RSC Advances

REVIEW

Cite this: *RSC Adv.*, 2024, **14**, 14374

Recent progress of electrospun nanofibers as burning dressings

Shengwei Zhang,†[a] Wei Yang,†[b] Wenjian Gong,[c] Yuhang Lu,[c] Deng-Guang Yu *[c] and Ping Liu*[b]

Received 27th February 2024
Accepted 25th April 2024

DOI: 10.1039/d4ra01514b

rsc.li/rsc-advances

Burns are a global public health problem, which brings great challenges to public health and the economy. Severe burns often lead to systemic infection, shock, multiple organ failure, and even death. With the increasing demand for the therapeutic effect of burn wounds, traditional dressings have been unable to meet people's needs due to their single function and many side effects. In this context, electrospinning shows a great prospect on the way to open up advanced wound dressings that promote wound repairing and prevent infection. With its large specific surface area, high porosity, and similar to natural extracellular matrix (ECM), electrospun nanofibers can load drugs and accelerate wound healing. It provides a promising solution for the treatment and management of burn wounds. This review article introduces the concept of burn and the types of electrospun nanofibers, then summarizes the polymers used in electrospun nanofiber dressings. Finally, the drugs (plant extracts, small molecule drugs and nanoparticles) loaded with electrospun burn dressings are summarized. Some promising aspects for developing commercial electrospun burn dressings are proposed.

1 Introduction

The skin is the largest organ in the human body, covering the surface of the body and accounting for approximately 10% of body weight.[1] Burns are injuries to the skin caused by high temperatures (flame or scald), electricity, chemicals, friction, or radiation.[2] The healing process of burn wounds is similar to that of most other wounds, and both go through a complex process. The wound healing process usually includes four stages: hemostasis, inflammation, cell proliferation, and tissue remodelling.[3] Mild burns can recover quickly with the aid of some medications. However, severe burns are often accompanied by complications such as bacterial infection, shock, and organ failure. Burns reduce the immunomodulatory function of the patient's skin, making the wound vulnerable to bacterial infection. Bacterial infection can cause an increase in wound exudate, which seriously hinders wound healing and brings huge challenges to wound treatment.[4]

When the skin damage is too severe and the autologous repair ability is not enough to restore the original structure and function, the traditional method of skin transplantation is generally used. In the past few decades, the survival rate of burn patients has been significantly improved due to the application of various skin grafts.[5] Despite widespread use, there are problems with limited donors for autologous skin grafts and immune rejection of allogeneic transplants.[6,7] With the development of biotechnology, the emergence of multifunctional wound dressings and nanofiber scaffold materials has alleviated the problem of skin transplantation to a certain extent. Wound dressings can cover the wound and provide a temporary barrier against external bacterial infections.[8] It can also serve as an induction template to guide skin cell recombination, host tissue infiltration, and integration, and has a significant effect on wound healing.[9] Traditional dressings such as gauze and bandages are often used in clinical practice to assist in wound treatment. They can absorb wound exudate and blood, while also providing mechanical protection. However, the disadvantage of traditional dressings is that they do not have anti-infection ability and are prone to adhesion to the wound, causing secondary damage to the patient, which is not conducive to wound healing. The ideal wound dressing should have the following properties: (1) absorb excess wound exudate and blood; (2) provide a moist environment for wound healing; (3) good breathability; (4) protect the wound from infection by external microorganisms and harmful substances; (5) good biocompatibility and degradability; (6) removing the dressing will not cause secondary damage to the patient's wound.

In addition to traditional dressings, common types of dressings include sponges, films, foams, hydrogels,

[a]*School of Health Science and Engineering, University of Shanghai for Science and Technology, Shanghai 200093, China. E-mail: 222302325@st.usst.edu.cn*

[b]*The Base of Achievement Transformation, Shidong Hospital Affiliated to University of Shanghai for Science and Technology, Shanghai 200443, China. E-mail: yangw278619@163.com; liupingmedicine@163.com*

[c]*School of Materials and Chemistry, University of Shanghai for Science and Technology, Shanghai 200093, China. E-mail: 223353279@st.usst.edu.cn; 2026010214@st.usst.edu.cn; ydg017@usst.edu.cn*

† These authors contributed equally to this work.

hydrocolloids, and nanofiber composites.[10–12] Different types of dressings have different characteristics and can be selected for specific types of wounds. Sponge dressing has a highly porous structure, which can absorb a lot of water and provide a moist environment for wound healing.[13] However, sponge dressings exhibit weak mechanical strength and may cause skin maceration. Film dressings are breathable and can reduce patient pain.[14] However, this type of dressing has weak water absorption, which can easily cause the accumulation of wound exudate and easily adhere to the wound.[15] Hydrogels are hydrophilic macromolecular networks that can absorb and retain wound exudates, and promote fibroblast proliferation and glial cell migration.[16] The mechanical stability of hydrogel becomes worse after water absorption and swelling. As a nanoscale material that is constantly being promoted for use, nanofibers are increasingly used as wound dressings. Nanofibers with nanoscale structures are similar to natural extracellular matrix, possessing good drug loading and delivery capabilities, and being able to absorb more wound exudates than other types of dressings.[17–19] The nanofibers prepared by electrospinning have good mechanical and biological properties.

The preparation methods of nanofibers include drawing methods, template synthesis, self-assembly, microphase separation, and electrospinning.[20–24] Electrospinning technology is widely used in the preparation of nanofibers because of its low cost, high efficiency, and simple operation. Electrospinning is an efficient method for preparing fibres with diameters between nanometres and micrometres.[25] The structure of electrospun nanofibers can be adjusted to adapt to various applications.[26–28] For example, in the biomedical field, electrospun nanofibers are used in wound dressings, tissue engineering scaffolds, and drug delivery.[29–33] Electrospun nanofiber wound dressings have many outstanding advantages. Firstly, electrospun nanofibers have a larger specific surface area, providing more adhesion and growth sites for cells.[34] Secondly, electrospun nanofibers have high porosity, maintaining good breathability and moisture permeability while blocking the invasion of external pathogens.[35,36] Finally, electrospun nanofibers have a controllable structure and can serve as drug carriers to load various bioactive ingredients and drugs to improve wound healing efficiency.[37–40] In addition, nanofiber wound dressings can also control the rate and time of drug release. Therefore, electrospun nanofibers show great potential in the field of biomedical applications.

In the "PubMed" and "Web of Science" databases, the relevant literature in the past ten years is searched by searching for the keywords "wound dressing" and "electrospun wound dressing". The search results are shown in Fig. 1. From the search results, it can be seen that there are thousands of literatures on wound dressings in both databases each year, and there is an increasing trend over time. Especially after 2018, the growth rate of related literature has increased significantly, which shows that the research on wound dressing has become a hot topic in the field of biomedicine. At the same time, the literature on electrospun nanofiber dressings also shows an increasing trend. It shows that with the development of electrospun nanofiber technology, the wound dressing prepared by nanofiber has been recognized by people. The main work of this paper is to review the common types of electrospun nanofibers, the polymers used, and various drugs with therapeutic or antimicrobial activity wrapped in electrospun nanofiber dressings.

2 Burn and wound healing

2.1 Burn

Burns are an underestimated form of trauma that can affect anyone, anytime and anywhere.[41] According to the severity of burns, they can be divided into four levels: first-degree burns, second-degree burns, third-degree burns, and fourth-degree burns.[11,42] First-degree burns only involve the epidermis, accompanied by redness and mild pain, which subsides within 48–72 hours.[43] This degree of burn does not require special treatment and will not leave scars. Second-degree burns are divided into superficial second-degree burns and deep second-degree burns. Superficial second-degree burns involve the epidermis and part of the dermis, accompanied by pain.[44] Deep second-degree burns involve the surface layer of skin and the deeper dermis because some pain receptors are destroyed and pain is felt slowly. This degree of burn requires surgical treatment and can form scars. If the wound is not infected, it will take 3–4 weeks to heal. Third-degree burns run through the entire dermis. Because nerve endings are damaged, they usually don't feel pain and need to be protected from infection.[41] Third-degree burns usually need to be treated by skin grafting. In addition, if the burn depth involves deep tissue, it is called a fourth-degree burn. It combines the characteristics of second and third-degree burns, penetrating from the epidermis to the subcutaneous tissue layer, damaging some muscles or bones.[45] Fig. 2 shows the depth of each level of burn. In general, superficial burns, like normal mechanical injuries, surgical wounds, *etc.*, undergo a natural wound healing process without much intervention. The difference, however, is that severe burns can disrupt the structural and functional integrity of the skin, increasing the likelihood of bacterial infection and bringing about a range of systemic reactions.[46] Patients with extensive deep burns often develop severe systemic inflammation, hypermetabolism, and catabolic responses, and if not treated with prompt surgical intervention, they can die from multiple organ failure.[47,48] In addition, burns can result in hypertrophic scars, which not only affect aesthetics but may also limit normal body function. The key to burn wound management is to prevent infection as well as to improve the scarring caused by burns. Therefore, the addition of antimicrobial drugs to burn dressings is the preferred method compared to normal wound dressings, and drugs with anti-inflammatory activity can also be added to inhibit scarring due to excessive inflammation.

2.2 Healing process of burn wounds

Wound healing is a dynamic and complex process that is coordinated by various cells, cytokines, growth factors, and neuroendocrine mechanisms.[49] Skin wound healing is usually divided into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling (Fig. 3).[50] When tissues and

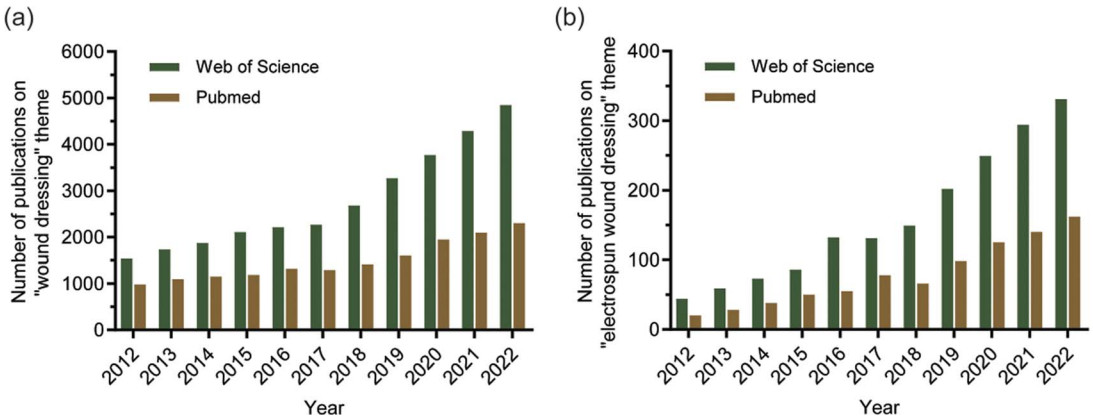

Fig. 1 The literature related to the past ten years was searched in the databases of "PubMed" and "Web of Science". (a) The number of literatures retrieved based on the theme "wound dressing"; (b) the number of literatures retrieved based on the theme "electrospun wound dressing".

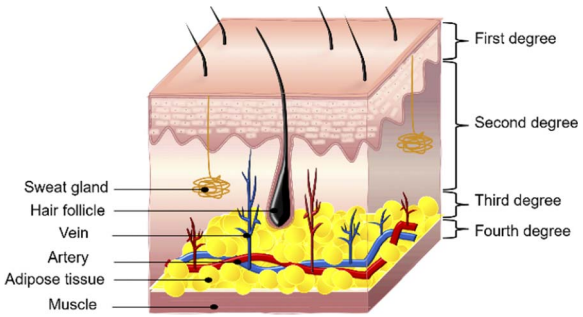

Fig. 2 Burns depth and level. Burns are classified into four grades based on the size and depth of skin damage: first-degree, second-degree, third-degree, and fourth-degree burns.

cells of the body are damaged, inflammatory mediators activate the host's vascular and leukocyte responses for hemostasis and inflammation. The release of various cytokines allows neutrophils to accumulate in the wound and remove bacteria and damaged tissue.[51,52] After some time, neutrophils gradually decrease and macrophages increase. Macrophages and neutrophils begin to phagocytose bacteria and nonfunctional host cells. Macrophages secrete fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), interleukin-1 (IL-1), and tumour necrosis factor (TNF) to further stimulate capillary angiogenesis and fibroblast proliferation. The proliferation, migration, and remodelling of endothelial cells is an important process of angiogenesis.[53] New capillaries and hyperplastic fibroblasts form granulation tissue, which is then remodeled and matures to form a scar. During the tissue remodelling phase, the wound undergoes epithelial regeneration *via* keratinized cells and extracellular matrix accumulation *via* fibroblasts and endothelial cells.[54]

There are many factors that affect the wound healing process, and bacterial infection is one of the most important. Bacterial infections can increase wound exudate and interfere with the normal growth of granulation tissue.[55] Bacterial infections may also prolong or prevent wound healing by maintaining the inflammatory phase of the healing process. It has been reported that about 75% of burn patients die from bacterial infections.[56] Therefore, antibacterial dressings can be used to assist in the treatment of burns. A qualified dressing can not only provide a suitable environment for wound healing but also have excellent anti-infection ability.

The researchers tried different methods to produce wound dressings with antibacterial activity, including the use of materials with inherent bactericidal activity, the improvement of surface structure, or the addition of antimicrobial agents.[57] In recent years, people have been trying to study a variety of bioactive compounds, combining these compounds with films, sponges, foams, hydrogels, and nanofibers to make advanced dressings. Advanced dressing has a better effect on promoting wound healing than traditional dressing. Among them, the preparation process of electrospun nanofiber dressing is simple and the cost is low, so it has a good development prospect in the field of wound treatment and management.

