Antibacterial properties and drug release study of cellulose acetate nanofibers containing ear-like Ag-NPs and Dimethyloxallyl Glycine/beta-cyclodextrin

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Abstract

In this paper, a multifunctional wound dressing with sustained-release and antibacterial properties was prepared using cellulose acetate (CA) as the matrix and Dimethyloxallyl Glycine (DMOG) and silver nanoparticles (Ag-NPs) as the drug loading component. The scanning electron microscopy shows that the microstructure of the nanofibers is uniform and droplet free, and the diameters of CA and CA/β-CD/DMOG nanofibers are mainly concentrated in the range of 40-120 nm, and the diameters of CA/DMOG/Ag-NPs nanofibers are mainly concentrated in the range of 120-200 nm. In vitro release test confirms that the CA/DMOG/Ag-NPs nanofiber can slowly release DMOG within about 84 hours, which abides by a typical diffusion, and the main driving force is the concentration gradient between the drug-carrying nanofibers and the releasing medium. The antibacterial performance test demonstrates that the material exhibits obvious antibacterial performance against both E. coli and B.subtilis bacteria with little adverse effects on cell viability proved by cell compatibility test. Taken together, CA/DMOG/Ag-NPs can be a wound dressing material with good application prospects to promote the healing of diabetic wounds.

Keywords:

Nanofiber, drug release, silver nanoparticles, antibacterial, wound dressing.

1. Introduction

As the body's largest organ in area, skin tissue is extremely important to the body[1]. It has the function of protecting and defending against the invasion of the outside world. When skin breaks, it usually heals itself[2]. However, some external factors, such as lower limb vascular disease, skin microvascular disease, and bacterial infection and other factors[3], can hinder the wound to heal normally, which can prevent normal wound healing, affect the quality of health, increase medical costs, and even lead to death[4]. Wound dressing is usually used to treat skin damage[5]. However, traditional wound dressing, such as dry gauze or oil gauze cannot meet the wound healing needs[6]. Such as microbial colonization often occurs causing wound infections, which can lead to longer healing times or even difficulty in healing. Therefore, we need to investigate new wound dressings that can protect the wound breakage while acting as antimicrobial and promoting wound healing[7].Therefore, it is of great research value to develop a wound dressing that can ensure a good wound environment and promote wound healing[8].

Electrospinning is a new technology for preparing nanofibers by using electric force to draw charged threads of polymer solutions[9]. The nanofibers prepared by this method have good characteristics such as bionic nanofiber structure, high porosity and high specific surface area[10]. These characteristics allow electrospun nanofibers to provide a good protective barrier for wounds as wound dressings. Furthermore, it can stabilize the wound environment, and has suitable air permeability and water absorption[11]. In addition, specific spinning parameters can be used to produce some

nanofibers with unique microstructure characteristics, similar to extracellular matrix fibrin (ECM) in diameter, porosity, and morphology[12]. It can promote the ability of cells to attach and proliferate and thus promoting wound healing[13]. Nanofibers also have the ability to carry a variety of small molecule drugs, as well as bioactive substances[14]. The release rate and time of the drug can be controlled by methods such as mixing and coaxial spinning[15]. Due to the rapid evaporation of the solvent during the spinning process, the drug or inclusion remains uniformly distributed in the nanofiber as if it were in solution. Drug molecules are released from the fibers into the external release medium by diffusion, and this process is significantly slower compared to the burst release of conventional drug release.

Cellulose acetate (CA), a derivative of natural cellulose, is an important component of the cell wall of green plants and is widely available and inexpensive[16]. Electrostatically spun CA nanofibers are biocompatible, degradable and non-toxic. In addition, the cellulose acetate nanofibers prepared by electrostatic spinning have high porosity, good air permeability and stable chemical properties, which make the nanofibers a good drug-carrying material and make them advantageous for use as biomedical materials[17-19].

Dimethyloxallyl Glycine (DMOG) is a small molecule drug that can penetrate cells. It is a competitive inhibitor of prolyl hydroxylases (PHDs)[20], which catalyzes the hydroxylation of hypoxia inducible factor 1(HIF-1). HIF-1 is a key transcription factor that regulates the expression of angiogenic genes. Therefore, DMOG can activate HIF-1 by inhibiting PHDS and thus positively regulate the expression of angiogenic

factor[21]. Therefore, DMOG has been widely used in tissue regeneration as a small molecule drug in recent years. Research has shown that fibrous membranes containing DMOG can effectively promote the healing of diabetic wounds by improving angiogenesis[22, 23]. However, DMOG may lead to increased red blood cell production and the risk of developing tumors. Therefore, it is necessary to design a controlled release system which enables the release of DMOG drugs at appropriate doses during the healing of diabetic wounds and last for enough time[24].

Cyclodextrin (CD) is a series of cyclic oligosaccharides produced by amylose under the action of cyclodextrin glucosyltransferase[25]. It usually contains 6 to 12 D-glucopyranose units**Error! Reference source not found.**. As the rim of the cyclodextrin is hydrophilic, while cavity is hydrophobic. Thus, it provides a combination of hydrophobic parts, which can be used as host to envelope various appropriate guests[26], such as organic molecules, inorganic ions and gas molecules, etc. Therefore, it can be prepared into inclusion complexes with some drug molecules that are not biocompatible[27]. It not only increases the biocompatibility of the drug, but also plays the role of slow release.

