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Research Article

Study on Photocatalytic Antibacterial and Sustained-Release Properties of Cellulose/TiO_2/β-CD Composite Hydrogel

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A novel cellulose/TiO_2/β-CD hydrogel with high photocatalytic antibacterial activity and sustained release of drug was prepared. TiO_2 sol with a diameter of about 9 nm in this hydrogel was the photoantibacterial agent. β-CD can significantly enhance photoantibacterial activity and the sustained-release effect of this hydrogel. The structure and property of this hydrogel composite were characterized by Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). *Escherichia coli* and *Staphylococcus aureus* were selected as model bacteria to evaluate the antibacterial activity of the composite hydrogel under natural light irradiation and darkness, respectively. The in vitro release experiment used curcumin as a model drug in PBS buffer solution. The influence of β-CD on the antibacterial activity and sustained-release effect of the composite hydrogel was investigated. The results showed that the hydrogel composite presented a good photoantibacterial property, while the antibacterial activity can be neglected under the condition of no light. The complete release of curcumin from the composite was achieved after 120 h. Therefore, the hydrogel system has the characteristics of low cost and high effect, which could be used for an antibacterial sustained-release material.

1. Introduction

Cellulose is one of the most abundant biomass materials and possesses many promising properties, which has been widely used in all areas of society. The application of cellulose-based materials has received great attention in recent years [1, 2].

Hydrogels are three-dimensional, cross-linked polymeric networks which possess an ability to swell in water without getting dissolved in it [3]. With the advantages of renewability, biocompatibility, biodegradability, and thermal and chemical stabilities, cellulose-based hydrogels can be used for wound healing [4], tissue engineering [5], and drug carrying [6].

However, due to a lack of bactericidal property and the inherent incompatibility between hydrophobic drugs and the hydrophilic nature of the cellulose net, the release of hydrophobic drugs from cellulose-based hydrogels cannot be controlled for a long duration [7].

β-CD contains a peculiar hydrophobic cavum and could form inclusion complexes with various guest molecules. Zhang et al. have synthesized cellulose hydrogels by the addition of β-CD cross-linked with epichlorohydrin (ECH) in a NaOH/urea aqueous solution; these hydrogels could complex 5-FU with β-CD that restrains the release from the hydrogels because the inclusion interactions are too strong to let 5-FU complex into the cavity of β-CD [8]. However, this hydrogel still lacks a bactericidal property, and the influence of β-CD with a cross-linker on the hydrogel formed has not been studied.

The addition of TiO_2 sol can improve the antimicrobial performance of the cellulose-based hydrogel. TiO_2 sol has been widely used in the fields of photovoltaics, photocatalysis, and antibiosis. It is now well established that TiO_2 produces electrons and holes upon exposure to light, subsequently leading to the formation of reactive oxygen species (ROS). These oxygen species are highly reactive

with both cell membrane and cytoplasmic materials. And the point of attack depends on the particle location upon excitation. Such oxidative reactions can affect cell integrity and the chemical arrangement of surface structures and are the main mechanisms of their photocatalytic antibacterial activities [9–11].

Nonetheless, photocatalytic antibacterial efficiency is still not high due to the rapid recombination of the electron and hole of TiO_2 particles [12]. To improve the effect of TiO_2, β-cyclodextrins (β-CD) are added as a photocatalytic promoter based on their hydrophobic inner cavity, the charge transfer rate from the photoexcited semiconductor to electron acceptors is accelerated, and the photocatalytic substrates onto the TiO_2 surface are concentrated [13].

To form a hydrogel from dissolved cellulose, a cross-linking process is required. The aim of the cross-linking process is to improve the insolubility, mechanical strength, stiffness, and rigidity of the polymer. One of the most common cross-linkers used is epichlorohydrin (ECH) [14]. Even though ECH is toxic in nature, its toxicity is diminished after a rinsing process [15]. For this reason, ECH was used to cross-link a cellulose-based composite hydrogel in this manuscript.

In this study, a novel cellulose/TiO_2/β-CD hydrogel composite was prepared. As illustrated in Scheme 1, we prepared the hydrogel by adding TiO_2 sol, which was synthesized in advance by a sol-gel method and a β-CD-to-cellulose solution; then, the mixture was cross-linked with epichlorohydrin (ECH). The structure and properties of the obtained hydrogel composite were characterized by Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), scanning electron microscopy (SEM), and transmission electron microscopy (TEM). *Escherichia coli* and *Staphylococcus aureus* were selected as model bacteria to evaluate the bactericidal activity of the hydrogel under natural light and darkness, respectively. The in vitro release experiment chose hydrophobic curcumin as the model drug in the PBS buffer solution (pH = 7.4). This hydrogel system possesses the characteristics of a simple preparation process, low cost, and high effect, which may be used as an antibacterial and sustained-release material.

