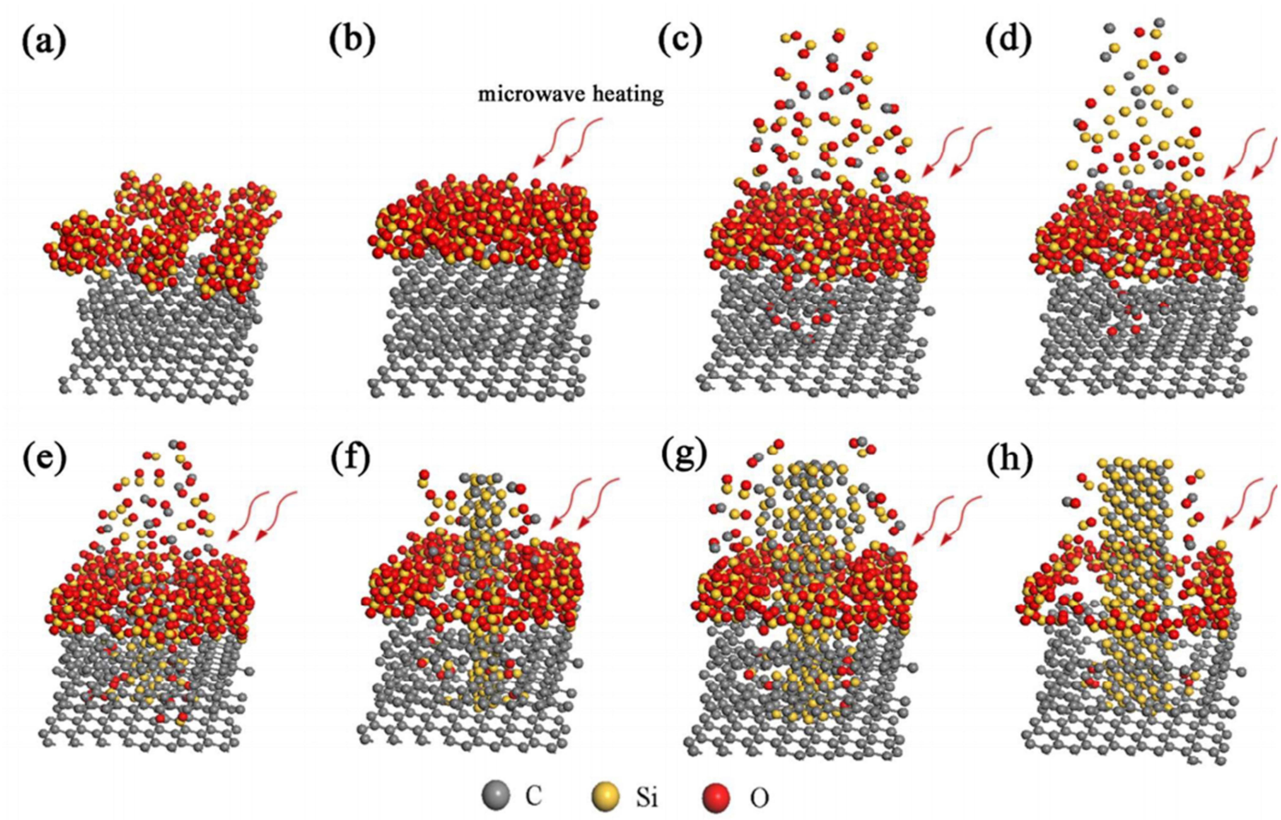

Figure 4 Diagram showing the atomic diffusion and growth process of SiC whiskers under microwave synthesis.

Notes: (**a**) Spherical SiO_2 adhered to the surface of C. (**b**) Microwave coupling of C resulted in heat generation and caused SiO_2 to melt. (**c**) Microwave coupling of C resulted in local thermal effects. (**d**) CO and SiO, in turn, activated the instantaneous microwave plasma. (**e**) Local interface reactions led to the formation of the SiC crystal nucleus. (**f**) The oriented arrangement of SiC crystallites led to the formation of whiskers driven by the escaping gases. (**g**) Newly formed SiC microcrystals adhered to the surface and generated crystallite knots. (**h**) The microwave coupling effect caused the atoms in the knots to diffuse and form smooth SiC whiskers. Used with permission of Royal Society of Chemistry from *Phys Chem Chem Phys*, Investigation on the growth mechanism of SiC whiskers during microwave synthesis, Song B, Zhao B, Lu Y, et al, Vol 20(40), 25799–25805, Copyright © 2018; permission conveyed through Copyright Clearance Center, Inc.[60]

the surface of the material source into gaseous atoms and molecules or to partially ionize them into ions under vacuum conditions. Subsequently, the vapor-phase feedstock is introduced into the low-temperature growth zone, where the vapor-phase feedstock has a low degree of supersaturation, and the vapor-phase coalesces to form nuclei and grows into whiskers. PVD is mainly used to prepare whiskers of metals with low melting points, such as Zn and Ge.

Liquid Phase Method

Whisker preparation by the liquid-phase method involves dissolving the raw material in a solvent and then controlling the crystallization conditions so that the raw material precipitates and grows into whiskers in the solution. The nucleation and growth of the crystals can be controlled by controlling the concentration, temperature, pH, and other parameters of the solution, and whiskers of desired shapes and sizes can be achieved. Whiskers prepared by the liquid-phase method have the advantages of a fast growth rate and high crystal quality.

The commonly used liquid-phase methods for whisker preparation include hydrothermal,[151–153] solvent-thermal,[4] and anti-solvent methods. The hydrothermal method is performed in a sealed pressure vessel using water as solvent. The temperature and pressure are adjusted to create an environment similar to the geological formation of high temperature and pressure conditions, so that the raw materials in the liquid- or vapor-phase chemical reaction, and ultimately the formation of whiskers. It is mainly used to prepare oxide whiskers with heat and corrosion resistance, such as MgO, Al_2O_3, and ZnO. In addition, the hydrothermal method can be used to prepare other whiskers with specific properties, such as metal sulfide whiskers with excellent electrical properties. The solvothermal method involves dissolving the raw material in an organic solvent and subjecting it to chemical reactions in the liquid phase to form whiskers under specific temperature and pressure conditions. This method is suitable for preparing whiskers with lower growth temperatures and lower growth rates, such as carbides, nitrides, and silicides. In the anti-solvent method, the anti-solvent is added to the solution, the rate of addition and concentration is controlled until the solution reaches a supersaturated state, and the formation of whiskers is promoted. This method is suitable for preparing salt whiskers with specific solubility, such as $CaCO_3$ and magnesium chloride (MgCl).