In addition, to ensure a good wound healing environment, the selected materials should have certain antibacterial properties and not excessive cytotoxicity. In recent years, with the increase of drug-resistant bacteria, more and more attention has been paid to antimicrobial biomaterials[28]. Silver is a kind of good natural antimicrobial substance with good antibacterial properties[29]. Some studies have shown that silver has better antibacterial properties when it is in the form of nanoparticles[30]. The

antibacterial mechanism of silver nanoparticles has not been fully investigated. It has been suggested that the long-lasting broad-spectrum antibacterial effect is achieved due to the denaturation of proteins and changes in cell membrane fluidity caused by silver nanoparticlesp[31]. In addition, nanosilver particles can achieve good antibacterial effect with lower silver content due to their ultra-high specific surface area, and lower silver content means lower cytotoxicity[31-34].As a new and safer substitute for antibacterial substances, silver nanoparticles have been widely used in this field[35].

Therefore, in this study, DMOG was selected as the loading drug, which was contained in β-CD and loaded in cellulose acetate nanofibers, and loaded with silver nanoparticles, so as to realize anti-infection and promote healing of diabetic wounds.

2. Experimental Procedures

2.1 Materials

Cellulose acetate (CA, acetyl content: 39.5%) was purchased from Aladdin Biochemical Technology Co., Ltd. (Shanghai, China). β-cyclodextrin (β-CD) was purchased from Macklin Biochemical Co.,Ltd. (Shanghai, China). Acetone was purchased from Macklin Biochemical Co.,Ltd. (Shanghai, China). N-N-Dimethylacetamide（DMAC）was purchased from Macklin Biochemical Co.,Ltd. (Shanghai, China). Dimethyloxallyl Glycine (DMOG) was purchased from Aladdin Biochemical Technology Co., Ltd. (Shanghai, China). NaOH was purchased from Macklin Biochemical Co.,Ltd.(Shanghai, China). Silver nitrate was purchased from

Macklin Biochemical Co.,Ltd.(Shanghai, China). All reagents were used without any purification.

2.2 preparation of DMOG/β-CD inclusion complexes

Firstly, exact 1.134 g of β-CD was dissolved in 50 mL of deionized water. Then the solution was magnetic stirred for 6h at 50 ℃. After the solution cooled down to normal atmospheric temperature, 0.175 g of DMOG was added into β-CD solution and keep stirring for 12h. so that the mass ratio of the two molecules in the solution is 1:1, resulting in a β-cyclodextrin/DMOG inclusion complex. Then the upper clarified solution was extracted and placed at 4 °C for 12h. The final product is obtained by freeze-drying.

2.3 preparation of wound dressings

The 10 wt% CA was mixed in DMAC and acetone (2:1) and stirred for 12h at room temperature. Then a certain amount of DMOG/β-CD inclusion (2.5 wt%, relative to the polymer) is then added to the cellulose acetate spinning solution to obtain the final spinning solution; The obtained solution was continuously stirred until a homogeneous solution was formed. Then the obtained solution was extracted with a plastic syringe. A blunt needle with a core diameter of 0.6 mm was assembled with a syringe for electrostatic spinning. The electrospinning process was conducted at a working positive voltage of 10 KV and a working negative of 0.98 KV, a flow rate of 0.4 mL/h and a collecting distance of 12 cm. The resulting nanofibers are collected on a negative roller collector.

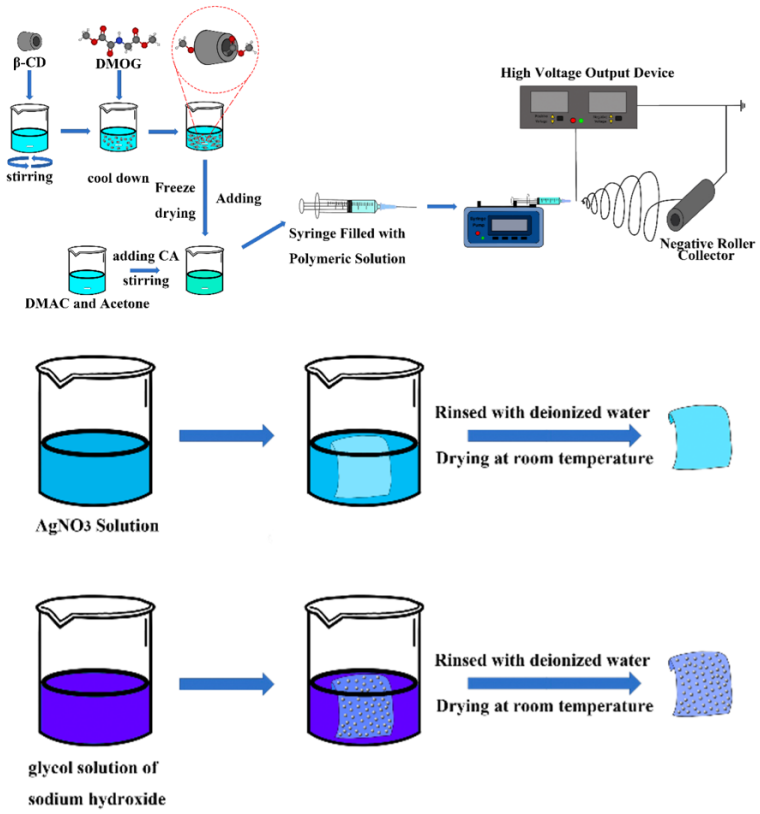


Fig. 1. Schematic diagram of nanofiber preparation process

The nanofibers were wetted with 0.001 g/mL $AgNO_3$ for 3h and rinsed with deionized water. Immersion of the resulting fibrous membrane into 0.16 g/50 mL Glycol solution of sodium hydroxide for 1h. The alkaline alcohol solution slowly reduces the silver ions to form fine-sized silver nanoparticles. Then the fibrous membrane was rinsed with deionized water and dried at normal atmospheric temperature. This process should be carried out in low light.