3 Electrospun nanofiber

3.1 Introduction to electrospinning technology

Electrospinning is a simple and versatile technique for preparing nanofibers containing bioactive compounds.[58,59] The diameters of electrospun nanofibers range from nanometers to microns, which are two to three orders of magnitude smaller than those made by traditional dry or wet spinning methods.[60–62] The electrospinning device is mainly composed of four parts: injection pump, syringe with spinneret, collection device, and high voltage power supply (Fig. 4). The specific electrospinning process is as follows. The prepared polymer solution is loaded into a syringe fixed to the syringe pump and the polymer solution is controlled at a constant flow rate to the spinneret. The high-voltage power supply applies high voltage to the spinneret, and the electrostatic charge accumulates in the polymer solution at the tip of the spinneret, gradually driving the droplet into a cone, known as the "Taylor cone".[63,64] When the strength of the electrostatic field exceeds the surface tension of the solution, the charged polymer solution ejects from the tip

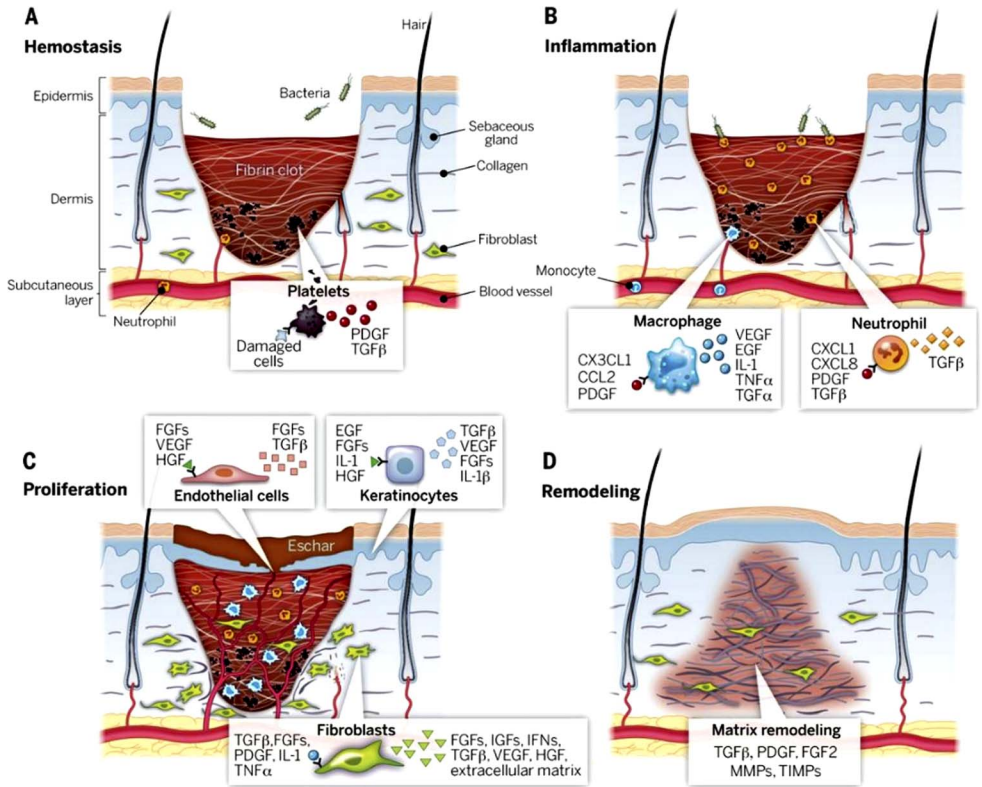

Fig. 3 Stages of wound healing: (A) hemostasis, (B) inflammation, (C) proliferation, (D) remodelling. Reproduced from ref. 50 with permission from Science, copyright 2003.

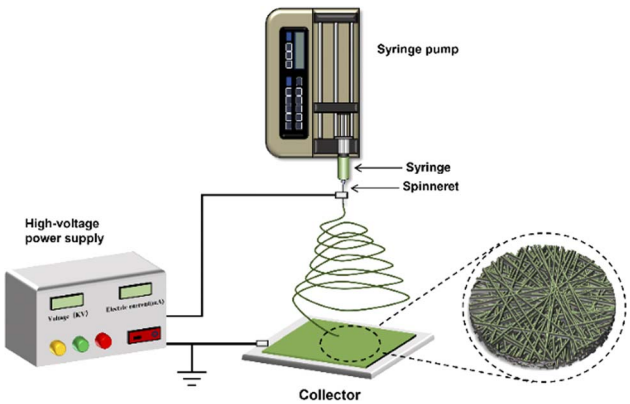

Fig. 4 Electrospinning device. The electrospinning device is mainly composed of an injection pump, a syringe connected with a spinneret, a high-voltage power supply, and a collector.

of the Taylor cone.[26] Under the action of the electric field force between the spinneret and the collecting device, the ejected polymer solution goes through bending and whipping stages and then falls on the collecting device. With the volatilization of the solvent, the stretched and cured polymer solution is deposited on the collection device, resulting in the formation of nanofibers.[65]

In the process of electrospinning, the size and shape of nanofibers can be changed by changing solution parameters (polymer type, viscosity, concentration, conductivity, and surface tension), process parameters (electric field strength, electrostatic potential, acceptance distance, pore diameter) and environmental conditions (temperature, humidity, local airflow).[66–70] Nanofibers with different morphological structures can realize the loading and precisely controlled release of various drugs. Sustained drug release ensures smooth drug concentration in the wound, reducing dosing frequency and improving compliance.[71,72] Electrospun nanofibers have facilitated the development of drug delivery systems and show promising prospects in wound healing and skin regeneration.[73,74] To provide more structures for nanofibers, many strategies have been developed to improve electrospinning technology. As shown in Fig. 5, there are various types of electrospun nanofibers: (1) single-fluid electrospinning: blending electrospinning and emulsion electrospinning; (2) double-fluid electrospinning: coaxial electrospinning and side-by-side electrospinning; (3) multi-fluid electrospinning.

3.2 Single fluid electrospinning

3.2.1 Blending electrospinning. Blending electrospinning is a commonly used method for preparing blended nanofibers containing two or more different polymers.[75,76] Before electrospinning, different polymers need to be added to the solvent in a certain proportion and mixed thoroughly. After testing, blending electrospinning can achieve the delivery of cell inhibitors, antibiotics, and therapeutic drugs with specific

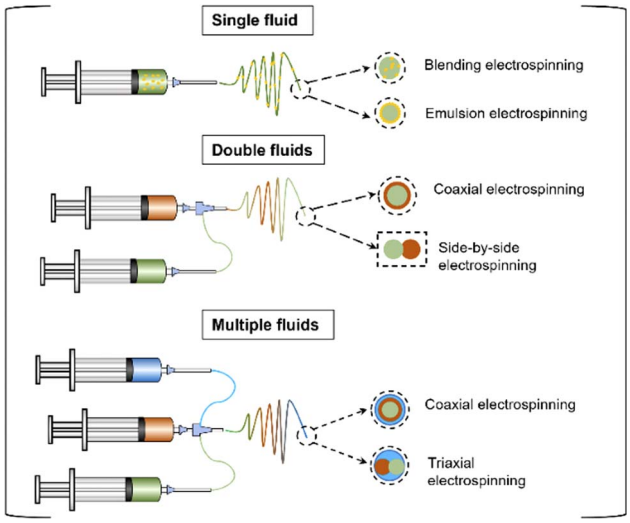

Fig. 5 According to the number of fluids, electrospinning can be divided into single-fluid electrospinning (blended electrospinning and emulsion electrospinning), double-fluid electrospinning (coaxial electrospinning and side-by-side electrospinning), and multi-fluid electrospinning.

functions.[77–81] The choice of solvent determines whether polymers and drugs can be fully dissolved. If the solvent that dissolves the polymer cannot dissolve the drug, it is necessary to dissolve the drug with a small amount of solvent that dissolves the drug, and then blend electrospinning with the polymer solution.[63,82,83] The disadvantage of blending electrospinning is also obvious. If the drug is not fully dissolved, it will accumulate on the surface of the nanofibers and cause sudden drug release.

3.2.2 Emulsion electrospinning. Emulsion electrospinning is a simple and effective method for the preparation of core–shell nanofibers, which improves the problem of sudden drug release caused by blending electrospinning.[84] Emulsion electrospinning usually uses two types of emulsions. One is a water-in-oil emulsion based on a lipophilic continuous phase and a hydrophilic liquid drop phase.[85] This type of emulsion is used to encapsulate hydrophilic small molecular proteins or drugs. The emulsion is stabilized by surfactants/emulsifiers with low hydrophilic and lipophilic balance.[86] The other is oil-in-water emulsion which is formed by lipophilic droplet phase and hydrophilic continuous phase. The hydrophobic drug was dissolved in the oil phase solvent and then diffused into the hydrophilic continuous phase. Compared with blending electrospinning, emulsion electrospinning has more advantages in the preparation of nanofibers containing low-solubility drugs. Compared with the drug-loaded nanofibers prepared by electrospinning of blends, the nanofibers based on emulsion electrospinning show more uniform drug distribution.[87] Jiang *et al.* reported the electrospinning of a Pickering emulsion loaded with a natural antimicrobial agent, tea tree oil (TTO), and stabilized with ZnO/Ag nanocomposites for antimicrobial dressings.[88] With the stabilization of ZnO and Ag nanoparticles, TTO could be uniformly distributed in the Pickering emulsion with good stability. The results showed that the prepared nanofiber dressings had excellent long-term bacteriostatic activity against both Gram-positive and Gram-negative bacteria, as well as good biocompatibility and blood compatibility. In addition, it effectively promoted cell proliferation and migration when the concentration of nanofiber samples was 800 μg ml^{-1} or less.

3.3 Double-fluid electrospinning

3.3.1 Coaxial electrospinning. Coaxial electrospinning can simultaneously use two kinds of polymer solutions to prepare nanofibers with core–shell structures. The advantage of this structure is that the drug is put into the core layer, which reduces the phenomenon of sudden drug release and prolongs the drug release time.[89–91] Coaxial electrospinning can use a combination of spinnable solution and non-spinnable solution, which is generally put into the core layer. When preparing core–shell nanofibers using coaxial electrospinning, it is necessary to consider the miscibility, viscosity, and conductivity between different layers of solutions.[92–94] Nanofiber burn dressings with dual drug loading of centella total glucoside and ciprofloxacin were prepared by coaxial electrospinning technique by Guo *et al.*[95] They placed centella total glucoside into the nuclear layer to avoid sudden release while prolonging the therapeutic effect of the drug. Antimicrobial experiments and *in vitro* cellular experiments showed that the prepared nanofibers had excellent antimicrobial activity and the ability to promote the proliferation of fibroblasts. In addition, rat burn experiments showed that the nanofiber dressing also significantly accelerated wound healing by promoting endothelial cell proliferation and angiogenesis. In another study, Ramalingam *et al.* prepared core–shell nanofibers, in which polycaprolactone/gelatin loaded minocycline hydrochloride as the shell, and gelatin containing *Gymnema sylvestre* extract as the core layer.[96] Compared with the blended nanofibers they prepared, the core–shell structure promotes the sustained release of bioactive components in the nanofibers. The plant extracts in the shell layer and the antibiotics in the core layer exerted a good synergistic effect, which together achieved antimicrobial activity and promoted cell proliferation. Experiments on second-degree burns in porcine skin demonstrated that the dressing could effectively promote collagen deposition and re-epithelialization. Coaxial electrospinning provides an effective method for encapsulating bioactive materials in biomedical nanofibers.[97,98]

3.3.2 Side-by-side electrospinning. Based on single-fluid electrospinning, Janus nanofibers can be prepared using parallel spinnerets. Unlike the core–shell structure, all parts of the Janus structure can be in direct contact with the external environment.[99,100] Janus nanofibers can achieve biphasic controlled release during drug release. Yang *et al.* prepared Janus nanofiber dressing loaded with ciprofloxacin and silver nanoparticles on both sides by side-by-side electrospinning.[101] Transmission electron microscopy images showed that the prepared Janus had a clear Janus structure. *In vitro* drug release experiments showed that the release of ciprofloxacin was almost complete within the first 30 minutes, which ensured that

the strongest antimicrobial activity was achieved in the early stage of wound healing. In addition, Janus nanofibers showed good antimicrobial activity against *Staphylococcus aureus* and *Escherichia coli* due to the synergistic effect of ciprofloxacin and silver nanoparticles. In a similar study, Shi *et al.* prepared amphiphilic Janus nanofiber membranes loaded with copper sulfide nanoparticles, mupirocin and valsartan using polyvinyl alcohol, polylactic acid-glycolic acid.[102] Their prepared Janus nanofiber membranes possessed obvious amphiphilic characteristics and were capable of sustained release of the antimicrobial agent mupirocin in a hydrophilic environment. In addition, the photothermal effect of the amphiphilic Janus nanofiber membrane can also control the release of the anti-inflammatory agent valsartan. Therefore, the wound dressing they prepared can effectively solve the problems of infection and inflammation in wound healing, providing a feasible method for clinical application. Presently, side-by-side electrospinning and the functionalizations of Janus nanofibers are hot topics in some scientific fields such as energy, electronic textiles, drug delivery, and environments.[103–107]

3.4 Multi-fluid electrospinning

Triaxial electrospinning can achieve more functions, such as loading drugs with different properties, longer drug release times, and solving the problem that some drugs are difficult to dissolve.[108,109] Curcumin possesses several excellent antibacterial, anti-inflammatory and antioxidant activities, but it is difficult to dissolve in water. In order to improve the utilization of curcumin's active ingredients, Liu *et al.* prepared nanofibers with controllable thickness of the sheath layer for the controlled release of curcumin using modified triaxial electrospinning.[110] They prepared nanofibers with uniform linear morphology and distinct core-sheath structure. The experimental results showed that the core-sheath nanofibers were able to precisely control the release of curcumin and showed good antibacterial activity against both *Staphylococcus aureus* and *Escherichia coli*. Triaxial electrospinning technology opens up a new way to prepare complex nanomaterials and shows great advantages in the formation of drug delivery systems with complex nanostructures.[111]