2. Experimental

2.1. Materials. Tetrabutyl titanate, β-CD (MW = 1134.98), disodium hydrogen phosphate (Na_2HPO_4), sodium chloride (NaCl), potassium chloride (KCl), sodium hydroxide (NaOH), urea, and curcumin were obtained from Aladdin Reagent Database Inc. (Shanghai, P.R. China). 1,3-Diphenylisobenzofuran (DPBF) was purchased from Acros Organics (Geel, Belgium). Qualitative filter paper was obtained from Titan Reagent Database Inc. (Shanghai, P.R. China). All reagents were of analytical grade and were used without further purification. Double-distilled water was used in the whole experiment.

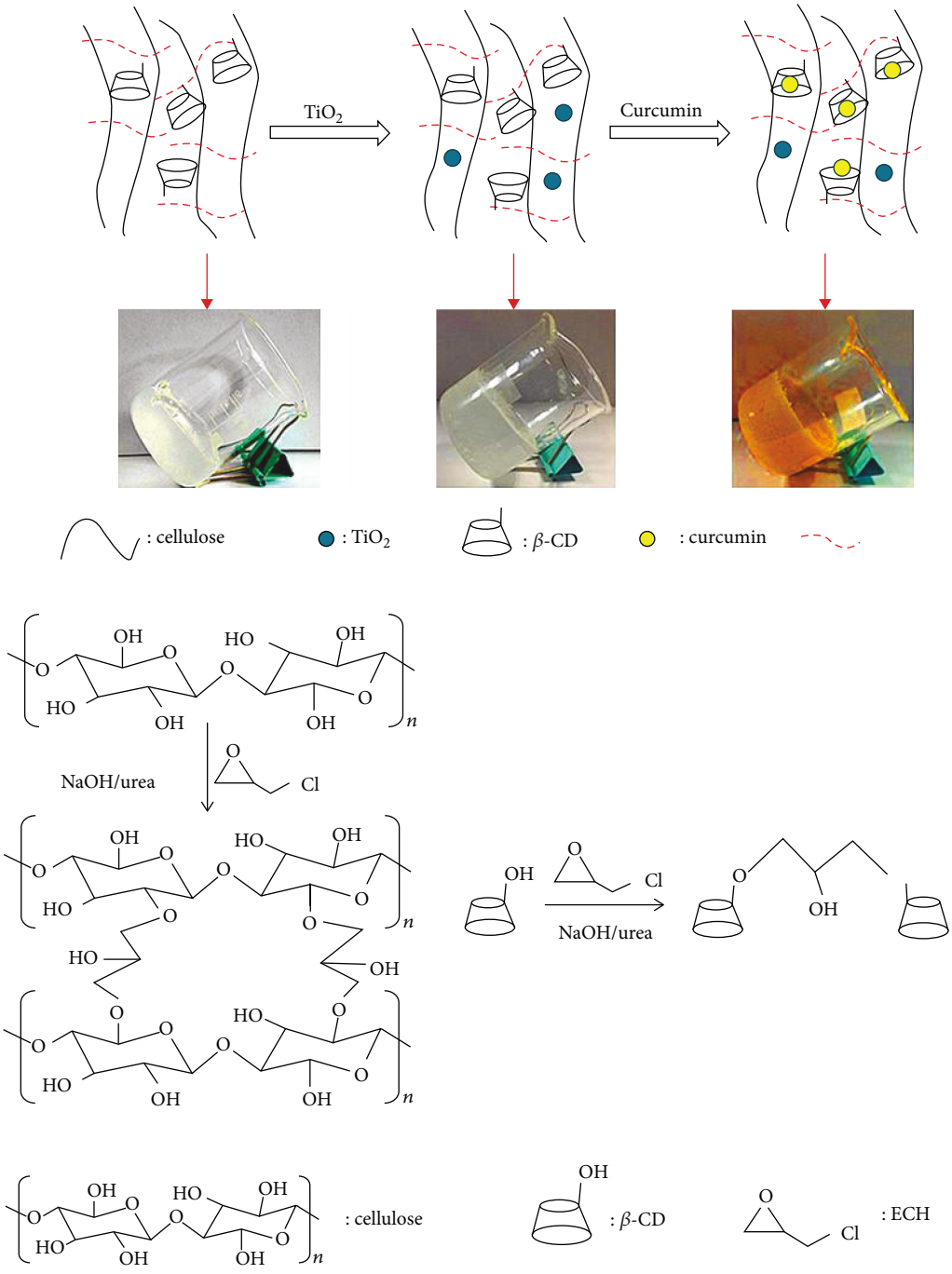
2.2. Synthesis of TiO_2 Sol. TiO_2 sol with a solid content of 25% was synthesized by the hydrolysis of tetrabutyl titanate. In brief, 3.5 mL of tetrabutyl titanate was added to a solution containing 47 mL of water and 8 mL of acetic acid. After magnetic stirring for 2 h, the nearly transparent appearance of sol was obtained. The sol was stored in a sealed vial to age overnight, and then the sol was stored in a fridge set at 4°C for a maximum period of one month, to prevent excessive ageing.