2.4 Characterization

Scanning Electron Microscopy (SEM, Sigma 300, Carl Zeiss) was used to observe the surface morphologies. The average fiber diameter and the diameter distribution were measured by software *Image-J*. The Fourier Transform Infrared (FT-IR,

PerkinElmer Frontier, England) was used with a scanning range of 4000-800 cm^{-1} to exam the chemical interactions. XRD patterns were obtained using X-ray diffraction (XRD, Rigaku D/MAX 2500V, Rigaku Corporation) with Cu Kα radiation at a scanning speed of 2°/min. The water contact angle is measured by a static contact angle measuring device (Kyruss, Germany) as an indication of the hydrophilicity/hydrophobicity of the wound dressing. The Epoch 2 microplate spectrophotometer (Biotek , USA) was used to compare the absorbance of each group and detect the cytocompatibility of the samples in each group.

2.4.1 Mechanical properties

All kinds of pairs of nanofiber films were cut into tensile test samples with a width of 2cm and length of 5cm. The mechanical properties of fiber samples were tested by Instron 1185 with a crosshead spee of 10 mm/min. Tensile testing of each sample should be conducted five times to take the average.

2.4.2 In vitro release test

The in vitro release ability of drug-loaded nanofiber membrane was tested by dynamic dialysis. 100 mg of the sample fibrous membrane was placed into a dialysis tube (molecular weight cut-off = 1000 Da) containing 5 mL of phosphate buffered saline (PBS, pH～7.4). The dialysis tube was suspended in a beaker containing 100 mL PBS with 2 vol% ethanol. The test was carried out in a shaker at 80 r/min at 37 ℃. Then 3 mL of the external release medium was periodically extracted from the beaker periodically. The content of DMOG was determined by spectrophotometer (UV-2600). The content of DMOG in the solution was determined by checking the absorption peak

of the external release medium at 230 nm. After each extraction, the same volume of PBS solution was added to the external release medium to keep the total volume of the external release medium unchanged.

The actual drug loading in the drug-loaded nanofiber membrane was measured by ultrasonic method. The 100 mg nanofiber membrane sample was immersed in 100 mL alcohol and treated with ultrasound for 1h. The concentration of DMOG in the sample was measured by ultraviolet spectrophotometer, and the actual drug loading of the sample was calculated.

2.4.3 Antibacterial activity test

Gram-negative E. coli (ATCC-25922) and Gram-positive B.subtilis (ATCC-25923) bacteria were used to test the antibacterial properties of the fibrous membrane samples by disk diffusion method.

2.4.4 Cytocompatibility evaluation

In cell viability analysis , MTT (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay was used to evaluate the cell viability and proliferation after co-incubated with material disks for 24 h and 48 h. The samples were cut into a 2 cm^2 round disk and sterilized by 75%vol alcohol and ultraviolet irradiation for 24h. The medium composition of L929 cells was Dulbecco's Modified Eagle's Medium (DMEM) (Gibco, USA)+10% fetal bovine serum (FBS)+1% penicillin/streptomycin. L929 cells were cultured in this medium, and the cells entered the exponential growth phase. Then the cells were transferred on a 24-well plates, 20000 cells/well, standing for 6h until the cells are adhered to the bottom. Then the

round disk sample was added into the wells, and the cells were cultured for 24 hours. 5 mg/ml MTT solution was added into the 24-well plate, 100μl per well. All samples should be incubated at 37°C for 4h. Then carefully aspirate the culture fluid from each well add DMSO 700μl to each well, and react at room temperature for 10 min. Succinate dehydrogenase in mitochondria of living cells can reduce MTT to water-insoluble blue-purple crystalline formazan and deposit it in the cells, while dead cells do not have this function. Dimethyl sulfoxide (DMSO) can dissolve the methyl stagger in cells, and its light absorption value can be measured at 570 nm by enzyme, which can indirectly reflect the number of living cells. The resulting data were analyzed for cytocompatibility using the following formula[36].

$$cell\ viability(\%) = \frac{sample\ absorbance - Blank\ abosrbance}{Control\ absorbance - Blank\ abosrbance} \times 100 \quad (1)$$

3. Results and discussion

3.1 Morphology of nanofibers

The microstructures of CA, CA/β-CD/DMOG and CA/DMOG/Ag electrospun nanofibers were studied by SEM images. As shown in Fig. 2(A), (B) aligned, droplet free nanofibers can be successfully prepared by electrospinning. It can be seen that the microstructure of all the samples exhibit good topological structure[37]. Previously research showed that aligned fiber, promotes cell migration and division . More studies have also demonstrated that the arrangement of fibers affects the direction and extent of cell extension and the migration of fibroblasts, ligament cells, and gliomas[38, 39].

In order to study the diameter distributions of three kinds of nanofibers, Image J software was used to measure the diameters of 100 fibers in the three fibers and conduct

distribution statistics. As shown in Fig. 2(D), (E) the addition of DMOG to CA nanofibers has no significant effect on the diameter of the nanofibers. The diameters of CA and CA/β-CD/DMOG nanofibers are mainly distributed in the range of 40-120 nm. This distribution of fiber diameters in the micron to nanometre range is thought to have a structure similar to that of the extracellular matrix**Error! Reference source not found.**. Various cell types respond differently when cultured on submicron diameter (less than 700 nm) versus electrospun fibers greater than 1 micron in diameter[40]. Furthermore, there are uniformly distributed ear-like Ag-NPs on the fiber surface, and the diameters of CA/DMOG/Ag-NPs nanofibers are mainly distributed in the range of 120-200 nm, as seen in Fig.2(C). The average diameter of the fibers increased slightly.