4 Polymer used for making electrospun nanofiber burn dressings

The selection of polymers for electrospun nanofibers is crucial for burn wound management as it affects the mechanical properties and therapeutic activity of dressings.[112] There are differences in viscosity, nanofiber morphology, biocompatibility, and mechanical strength of polymer spinning solutions from different sources.[113] Both natural polymers and synthetic polymers are feasible choices. Natural polymers have better biocompatibility, while synthetic polymers have better mechanical properties.[114] Table 1 summarizes the natural and synthetic polymers used in the preparation of electrospun nanofiber burn dressings. These polymers mainly include natural ones such as chitosan,[115–120] gelatin,[121–123] silk fibroin,[118,124,125] sodium alginate,[126,127] and synthetic polymers such as poly(ε-caprolactone),[128–132] poly(vinyl alcohol),[119,125,133] poly(ethylene oxide),[120,127,131] poly(vinyl pyrrolidone),[132] polyurethane[126] and polylactic acid.[134]

Table 1 Polymers for preparation of electrospun nanofibers

Polymer type	Polymer	Ref.
Natural polymer	Chitosan	115–120
	Gelatin	121–123
	Silk fibroin	118, 124 and 125
	Sodium alginate	126 and 127
Synthetic polymer	Poly(ε-caprolactone)	116, 122, 124 and 128–131
	Poly(vinyl alcohol)	119, 125 and 133
	Poly(ethylene oxide)	120, 127 and 131
	Poly(vinyl pyrrolidone)	132
	Polyurethane	126
	Polylactic acid	134

4.1 Natural polymers

4.1.1 Chitosan. Chitosan (CS) is a natural polymer derived from chitin. It has excellent biocompatibility, biodegradability, antioxidant, and antibacterial activity.[135] Due to its unique biological activity, CS is widely used in drug delivery, wound dressings, and tissue engineering scaffolds.[136–138] It is not easy to prepare nanofibers from a single CS solution using electrospinning technology. To solve this problem, Shabunin *et al.* added chitin nanofibril to the CS solution, which significantly improved the formation rate of CS nanofibers.[115] The wound dressing has two layers, and the outer layer is composed of polyamide nanofibers to provide mechanical strength for the wound dressing and prevent the invasion of external bacteria. The inner layer is composed of CS mixed with chitin nanofibril, which is mainly responsible for sterilizing and absorbing wound exudate. Liu *et al.* chose polycaprolactone (PCL) with excellent mechanical properties to blend with chitosan to improve the physical properties of chitosan.[116] The PCL/CS graft copolymer has both the biological activity of CS and the mechanical stability of PCL. The results of clinical experiments showed that PCL/CS nanofiber dressing had better antibacterial activity and mechanical properties than traditional dressing.

Unlike most other polysaccharides, CS is a natural cationic polymer that can be blended with other negatively charged natural or synthetic polymers.[139] The antibacterial activity of chitosan due to the interaction between the positive charge of chitosan and the negative charge on the surface of bacteria, resulting in the rupture of bacterial biofilm.[140] Mirhaj *et al.* designed a bilayer wound dressing simulating the skin tissue structure, with chitosan/polyethylene glycol containing advanced platelet-rich fibrin (A-PRF) in the upper layer and chitosan electrospun nanofibers loaded with L-arginine in the lower layer.[117] The results showed that the prepared bilayer dressing possessed excellent antimicrobial activity and potential to promote blood vessel formation. This was attributed to the synergistic antimicrobial effect of the positively charged L-arginine with the equally positively charged chitosan. Studies

have shown that arginine has the ability to stimulate vascular regeneration and enhance collagen synthesis.[141] Therefore, the L-arginine in this wound dressing together with A-PRF promotes angiogenesis and accelerates wound healing.

4.1.2 Gelatin. Gelatin, which is mainly extracted from collagen in animal skin, muscle, and bone, is a heterogeneous mixture of highly hydrophilic peptides.[142,143] Gelatin is widely used in biomedical fields, such as biological stents, vaccine development, anticancer drugs, and wound dressings.[144–146] However, gelatin needs to be blended with other polymers to enhance its mechanical properties. Poly(L-lactic-*co*-caprolactone) nanofibrous membranes loaded with Epigallocatechin-3-O-gallate (EGCG) were prepared by Li *et al.* using coaxial electrospinning, and gelatin was added to enhance the hydrophilicity and biocompatibility of nanofibrous membranes.[121] The results showed that the wound dressing had good biocompatibility, antimicrobial, antioxidant, and ability to promote wound closure. Leung *et al.* used gelatin and polycaprolactone to prepare a chondroitin sulphate-loaded blend and coaxial nanofiber composite dressings.[122] They established a pig skin burn model to test the effect of two kinds of nanofibers on wound healing. Compared with polycaprolactone/gelatin blend nanofibers, core–shell nanofibers were easier to promote cell growth and achieved controlled drug release. During the healing process of burn wounds, a large amount of exudate is produced, which can hurt wound healing. Considering this problem, Zhou *et al.* prepared an asymmetric wettable fibre membrane by electrospinning.[123] The inner layer was composed of hydrophilic gelatin and ginsenoside Rg1, and the outer layer was a mixture of black phosphorus grafted chitosan and poly(lactic-glycolic) acid (Fig. 6). Similar to the dermis of human skin, the hydrophilic inner layer can not only remove excess wound exudate but also provide a moist environment for the wound.

4.1.3 Silk fibroin. Silk fibroin (SF) is a natural macromolecular fibrin extracted from silkworm cocoons.[147] Compared with other synthetic and natural polymers, SF has better biocompatibility, non-toxicity, biodegradability, resistance, and thermal stability.[148,149] In addition, SF has excellent toughness and is often mixed with other polymers to improve the mechanical properties of nanofibers. Khosravimelal prepared CS/SF electrospun nanofibers containing cationic antimicrobial peptides as wound dressings.[118] The combination of cationic antimicrobial peptide and chitosan can significantly improve the antibacterial effect of nanofiber dressings. SF can improve the weak mechanical properties of chitosan, which is well proved by the results of the stress–strain curve. Mollaghadimi used SF and PCL to prepare nanofiber wound dressings and added allicin to improve the antibacterial properties.[124] Yerra *et al.* prepared electrospun nanofibers by blending silk fibroin, polyvinyl alcohol, and antibiotics.[125] The wound therapeutic effect of nanofiber dressing was tested by a rat burn model. The results showed that the dressing had excellent antibacterial ability, and it also promoted the cell viability and cell adhesion of fibroblasts. SF comes into direct contact with the wound and releases antibiotics to remove pathogens. The activity of silk fibroin/polyvinyl alcohol nanofiber dressings is mainly reflected in the biodegradability of SF and the release rate of drugs.

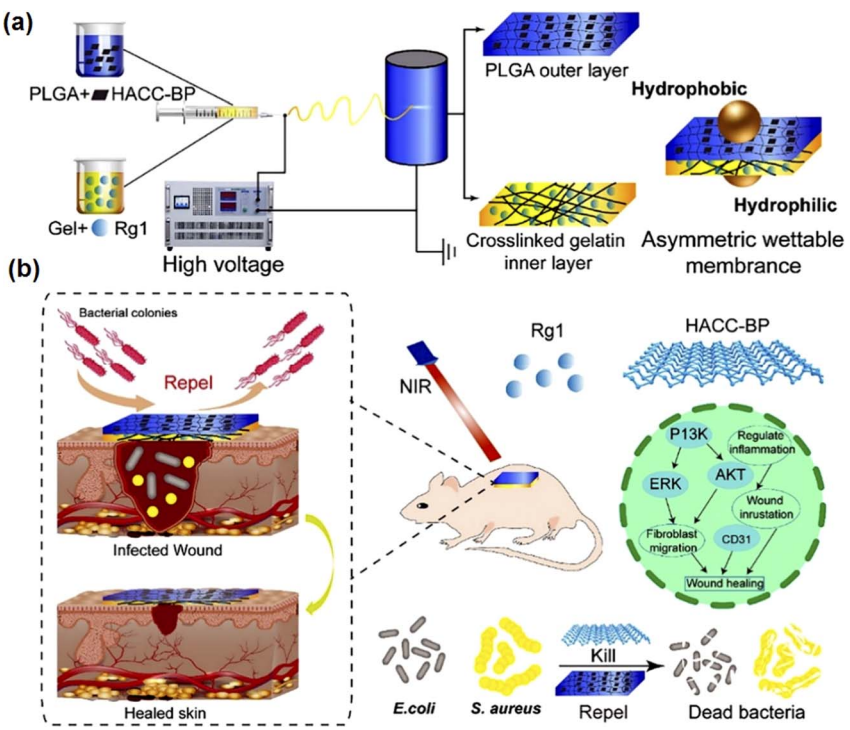

Fig. 6 (a) Preparation process of the asymmetric wettable membrane. (b) The antibacterial and wound healing properties of asymmetric wettable film. Reproduced from ref. 123 with permission from Wiley, copyright 2022.

4.1.4 Sodium alginate. Sodium alginate is a natural polysaccharide polymer extracted from brown algae.[150] Because of its non-toxicity, antioxidation, biocompatibility, and biodegradability, it has aroused great interest in biomedical applications.[151] The polymer synthesized from sodium alginate has weak mechanical properties and needs to be mixed with other polymers to maintain structural integrity. A series of nanofiber burn dressings based on polyurethane (PU), hydroxypropyl trimethyl ammonium chloride chitosan (HACC) and sodium alginate (SA) were prepared by Guo *et al.*[126] The natural anionic polysaccharide SA absorbs wound exudate and maintains a moist environment, and also interacts with the cationic HACC to reduce its cytotoxicity. Cellular experiments showed that the SA-containing nanofibers significantly promoted the proliferation and migration of keratinocytes and fibroblasts. Huang *et al.* reported a multilayer nanofiber film, the upper and lower layers of which were poly(ethylene oxide)/sodium alginate electrospun nanofiber films, and the intermediate layer was nanofibers loaded with tetracycline hydrochloride.[127] The multilayer nanofiber membrane has a regular arrangement structure and many voids, which provides an ideal environment for cell adhesion and proliferation. In addition, the fibre membrane also had an excellent drug-controlled release (release period of more than 10 days) and antibacterial effect. Sodium alginate can release bioactive substances and reduce the expression of proinflammatory factors, which shows great potential in the treatment of burns.

4.2 Synthetic polymers

4.2.1 Poly(ε-caprolactone). Poly(ε-caprolactone) (PCL) is a biodegradable, safe, and non-toxic hydrophobic synthetic polymer, which has been approved by FDA for biomedical applications.[152] Because of its good mechanical properties and biocompatibility, it has been widely used as a raw material for the preparation of electrospun nanofibers. However, the electrospun nanofibers based on PCL are not hydrophilic, which may not provide an ideal environment for cell adhesion and proliferation.[153] PCL needs to be blended with other hydrophilic polymers or drugs to improve hydrophilicity. Zhou *et al.* prepared chitosan oligosaccharide/polycaprolactone nanofiber membranes loaded with rutin and quercetin.[128] The authors explained that blending chitosan oligosaccharides with PCL can improve the hydrophilicity of nanofiber membranes and provide a moist environment for wound healing. The experimental results showed that the prepared nanofiber membrane had good hydrophilic, antioxidant, and antibacterial properties, and could promote wound healing. Bayat *et al.* prepared kiwifruit extract (KE) loaded nanofibers by blending hydrophilic cellulose acetate with PCL and evaluated their properties of promoting burn wound healing.[129] In the test of wound healing effect for more than 21 days, PCL/CA/KE nanofiber dressing had a better effect than KE. In addition, PCL/CA/KE effectively promoted the proliferation of fibroblasts. Guo *et al.* prepared electrospun nanofiber mats using PCL and α-lactalbumin (ALA).[130] The wettability and mechanical properties of nanofiber wound dressings were improved by adjusting the mass ratio of ALA to PCL. The results proved that the prepared nanofibers had a significant effect on promoting wound healing and reducing scar.

4.2.2 Poly(vinyl alcohol). Polyvinyl alcohol (PVA) is a kind of synthetic polymer with semi-crystalline properties.[154] Because of its excellent hydrophilicity, biocompatibility, and biodegradability, it is widely used in the preparation of medical biomaterials such as hydrogels, films, scaffolds, and nanofibers.[155,156] Morais *et al.* prepared electrospun nanofiber mats by mixing PVA, CS, green propolis extract, and nystatin.[119] The combination of PVA and CS makes the biodegradable nanofiber mat have better water absorption and swelling ability, which is beneficial to the absorption of wound exudate. Ramkumar *et al.* prepared PVA nanofiber scaffolds doped with molybdenum nanoparticles.[133] The experimental results showed that the nanofiber scaffold was compatible with red blood cells and had excellent biocompatibility. The diameter of the bacteriostatic circle was more than 7 mm, which proved that it had better antibacterial performance. Their research confirms the advantages of polyvinyl alcohol nanofibers mixed with metal nanoparticles in promoting cell growth.

4.2.3 Poly(ethylene oxide). Poly(ethylene oxide) (PEO) is a kind of synthetic polymer, which shows excellent biocompatibility, biodegradability, and water solubility.[157] Singh *et al.* used PEO, PCL, and silver sulfadiazine to prepare nanofibers with core–shell structure.[131] PEO mixed with silver sulfadiazine as the core layer (Fig. 7A(a)). The prepared core–shell nanofibers showed sudden drug release in the initial stage (Fig. 7A(c)). This is because PEO tends to absorb water and expand, resulting in the release of drugs too quickly. With the gradual degradation of the core layer, the release curve gradually tended to be stable, and the long-term sustained release of silver sulfadiazine was realized. Abid *et al.* used CS and PEO to prepare nanofiber burn dressings loaded with ZnO nanoparticles (Fig. 7B).[120] Because it was too difficult to spin with a single CS solution, the author added PEO to improve the spinnability of the CS solution. The results showed that the prepared nanofibers had good antibacterial activity, biocompatibility, and stability.