2.3. Cellulose/TiO_2/β-CD Hydrogel Preparation. The cellulose solution was prepared according to methods reported by literature. 4 g of qualitative filter paper was dissolved in 81 mL of deionized water containing 7 g of NaOH and 12 g of urea which were filtered with a G2 sand filter. The solution was stirred for 5 min and stored in a refrigerator for 12 h; the solution was then brought back to room temperature, stirred extensively to obtain a colorless and transparent solution, and then centrifuged for 15 min (7200 rpm) at 15°C. Then, β-CD was added at concentrations of 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, and 10 wt%, and the TiO_2 sol was added to the β-CD/cellulose solutions with the concentration of 5% (v/v). 10 mL of ECH was added into the cellulose/TiO_2/β-CD mixture solution and reacted for 30 min under room temperature and then kept at 50°C for 5 h to obtain the composite hydrogel [8, 16].

2.4. Characterization. The FTIR spectra of the cellulose/-TiO_2/β-CD hydrogel were collected with a Bruker Tensor II Fourier transform infrared spectrometer. The test specimens were prepared by the KBr-disc method. The particle sizes of the TiO_2 were measured by a Nano ZS (Malvern Co., U.K.). The phase structure and purity of the TiO_2 were examined by X-ray diffraction (XRD) using a MAP18XAHF with a diffract meter with Cu Kα radiation ($\lambda = 1.54$ Å) at a scanning rate of 2°/min. The morphology and microstructure were characterized by a SEM instrument (Hitachi S-4800, Japan) and an EDX (Oxford Instruments Link ISIS). The fractured surfaces of the hydrogels were sputtered with gold before they were observed and photographed. The UV-vis absorbance was measured by using a UV-1800 spectrophotometer (Shimadzu, Japan).

2.5. Swelling Experiments. The swelling capacity of the cellulose/TiO_2/β-CD hydrogel with respect to time was carried out. The experiment was performed using a definite quantity of the material, which was transferred to a previously weighed tea bag and then placed in a beaker containing 100 mL of distilled water at room temperature for 24 h to attain equilibrium. The samples were collected from the distilled water at regular intervals. Before the weights of the hydrogel were recorded, the surfaces of the hydrogels had been wiped with filtered paper to remove water. The sample weights were recorded as the average of three measurements.

2.6. Antibacterial Studies. The antibacterial activity of the final product was screened by the disc diffusion method using *Escherichia coli* and *Staphylococcus aureus*. Cellulose/-TiO_2/β-CD hydrogels were cut into a disc shape with a diameter of 10 mm (360 mg by weight), which was the same size as the samples. Next, fresh precultures of *Escherichia coli* and *Staphylococcus aureus* were spread on the agar plate, and the samples were placed on top and incubated at 37°C



Scheme 1: Schematic illustration of the curcumin-carrying composite hydrogel and the proposed mechanism for the cross-linking reaction of ECH with β-CD and cellulose.

for 24 h exposed to natural light. Finally, the inhibition zones were measured. To test the contribution of β-CD to the antimicrobial activity, the ring of inhibition was measured for different composites with the same cellulose/-TiO_2 concentrations. In addition, the dark reaction and the blank experiments of the composite hydrogels were also done. In blank experiments, the antibacterial effect of the cellulose/β-CD (4 wt%) hydrogel without TiO_2 sol and with 1 mL, 2 mL, and 3 mL TiO_2 sol was compared with light irradiation.