These particles were analyzed by EDS, and the results were shown in Fig. 3. Obviously, appreciable amount of Ag is found in CA/DMOG/Ag nanofibers. EDS analysis proves that Ag nanoparticles are successfully synthesized on the surface of nanofibers.

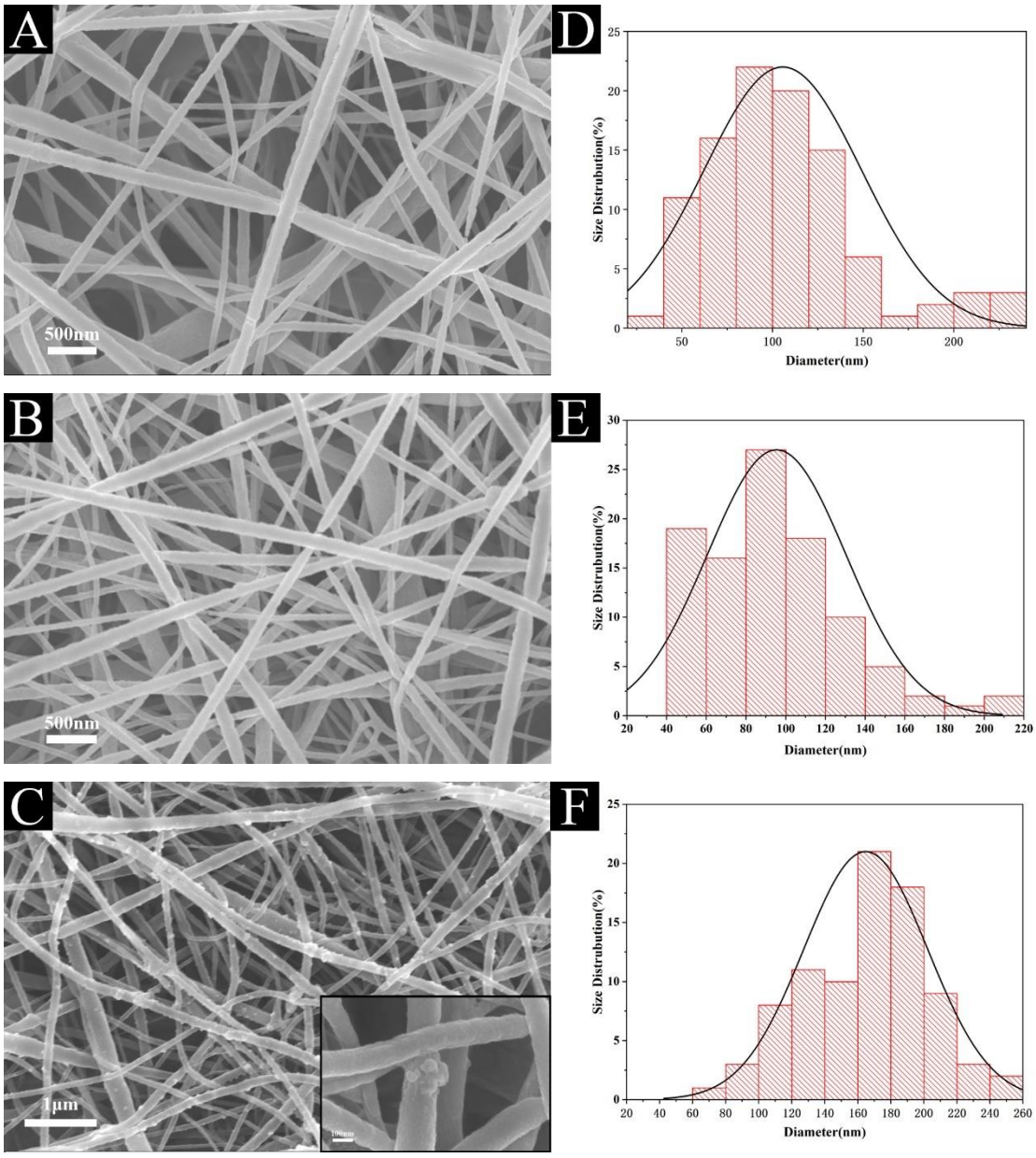
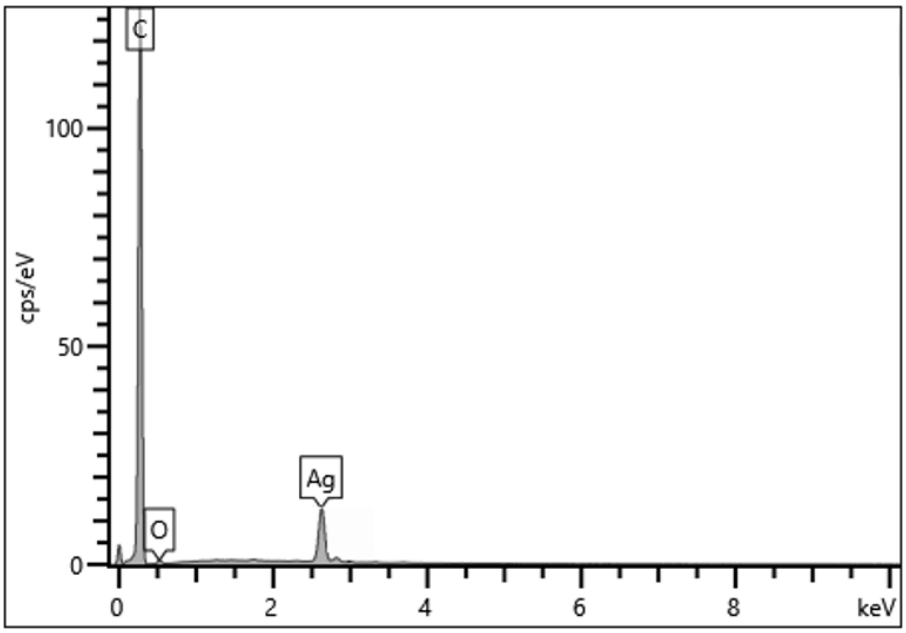