Solid-Phase Method

The solid-phase method of whisker preparation involves the formation of whiskers from raw materials through physical or chemical reactions.[176] In the solid state, atoms or molecules move slowly and require higher temperature and pressure conditions to activate reactions. Under high temperature and pressure conditions, the speed of movement of the atoms or molecules in the raw material and the frequency of their mutual collisions are increased, thus facilitating the reaction. When the reaction reaches a certain level, nuclei begin to form and gradually grow into whiskers.

Common solid-phase methods for preparing whiskers include hot pressing,[56] melting,[177] and reaction methods.[47] Hot pressing involves heating the raw materials to high temperatures and reacting and sintering them under pressure to finally form whiskers. This method is suitable for preparing high-purity and high-crystallinity whiskers, such as oxides and carbides.The melting method involves heating the raw material above the melting point to form a molten state and then forming whiskers by controlling the cooling rate and crystallization conditions. It is suitable for preparing whiskers with lower melting points, such as sulfides and nitrides. In the reaction method, the raw materials and reactants are mixed and allowed to undergo chemical reactions under specific temperature and pressure conditions to generate the required whiskers. This method is suitable for the preparation of whiskers with complex chemical compositions, such as composite materials, and functional materials.

Electrolytic Method

The electrolytic method of preparing whiskers involves the electrolysis of a specific solution so that the ions undergo a reduction or oxidation reaction under the action of the electric field. This method uses a metal or alloy as an anode to precipitate the whiskers on the cathode with high purity, crystallinity, and good mechanical properties. The advantages of this method include the fast growth rate and high purity of the whiskers, and the controllability of the process. The anodic oxidation and electrolytic crystallization methods of whisker preparation are commonly used; they are mainly applicable to the preparation of metal and some non-metal whiskers, such as Mo,[178,179] and Si.[180]

Other whisker preparation methods include mechanical alloying, sol-gel, template, and laser methods. The mechanical alloying method is used to prepare metal powders into whiskers via high-energy ball milling. The metal powder can be alloyed, and whiskers can be generated by controlling conditions, such as the ball milling time, ball material ratio, and ball milling medium. The sol-gel method involves dissolving raw materials in a solvent to form a sol, followed by gelation under specific conditions and heat treatment to grow the crystals into whiskers. The template method involves filling the template holes with template material and performing crystal growth under specific conditions so that the crystals grow in the direction of the template holes to form whiskers.In the laser method, crystals are subjected to large amounts of energy via laser irradiation, resulting in the formation of whiskers. The laser whisker preparation has the advantages of high controllability and efficiency. Commonly used laser whisker preparation methods include laser fusion and laser induction.

Application of Whiskers in Dentistry

Bone Regeneration

Whiskers have a high degree of crystallinity and orientation, and can exert a strong mechanical interlocking effect on the surface of the material, thus improving the interfacial bonding.[131] During osseointegration, the mechanical interlocking action helps to increase the strength of the connection between the jawbone and the implant material, improving the overall stability, additionally, whiskers facilitate osseointegration through a range of biological and biomechanical mechanisms.[181–183] They can induce the differentiation of bone marrow mesenchymal stem cells to osteoblasts, thus promoting a tight bond between the jawbone and the implant material.[184] In addition, whiskers accelerate the process of osseointegration by modulating the inflammatory response and tissue regeneration processes. Wang et al[185] composited calcium silicate whiskers (CSws) with poly(ether-ether-ether-ketone) (PEEK) to prepare PEEK/CSw composites. The tensile, compressive, and flexural strengths of the PEEK/CSws composites were increased by 20%, 18%, and 52%, respectively, compared to those of PEEK. In addition, the PEEK/CSw composites significantly improved bone formation and osseointegration and possessed higher bone repair capability than PEEK.

Whiskers are biologically active and can demonstrate good biocompatibility with the jawbone, providing a suitable environment for the growth of bone cells. Whiskers help to improve the speed and quality of bone healing and accelerate the process of osseointegration by promoting bone growth. They accelerate the repair of jawbone injuries by stimulating the activity of osteoblasts and promoting the formation and mineralization of the bone matrix,[186] thus shortening the recovery time and improving the quality of the bone repair. Huang et al[41] uniformly dispersed chitin whiskers with an average length and width of 300 and 20 nm, respectively, in a negatively charged aqueous sodium alginate solution, which resulted in a homogeneous nanocomposite hydrogel. Strong electrostatic interactions between chitin whiskers and alginate inhibited the swelling tendency and improved the mechanical properties of alginate hydrogels, while the incorporation of chitin whiskers significantly promoted the adhesion and proliferation of osteoblasts (Figure 5). Owing to their unique properties, such as enhancing the interfacial bonding, promoting bone growth, improving the mechanical properties, promoting bone repair, and facilitating osseointegration, whiskers play a significant role in improving jaw health and have broad application prospects in the biomedical field.