The ROS generated from the cellulose/TiO_2/β-CD hydrogel with different concentrations of β-CD under natural light irradiation was determined by decomposing 1,3-diphenylisobenzofuran (DPBF) in ethanol at 410 nm, which can be measured by using a UV-1800 spectrophotometer.

2.7. Drug Loading and In Vitro Release. Curcumin was chosen as the model drug for sustained release by a swelling equilibrium method [17]. Curcumin loading was carried out by dispersing 100 mg of the dried cellulose/TiO_2/β-CD

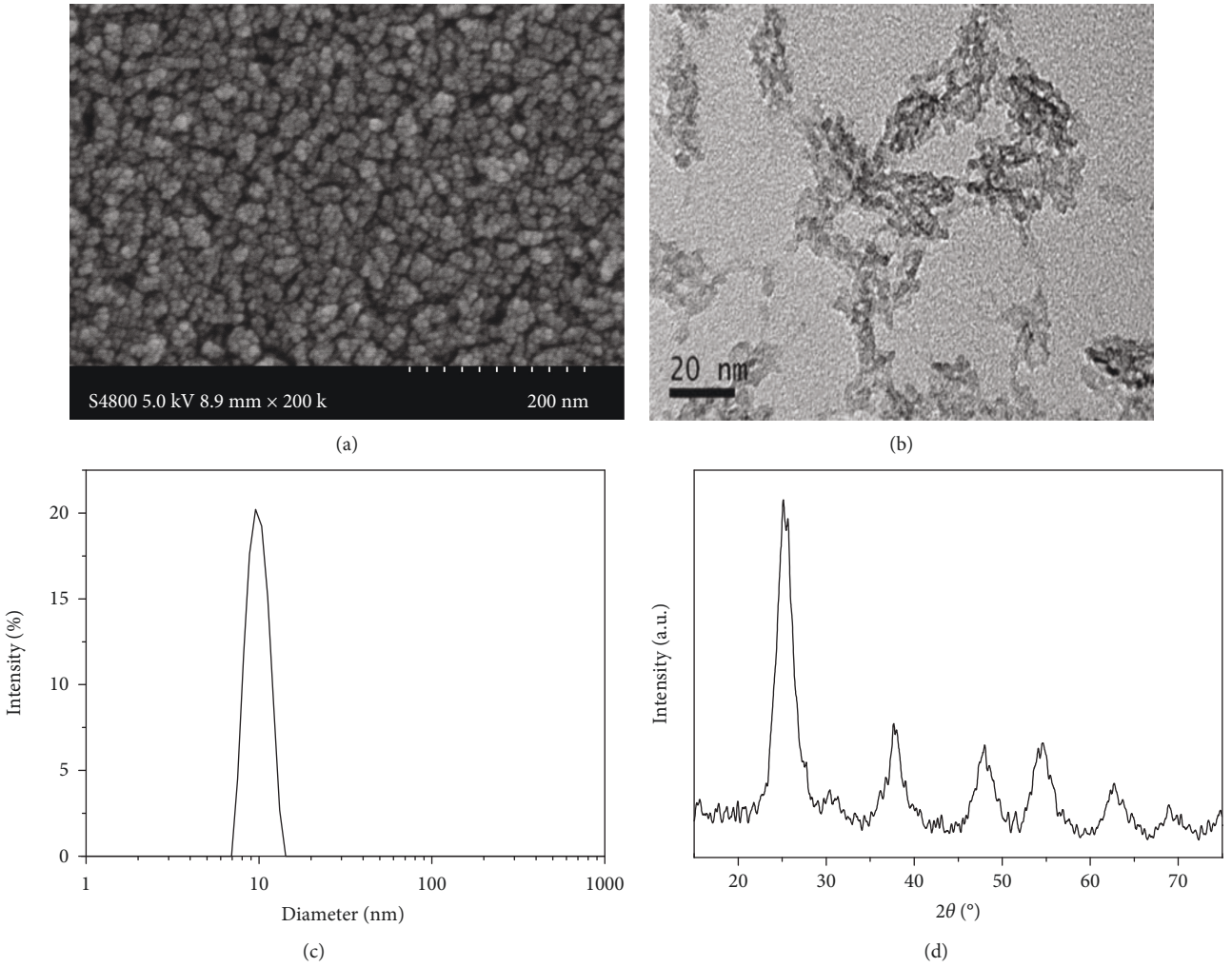


Figure 1: (a) SEM image, (b) TEM image, (c) size distribution curve, and (d) XRD pattern of the prepared TiO_2 sol.