Fig. 2. SEM images of electrospun fibrous membrans (A) CA, (B) CA/β-CD/DMOG, (C)CA/β-CD/Ag-NPs and (D)(E)(F) respective average diameter distribution.



Element	Line	Apparent concentration	k ratio	Wt%	Wt% Sigma
C	K	171.61	1.71610	96.12	0.13
O	K	1.98	0.00665	3.59	0.13
Ag	L	0.45	0.00447	0.29	0.04
total:				100.00	

Fig. 3. EDS spectra of CA/β-CD/Ag-NPs nanofiber membranes

3.2 Mechanical strength

The stress-strain curves of the three nanofiber membranes are shown in Fig. 4. The results show that adding drugs or loading silver nanoparticles on the surface of cellulose acetate nanofiber membrane can reduce the tensile strength of nanofiber membrane. The highest tensile strength of pure cellulose acetate nanofiber membrane is 4.16±0.74 MPa. However, the tensile strength of samples with DMOG and Ag-NPs decreased to 1.97±0.53 and 1.349±0.23 MPa, respectively. It is attributed to the addition of β-

cyclodextrin and the treatment of alkaline conditions. Studies have shown that the tensile strength of human skin is about 1-32 MPa[41]. Therefore, the nanofiber membrane prepared in this study preliminarily meets the requirements of biological application. However, if higher tensile strength is required in practical applications, it can be combined with other materials with high tensile strength to meet the requirements.

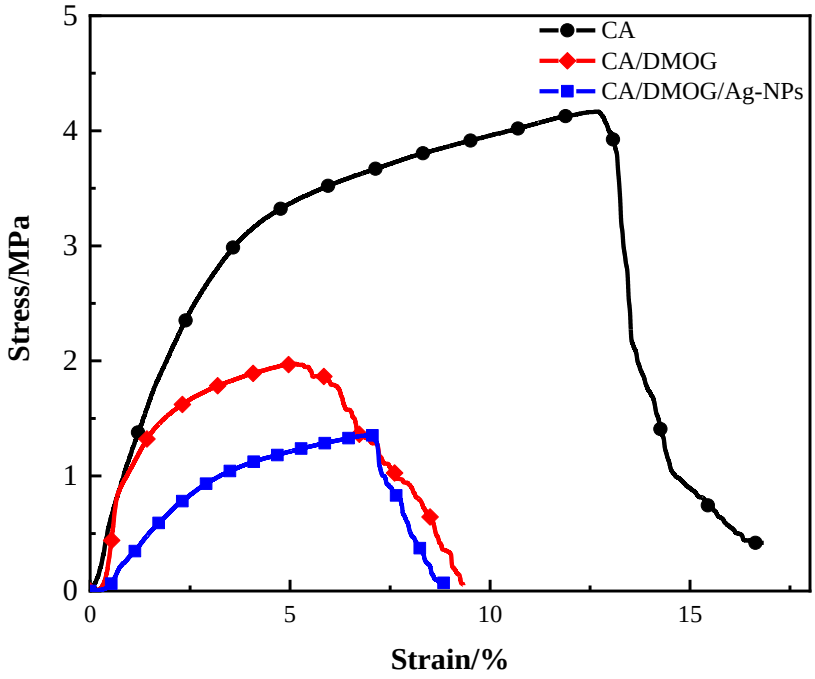


Fig. 4. Typical stress–strain curves of three types of nanofiber membranes

3.3 Wettability

Fig. 5. shows the water contact angles (WCA) of CA, CA/β-CD/DMOG and CA/DMOG/Ag-NPs nanofiber membranes. As shown in Fig.6(a), CA nanofiber membrane is hydrophobic with an average WCA of ~126.7°. However, the

hydrophobicity of CA nanofiber membrane containing DMOG increased obviously by 42.6% (Fig. 6(b)), The reason may be due to the addition β-CD molecule which contain a hydrophilic outer surface. Therefore, the hydrophilicity of the material improves. After loading nano-silver particles on the nanofibers, the hydrophilicity of the material decreases slightly, as shown in Fig.6(c). However, it is still below 90°, indicating that the material is still hydrophilic. Some researchers believe that it is the nanosilver particles that cover the pores on the surface of nanofibersp[42]. I speculate that perhaps the process of nanosilver particle generation preferentially nucleates the unsmooth parts of the fiber surface, and this tendency to change the microscopic morphology of the fiber surface leads to this change in hydrophilicity. High hydrophilicity helps cells to attach and divide, thereby promotes wound healing to a certain extent[43].