Periodontal Regeneration

Periodontal disease is one of the leading causes of tooth loss, and periodontal tissue regeneration is an important treatment for this disease.[187] Whiskers have excellent biocompatibility and bioactivity and can effectively promote periodontal tissue regeneration.[188] The mechanical properties of these materials are similar to those of periodontal tissues, hence, they can be used as a replacement or supplemental material for periodontal tissues to provide the

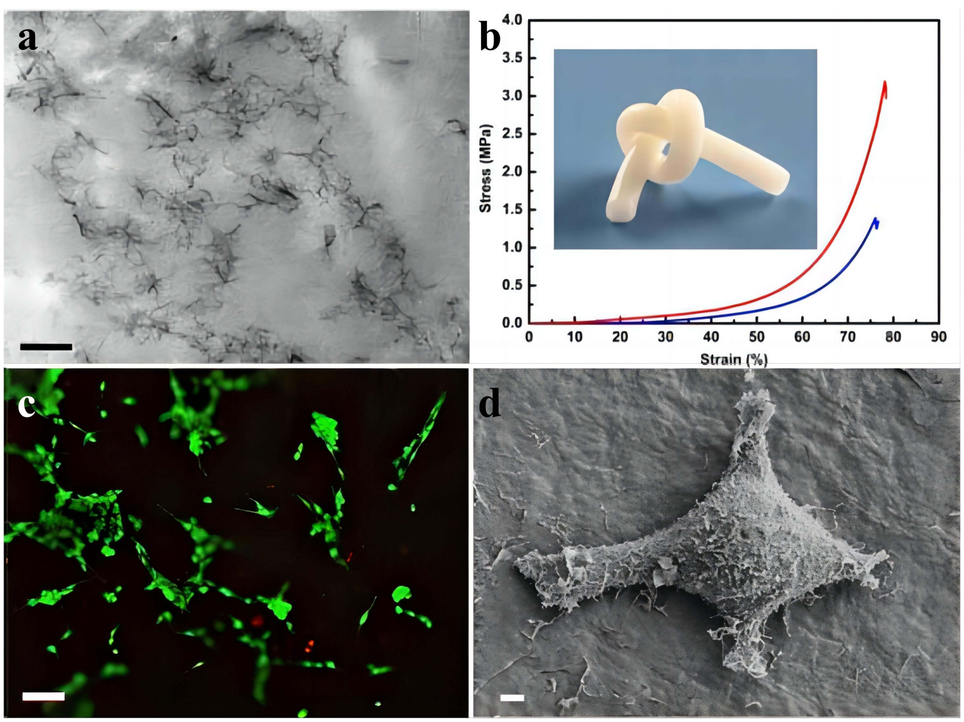

Figure 5 (**a**) TEM images of the ultrathin 2 section of SC4-4 hydrogel. (**b**) Compressive stress-strain curves of the composite hydrogels. (**c**) Fluorescence micrographs of composite hydrogels. (**d**) SEM images of the osteoblasts spreading on the composite hydrogels.

Note: Reprinted with permission from Huang Y, Yao M, Zheng X, et al. Effects of Chitin Whiskers on Physical Properties and Osteoblast Culture of Alginate Based Nanocomposite Hydrogels. *Biomacromolecules*. 2015;16(11):3499–3507. Copyright © 2015 American Chemical Society.[41]

necessary support and stability. The structure and function of periodontal tissues can be enhanced by implanting or filling whiskers, thus promoting tissue regeneration and repair. Nanostructures on the surfaces of whiskers can interact with cell membranes and activate intracellular signaling pathways, which regulate cell proliferation, differentiation, migration, and other biological processes to promote periodontal tissue regeneration and repair.[23] Furthermore, whiskers can induce stem cells to differentiate into various cells in periodontal tissues, such as osteoblasts, odontogenic osteocytes, and adipocytes, thus promoting the regeneration of periodontal tissues. They can promote the proliferation and migration of vascular endothelial cells, thereby promoting the formation of new blood vessels. In addition, whiskers can regulate the expression of angiogenesis-related factors, such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), to further promote angiogenesis.[189,190] Whiskers reduce the inflammatory response by inhibiting the production and release of inflammatory mediators. They promote the differentiation of immune cells and regulate the immune response by regulating the activity of immune cells, thus contributing to the reduction of inflammatory damage to periodontal tissues and the regeneration of periodontal tissues. Whiskers effectively promote periodontal tissue regeneration through mechanisms that promote cell proliferation and differentiation, guide tissue growth, promote angiogenesis, and facilitate anti-inflammation and immunomodulation. However, the application of whiskers in periodontal tissue regeneration needs to be further investigated and explored in more detail. Future studies should focus on optimizing the preparation and properties of whiskers and exploring their application in clinical treatment to provide a more effective periodontal disease treatment.

Treatment and Prevention of Oral Cancer

Oral cancer is a common malignant tumor that poses a serious threat to human health. The immune system is the body's vital defense against foreign pathogens and tumors. Whiskers prevent and treat oral cancer by enhancing the function of the immune system. The active groups on the surfaces of the whiskers can interact with immune cells, activate the immune cells, and improve their ability to kill tumor cells. Whiskers can be used as carrier materials, loaded with antitumor drugs or immunomodulators, combining the drugs with whiskers via physical adsorption or chemical bonding can help achieve controlled release and targeted drug delivery, and inhibit tumor growth through direct administration or stimulation of immune response.[191–193] Xu et al[42] piggybacked TiO_2 whiskers with the anticancer drug garcinia cambogia for potential application in photodynamic therapy, the TiO_2 whiskers, which had the same diameter distribution and a high degree of conjugation, were safe and effective sensitizers. Additionally, the TiO_2 whiskers could enhance the efficacy and attenuate the side effects of garcinia cambogia. In the study by Qing et al,[85] the drug-releasing effect of TiO_2 whiskers led to an increase in the therapeutic concentration in cancer cells and improved the dosage efficiency of the drugs, thus addressing some of the limitations of anticancer drugs (Figure 6).

Whiskers can inhibit tumor growth through multiple mechanisms. They can inhibit the proliferation of tumor cells, the active groups on the surfaces of whiskers can bind to receptors on the tumor cell membranes, interfere with the signal transduction pathway and inhibit their proliferation and division. Whiskers can induce apoptosis of tumor cells by regulating the expression of apoptosis-related genes, triggering programmed death, and inhibiting tumor growth.[194] In addition, whiskers can inhibit tumor growth and proliferation by inhibiting tumor angiogenesis. They can inhibit the proliferation and migration of vascular endothelial cells, thus cutting off the nutrient supply to tumor cells and inhibiting their growth.

Whiskers reduce the inflammatory response, which helps to prevent and treat oral cancer. They can inhibit the release of inflammatory mediators, reduce the degree of inflammatory response, and decrease the inflammatory damage to the oral mucosa. The active groups on the surfaces of whiskers can interact with oral mucosal cells, promote cell proliferation and differentiation, and accelerate the regeneration of oral mucosal tissues. In addition, whiskers can be used as scaffolding materials to provide support for the attachment and growth of oral mucosal cells, promoting tissue repair and functional recovery. Studying the interaction mechanism between whiskers and oral cancer and optimizing the preparation and application technology of whiskers can provide a novel and effective therapeutic strategy for the prevention and treatment of oral cancer.