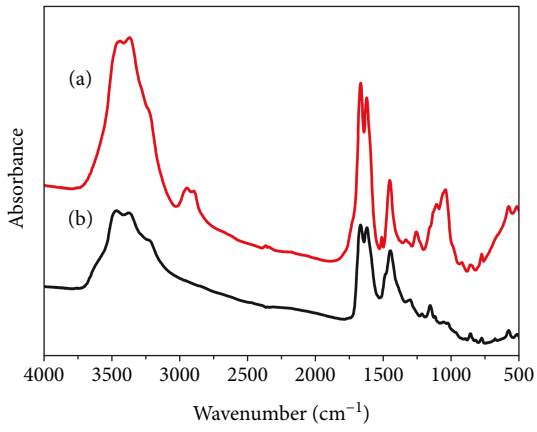


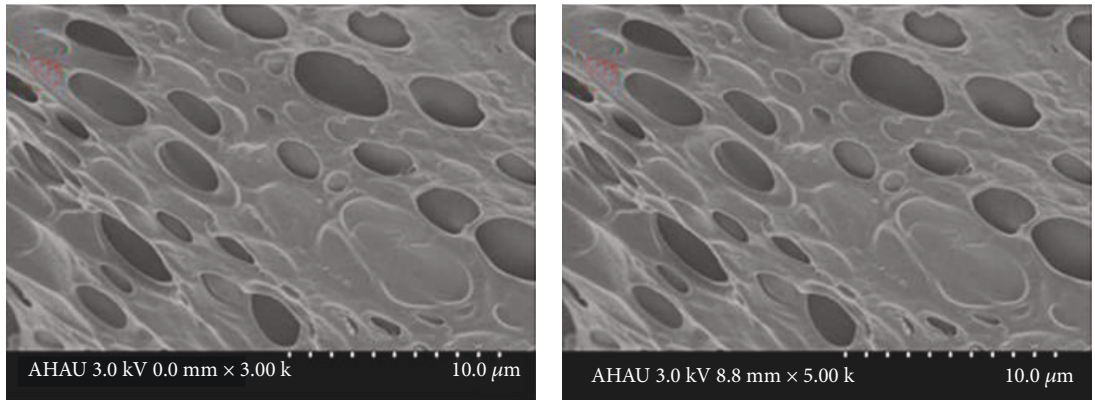
Figure 2: FTIR spectra of the cellulose/TiO_2/β-CD hydrogel before (a) and after (b) cross-linking by ECH.

hydrogel in a mixture of 1 mg/mL curcumin aqueous solution and 50 mL phosphate buffer solution (PBS, pH = 7.4) and then stirring for 24 h to reach the equilibrium state at 37°C. The mixed solution was centrifuged, and the supernatant was collected and subjected to UV-vis analysis at λ_{max} = 440 nm [18]. The loading efficiency was calculated using the following:

$$\text{Loading efficiency}(\%) = \frac{\text{total curcumin} - \text{free curcumin}}{\text{total curcumin}}. \quad (1)$$

Then, the hydrogel was fetched out and vacuum dried at 45°C. The in vitro release was carried out at 37°C in phosphate buffer solution (PBS, pH = 7.4). The release study was performed by immersing the above drug-loaded hydrogel in a glass bottle filled with PBS. After specified time intervals (12 h), it was centrifuged and the supernatant solution was collected and subjected to UV-vis analysis at λ_{max} = 440 nm. The percentage amount of curcumin released was calculated and plotted versus time according to the following [19]:

$$\text{Drug release}(\%) = \frac{\text{released curcumin}}{\text{total curcumin}}. \quad (2)$$



(a) (b)

Figure 3: SEM images of the cellulose/TiO_2 hydrogel (a) and cellulose/TiO_2/β-CD hydrogel (b).