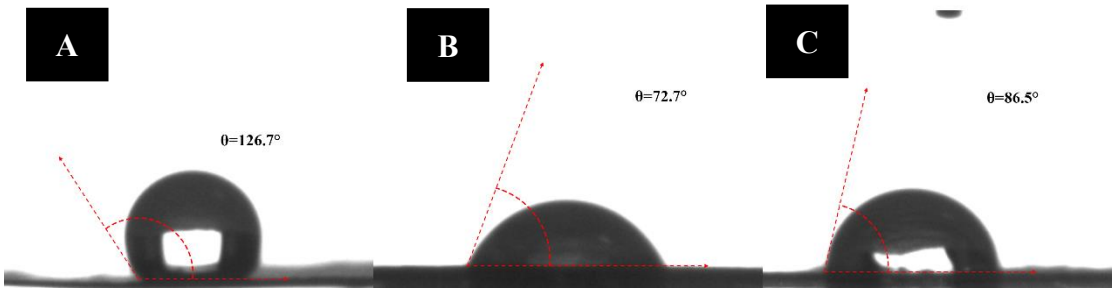


Fig. 5. Water stability of three types of nanofiber membranes

3.4 physical statues analysis

XRD was used to analyze the target drug DMOG, β-CD, and CA nanofiber membranes containing β-CD encapsulated DMOG, as shown in Fig. 6(a). It can be seen that both the original DMOG and β-CD show obvious crystal characteristics. A large

number of characteristic diffraction peaks occur in the range of 10° to 50°. This result suggests that both DMOG and β-CD are usually present in crystalline form. On the other hand, the diffraction spectrum of CA exhibits several broad diffraction halos, which illustrates that CA has typical amorphous characteristics[44]. In contrast, DMOG and β-CD in CA/β-CD/DMOG nanofibers do not exhibit distinct crystallographic features in the spectra.

This may be due to the rapid evaporation of solvents during electrospinning, which prevents crystal lattice formation[27]. In addition, the diffraction spectrum of CA / β-CD /DMOG nanofibers exhibits some small diffraction peaks of DMOG and β-CD crystals，suggesting the presence of DMOG contained by β-CD in this fiber.

Fig.6.(b) shows the FTIR spectra of CA/DMOG/Ag-NPs nanofiber membranes and its raw materials. In the CA spectrum, there is carbonyl ester group at 1745 cm^{-1}, which is the fingerprint peak of CA. The bands at 1243 and 2916 cm^{-1} are the stretching vibration peaks of alkene C-H and alkane C-H, respectively. In addition, the absorption peaks of C-O-C and C-O are corresponding to the bands of 1099and 1329 cm^{-1} respectively. The β-CD structure results in a strong and wide band at 3300 cm^{-1}, which is caused by O-H stretching vibration. The asymmetric stretching motion of CH_2 shows a band of 2925 cm^{-1} in the spectrum[45]. The bands at 1021 and 1079 cm^{-1} correspond to the stretching vibration peaks of C-O and C-O-C respectively. The whole spectrum distribution of the electrospun fiber samples illustrate the characteristics of both CA and β-CD. However, the overall peak intensity of the characteristic peak area has decreased in the spectrum of the electrospun fiber samples. The wide band at 3426 cm^{-}

[1] is caused by the vibration of the amide N-H bond. In addition, a shift of the peak at 1021 in the β-CD spectrum to 1030 cm^{-1} was also observed. The changes in these characteristics can be considered to be that DMOG is successfully included in β-CD and added to the CA nanofibers through electrospinning technology.

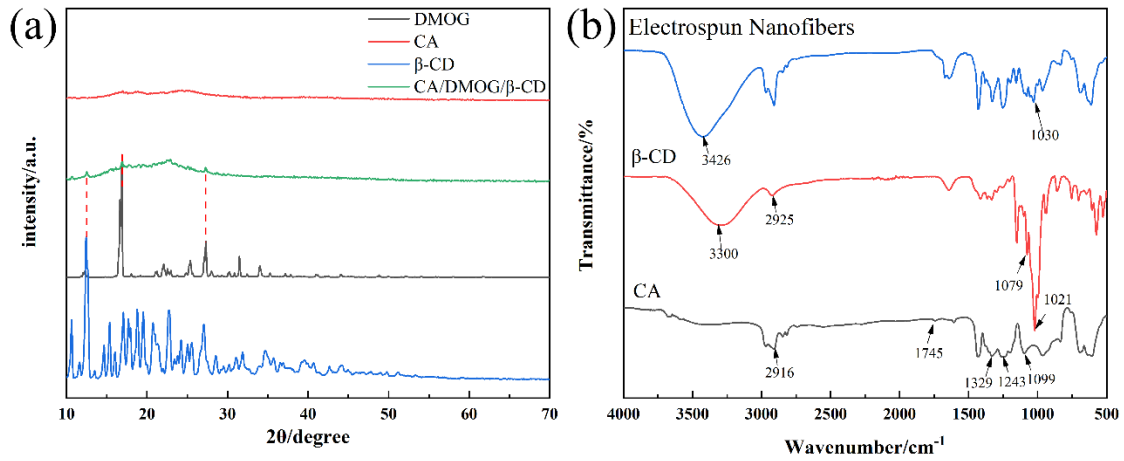


Fig.6. (a) XRD patterns (b) FT-IR spectra of CA/DMOG/Ag-NPs nanofiber membranes and its raw materials

3.6 In vitro drug release

The explosive release of drugs and the side effects caused by high concentration of drugs are one of a major concern that must be considered in the practical application of drugs. The Fig. 7. (a) shows the drug release curve of drug-loaded cellulose acetate nanofiber membrane in vitro drug release test. It is clearly observed that DMOG can be sustained and controlled release from the drug-carrying nanofibers. The explosive release of DMOG occurred in the first hour, and the release amount reaches 52% of the total drug load. After that, the release rate slows down, and 34.78% of the total drug

load was released gradually in about 84h.