4.2.4 Poly(vinyl pyrrolidone). Water-soluble polymer polyvinylpyrrolidone (PVP) has excellent film-forming, biodegradability, high polar groups, and is non-toxic.[158,159] Khataei *et al.* reported a composite nanofiber wound dressing using polyamide-6, PVP, and tea tree essential oil produced by electrospinning.[132] The results of mechanical property tests showed that PVP improved the mechanical strength of the nanofibers, thus protecting the wound from external forces during the healing process. As the molecular weight of PVP increased, the nanofibers exhibited higher porosity, water vapor permeability, and surface wettability, thereby promoting cell adhesion and proliferation. In addition, the produced nanofibers containing tea tree essential oil exhibited excellent antioxidant and antimicrobial properties. This explains why the nanofiber dressings they prepared can effectively promote wound healing.

4.2.5 Polyurethane. Polyurethane has been widely used in the biomedical field due to its excellent biocompatibility and tensile strength.[160] Guo *et al.* prepared composite nanofiber dressings loaded with ginsenoside Rg3 using polyurethane and

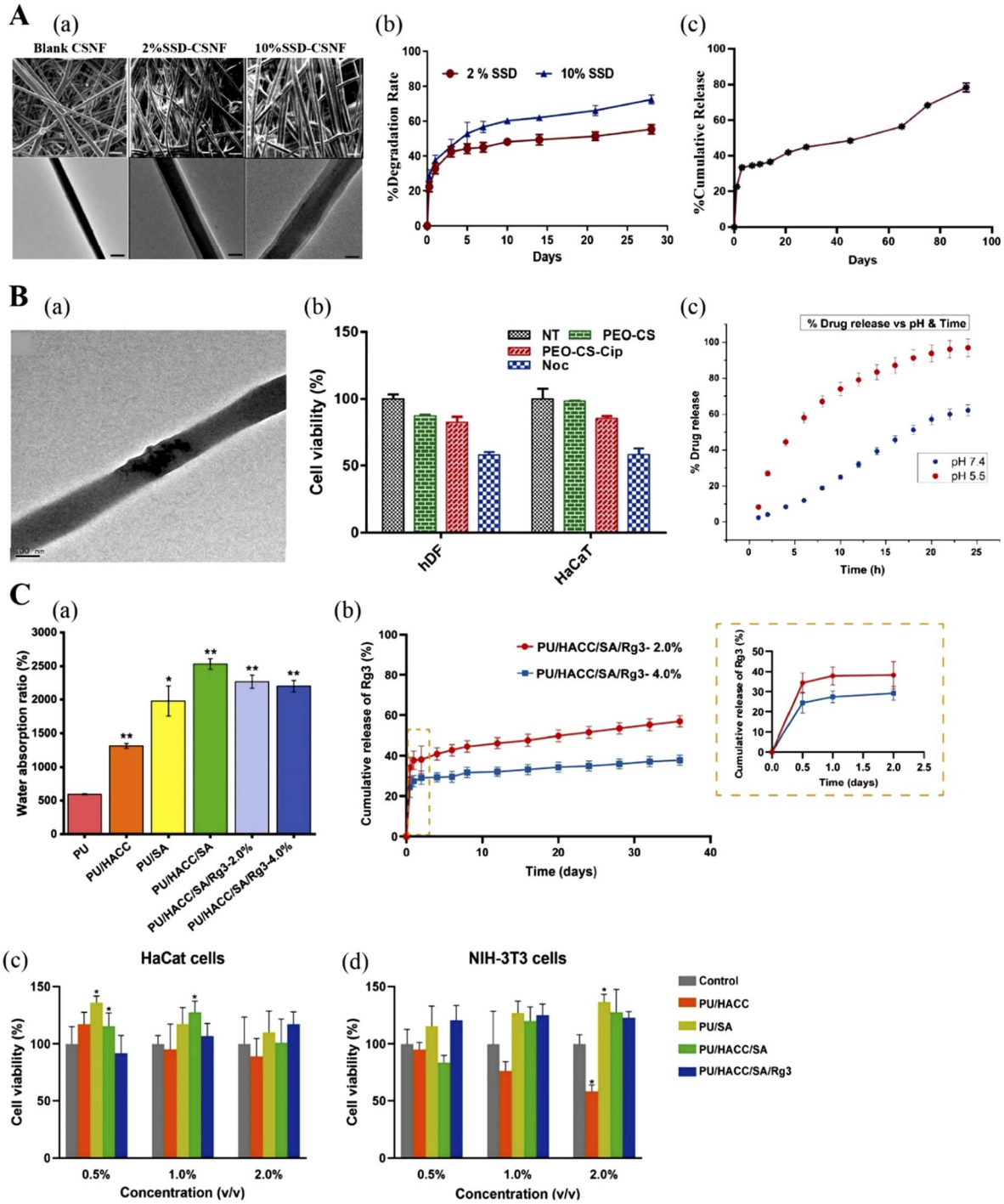

Fig. 7 (A) Silver sulfadiazine (SSD) loaded core–shell nanofibers: (a) SEM and TEM images of core–shell nanofibers (CSNF), 2% SSD loaded and 10% SSD loaded core–shell nanofibers (SSD-CSNF); (b) degradation profile of 2% SSD-CSNF; (c) the release profile of 2% and 10% SSD-CSNF. Adapted from ref. 131 with permission from Elsevier, copyright 2022. (B) Poly(ethylene oxide)-chitosan nanofibers: (a) TEM image of ciprofloxacin-loaded nanofibers with a size of 100 nm; (b) cytotoxicity of nanofibers to human dermal fibroblasts and keratinocytes; (c) commutative drug release % *vs.* pH and time. Adapted from ref. 120 with permission from Elsevier, copyright 2019. (C) Ginsenoside Rg3-loaded polyurethane/marine polysaccharide-based nanofiber dressings: (a) water absorption; (b) release curve of ginsenoside Rg3 with time; (c) and (d) are the effects of different concentrations of nanofiber dressing extracts on the proliferation of keratinocytes and fibroblasts. Adapted from ref. 126 with permission from Elsevier, copyright 2023.

marine polysaccharides (Fig. 7C).[126] This composite dressing showed a significant promoting effect on the growth of fibroblasts and keratinocytes (Fig. 7C(c) and (d)). According to the results of 21 days of treatment on a third-degree burn rat model, the composite nanofiber dressing had a significant effect on promoting burn wound healing. The results indicate that

composite dressings exhibit superior wound healing potential compared to conventional dressings in many aspects.

4.2.6 Polylactic acid. Polylactic acid (PLA) is a polyester polymer obtained by polymerizing lactic acid as the main raw material, which has good biocompatibility and biodegradability and shows great potential in tissue engineering and drug delivery.[161] Liu *et al.* prepared degradable nanofiber dressings loaded with astragaloside IV using chitosan and polylactic acid.[134] Since polylactic acid possesses certain hydrophobicity, it can be combined with hydrophilic chitosan, enabling the nanofiber dressings to resist the intrusion of foreign aqueous solutions while slowly absorbing wound exudate. However, the antimicrobial activity of PLA is poor, and the antimicrobial activity of the prepared dressings mainly comes from the synergistic effect of astragaloside IV and chitosan. The results showed that the wound dressing they prepared had satisfactory antibacterial and wound healing promotion effects, and was a safe and effective wound dressing.

Polymers are always playing an important role in developing all kinds of medicated materials.[162–164] Electrospinning initially was just a method for converting polymeric solution into solid nanofibers. Along with the fast developments of electrospinning techniques and the polymer sciences, more and more polymers will be introduced into the applications of burn dressings in the form of electrospun fibrous mats.[165–170]

5 Drugs loaded in electrospun nanofiber burn dressings

In order to enhance the performance of nanofiber burn dressings, various therapeutic and antimicrobial agents are incorporated into the nanofibers, including plant extracts, small molecule drugs, and nanoparticles. Table 2 Classification of nanofiber-loaded drugs according to their biological effects. These compounds have different functional performances, *e.g.*, accelerating wound healing,[171] antibacterial,[172] preventing scar formation,[126] and multi-function.[174,175] They can be loaded into the nanofibers alone, but can also be encapsulated jointly for a synergistic effect.

Table 2 Bioactive compounds loaded on electrospun nanofiber dressings

Biological effect	Bioactive compounds	Ref.
Accelerate wound healing	Curcumin	116
	Ginsenoside Rg1	123
	Kiwi extract	129
	Bromelain	171
Antibacterial	Allicin	124
	Berberis lycium extract	172
	Gymnema sylvestre extract	96
	Silver sulfadiazine	131
	Zinc oxide	173
Reduce scar formation	α-Lactalbumin	130
	Ginsenoside Rg3	126
Multifunction	Quercetin/rutin	128
	Lavender essential oil	174
	Astragaloside IV	175

5.1 Accelerate wound healing

5.1.1. Curcumin. Turmeric is a perennial herb widely used in Asia. Curcumin is the main bioactive component of turmeric, which has many properties, such as anti-inflammation, antioxidation and anti-infection.[176] Persistent bacterial infection in the process of wound healing will cause long-term chronic inflammation, which will seriously affect the speed of wound healing. Curcumin, a natural active ingredient, can reduce wound inflammation by decreasing pro-inflammatory factors expression.[177] Using PCL/CS as shell, zein (ZE) and curcumin (CUR) as core, Liu *et al.* prepared PCL/CS graft copolymer-zein-curcumin (PCL/CS-ZE-CUR) electrospun nanofibers.[116] In the antibacterial experiment, the total infection rate of the traditional dressing group decreased by 13.8%, while the new nanofiber dressing group decreased by 78.2%, which proved the antibacterial activity of the new nanofiber dressing. Judging from the healing of the burn wound, PCL/CS-ZE-CUR electrospun nanofiber dressing had a better therapeutic effect than traditional dressing. Curcumin's excellent ability of anti-inflammation and scavenging oxygen free radicals can accelerate wound healing and is expected to provide beneficial improvements for wound management.

5.1.2. Ginsenoside Rg1. Ginsenoside Rg1 is a kind of protopanaxatriol saponin extracted from traditional Chinese medicine Ginseng, which has anti-inflammatory, antioxidant, and neuroprotective activities.[178,179] Zhou *et al.* produced a double-layer structure electrospun asymmetric fibre membrane containing ginsenoside Rg1.[123] *In vitro*, cytotoxicity tests showed that ginsenoside Rg1 could promote the migration of human umbilical vein endothelial cells and the formation of capillaries (Fig. 8A(b)). The experimental results *in vivo* showed that the fibre membrane could regulate inflammatory factors and growth factors, and it also achieved anti-inflammation and promoted collagen deposition (Fig. 8A(d)). The prepared asymmetric wettable membrane inhibits pro-inflammatory factors by enhancing the expression of anti-inflammatory factors, promotes macrophage M2 polarization, and inhibits macrophage M1 polarization. This also explains why the wound dressing they prepared can accelerate wound healing (Fig. 8A(c)).

5.1.3. Kiwi extract. Kiwi extract (KE) contains a variety of bioactive components, such as phenols, vitamins C and E, which are considered to have anti-aging, anti-inflammatory, and antioxidant effects.[180] Bayat *et al.* prepared nanofibers containing polycaprolactone, cellulose acetate (CA), and kiwifruit extract (PCL/CA/KE).[129] PCL/CA/KE nanofibers have 30% higher water absorption than PCL/CA. The results of cell experiments *in vitro* showed that PCL/CA/KE nanofibers had no cytotoxicity and effectively promoted the proliferation and attachment of fibroblasts. The authors used a mouse burn model to test the ability of nanofiber membranes to promote wound healing. After 21 days, the ability of PCL/CA/KE to promote burn wound healing was significantly higher than that in the control group. The completion of the epithelialization process and the significant reduction of inflammatory cells better prove that PCL/CA/KE nanofiber is an effective dressing to promote burn wound healing.5.1.4 Bromelain.