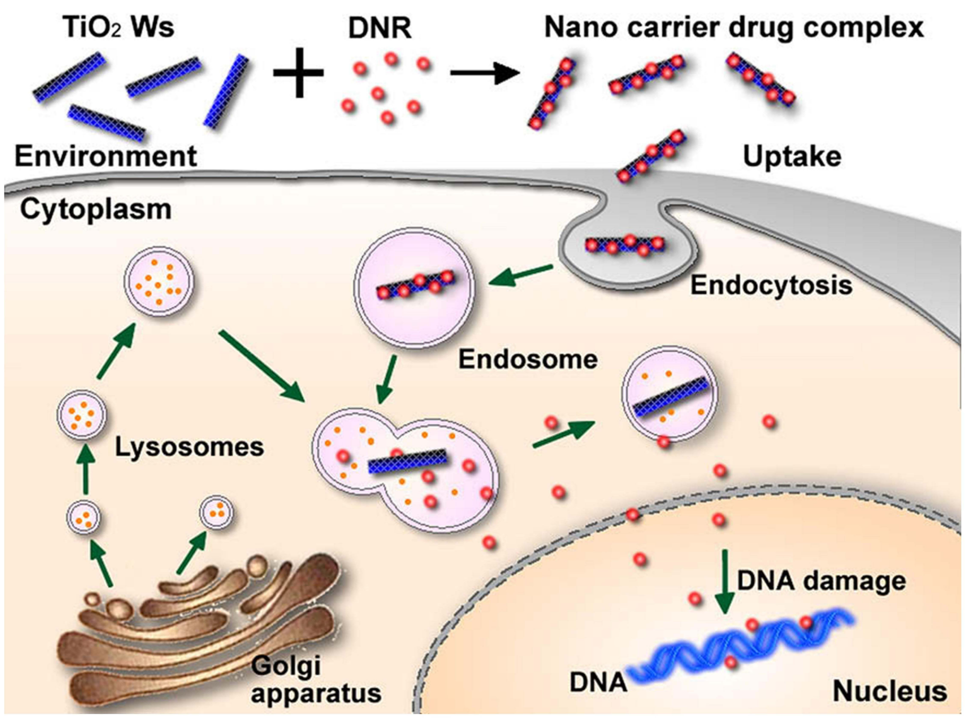

Figure 6 Illustration of the possible mechanism involved in enhancing the uptake of daunorubicin into SMMC-7721 cells via TiO_2 whiskers drug delivery.
Note: Reprinted from *Biomaterials*, Vol 30(27), Li Q, Wang X, Lu X, et al, The incorporation of daunorubicin in cancer cells through the use of titanium dioxide whiskers, 4708–4715, Copyright © 2009, with permission from Elsevier.[85]

Control of the Infection

The antimicrobial properties of whiskers are mainly attributed to their sharp shape and good biocompatibility.[43] Whiskers can kill bacteria by piercing the cell wall and destroying the cell structure. Some whiskers can also inhibit infection by adsorbing onto the surface of the bacteria and preventing them from reproducing and spreading.[195,196] Niu et al[197] verified the hypothesis that tetrapod-like ZnO whiskers (T-ZnOw) simultaneously enhance the antimicrobial activity and mechanical properties of a two-component composite resin. The antimicrobial activity of the material was evaluated using the broth dilution and direct contact tests. Optical microscopy, SEM, flexural strength, compressive strength, and radial tensile strength were used for mechanical characterization. The results showed that T-ZnOw provided the resin with strong antimicrobial activity and better mechanical properties in all tested groups. The T-ZnOw antimicrobial agent was doped into the composite resin to improve its antimicrobial properties, which were better than those observed after doping the silver-based inorganic antimicrobial agent into the composite resin. Chen et al[63] mixed silanized aluminum borate whiskers (ABW), silanized ZrO_2 nanoparticles (nano-ZrO_2), and poly(methyl methacrylate) (PMMA) powder to obtain ZrO_2-ABW/PMMA composites.TiO_2, silver-supported TiO_2 (Ag/TiO_2), silver-supported zirconium phosphate (Novaron), and T-ZnOw were mixed with ZrO_2-ABW/PMMA composites. The colony- forming units in the plaque biofilm were examined, and the cytotoxicity and mechanical properties of the materials were also evaluated. All the composites showed good antimicrobial activity and mechanical properties.

Whiskers contribute to the healing of damaged oral mucosa, acceleration of tissue repair, reduction in mucosal damage by oral infections, and improvement in the oral mucosa's ability to resist infections by stimulating cell growth and promoting neovascularization.[106,198] Grizzo et al[135] synthesized multifunctional bilayer membranes from poly(lactic acid), β-chitin whiskers, and silver nanoparticles (Figure 7), the bilayer membranes had high surface area and porosity (>80%), significant stability in aqueous media, and good mechanical properties, which are useful for applications in wound healing.

Whiskers can promote the adhesion and proliferation of oral mucosal cells, forming a dense mucosal layer, reducing the invasion of bacteria and other microorganisms, enhancing the barrier function of the oral mucosa, and improving the oral mucosa's ability to resist infection. They have good biocompatibility and degradability, and can be gradually