Peppas mathematical model is introduced to study the mechanism of drug release from nanofibers[46]. The Korsmeyer-Peppas model was expressed as:

$$\frac{M_t}{M_\infty} = k_{kp}t^n \qquad (2)$$

Where $\frac{M_t}{M_\infty}$ is the cumulative release of the drug during time t, k_{kp} is the kinetic constant, and n is the diffusion constant[47]. Fig. 7. (b) shows the drug release curve fitted by Korsmeyer-Peppas model. The formula is fitted to be: $\frac{M_t}{M_\infty}$=$51.27731t^{0.1221}$. It can be seen that the drug diffusion constant of CA/DMOG/Ag-NPs nanofiber membrane is 0.1221. The drug release mechanism in this model can be judged by the n-value. When $n \leq 0.5$ the drug release mechanism is Fickian dispersion. When $0.5 < n < 1$, the drug release mechanism is non-Fickian diffusion mechanism. When $n \geq 1$, the drug release mechanism is skeleton corrosion. Thus, it can be figured out that the release of DMOG is a pure Fickian diffusion controlled process.

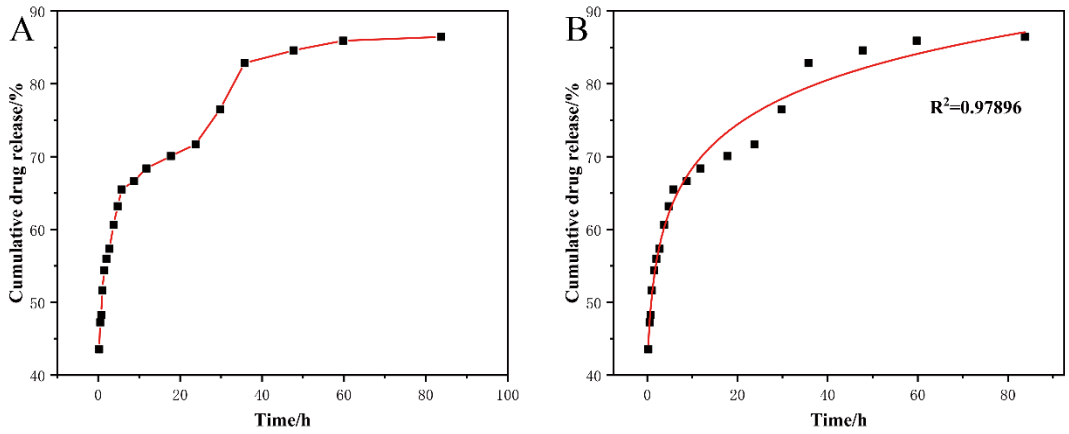


Fig. 7. In vitro release profiles: (A) The cumulative release of DMOG from CA/DMOG/Ag-NPs fibrous matrix; (B) Mathematical fitting curves of CA/DMOG/Ag-NPs fibrous matrix.

3.7 Antibacterial activity

The antimicrobial performance test results are shown in Fig. 8. (a)(b)(c) are the 12, 24 and 48h antibacterial test results of E.coli, (D)(E)(F) are the 12, 24 and 48h antibacterial test results of S. aureus, (a-c) are CA, CA/β-CD/DMOG and CA/DMOG/Ag-NPs nanofiber membrane samples respectively. The results indicate that the nanofiber membrane loading with silver nanoparticles exhibits obvious inhibition zone in the tests against Gram-negative (E.coli) and Gram-positive (S. aureus) bacteria. Therefore, it can be proved that the drug-loaded CA containing Ag-NPs has good antibacterial properties. However, the CA nanofiber membrane and CA/β-CD/DMOG nanofiber membrane exhibit no obvious antibacterial effect against both Gram-negative and Gram-positive bacteria. Therefore, it can be proved that the antibacterial performance of CA/DMOG/Ag-NPs nanofiber membrane sample is directly related to the presence of silver nanoparticles. The diameters of the antibacterial zone around the samples containing Ag-NPs after 12, 24 and 48 h were compared. The diameters of the antibacterial zone were positively correlated with time. It can be found that most of the bacteriostatic rings are formed in the first 12 h, and the diameters of the bacteriostatic rings increased slowly in the first 12 to 24 h. The diameters of the bacteriostatic zones hardly change in the next 24 to 48 h, indicating that the antimicrobial effect has stabilized the diameter of the inhibition ring no longer changes indicating a dynamic equilibrium. This indicates that the Ag-NPs will not develop resistance for at least 48 h. However, silver is a heavy metal element after all. While sterilization, silver ions will also cause certain damage to human cells. High content of

silver will accumulate in various systems and organs, and it is difficult to be discharged in a short time[48]. Therefore, while the antimicrobial properties of silver-containing materials are of concern, it is also important to ensure that they do not have too high a level of cytotoxicity.