3. Results and Discussion

3.1. Characterization of TiO_2 Sol. The TiO_2 sol was prepared by the sol-gel method. The SEM and TEM analyses of the prepared TiO_2 sol exhibiting an irregular shape are shown in Figures 1(a) and 1(b). The size distribution of TiO_2 sol determined by dynamic light scattering (DLS) is presented in Figure 1(c). The average particle size of TiO_2 sol is about 9 nm. It is well known that the small size of TiO_2 sol has a much higher active surface energy, and it can be used as a highly efficient photoantibacterial agent.

The XRD pattern of TiO_2 sol (Figure 1(d)) exhibits six major reflection peaks at 2θ of 25.2°, 38.5°, 48.0°, 55.0°, 62.6°, and 70.3°, which can be well indexed to the (101), (112), (200), (211), (204), and (220) planes of anatase TiO_2 (JCPDS Card No. 21-1272), respectively [20].

3.2. Preparation of Cellulose/TiO_2/β-CD Composite Hydrogel. A cellulose solution with a concentration of 4.0 wt% was prepared according to the previous method. The cellulose/-TiO_2/β-CD composite hydrogel was synthesized with different concentrations of TiO_2 sol and β-CD in the cellulose solution with ECH as a cross-linking agent. The proper quantity of TiO_2 sol to the volume ratio of the cellulose solution is 5% (v/v). This ratio is adopted in the following results.

As plenty of hydroxyls in β-CD could react with ECH, the content of β-CD may impact the gelation properties of the composite hydrogel. The hydrogel was very soft when the β-CD content was below 3 wt%, and the hydrogel became harder as the β-CD content was higher than 4 wt%.

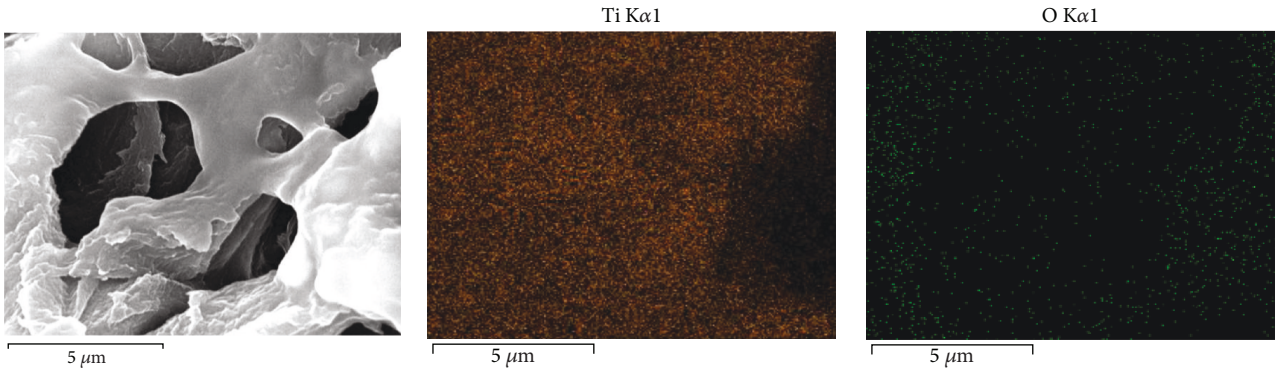
3.3. Characterizations of the Hydrogel Composite. The FTIR spectra of the obtained cellulose/TiO_2/β-CD hydrogel before and after cross-linking by ECH can be seen in Figure 2. The FTIR of β-CD showed strong absorption peaks at 3400 cm^{-1} (O-H), 2929 cm^{-1} (C-H), 1635 cm^{-1} (H-O-H bending), and 1156 cm^{-1} (C-O). In the spectra of ECH cross-linked with the cellulose/TiO_2/β-CD hydrogel, the strength of the absorption peaks at 2929 cm^{-1} was obviously diminished maybe by the decreases of the hydrophobic saturated C-H groups with the hydrogel cross-linked by ECH [21]. And the strengths of absorption peaks at 3400 and 1052 cm^{-1} for the hydroxyl groups and hydrogen bonds were obviously diminished, indicating that a lot of the hydroxyls both in cellulose and β-CD reacted with the ECH cross-linking agent that occurred in the cellulose/TiO_2/β-CD sample.

To investigate the influence of β-CD on the structure of the composite hydrogel, the surface morphology of cellulose/TiO_2 and cellulose/TiO_2/β-CD hydrogels were observed using SEM, and the result can be seen in Figure 3. Interpenetrated porous and network structures of both hydrogels were clearly observed in Figure 3. It can be observed that the network structure formed with β-CD was more dense, and the hydrogel formed without β-CD was looser. This phenomenon could be explained by the observation that β-CD in the composite hydrogel could actively participate in the cross-linking reaction, just as it was mentioned previously.