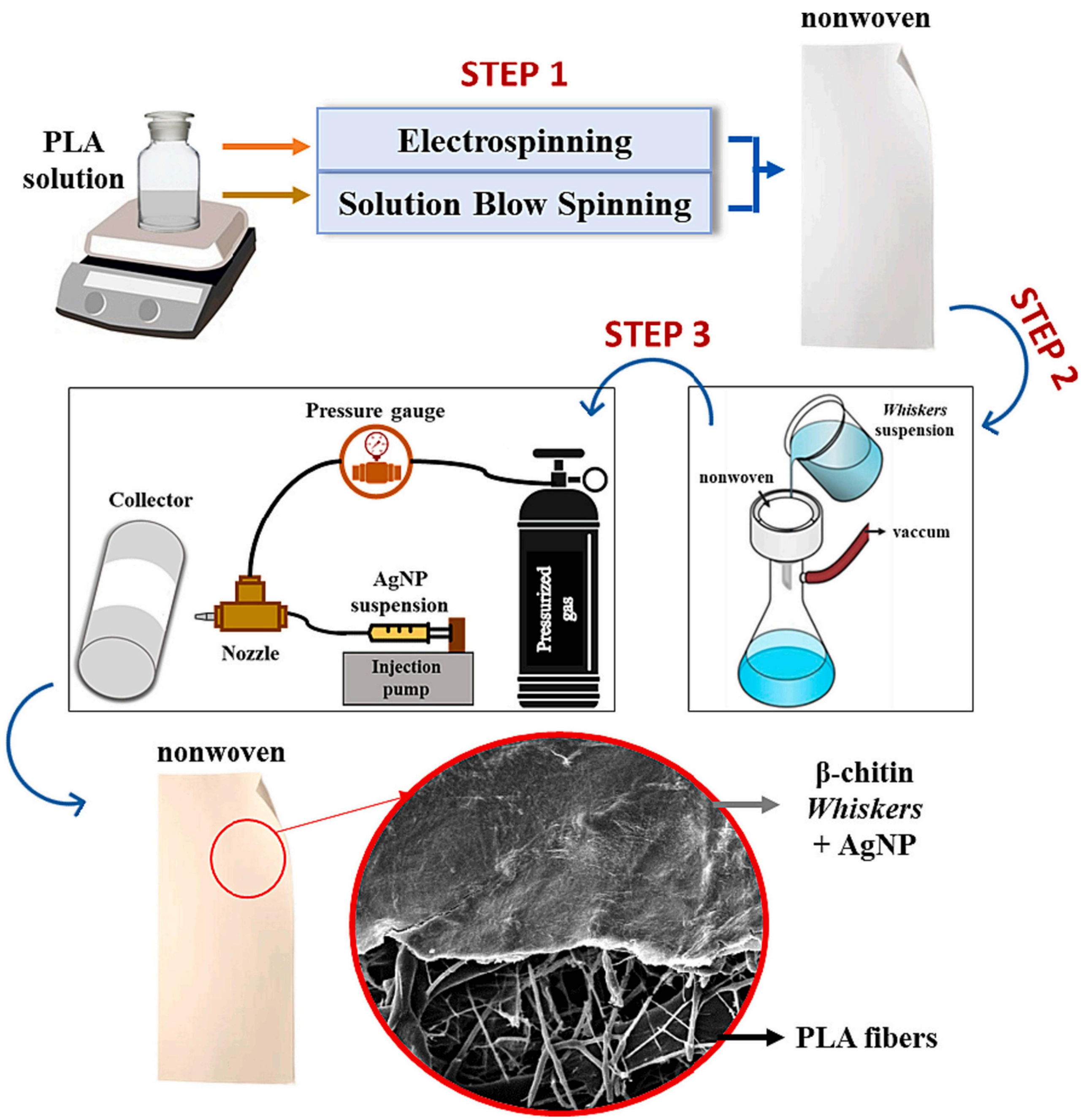

Figure 7 Schematic of the production method of bilayer membranes.

Note: Reprinted from *International Journal of Biological Macromolecules*, Vol 251, Grizzo A, Dos Santos DM, da Costa VPV, et al, Multifunctional bilayer membranes composed of poly(lactic acid), beta-chitin whiskers and silver nanoparticles for wound dressing applications, 126314, Copyright © 2023, with permission from Elsevier.[135]

degraded in the oral environment without toxic side effects or allergic reactions.Pang et al[199] doped chitin nanowhiskers (CtNWs) with carboxymethyl chitosan (CMCS) and dextran dialdehyde (DDA) into Schiff base cross-linked hydrogels to construct a mechanically reinforced tissue adhesive. The composite hydrogel demonstrated anti-swelling properties in phosphate-buffered saline with optimal antimicrobial and hemostatic capabilities, in the in vivo experiments, the composite hydrogel demonstrated the ability to promote wound healing without causing an inflammatory response.

The properties of whiskers make them a potential material for oral infection control. However, in-depth research on their clinical applications is warranted. Future research directions should include improving the preparation process of whiskers, enhancing their antimicrobial and tissue regeneration properties, and exploring their synergistic effects with other materials.

Pulp Regeneration

Patients with pulpitis and apical periodontitis are treated via root canal therapy, which inevitably leads to permanent loss of the vitality and sensitivity of the tooth.[200,201] Therefore, regeneration of functional pulp in the deactivated pulp space is a promising alternative for restoring the biological function of the tooth.[202] Dental pulp regeneration is a complex biomedical process involving the synergistic action of multiple factors, such as stem cells, growth factors, and specific microenvironments. Although whiskers do not have pulp regeneration ability, they can be used as biological scaffolds or enhancement materials that combine with stem cells and growth factors to participate in the pulp regeneration process.[203] They can be used as biological scaffolds in combination with cells, such as pulp stem cells or gingival tissue. Whisker scaffolds can provide space and guidance for cells to grow and promote the regeneration of pulp tissue. Furthermore, whiskers can stimulate the proliferation and differentiation of pulp stem cells, promote the growth of newborn pulp tissue, and improve the effectiveness of pulp regeneration. In addition, they can be combined with biologically active substances, such as growth factors, to further enhance the effect of pulp regeneration. Wang et al[24] reported that exosome-loaded hydroxypropyl chitosan (HPCH)/chitosan whisker (CW) thermosensitive hydrogels had strong mechanical properties and bioactivity. In vitro, cellular experiments demonstrated that the value-added differentiation of whiskers and exosome delivery significantly enhanced the hydrogel's ability to promote gingival generation and angiogenesis. In vivo, animal experiments revealed the formation of new pulp-like tissues in dental models. The whiskers demonstrated excellent mechanical properties and stability and provided the necessary support and protection during pulp regeneration to promote the formation of new tissues (Figure 8).