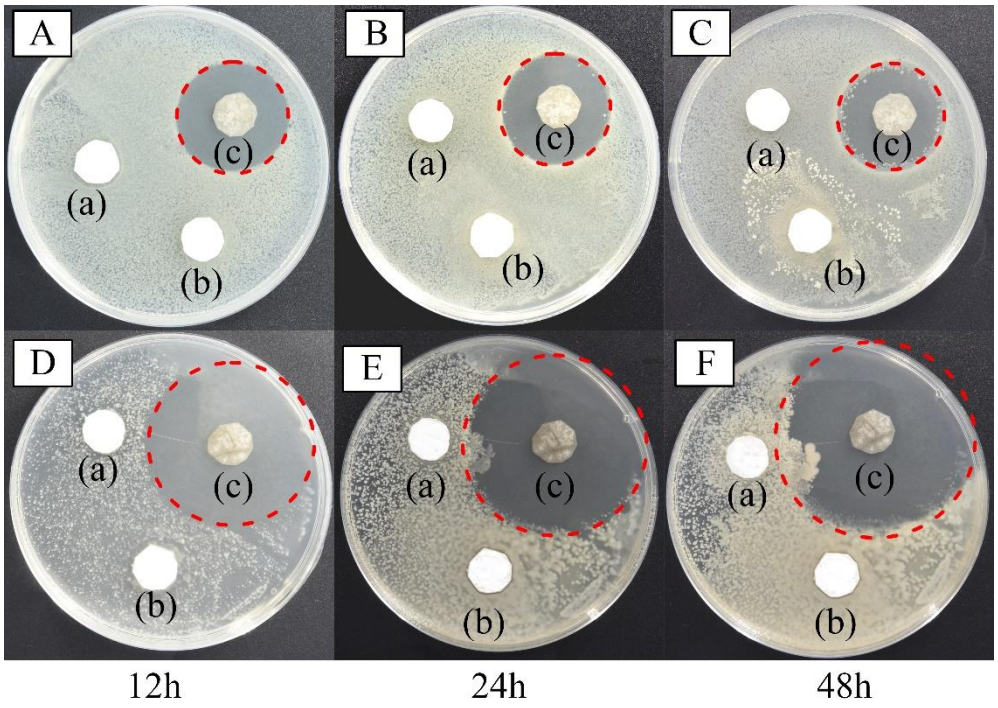


Fig. 8. Antibacterial activity against E.coli (A)(B)(C) and S. aureus (D)(E)(F) of nanofibrous membranes for 12, 24 and 48h.

3.8 In vitro cell viability

The cytocompatibility of CA, CA/β-CD/DMOG and CA/DMOG/Ag-NPs nanofiber membranes were analyzed by MTT assay. Cells inoculated on a tissue culture plate (TCP) without material were used as a control group, as shown in Fig 9, none of the three materials showed inhibitory effect on cell proliferation. After 24 h and 48 h of culture, all three materials showed higher cell viability relative to TCP. The most

probable reason is that CA fiber membrane has appropriate porosity, similar to the structure of extracellular matrix, good hydrophilicity and other reasons to promote the proliferation of cells. In addition, the cell activity of CA/DMOG/Ag-NPs samples after 24 h culture was the lowest among the three groups of samples. This indicates that the silver-containing materials have certain toxicity to cells. The results of 48h cytocompatibility test showed the same trend of promoting cell proliferation after 48h of direct contact incubation of l929 cells with the samples as before.The cell survival rate of CA/DMOG/Ag-NPs samples in the 48h test decreased slightly compared to the results in the 24h test, but was still higher than in the TCP experimental group, showing a promotion of cell proliferation. However, a comprehensive analysis of the experimental results can be concluded that the nano-silver particle with appropriate amount is beneficial to antibacterial properties and good cell compatibility of the material.

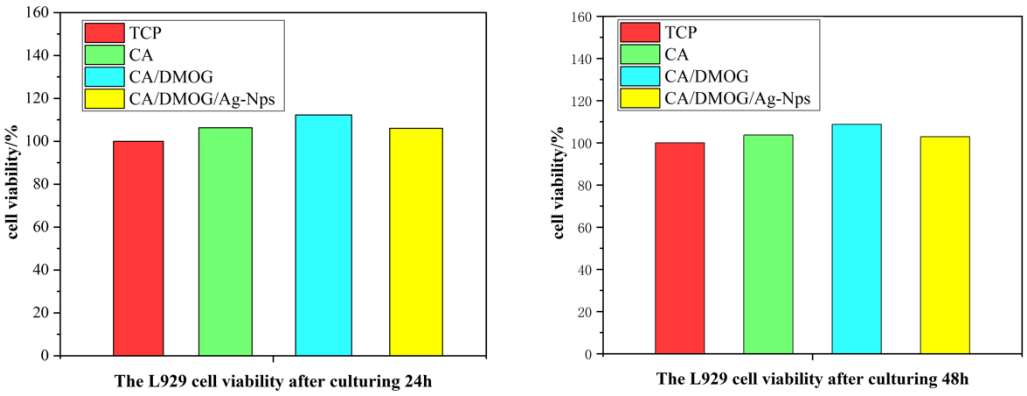


Fig. 9. The L929 cell viability after culturing 24 h and 48 h.

4. Conclusions

In this study, DMOG, nano silver particles and cellulose acetate were used to prepare a

dual-functional nanofiber capable of achieving sustained drug release and antibacterial DMOG through electrospinning technology. DMOG, as a drug to promote wound healing, is packaged with β-CD and then combined with CA to prepare spinning solution. Ag-NPs as antibacterial substances are directly synthesized on the surface of drug-loaded CA nanofiber membranes through in-situ synthesis. Through microscopic morphology analysis, mechanical strength analysis, and wettability analysis, it can be concluded that the prepared nanofiber membrane has good microscopic morphology, appropriate mechanical properties, and wettability. In vitro release test proves that the material can achieve sustained release of DMOG in about 84 h. In vitro cell viability test shows that the material not only possesses the good cell compatibility of electrospun nanofibers, promotes cell growth, but also has the antibacterial properties of Ag-NPs. In addition, the antibacterial effect is stable for at least 48 h and no drug resistance will be produced. All these results indicate that the material can be used as a good antibacterial wound dressing for promoting diabetic wound healing.

Data availability

The raw/processed data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study.

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