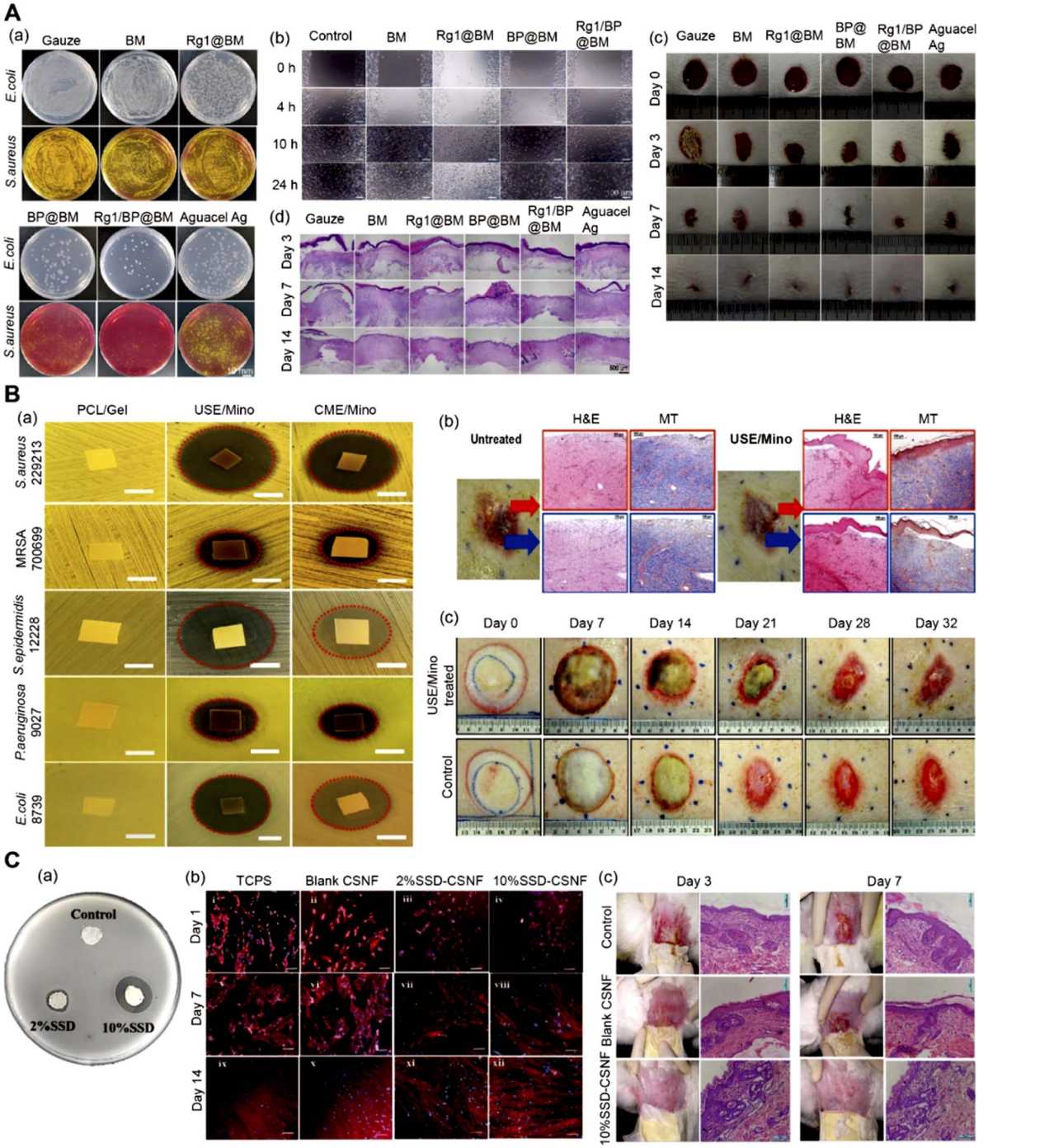

Fig. 8 (A) Multifunctional nanofiber membranes containing black phosphorus/Rg1: (a) *Escherichia coli* and *Staphylococcus aureus* colonies remaining in the wound area on the third day; (b) image of umbilical vein endothelial cells *in vitro* wound healing experiment; (c) pictures of wounds treated with different materials on days 0, 3, 7 and 14; (d) H&E staining of wound tissues. Adapted from ref. 123 with permission from Wiley, copyright 2022. (B) Core–shell structured anti-microbial nanofiber dressings (a) disk diffusion diagram of antibacterial activity of different core–shell nanofibers; (b) histological images of wounds untreated and treated with nanofiber dressings; (c) comparative images of wound treatment results at different time intervals. Adapted from ref. 96 with permission from ACS, copyright 2021. (C) Application of core–shell nanofibers in burn treatment: (a) antibacterial effect of different core–shell nanofibers; (b) fluorescence microscope image of human dermal fibroblasts cultured on core–shell nanofibers; (c) histological sections of different groups on the 3rd and 7th day. Adapted from ref. 131 with permission from Elsevier, copyright 2022.

Pineapple is a tropical fruit loved by people around the world. Bromelain, which is extracted from the stems, leaves, and fruit of the pineapple plant, also has great appeal. Research shows that bromelain has anti-inflammatory, antioxidant, immunomodulatory, cardioprotective, and anti-cancer properties.[181] In addition, bromelain is widely used in the food

industry, cosmetics, and pharmaceutical industries due to its unique pharmacological and chemical properties.[182] Hasannasab *et al.* combined the therapeutic properties of bromelain and ZnO nanoparticles with the structural properties of silk fibroin to prepare a wound dressing with antibacterial properties.[171] The results of antibacterial experiments showed that bromelain did not affect the antibacterial activity of excipients, and it was ZnO nanoparticles that made the dressing have antibacterial activity. However, compared with pure silk fibroin nanofibers, bromelain can accelerate the removal of necrotic tissue to promote wound re-epithelialization.

5.2 Antibacterial

5.2.1 Allicin. Allicin is a thiosulfinate extracted from garlic. Allicin has many properties that are beneficial to human health, such as antibacterial, cholesterol-lowering, blood pressure-lowering, and anti-tumour properties.[183] Some studies have shown that allicin can redox with mercaptan groups in protein and glutathione, which is crucial for the biological activity of allicin.[184] All kinds of bacteria, fungi, and cells can be inhibited or killed by adjusting the concentration of allicin. Mollaghadimi added allicin to PCL and SF to make nanofiber wound dressings.[124] The effect of allicin is to expand the antibacterial properties of nanofibers. In the antibacterial experiment, the diameter of the inhibitory zone of bacterial growth was measured. Compared with the sample without allicin, the inhibition band of the nanofiber containing allicin increased to more than 3 mm, showing a good antibacterial effect.

5.2.2 *Berberis lycium* extract. *Berberis lycium* is rich in phenols, alkaloids, and other bioactive compounds, which have anti-inflammatory, antibacterial, and antioxidant effects.[185] Khan reported a polyvinyl alcohol/montmorillonite electrospun nanofiber containing root extract of *Berberis lycium*.[172] The results showed that the nanofibers containing 0.8 g of extract showed the highest antibacterial activity. And the inhibitory effect on *Pseudomonas aeruginosa* was better than that of *Staphylococcus aureus*. Compared with the control group, the wound treated with nanofibers with extract showed the best healing effect and reduced inflammation. Because the extract has anti-inflammatory and antibacterial activity, it quickly enters the stage of cell proliferation after a short period of inflammation.

5.2.3 *Gymnema sylvestre* extract. *Gymnema sylvestre* is a slow-growing medicinal woody plant with effective anti-obesity and anti-diabetes activities.[186] The extract also has the properties of anti-bacterial, anti-inflammatory, anti-high cholesterol, and anti-sugar. Ramalingam *et al.* prepared coaxial nanofibers in which the core layer was loaded with *G. sylvestre* extract and the shell layer was loaded with minocycline hydrochloride.[96] The joint action of the extract and minocycline hydrochloride enhances the permeability of the bacterial cell wall, so it shows an obvious synergistic effect on Gram-positive bacteria (Fig. 8B(a)). The prepared core–shell nanofiber mats effectively promoted wound healing compared with the untreated control group (Fig. 8B(b) and (c)).

5.2.4 Silver sulfadiazine. The silver ions released from silver sulfadiazine are an effective antibacterial agent that can eliminate a variety of bacteria including Gram-positive and Gram-negative bacteria. Dressings containing silver sulfadiazine are often chosen for burn wound management.[187] Singh *et al.* prepared core–shell nanofibers loaded with silver sulfadiazine using PEO and PCL.[131] When the concentration of silver sulfadiazine is greater than 5 μg ml^{-1}, bacterial growth will be completely inhibited (Fig. 8C(a)). The results showed that the core–shell nanofibers loaded with silver sulfadiazine had higher cell proliferation ability and no toxicity to cell growth (Fig. 8C(b)). Compared with the control group, there was no obvious inflammation in the wound images of the nanofiber group (Fig. 8C(c)).

5.2.5 Zinc oxide. The tremendous development of nanotechnology has led to a wide range of applications of metal and its oxide nanoparticles in the fields of biology, medicine, chemistry and environment.[188] Among the many metal and its oxide nanoparticles, zinc oxide nanoparticles have attracted attention for their many distinctive properties. In the biomedical field, zinc oxide nanoparticles exhibit excellent anticancer, antibacterial, and antioxidant properties, as well as the potential to promote wound healing. [189] A hyaluronic acid-silk fibroin core–shell nanofiber dressing with ZnO encapsulated in the core layer was designed for burn treatment by Hadisi *et al.*[170] The results showed that the addition of ZnO improved the antimicrobial properties of the nanofiber dressing, which inhibited both *Escherichia coli* and *Staphylococcus aureus*, with an antimicrobial effect of more than 14 days. Although high concentration of ZnO will have better antibacterial effect, it will also be toxic to the cells. *In vitro* and *in vivo* studies have shown that 3 wt% ZnO promotes cell proliferation, collagen deposition, and effectively improves burn wound healing. ZnO nanoparticles possess significant antimicrobial properties and are not prone to the problem of bacterial resistance, and thus can be used as a viable alternative to antibiotics.

5.3 Reduce scar formation

5.3.1 α-Lactalbumin. Alpha-lactalbumin (ALA) is an acidic small molecule globular protein found in mammalian whey.[190] Its main function is to promote the synthesis of lactose in the mammary gland. The abundant tryptophan in α-lactalbumin is an important precursor for the synthesis of the neurotransmitter serotonin. Serotonin can promote the proliferation and migration of fibroblasts and keratinocytes, thereby promoting wound healing.[191] Guo *et al.* explored the role of ALA in accelerating burn wound healing and reducing scar formation by synthesizing electrospun nanofiber pads of α-lactalbumin and polycaprolactone.[130] The results showed that the wound treated with ALA/PCL dressing showed higher collagen deposition and collagen fibres were more mature than other groups. Studies have shown that mature collagen fibres can promote extracellular matrix reconstruction and skin tissue growth.[192] Compared with the control group, myofibroblasts were significantly reduced in the ALA/PCL nanofiber mat group. In addition, on day 12 after treatment, collagen I had a higher

expression level than collagen III. All of the above results can prove that ALA/PCL nanofiber pads can significantly promote wound healing and reduce scars.

5.3.2 Ginsenoside Rg3. 20(*R*)-ginsenoside Rg3 is a tetracyclic triterpene saponin present in red ginseng and has a wide range of pharmacological activities, such as cardiovascular regulation, antioxidant and anti-cancer.[193] An experiment by Tang *et al.* showed that ginsenoside Rg3 could significantly reduce the expression of interleukin-6 (IL-6), connective tissue growth factor (CTGF), tumour necrosis factor α (α-TNF) and α-smooth muscle actin (α-SMA), and enhance the expression of anti-fibrosis genes such as transforming growth factor-β (TGF-β).[194] Thus, reducing the production of collagen and the accumulation of extracellular matrix. Guo *et al.* prepared composite nanofibers blended with polyurethane and marine polysaccharides loaded with ginsenoside Rg3 and tested their ability to inhibit scar formation.[126] The results confirmed that the nanofiber dressing loaded with ginsenoside Rg3 can effectively adjust the ratio of type I collagen and type III collagen to inhibit the formation of wound scars. The composite nanofiber dressing has great advantages in promoting burn skin healing and inhibiting scar formation.

5.4 Multifunction

5.4.1 Quercetin/rutin. Quercetin is a bioactive substance produced by the hydrolysis of rutin, and it is also the most studied flavonoid. Studies have shown that quercetin/rutin can remove oxidizing substances produced by inflammation and promote wound healing.[195,196] Zhou *et al.* reported a new nanofiber membrane composed of polycaprolactone, chitosan oligosaccharide, and quercetin/rutin.[128] The antioxidant experiment showed that quercetin/rutin had a certain oxygen-free radical scavenging ability. The antibacterial activity of nanofiber membrane was studied with *Staphylococcus aureus* and *Escherichia coli*. The results showed that the inhibitory effect of the nanofiber membrane on *Staphylococcus aureus* was better than that of *Escherichia coli*. This result may be due to the unique outer membrane structure of *E. coli* that blocks the infiltration of external drug molecules. All in all, this new type of nanofiber membrane has good antibacterial and antioxidant activity but also has a certain hydrophilic ability, so it is an ideal burn dressing.

5.4.2 Lavender essential oil. Lavender has a long history of use, and its essential oil shows excellent pharmacological properties, which has attracted special attention.[197] Lavender essential oil is considered to be one of the most commonly used over-the-counter herbs for the treatment of mental disorders, anxiety, and depression.[198] Studies have shown that lavender essential oil can enhance the activity of proteins involved in wound tissue remodelling and accelerate wound contraction.[199] Sofi *et al.* prepared polyurethane electrospun nanofibers loaded with lavender essential oil and silver nanoparticles simultaneously.[174] Lavender essential oil improves the hydrophilicity of polyurethane rice fibre, provides an environment similar to the extracellular matrix for cell proliferation, and improves the vitality of fibroblasts. The results of antibacterial activity showed that lavender essential oil and silver nanoparticles had significant synergistic antibacterial effects. All in all, lavender essential oil has potential therapeutic value for burn wound healing, and it has great potential in the preparation of wound dressings.

5.4.3 Astragaloside IV. Astragaloside IV is one of the important bioactive substances in the traditional Chinese medicine plant *Astragalus membranaceus*, which has been proven to have the properties of anti-inflammation, anti-oxidation, anti-cancer, anti-hypertension, and anti-fibrosis.[200,201] Astragaloside IV can inhibit oxidative stress and extracellular matrix deposition.[202] During the wound healing process, Astragaloside IV promotes wound healing and reduces scar formation by reducing collagen deposition and reducing the expression of inflammation. Zhang *et al.* prepared silk fibroin/gelatin electrospun nanofibers loaded with Astragaloside IV and tested their effect on wound treatment.[175] The results showed that the ratio of I/III collagen in the nanofiber dressing group loaded with Astragaloside IV was close to that of normal skin, which decreased the expression level of α-smooth muscle actin and inhibited scar formation. Silk fibroin/gelatin nanofiber dressings loaded with Astragaloside also accelerate wound healing by promoting angiogenesis, increasing the number of wound macrophages, and improving local anti-inflammation.

6 Conclusions and perspectives

Burns, as an uncontrollable accidental injury, seriously affect the physical and mental health of patients. Nanofiber dressings are often used for burn wound management. Electrospinning is widely used in the preparation of nanofibers due to its simple operation and low cost. Electrospun nanofibers show great potential in promoting wound healing due to their unique structure and physicochemical properties. First of all, this review introduces the common types of electrospun nanofibers. With the continuous improvement of electrospinning technology, there are blending electrospinning, emulsion electrospinning, coaxial electrospinning, side-by-side electrospinning, and triaxial electrospinning. Among them, the nanofibers with core–shell structures can control the rate of drug release and achieve long-term continuous drug delivery. Secondly, the polymers used for electrospinning nanofibers are reviewed, including natural polymers and synthetic polymers. Natural polymers are generally extracted from plants or animals, which have good biocompatibility and similar characteristics to natural tissue matrix, showing the potential to promote skin regeneration. However, the film-forming properties of natural polymers are poor and need to be improved by blending with other polymers. Researchers usually choose synthetic polymers with strong mechanical properties and natural polymers to improve the overall properties of electrospun nanofibers. Finally, the bioactive substances wrapped in nanofiber dressings are introduced in this paper. Nanofibers have biological activity by adding antibiotics, natural active substances, and nanoparticles, which can prevent bacterial infection and accelerate wound healing at the same time.