Whiskers have antimicrobial properties that can effectively inhibit the growth of bacteria in the oral cavity, reduce the risk of infection, and create a favorable environment for pulp regeneration. They have good compatibility with human tissues, thus reducing the chances of rejection and facilitating cell growth and tissue fusion during pulp regeneration. Whiskers are malleable and degradable, can be formed into different shapes and sizes according to the needs, and degrade on their own within a certain period of time with no long-term side effects on the surrounding tissues.

Due to their good biocompatibility, stable physical and chemical properties, ability to promote cell proliferation and differentiation, antimicrobial properties, plasticity, and degradability, whiskers are a promising material in the field of pulpal regeneration and may be used for the treatment of pulpal injuries.

Improvement of Medical Devices

Whiskers have high strength, high modulus of elasticity, and low density. These properties may aid in the reinforcement and support of medical devices and improve their durability and reliability.[204] Whiskers have good chemical stability, which is beneficial for maintaining a stable performance in physiological environments.[39,205,206] T-ZnOw has the same perfect surface as conventional whiskers. Unlike conventional whiskers, T-ZnOw has a unique three-dimensional structure with four needles growing from a single point and an angle of 109.28° between two needles.[207] This special structure gives T-ZnOw-filled dental resin composites tropical rather than anisotropic properties, which means that forces can be more evenly distributed inside them. The filler needles can create a more robust interface by increasing integration with the resin matrix.[132] Zhang et al[208] prepared ZrO_2-ABW/PMMA composites by mixing modified nano-ZrO_2 and ABWs with PMMA, the mechanical properties of silanized ZrO_2-ABW/PMMA composites were significantly improved. The flexural strength reached a maximum value of 108.01 ± 5.54 MPa when 2 wt% of nano-ZrO_2 was mixed with ABWs at a ratio of 1:2, which was 52% higher than pure PMMA. The surface hardness reached a maximum value of 22.50 ± 0.86 MPa when 3 wt% of nano-$ZrO_2$was blended with ABWs at the same ZrO_2/ABW ratio, which was a 27% increase compared to that of pure PMMA. Zhu et al[209] prepared a two-component thermal/photodual dual-sensitive hydrogel (M/C) by physically and chemically cross-linking chitin whiskers (CHW) and methacrylated hydroxybutyl chitosan (MHBC) as raw materials (Figure 9). The introduction of CHW significantly enhanced the mechanical properties of the M/C hydrogel and improved the resistance to deformation.

Xu et al[210] fused silica particles onto SiC whiskers to promote silanization and improve whisker retention in the matrix. Hardened glass ionomers were ground to a fine powder, mixed with whiskers, and used as fillers in dental resins. The materials were tested for flexural strength, modulus of elasticity, and fracture toughness, and a fluoride ion selective electrode was used to measure the fluoride release. The whisker-added resin exhibited moderate fluoride release and

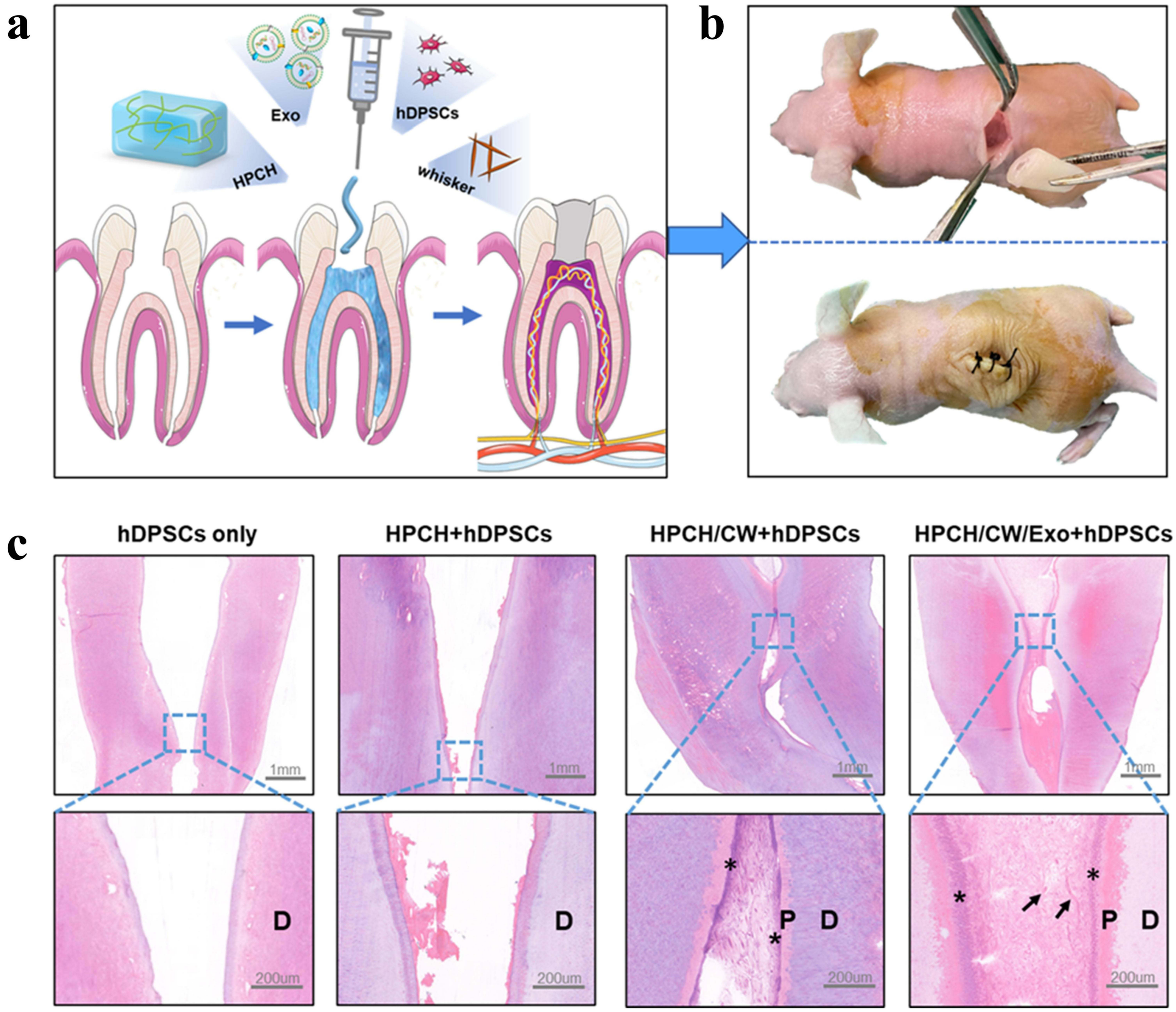

Figure 8 (**a**) Schematic diagram of a tooth root model filled with hDPSC encapsulated hydrogels. (**b**) Photographs of a nude mouse model for tooth root implantation. (**c**) HE staining images of the regenerated pulp-like tissues in the endodontic space.