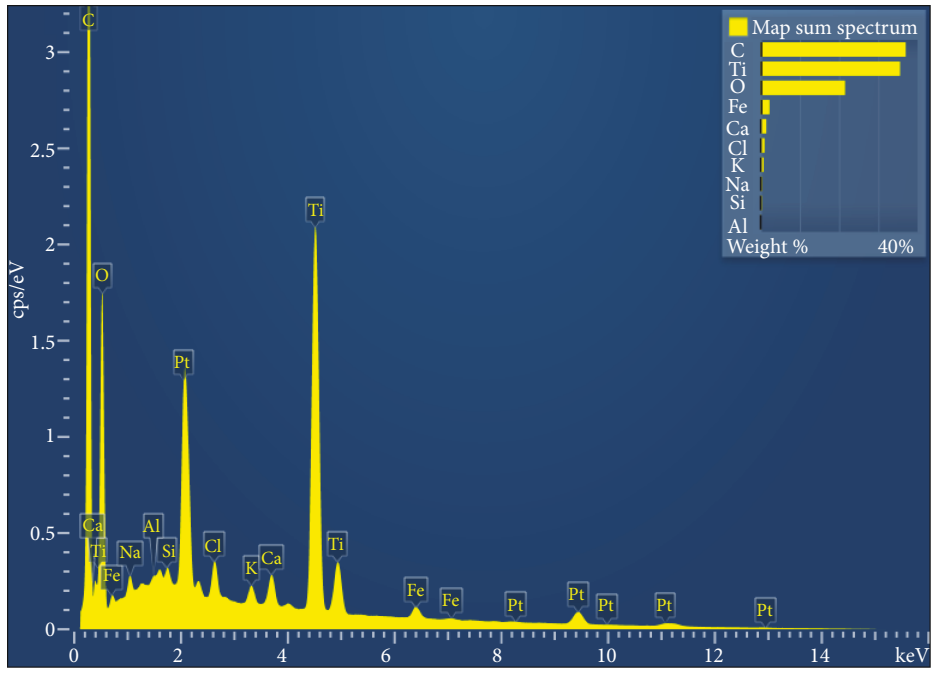
The pore diameters of the cellulose/TiO_2 hydrogel and cellulose/TiO_2/β-CD hydrogel ranged from 200 to 300 nm (Figure 3(a)) and 100 to 200 nm (Figure 3(b)), respectively, as it is feasible for a material with smaller pores to get a larger specific surface area, which facilitated the uptake of a large amount of solvent. Furthermore, the porous architecture of the material could also load all kinds of drugs and control drug release. Therefore, the cellulose/TiO_2/β-CD hydrogel might be a good carrier for sustained and controlled drug release.

In order to prove that TiO_2 was successfully introduced into the composite hydrogels and get the accurate data, the SEM-EDS and EDX mapping techniques were used to determine precisely the microstructure, component, and content of TiO_2 in Figure 4. The elemental EDX mapping of the sample clearly demonstrated the existence of Ti and O in the hydrogel with 4 wt% of β-CD, and the distribution of these elements was quite uniform and the TiO_2 content obtained is about 35 wt%. Similar results were obtained for different morphologies of the hydrogels with 3 wt% and 5 wt% of β-CD in Figures 4(e)–4(l). All data fully documented that TiO_2 was successfully introduced into the composite hydrogels.