There are still many challenges in the application of electrospun nanofibers in burn wound dressings. Microbial infection and persistent inflammation will affect the speed of wound healing. Considering the complexity of the burn wound healing process, it is very important to choose a suitable dressing. At present, people are not only paying attention to the antibacterial activity of nanofiber dressings and their ability to accelerate wound healing but also whether the dressings can inhibit scarring. Researchers try to use a variety of materials to make nanofiber dressings have more functions, but it still requires a large number of clinical trials to prove the effectiveness and safety of nanofiber dressings. The application of nanofibers in biomedicine is expanding, and it also shows a great prospect in wound management. This review provides some reference for the application of nanofiber dressing in clinical burn treatment. In the future, it is necessary to further improve the preparation methods of nanofibers and find more bioactive substances to improve the therapeutic effect and reduce the cost. As a special applied field, wound dressing is able to always rely on the appearances of new electrospinning techniques,[202–206] and also its combinations with electrospraying and other traditional chemical and physical methods.[207–217]

Author contributions

Conceptualization, S. Z., W. Y. and D.-G. Y.; methodology, S. Z., W. Y., W. G., Y. L. and D.-G. Y.; writing—original draft preparation, S. Z. and W. Y.; writing—review and editing, D.-G. Y. and P. L.; visualization, W. G. and Y. L.; supervision, D.-G. Y. and P. L.; project administration, D.-G. Y. and P. L.; funding acquisition, P. L. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

The financial support provided by the following funds is appreciated: the Shanghai Natural Science Foundation (No. 21ZR1459500), the Shanghai Industrial Collaboration Project (HCXBCY-2023-042), the Municipal Commission of Health and Family Planning Foundation of Shanghai (No. 202140413), the Natural Science Foundation of Shandong Province (No. ZR2021MH129), and the Medical Health Science and Technology Innovation Plan of Jinan (No. 202134037).

References

1 L. F. Qi, C. L. Zhang, B. Wang, J. B. Yin and S. F. Yan, *Macromol. Biosci.*, 2022, **22**, e2100475.
2 Z. Y. Li, F. Zhou, Z. Y. Li, S. Y. Lin, L. Chen, L. X. Liu and Y. M. Chen, *ACS Appl. Mater. Interfaces*, 2018, **10**, 25194–25202.
3 A. Gholipour-Kanani, S. H. Bahrami and S. Rabbani, *IET Nanobiotechnol.*, 2016, **10**, 1–7.
4 M. M. Chen, J. Tian, Y. Liu, H. Cao, R. Li, J. H. Wang, J. L. Wu and Q. Q. Zhang, *Chem. Eng. J.*, 2019, **373**, 413–424.
5 A. Shpichka, D. Butnaru, E. A. Bezrukov, R. B. Sukhanov, A. Atala, V. Burdukovskii, Y. Y. Zhang and P. Timashev, *Stem Cell Res. Ther.*, 2019, **10**, 94.
6 B. S. Atiyeh and M. Costagliola, *Burns*, 2007, **33**, 405–413.
7 H. Luze, S. P. Nischwitz, C. Smolle, R. Zrim and L. P. Kamolz, *Medicina*, 2022, **58**, 912.
8 D. Simões, S. P. Miguel, M. P. Ribeiro, P. Coutinho, A. G. Mendonça and I. J. Correia, *Eur. J. Pharm. Biopharm.*, 2018, **127**, 130–141.
9 Y. P. Liang, J. H. He and B. L. Guo, *ACS Nano*, 2021, **15**, 12687–12722.
10 A. E. Stoica, C. Chircov and A. M. Grumezescu, *Molecules*, 2020, **25**, 2699.
11 Y. X. Yao, A. D. Zhang, C. S. Yuan, X. G. Chen and Y. Liu, *Biomater. Sci.*, 2021, **9**, 4523–4540.
12 K. Chen, Y. H. Li, Y. B. Li, Y. F. Tan, Y. S. Liu, W. S. Pan and G. X. Tan, *J. Nanobiotechnol.*, 2023, **21**, 237.
13 Y. F. Shi, H. J. Zhang, X. Zhang, Z. Chen, D. Zhao and J. Ma, *Regener. Biomater.*, 2020, **7**, 63–70.
14 P. I. Sandhya, P. Subramaniyan and V. G. Sujata, *Wounds*, 2023, **35**, 41–46.
15 E. A. Kamoun, E. S. Kenawy and X. Chen, *J. Adv. Res.*, 2017, **8**, 217–233.
16 U. N. Tak, S. Rashid, P. Kour, N. Nazir, M. I. Zargar and A. A. Dar, *Int. J. Biol. Macromol.*, 2023, **234**, 123718.
17 Z. Hadisi, J. Nourmohammadi and S. M. Nassiri, *Int. J. Biol. Macromol.*, 2018, **107**, 2008–2019.
18 X. X. Chen, R. Zhao, X. Wang, X. Li, F. Peng, Z. G. Jin, X. Gao, J. A. Yu and C. Wang, *J. Biomater. Sci., Polym. Ed.*, 2017, **28**, 162–176.
19 D. G. Yu and C. Huang, *Biomolecules*, 2023, **13**, 1152.
20 D. Jao and V. Z. Beachley, *ACS Macro Lett.*, 2019, **8**, 588–595.
21 K. C. K. Cheng, M. A. Bedolla-Pantoja, Y. K. Kim, J. V. Gregory, F. Xie, A. de France, C. Hussal, K. Sun, N. L. Abbott and J. Lahann, *Science*, 2018, **362**, 804–808.
22 S. G. Zhang, *Adv. Cancer Res.*, 2008, **99**, 335–362.
23 S. H. Ji and J. S. Yun, *Nanomaterials*, 2022, **12**, 404.
24 I. Kohsari, Z. Shariatinia and S. M. Pourmortazavi, *Carbohydr. Polym.*, 2016, **140**, 287–298.
25 A. Z. Bazmandeh, E. Mirzaei, M. Fadaie, S. Shirian and Y. Ghasemi, *Int. J. Biol. Macromol.*, 2020, **162**, 359–373.
26 E. Mele, *Biotechnol. Bioeng.*, 2023, **120**, 1229–1240.
27 H. B. Wang, Y. Y. Lu, H. S. Yang, D.-G. Yu and X. H. Lu, *Front. Mol. Biosci.*, 2023, **10**, 4676.
28 D. G. Yu and L. Xu, *Curr. Drug Delivery*, 2023, **21**, 360–367.
29 A. Sadeghi, M. Zandi, M. P. Modaress and S. Rajabi, *Int. J. Biol. Macromol.*, 2019, **132**, 63–75.
30 E.-R. Kenawy, M. S. A. El-Moaty, M. Ghoneum, H. M. A. Soliman, A. A. El-Shanshory and S. Shendy, *RSC Adv.*, 2024, **14**, 4930–4945.
31 D. J. Patty, A. D. Nugraheni, I. D. Ana, Y. W. Sari and Y. Yusuf, *RSC Adv.*, 2023, **13**, 34427–34438.
32 Q. l. Zheng, Y. W. Xi and Y. X. Weng, *RSC Adv.*, 2024, **14**, 3359–3378.

33 X. Q. Wang and C. L. Feng, *WIREs Nanomed. Nanobi.*, 2023, **15**, e1847.
34 A. Schneider, X. Y. Wang, D. L. Kaplan, J. A. Garlick and C. Egles, *Acta Biomater.*, 2009, **5**, 2570–2578.
35 Y. Q. Liu, T. Y. Li, Y. F. Han, F. J. Li and Y. Liu, *Curr. Opin. Biomed. Eng.*, 2021, **17**, 100247.
36 H. Duan, H. N. Chen, C. R. Qi, F. M. Lv, J. Wang, Y. C. Liu, Z. P. Liu and Y. Liu, *Int. J. Pharm.*, 2024, **650**, 123660.
37 B. F. Finina and A. K. Mersha, *RSC Adv.*, 2024, **14**, 5290–5308.
38 J. F. Zhou, L. Z. Wang, W. J. Gong, B. Wang, D. G. Yu and Y. J. Zhu, *Biomedicines*, 2023, **11**, 2146.
39 Y. Wang, D. G. Yu, Y. Liu and Y. N. Liu, *J. Funct. Biomater.*, 2022, **13**, 289.
40 S. Tabakoglu, D. Kołbuk and P. Sajkiewicz, *Biomater. Sci.*, 2023, **11**, 37–61.
41 M. G. Jeschke, M. E. van Baar, M. A. Choudhry, K. K. Chung, N. S. Gibran and S. Logsetty, *Nat. Rev. Dis. Primers*, 2020, **6**, 11.
42 M. Burgess, F. Valdera, D. Varon, E. Kankuri and K. Nuutila, *Cells*, 2022, **11**, 3073.
43 C. Johnson, *Surgery*, 2018, **36**, 435–440.
44 R. M. Johnson and R. Richard, *Adv. Skin Wound Care*, 2003, **16**, 178–187.
45 A. Markiewicz-Gospodarek, M. Kozioł, M. Tobiasz, J. Baj, E. Radzikowska-Büchner and A. Przekora, *Int. J. Environ. Res. Public Health*, 2022, **19**, 3073.
46 S. Tejiram and J. W. Shupp, *Surgery*, 2024, **175**, 1259–1261.
47 D. G. Greenhalgh, *N. Engl. J. Med.*, 2019, **380**, 2349–2359.
48 P. E. Wischmeyer, *Nutr. Clin. Pract.*, 2019, **34**, 681–687.
49 L. H. Evers, D. Bhavsar and P. Mailänder, *Exp. Dermatol.*, 2010, **19**, 777–783.
50 B. K. Sun, Z. Siprashvili and P. A. Khavari, *Science*, 2014, **346**, 941–945.
51 A. N. Dehkordi, F. M. Babaheydari, M. Chehelgerdi and S. R. Dehkordi, *Stem Cell Res. Ther.*, 2019, **10**, 111.
52 P. Rousselle, M. Montmasson and C. Garnier, *Matrix Biol.*, 2019, **75**, 12–26.
53 H. J. Park, Y. L. Zhang, S. P. Georgescu, K. L. Johnson, D. Kong and J. B. Galper, *Stem Cell Rev.*, 2006, **2**, 93–102.
54 A. E. Ayadi, J. W. Jay and A. Prasai, *Int. J. Mol. Sci.*, 2020, **21**, 1105.
55 N. Akombaetwa, A. Bwanga, P. A. Makoni and B. A. Witika, *Polymers*, 2022, **14**, 2931.
56 Y. Liang, Y. Liang, H. Zhang and B. Guo, *Asian J. Pharm. Sci.*, 2022, **17**, 353–384.
57 K. Vig, A. Chaudhari, S. Tripathi, S. Dixit, R. Sahu, S. Pillai, V. A. Dennis and S. R. Singh, *Int. J. Mol. Sci.*, 2017, **18**, 789.
58 M. Roopesh, D. Davis, M. S. Jyothi, M. Vandana, B. S. Thippeswamy, G. Hegde, T. P. Vinod and R. S. Keri, *RSC Adv.*, 2023, **13**, 24320–24330.
59 D.-G. Yu and J. F. Zhou, *J. Pharm. Sci.*, 2023, **112**, 2719–2723.
60 E. B. Abdelazim, T. Abed, S. S. Goher, S. H. Alya, H. A. S. El-Nashar, S. H. El-Moslamy, E. M. El-Fakharany, E. A. Abdul-Baki, M. M. Shakweer, N. G. Eissa, M. Elsabahy and E. A. Kamoun, *RSC Adv.*, 2024, **14**, 101–117.
61 D.-G. Yu and J. F. Zhou, *Next Mater.*, 2024, **2**, 100119.
62 L. T. Yao, C. P. Sun, H. Lin, G. S. Li, Z. C. Lian, R. X. Song, S. L. Zhuang and D. W. Zhang, *J. Mater. Sci. Technol.*, 2023, **150**, 114–123.
63 A. Kim, J. K. Dash and R. Patel, *Membranes*, 2023, **13**, 183.
64 X. Y. Cao, W. Chen, P. Zhao, Y. Y. Yang and D. G. Yu, *Polymers*, 2022, **14**, 3990.
65 M. Rahmati, D. K. Mills, A. M. Urbanska, M. R. Saeb, J. R. Venugopal, S. Ramakrishna and M. Mozafari, *Prog. Mater. Sci.*, 2021, **117**, 100721.
66 E. Ahmed, B. S. Lalia and R. Hashaikeh, *Desalination*, 2015, **356**, 15–30.
67 R. Augustine, S. R. U. Rehman, R. Ahmed, A. A. Zahid, M. Sharifi, M. Falahati and A. Hasan, *Int. J. Biol. Macromol.*, 2020, **156**, 153–170.
68 M. G. Lin, J. L. Shen, B. B. Wang, Y. G. Chen, C. Y. Zhang and H. Qi, *RSC Adv.*, 2023, **13**, 30680–30689.
69 M. Sivan, D. Madheswaran, J. Valtera, E. K. Kostakova and D. Lukas, *Mater. Des.*, 2022, **213**, 110308.
70 M. Sivan, D. Madheswaran, S. Hauzerova, V. Novotny, V. Hedvicakova, V. Jencova, E. K. Kostakova, M. Schindler and D. Lukas, *Mater. Today Chem.*, 2022, **26**, 101025.
71 J. K. Patra, G. Das, L. F. Fraceto, E. V. R. Campos, M. D. P. Rodriguez-Torres, L. S. Acosta-Torres, L. A. Diaz-Torres, R. Grillo, M. K. Swamy, S. Sharma, S. Habtemariam and H. S. Shin, *J. Nanobiotechnol.*, 2018, **16**, 71.
72 Y. Z. Wang, H. Kang, J. Hu, H. M. Chen, H. M. Zhou, Y. Wang and H. Z. Ke, *RSC Adv.*, 2023, **13**, 21633–21642.
73 M. L. Wang, X. W. Huang, H. X. Zheng, Y. M. Tang, K. Zeng, L. Q. Shao and L. Li, *J. Controlled Release*, 2021, **337**, 236–247.
74 C. G. Qian, Y. B. Liu, S. Chen, C. Y. Zhang, X. H. Chen, Y. H. Liu and P. Liu, *Front. Bioeng. Biotechnol.*, 2023, **11**, 5252.
75 S. Nagam Hanumantharao and S. Rao, *Fibers*, 2019, **7**, 66.
76 X. J. Chen, S. Yan, S. S. Wen, J. J. Chen, J. Q. Xu, C. Wang and X. F. Lu, *J. Colloid Interface Sci.*, 2023, **641**, 782–790.
77 W. Gao, L. Sun, X. Fu, Z. Lin, W. Xie, W. Zhang, F. Zhao and X. Chen, *J. Mater. Chem. B*, 2018, **6**, 277–288.
78 L. J. del Valle, L. Franco, R. Katsarava and J. Puiggalí, *AIMS Mol. Sci.*, 2016, **3**, 52–87.
79 J. Hu, H.-Y. Li, G. R. Williams, H.-H. Yang, L. Tao and L.-M. Zhu, *J. Pharm. Sci.*, 2016, **105**, 1104–1112.
80 A. Bhattacharjee, K. Kumar, A. Arora and D. S. Katti, *Mater. Sci. Eng. C*, 2016, **63**, 266–273.
81 J. Jalvandi, M. White, Y. Gao, Y. B. Truong, R. Padhye and I. L. Kyratzis, *Mater. Sci. Eng.*, 2017, **73**, 440–446.
82 L. Bardoňová, A. Kotzianová, K. Skuhrovcová, O. Židek, H. Vágnerová, J. Kulhánek, T. Hanová, M. Knor, J. Starigazdová, K. Mamulová Kutláková and V. Velebný, *Int. J. Biol. Macromol.*, 2022, **194**, 726–735.
83 S. X. Kang, S. C. Hou, X. W. Chen, D. G. Yu, L. Wang, X. Y. Li and G. R. Williams, *Polymers*, 2020, **12**, 2421.
84 M. M. Abdul Hameed, S. A. P. Mohamed Khan, B. M. Thamer, A. M. Al-Enizi, A. Aldalbahi, H. El-Hamshary and M. H. El-Newehy, *J. Macromol. Sci. A*, 2020, **58**, 130–144.