Note: The bottom images are magnified views of the images above. D, dentin matrix; P, predentin-like tissue; star indicates odontoblast-like cells. The arrow indicates newly formed blood vessels. Used with permission of Royal Society of Chemistry from *J Mater Chem B*, Fabrication of an exosome-loaded thermosensitive chitin-based hydrogel for dental pulp regeneration, Wang S, Xing X, Peng W, et al, Vol 11(7), 1580–1590, Copyright © 2023; permission conveyed through Copyright Clearance Center, Inc.[24]

superior mechanical properties. In another study, Yang et al[204] compared the properties of whisker-reinforced calcium fluoride-containing composite resins with those of resin-modified glass ionomer cement. The reinforcement of SiC whiskers increased the mechanical properties of the composites. The addition of whiskers promoted the release of calcium, phosphate, and fluoride ions from the materials, which showed superior remineralization effects in the dentin of the lesions.

The whiskers significantly enhanced the mechanical properties of the material through various mechanisms, such as crack bridging, crack deflection, and pullout effect, this improved the toughness, crack extension resistance, and fatigue life of the composite material, thus enhancing the overall performance of the material.[211–213] Whiskers have good compatibility with human tissues and are less likely to cause rejection or inflammation in the body, which is conducive to the safe use of medical devices. Additionally, they have antimicrobial properties, which help prevent medical devices from causing infections during use, further improving the safety and reliability of the devices. With the advancement of new materials and processes, whisker-reinforced composites are expected to continue to improve performance and reduce costs. Furthermore, their application areas will be expanded to provide stronger material support in aerospace,

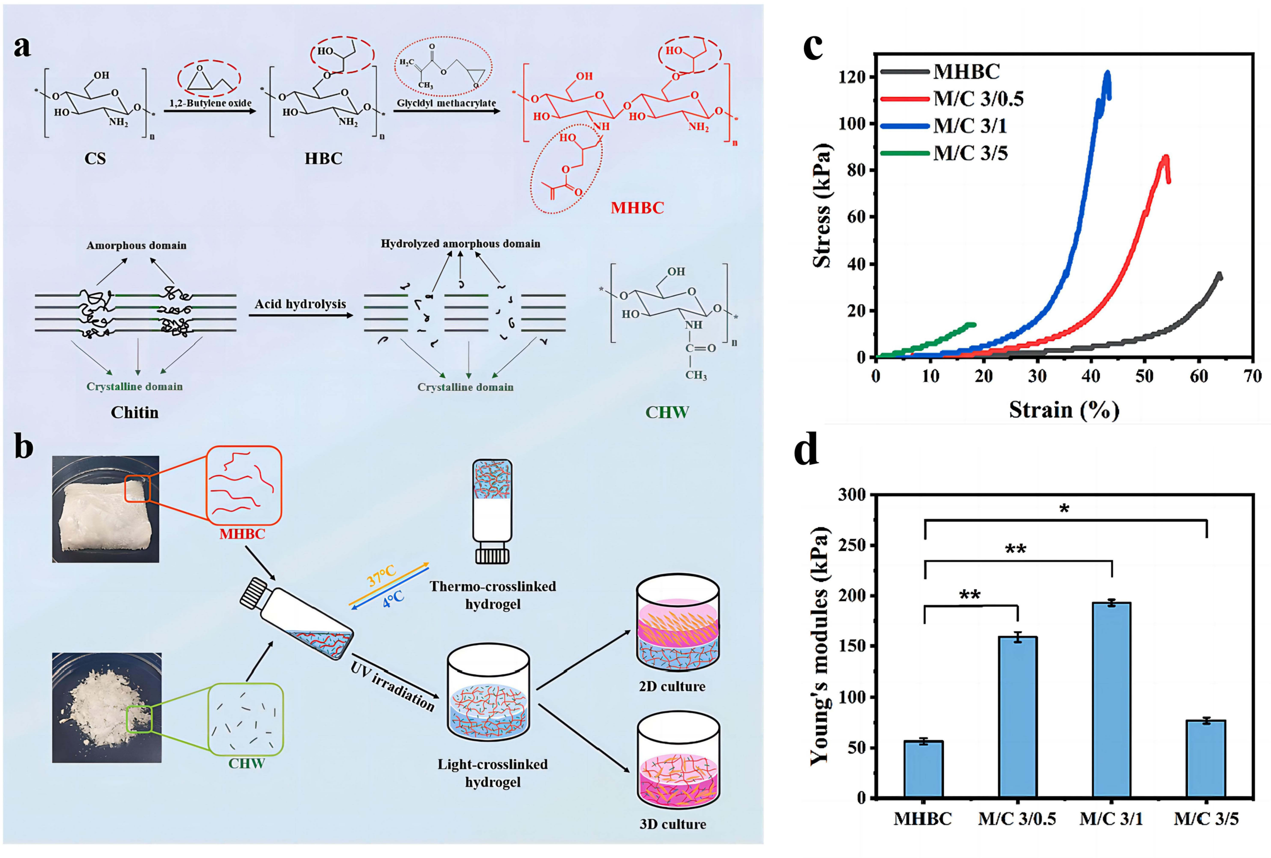

Figure 9 (**a**) Schematics of the MHBC and CHW synthesis. (**b**) Schematic representation of the thermo-crosslinked hydrogel and photo-crosslinked hydrogel preparation and the 2D/3D cell culture based on the hydrogel scaffold. (**c**) Compressive stress-strain curves of hydrogels. (**d**) The Young's modulus values of the hydrogels (**p*<0.05, ***p*<0.01).