85 M. Buzgo, A. Mickova, M. Rampichova and M. Doupnik, in *Core–Shell Nanostructures for Drug Delivery and Theranostics*, ed. M. L. Focarete and A. Tampieri, Woodhead Publishing, 2018, pp. 325–347, DOI: 10.1016/B978-0-08-102198-9.00011-9.

86 X. Q. Li, Y. Su, S. P. Liu, L. J. Tan, X. M. Mo and S. Ramakrishna, *Colloids Surf., B*, 2010, **75**, 418–424.

87 S. Agarwal and A. Greiner, *Polym. Adv. Technol.*, 2011, **22**, 372–378.

88 T. Jiang, D. Wang, X. Zhang, Q. Yang, Q. Huang, X. Ju, L. Li, X. Kang and C. Li, *Mater. Chem. Phys.*, 2024, **311**, 128561.

89 Y. R. Lv, Y. F. Han, Z. G. Yu, J. Chen, C. X. Li, C. Wang, P. Hu and Y. Liu, *Prog. Biomater.*, 2022, **11**, 253–261.

90 D. Han and A. J. Steckl, *Chempluschem*, 2019, **84**, 1453–1497.

91 L. Xu, H. He, Y. T. Du, S. W. Zhang, D.-G. Yu and P. Liu, *Pharmaceutics*, 2023, **15**, 2314.

92 A. K. Moghe and B. S. Gupta, *Polym. Rev. (Philadelphia, PA, U. S.)*, 2008, **48**, 353–377.

93 X. Y. Huang, W. L. Jiang, J. F. Zhou, D. G. Yu and H. Liu, *Polymers*, 2022, **14**, 4947.

94 Y. T. Du, Z. L. Yang, S. X. Kang, D. G. Yu, X. R. Chen and J. Shao, *Sensors*, 2023, **23**, 3685.

95 J. Guo, T. Wang, Z. Yan, D. Ji, J. Li and H. Pan, *Int. J. Pharm.*, 2022, **629**, 122410.

96 R. Ramalingam, C. Dhand, V. Mayandi, C. M. Leung, H. Ezhilarasu, S. K. Karuppannan, P. Prasannan, S. T. Ong, N. Sunderasan, I. Kaliappan, M. Kamruddin, V. A. Barathi, N. K. Verma, S. Ramakrishna, R. Lakshminarayanan and K. D. Arunachalam, *ACS Appl. Mater. Interfaces*, 2021, **13**, 24356–24369.

97 H. Li, C. G. Zhao, Z. X. Wang, H. Zhang, X. Y. Yuan and D. Kong, *J. Biomater. Sci., Polym. Ed.*, 2010, **21**, 803–819.

98 Y. X. Ji, H. Zhao, H. Liu, P. Zhao and D.-G. Yu, *Gels*, 2023, **9**, 700.

99 W. B. Chen, Z. J. Ma, X. Z. Pan, Z. L. Hu, G. P. Dong, S. F. Zhou, M. Y. Peng, J. R. Qiu and P. Gouma, *J. Am. Ceram. Soc.*, 2014, **97**, 1944–1951.

100 J. J. Li, Q. Du, J. G. Wan, D.-G. Yu, F. Tan and X. L. Yang, *Mater. Des.*, 2024, **238**, 112657.

101 J. Yang, K. Wang, D.-G. Yu, Y. Yang, S. W. A. Bligh and G. R. Williams, *Mater. Sci. Eng., C*, 2020, **111**, 110805.

102 Y. Shi, M. Zhou, S. Zhao, H. Li, W. Wang, J. Cheng, L. Jin and Y. Wang, *Mater. Des.*, 2023, **227**, 111778.

103 Z. B. Feng, Z. Q. Zhao, Y. A. Liu, Y. K. Liu, X. Y. Cao, D.-G. Yu and K. Wang, *Adv. Mater. Technol.*, 2023, **8**, 2300021.

104 Y. Y. Yang, W. Chen, M. L. Wang, J. C. Shen, Z. Tang, Y. M. Qin and D. G. Yu, *Polymers*, 2023, **15**, 2237.

105 H. Lv, Y. Y. Liu, P. Zhao, Y. B. Bai, W. X. Cui, S. L. Shen, Y. Liu, Z. Wang and D.-G. Yu, *Appl. Catal., B*, 2023, **330**, 122623.

106 W. L. Song, Y. X. Tang, C. Qian, B. J. Kim, Y. Z. Liao and D.-G. Yu, *Innovation*, 2023, **4**, 100381.

107 Y. B. Bai, Y. A. Liu, H. Lv, H. P. Shi, W. Zhou, Y. Liu and D.-G. Yu, *Polymers*, 2022, **14**, 4311.

108 E. J. Torres-Martinez, J. M. Cornejo Bravo, A. Serrano Medina, G. L. Pérez González and L. J. Villarreal Gómez, *Curr. Drug Delivery*, 2018, **15**, 1360–1374.

109 M. L. Wang, J. S. Hou, D.-G. Yu, S. Y. Li, J. W. Zhu and Z. Z. Chen, *J. Alloys Compd.*, 2020, **846**, 156471.

110 Y. Liu, X. Chen, Y. Gao, Y. Liu, D. G. Yu and P. Liu, *Biomolecules*, 2022, **12**, 1057.

111 K. Ghosal, R. Augustine, A. Zaszczynska, M. Barman, A. Jain, A. Hasan, N. Kalarikkal, P. Sajkiewicz and S. Thomas, *React. Funct. Polym.*, 2021, **163**, 104895.

112 A. T. Prabhu, V. Baliga, S. Bhat, S. T. Thenkondar, Y. Nayak and U. Y. Nayak, *Pharmaceutics*, 2023, **15**, 1560.

113 Y. Liu, S. Y. Zhou, Y. L. Gao and Y. L. Zhai, *Asian J. Pharm. Sci.*, 2019, **14**, 130–143.

114 S. Homaeigohar and A. R. Boccaccini, *Acta Biomater.*, 2020, **107**, 25–49.

115 A. S. Shabunin, V. E. Yudin, I. P. Dobrovolskaya, E. V. Zinovyev, V. Zubov, E. M. Ivan'kova and P. Morganti, *Cosmetics*, 2019, **6**, 16.

116 Q. Liu, L. P. Yang and Q. R. Peng, *Mater. Express*, 2021, **11**, 1420–1437.

117 M. Mirhaj, M. Tavakoli, J. Varshosaz, S. Labbaf, S. Salehi, A. Talebi, N. Kazemi, V. Haghighi and M. Alizadeh, *Carbohydr. Polym.*, 2022, **292**, 119648.

118 S. Khosravimelal, M. Chizari, B. Farhadihosseinabadi, M. Moosazadeh Moghaddam and M. Gholipourmalekabadi, *J. Mater. Sci.: Mater. Med.*, 2021, **32**, 114.

119 M. S. Morais, D. P. F. Bonfim, M. L. Aguiar and W. P. Oliveira, *J. Pharm. Innovation*, 2022, 1–15, DOI: 10.1007/s12247-022-09681-7.

120 S. Abid, T. Hussain, A. Nazir, A. Zahir, S. Ramakrishna, M. Hameed and N. Khenoussi, *Int. J. Biol. Macromol.*, 2019, **135**, 1222–1236.

121 A. Li, L. Li, B. a. Zhao, X. Li, W. Liang, M. Lang, B. Cheng and J. Li, *Int. J. Biol. Macromol.*, 2022, **194**, 914–923.

122 C. M. Leung, C. Dhand, V. Mayandi, R. Ramalingam, F. P. Lim, V. A. Barathi, N. Dwivedi, G. Orive, R. W. Beuerman, S. Ramakrishna, Y. C. Toh, X. J. Loh, N. K. Verma, A. W. C. Chua and R. Lakshminarayanan, *Biomater. Sci.*, 2020, **8**, 3454–3471.

123 L. M. Zhou, N. N. Liu, L. B. Feng, M. Y. Zhao, P. Wu, Y. F. Chai, J. Liu, P. Zhu and R. Guo, *Bioeng. Transl. Med.*, 2022, **7**, e10274.

124 B. Mollaghadimi, *IET Nanobiotechnol.*, 2022, **16**, 239–249.

125 A. Yerra and M. M. Dadala, *J. Appl. Polym. Sci.*, 2021, **139**, 51930.

126 X. Guo, F. F. Xiu, H. Bera, Y. F. Abbasi, Y. Chen, L. W. Si, P. X. Liu, C. W. Zhao, X. Tang, Y. Feng, D. M. Cun, X. Zhao and M. S. Yang, *Carbohydr. Polym.*, 2023, **317**, 121085.

127 Y. F. Huang, L. Wang, L. Yi, B. J. Xin and T. X. Li, *J. Text. Inst.*, 2024, **115**, 208–217.

128 L. Z. Zhou, L. Cai, H. J. Ruan, L. Zhang, J. Wang, H. J. Jiang, Y. Wu, S. W. Feng and J. Chen, *Int. J. Biol. Macromol.*, 2021, **183**, 1145–1154.

129 G. Bayat, M. Fallah-Darrehchi, P. Zahedi, A. B. Moghaddam, P. Ghaffari-Bohlouli and H. Jafari, *J. Biomater. Sci., Polym. Ed.*, 2023, **34**, 72–88.

130 X. Guo, Y. N. Liu, H. Bera, H. T. Zhang, Y. Chen, D. M. Cun, V. Fodera and M. S. Yang, *ACS Appl. Mater. Interfaces*, 2020, **12**, 45702–45713.

131 R. Singh, P. Roopmani, M. Chauhan, S. M. Basu, W. Deeksha, M. D. Kazem, S. Hazra, E. Rajakumara and J. Giri, *Int. J. Pharm.*, 2022, **613**, 121358.

132 S. Khataei, M. H. Al-Musawi, K. Asadi, S. Ramezani, M. Abbasian and M. Ghorbani, *J. Drug Delivery Sci. Technol.*, 2023, **82**, 104310.

133 S. Ramkumar, A. S. Nivetha, S. Saravanan, R. Harchana, B. Sathyasri and N. Sammeta, *J. Mater. Res.*, 2022, **37**, 4360–4367.

134 Z. Liu, Y. Lv, G. Zheng, W. Wu and X. Che, *AAPS PharmSciTech*, 2023, **24**, 202.

135 J. Venkatesan and S.-K. Kim, *Mar. Drugs*, 2010, **8**, 2252–2266.

136 P. S. Bakshi, D. Selvakumar, K. Kadirvelu and N. S. Kumar, *Int. J. Biol. Macromol.*, 2020, **150**, 1072–1083.

137 S. Peers, A. Montembault and C. Ladavière, *J. Controlled Release*, 2020, **326**, 150–163.

138 W. M. Kedir, G. F. Abdi, M. M. Goro and L. D. Tolesa, *Heliyon*, 2022, **8**, e10196.

139 M. E. Abd El-Hack, M. T. El-Saadony, M. E. Shafi, N. M. Zabermawi, M. Arif, G. E. Batiha, A. F. Khafaga, Y. M. Abd El-Hakim and A. A. Al-Sagheer, *Int. J. Biol. Macromol.*, 2020, **164**, 2726–2744.

140 M. Kong, X. G. Chen, K. Xing and H. J. Park, *Int. J. Food Microbiol.*, 2010, **144**, 51–63.

141 H. P. Shi, S. M. Wang, G. X. Zhang, Y. J. Zhang and A. Barbul, *Wound Repair Regen.*, 2007, **15**, 66–70.

142 H. R. El-Seedi, N. S. Said, N. Yosri, H. B. Hawash, D. M. El-Sherif, M. Abouzid, M. M. Abdel-Daim, M. Yaseen, H. Omar, Q. Shou, N. F. Attia, X. Zou, Z. Guo and S. A. M. Khalifa, *Heliyon*, 2023, **9**, e16228.

143 M. C. Gómez-Guillén, B. Giménez, M. E. López-Caballero and M. P. Montero, *Food Hydrocolloids*, 2011, **25**, 1813–1827.

144 A. I. Cernencu, G. M. Vlasceanu, A. Serafim, G. Pircalabioru and M. Ionita, *RSC Adv.*, 2023, **13**, 24053–24063.

145 B. Salahuddin, S. Wang, D. Sangian, S. Aziz and Q. Gu, *ACS Appl. Bio Mater.*, 2021, **4**, 2886–2906.

146 N. Sahoo, R. K. Sahoo, N. Biswas, A. Guha and K. Kuotsu, *Int. J. Biol. Macromol.*, 2015, **81**, 317–331.

147 Ł. Mazurek, M. Szudzik, M. Rybka and M. Konop, *Biomolecules*, 2022, **12**, 1852.

148 Z. Y. Zhou, J. Cui, S. L. Wu, Z. Geng and J. C. Su, *Theranostics*, 2022, **12**, 5103–5124.

149 P. Du, X. Chen, Y. Chen, J. Li, Y. C. Lu, X. X. Li, K. Hu, J. F. Chen and G. Z. Lv, *Heliyon*, 2023, **9**, e13506.

150 E. Manaila, G. Craciun and I. C. Calina, *Int. J. Mol. Sci.*, 2022, **24**, 104.

151 M. U. A. Khan, S. I. A. Razak, S. Haider, H. A. Mannan, J. Hussain and A. Hasan, *Int. J. Biol. Macromol.*, 2022, **208**, 475–485.

152 A. A. Shitole, P. Raut, P. Giram, P. Rade, A. Khandwekar, B. Garnaik and N. Sharma, *Mater. Sci. Eng., C*, 2020, **110**, 110731.

153 J. Wang, V. Planz, B. Vukosavljevic and M. Windbergs, *Eur. J. Pharm. Biopharm.*, 2018, **129**, 175–183.

154 M. Aslam, M. A. Kalyar and Z. A. Raza, *Polym. Eng. Sci.*, 2018, **58**, 2119–2132.

155 M. A. Najim, B. I. Khalil and A. A. Hameed, *Heliyon*, 2022, **8**, e11423.

156 Y. H. Shen, X. Yu, J. Cui, F. Yu, M. Y. Liu, Y. J. Chen, J. L. Wu, B. B. Sun and X. M. Mo, *Biomolecules*, 2022, **12**, 1245.

157 C. Gaidău, M. Râpă, L. M. Stefan, E. Matei, A. C. Berbecaru, C. Predescu and L. Mititelu-Tartau, *Fibers*, 2023, **11**, 87.

158 F. H. Alshammari, *Radiat. Phys. Chem.*, 2023, **209**, 110989.

159 J. F. Zhou, Y. L. Dai, J. H. Fu, C. Yan, D. G. Yu and T. Yi, *Biomolecules*, 2023, **13**, 1011.

160 H. Wang, J. X. Zhang, H. Liu, Z. G. Wang, G. W. Li, Q. P. Liu and C. Y. Wang, *Int. J. Biol. Macromol.*, 2023, **253**, 126294.

161 B. Mutlu, F. Çiftçi, C. B. Üstündağ and R. Çakır-Koç, *Int. J. Biol. Macromol.*, 2023, **253**, 126932.

162 N. Ajalli, M. Pourmadadi, F. Yazdian, M. Abdouss, H. Rashedi and A. Rahdar, *Curr. Drug Delivery*, 2023, **20**, 1569–1583.

163 T. R. Zhang, L. Li, S. Chunta, W. Wu, Z. J. Chen and Y. Lu, *J. Controlled Release*, 2023, **354**, 146–154.

164 F. L. Man, Y. Q. Yang, H. S. He, J. P. Qi, W. Wu and Y. Lu, *Mol. Pharm.*, 2023, **20**, 2579–2588.

165 M. D. Köse, N. Ungun and O. Bayraktar, *Curr. Drug Delivery*, 2022, **19**, 547–559.

166 D.-G. Yu and P. Zhao, *Biomolecules*, 2022, **12**, 1234.

167 W. L. Song, Y. Zhang, C. H. Tran, H. K. Choi, D.-G. Yu and I. Kim, *Prog. Polym. Sci.*, 2023, **142**, 101691.

168 Q. Liao, E. J. Kim, Y. X. Tang, H. L. Xu, D. G. Yu, W. L. Song and B. J. Kim, *J. Polym. Sci.*, 2023, **62**, 1517–1535.

169 M. L. Wang, R.-L. Ge, F. Y. Zhang, D.-G. Yu, Z.-P. Liu, X. Y. Li, H. Shen and G. R. Williams, *Biomater. Adv.*, 2023, **150**, 213404.

170 N. Song, S. Y. Ren, Y. Zhang, C. Wang and X. L. Lu, *Adv. Funct. Mater.*, 2022, **32**, 2204751.

171 M. Hasannasab, J. Nourmohammadi, M. M. Dehghan and A. Ghaee, *Int. J. Pharm.*, 2021, **610**, 121227.

172 A. K. Khan, S. Kaleem, F. Pervaiz, T. A. Sherazi, S. A. Khan, F. A. Khan, T. Jamshaid, M. I. Umar, W. Hassan, M. Ijaz and G. Murtaza, *J. Drug Delivery Sci. Technol.*, 2023, **79**, 3987.

173 Z. Hadisi, M. Farokhi, H. R. Bakhsheshi-Rad, M. Jahanshahi, S. Hasanpour, E. Pagan, A. Dolatshahi-Pirouz, Y. S. Zhang, S. C. Kundu and M. Akbari, *Macromol. Biosci.*, 2020, **20**, 1900328.

174 H. S. Sofi, T. Akram, A. H. Tamboli, A. Majeed, N. Shabir and F. A. Sheikh, *Int. J. Pharm.*, 2019, **569**, 118590.

175 D. P. Zhang, L. J. Li, Y. H. Shan, J. Xiong, Z. J. Hu, Y. Zhang and J. Q. Gao, *J. Drug Delivery Sci. Technol.*, 2019, **52**, 272–281.

176 M. Prasathkumar and S. Sadhasivam, *Int. J. Biol. Macromol.*, 2021, **186**, 656–685.

177 K. Huang, W. B. Liu, W. Y. Wei, Y. A. Zhao, P. Z. Zhuang, X. X. Wang, Y. F. Wang, Y. Hu and H. L. Dai, *ACS Nano*, 2022, **16**, 19491–19508.

178 Y. Gao, J. T. Li, S. F. Chu, Z. Zhang, N. H. Chen, L. Li and L. Zhang, *Eur. J. Pharmacol.*, 2020, **866**, 172801.
179 J. Gao, P. Bai, Y. Y. Li, J. Z. Li, C. X. Jia, T. S. Wang, H. B. Zhao, Y. C. Si and J. X. Chen, *J. Proteome Res.*, 2020, **19**, 2676–2688.
180 A. Aires and R. Carvalho, *J. Food Sci. Technol.*, 2020, **57**, 4265–4276.
181 P. Hikisz and J. B-Slomczewska, *Nutrients*, 2021, **13**, 4313.
182 C. Varilla, M. Marcone, L. Paiva and J. Baptista, *Foods*, 2021, **10**, 2249.
183 J. Borlinghaus, F. Albrecht, M. C. Gruhlke, I. D. Nwachukwu and A. J. Slusarenko, *Molecules*, 2014, **19**, 12591–12618.
184 E. Catanzaro, D. Canistro, V. Pellicioni, F. Vivarelli and C. Fimognari, *Pharmacol. Res.*, 2022, **177**, 106118.
185 A. Sharma, N. V. Tirpude, N. Bhardwaj, D. Kumar and Y. Padwad, *Inflammopharmacology*, 2022, **30**, 655–666.
186 R. Pothuraju, R. K. Sharma, J. Chagalamarri, S. Jangra and P. Kumar Kavadi, *J. Sci. Food Agric.*, 2014, **94**, 834–840.
187 Z. Aziz and B. Abdul Rasool Hassan, *Burns*, 2017, **43**, 50–57.
188 B. Sadanandan, P. Murali Krishna, M. Kumari, V. Vijayalakshmi, B. M. Nagabhushana, S. Vangala, H. K. Singh, B. R. Divya Swaroopa and V. Megala, *J. Mol. Struct.*, 2024, **1305**, 137723.
189 M. Y. Al-darwesh, S. S. Ibrahim and M. A. Mohammed, *Results Chem.*, 2024, **7**, 101368.
190 E. A. Permyakov, *Biomolecules*, 2020, **10**, 1210.
191 A. Sadiq, A. Shah, M. G. Jeschke, C. Belo, M. Qasim Hayat, S. Murad and S. Amini-Nik, *Int. J. Mol. Sci.*, 2018, **19**, 1034.
192 S. Q. Yan, Q. Zhang, J. N. Wang, Y. Liu, S. Z. Lu, M. Z. Li and D. L. Kaplan, *Acta Biomater.*, 2013, **9**, 6771–6782.
193 M. Y. Sun, Y. Ye, L. Xiao, X. Y. Duan, Y. M. Zhang and H. Zhang, *Int. J. Mol. Med.*, 2017, **39**, 507–518.
194 M. Y. Tang, W. B. Wang, L. Y. Cheng, R. Jin, L. Zhang, W. W. Bian and Y. G. Zhang, *Iran. J. Basic Med. Sci.*, 2018, **21**, 309–317.
195 E. Başaran, A. A. Öztürk, B. Şenel, M. Demirel and Ş. Sarica, *Eur. J. Pharm. Sci.*, 2022, **172**, 106153.
196 S. Faraji, N. Nowroozi, A. Nouralishahi and J. Shabani Shayeh, *Life Sci.*, 2020, **257**, 118062.
197 W. S. Yap, A. V. Dolzhenko, Z. Jalal, M. A. Hadi and T. M. Khan, *Sci. Rep.*, 2019, **9**, 18042.
198 V. López, B. Nielsen, M. Solas, M. J. Ramírez and A. K. Jäger, *Front. Pharmacol*, 2017, **8**, 280.
199 R. Samuelson, M. Lobl, S. Higgins, D. Clarey and A. Wysong, *J. Altern. Complementary Med.*, 2020, **26**, 680–690.
200 T. Q. Chen, P. Y. Yang and Y. J. Jia, *Int. J. Mol. Med.*, 2021, **47**, 4846.
201 L. Li, X. J. Hou, R. F. Xu, C. Liu and M. Tu, *Fundam. Clin. Pharmacol.*, 2017, **31**, 17–36.
202 W. B. Qian, X. R. Cai, Q. H. Qian, W. Zhang and D. L. Wang, *J. Cell. Mol. Med.*, 2018, **22**, 4354–4365.
203 H. P. Shi, Y. N. Liu, Y. B. Bai, H. Lv, W. Zhou, Y. Liu and D.-G. Yu, *Sep. Purif. Technol.*, 2024, **330**, 125247.
204 J. F. Zhou, T. Yi, Z. Y. Zhang, D.-G. Yu, P. Liu, L. Z. Wang and Y. J. Zhu, *Adv. Compos. Hybrid Mater.*, 2023, **6**, 189.
205 P. Zhao, K. Zhou, Y. Xia, C. Qain, D. G. Yu, Y. Xie and Y. Liao, *Adv. Fiber Mater.*, 2024, **5**, DOI: **10.1007/s42765-024-00397-6**.
206 D.-G. Yu, W. Gong, J. Zhou, Y. Liu, Y. Zhu and X. Lu, *WIREs Nanomed. Nanobiotechnol.*, 2024, **16**, 1964.
207 Z.-C. Yao, C. C. Zhang, Z. Xing, Z. Ahmad, Q. P. Ding and M.-W. Chang, *Chem. Eng. J.*, 2022, **429**, 132221.
208 Y. N. Lang, B. L. Wang, M.-W. Chang, R. Y. Sun and L. F. Zhang, *Colloids Surf., A*, 2023, **668**, 131399.
209 X. Jiang, Y. E. Zeng, C. Li, K. Wang and D. G. Yu, *Front. Bioeng. Biotechnol.*, 2024, **12**, 1354286.
210 Y. Wang, L. Liu, Y. J. Zhu, L. Z. Wang, D.-G. Yu and L.-Y. Liu, *Pharmaceutics*, 2023, **15**, 2561.
211 C. Huang, M. Wang, S. Yu, D. G. Yu and S. W. A. Bligh, *Nanomaterials*, 2024, **14**, 646.
212 S. Chen, J. F. Zhou, B. Y. Fang, Y. Ying, D.-G. Yu and H. He, *Macromol. Mater. Eng.*, 2023, **309**, 2300361.
213 L. Sun, J. F. Zhou, Y. M. Chen, D.-G. Yu and P. Liu, *Front. Bioeng. Biotechnol.*, 2023, **11**, 4.
214 X. H. Chen, Y. B. Liu and P. Liu, *Mol. Pharm.*, 2024, **21**, 173–182.
215 Q. Q. Lv, X. F. Ma, C. M. Zhang, J. Q. Han, S. J. He, K. M. Liu and S. H. Jiang, *Int. J. Biol. Macromol.*, 2024, **259**, 129268.
216 Y. Zhu, C. Zhang, Y. Liang, J. Shi, Q. Yu, S. Liu, D. G. Yu and H. Liu, *Biomater. Sci.*, 2024, **17**, 1643–1661.
217 J. Zhou, H. Pan, W. Gong, D. G. Yu and Y. Sun, *Nanoscale*, 2024, DOI: **10.1039/D4NR00893F**.