Note: Reprinted from *Carbohydrate Polymers*, Vol 304, Zhu Y, Qin D, Liu J, et al, Chitin whiskers enhanced methacrylated hydroxybutyl chitosan hydrogels as anti-deformation scaffold for 3D cell culture, 120483, Copyright © 2023, with permission from Elsevier.[209]

automotive, electronics, new energy, environmental protection, biomedicine, and other cutting-edge fields. However, although whisker-reinforced composites have mechanical advantages, the biocompatibility, long-term stability, and safety of the manufacturing process of the materials need to be rigorously evaluated before they are applied to medical devices.

In summary, the rapid development of whiskers has revolutionized the advancement of dentistry by providing new strategies, such as drug delivery, tissue regeneration, material toughening, and bioimaging, for the prevention, diagnosis, and treatment of oral diseases. High-strength and high modulus of elasticity whiskers become ideal scaffold materials for oral tissue engineering and regenerative medicine.[23,24] Whiskers can enhance the mucosal barrier function and inhibit the proliferation of tumor cells, achieving inflammation control and cancer prevention and proliferation.[29,30] They exhibit excellent drug carrier function, which can aid in precisely delivering drugs to the lesion site, thus enabling the efficient and precise treatment of diseases.[214,215] In addition, whiskers can be added to dental composites and medical devices as reinforcement with excellent mechanical properties and good biocompatibility, which can significantly improve the mechanical properties and durability of the materials.[216,217] In conclusion, whiskers have become a new hotspot for clinical research by virtue of their unique physicochemical and biological properties and nanoscale characteristics. They may be expected to deliver more innovations and breakthroughs in the field of oral health and promote the continuous development of dentistry.

Prospects

Whiskers are short micro- and nano-sized fibers grown from high-purity single crystals with extremely high aspect ratios. Whiskers are generally grown in high purity on merit, with a highly ordered atomic arrangement and a strength close to the theoretical value of intact crystals. Ceramic whiskers with high strength and good biocompatibility can be used as biomaterials to replace diseased or damaged tissues. For example, they can be used to make artificial joints,[218,219] teeth,[47,220] and bones.[221–225] Metal whiskers can be used to prepare biosensors and medical devices to improve the sensitivity and biocompatibility of the devices.[97] Cellulose and polymer whiskers have good biocompatibility and bioactivity and can be used to prepare biomedical materials,[226] drug carriers,[104] and tissue engineering scaffolds.[227] The targeted delivery and slow release of drugs can be realized by loading drugs or bioactive molecules onto whiskers; this can improve the therapeutic effect and reduce the side effects. Furthermore, whiskers can be used to construct tissue-engineered scaffolds with specific structures and functions to promote cell growth and tissue regeneration. Ceramic and metal whiskers with high hardness, high toughness, and excellent thermal and chemical stability are widely used for the reinforcement and toughening of composite materials to significantly improve the mechanical properties, thermal stability, and corrosion resistance.[68,228] As a high-performance material, whiskers show great potential in many fields. Incomplete statistics, the total annual production of whiskers has exceeded 10,000 tons. Currently on the market has been sold whiskers are mainly K_4TiO_4 whiskers and its conductive whiskers, magnesium salt (alkali sulfur, Mg) whiskers, SiC whiskers, H_3AlBO_2 whiskers, oxide whiskers, graphite whiskers and Fe_2O_3 whiskers.

The application of whiskers in dentistry has attracted widespread attention and demonstrated remarkable progress in some areas. However, several problems associated with the clinical application and translation of whiskers remain and must be addressed. The biocompatibility of whiskers is one of the key issues in their medical applications. Whiskers are synthetic materials; hence, the temperature, humidity, and pH of the oral environment can affect their biocompatibility. Studies have shown that whiskers may trigger an immune response or produce inflammation, which may affect patient health. Therefore, improving the biocompatibility of whiskers for their application in dentistry is a hot research topic. In addition, studies on the specific application mechanism and principle of action of whiskers in dentistry are limited. Although some studies have shown that whiskers can enhance the performance of oral restorative materials and promote the regeneration of oral tissues, the complexity of their interactions with oral tissue cells, signaling, and gene expression at multiple levels requires further research. Moreover, the long-term safety and efficacy of whiskers in dentistry remain to be verified. Whiskers have good biocompatibility, but strong corrosive properties exist in the oral environment. The potential risks of the long-term use of whiskers and their composites in the oral environment need to be evaluated with more clinical data and long-term observations. The complexity and high cost of the preparation process of whiskers also limit their application in dentistry. Thus, developing more efficient and economical preparation methods and reducing their production costs are warranted.

Whiskers show great promise as a high-performance material for future research. Materials with special properties can be developed using innovative synthesis methods, and the combination of whiskers with other dental materials and technologies can be explored to develop more advanced and effective oral treatment programs. Systematic information from proteomics, genomics, transcriptomics, and metabolomics to capture the changes in the metabolism, signaling pathways, and biological functions of whiskers might help realize the potential of the applications of this material in dentistry. Additionally, in-depth explorations of the interactions between whiskers and oral cells and tissues will provide a more solid theoretical basis for its use in preventing, diagnosing, and treating oral diseases. Additional clinical trials and long-term observational studies are warranted to verify the long-term safety and efficacy of whiskers in dentistry.

Conclusion

Whiskers have a wide range of applications in bone, periodontal, and pulp regeneration due to their unique physico-chemical and biological properties. They can control inflammation and prevent the spread of cancer by enhancing the mucosal barrier function and inhibiting the proliferation of tumor cells. Furthermore, the excellent mechanical properties and biocompatibility of this material enable their use as reinforcing and toughening materials to significantly improve the mechanical properties and durability of composite materials and medical devices. The excellent properties of whiskers give them great potential in the field of medicine. However, despite the potential advantages and application Prospects of whiskers in dentistry, several problems remain to be addressed. Thus, further research and development are needed to solve these problems and make full use of the advantages of the material. Additionally, long-term clinical trials and studies are needed to evaluate the long-term safety and efficacy of whiskers in dentistry.

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Disclosure

The authors report no conflicts of interest in this work.

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