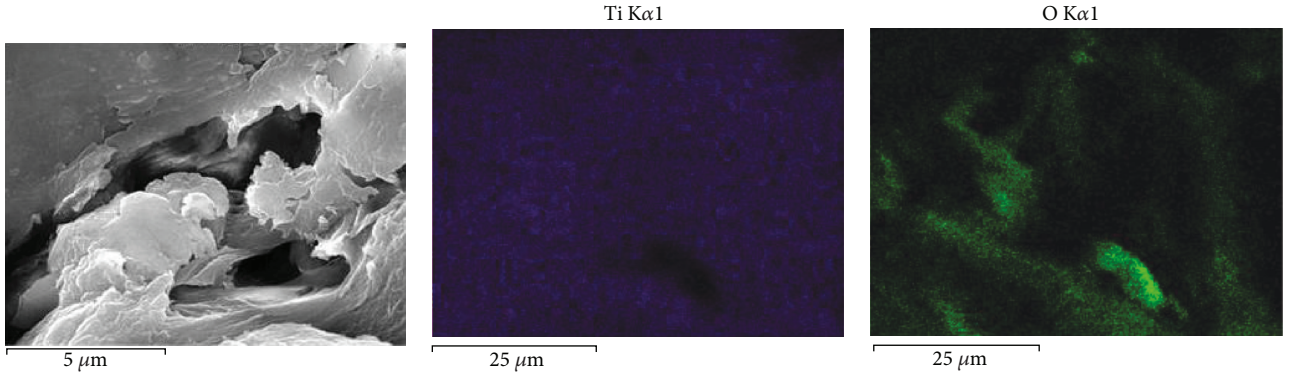
The hydrogels were further examined by TEM. Figure 5(a) is the TEM image of the cellulose/TiO_2 hydrogel without β-CD, and Figure 5(b) is the cellulose/TiO_2/β-CD hydrogel. It was observed that TiO_2 exhibits a sphere



(a) (b) (c)

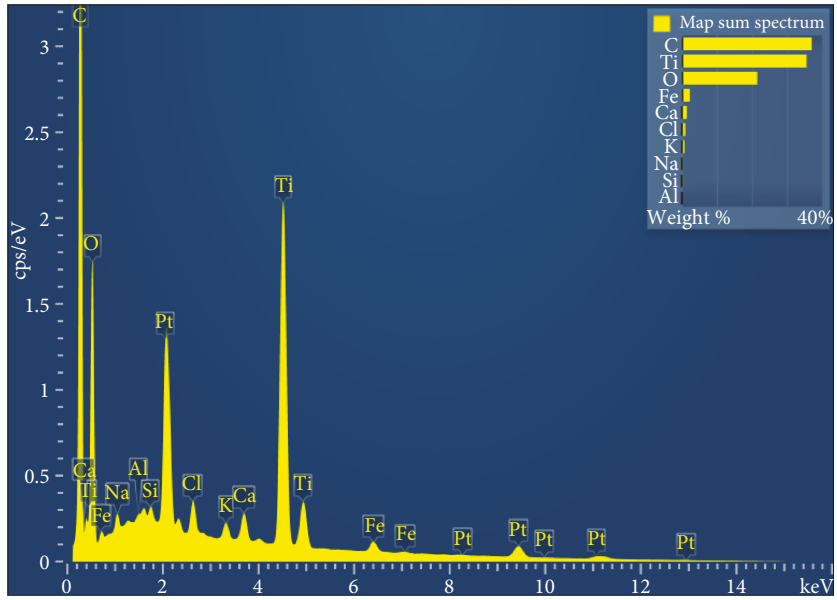


(d)

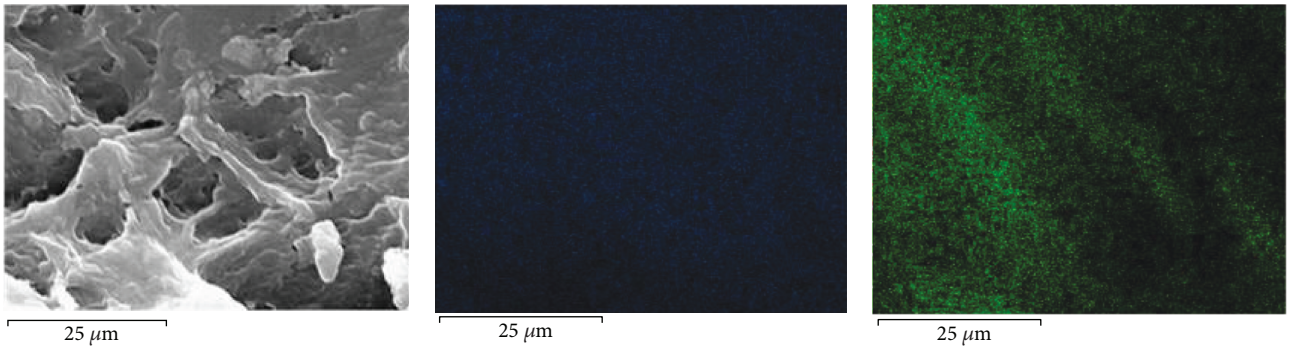


(e) (f) (g)

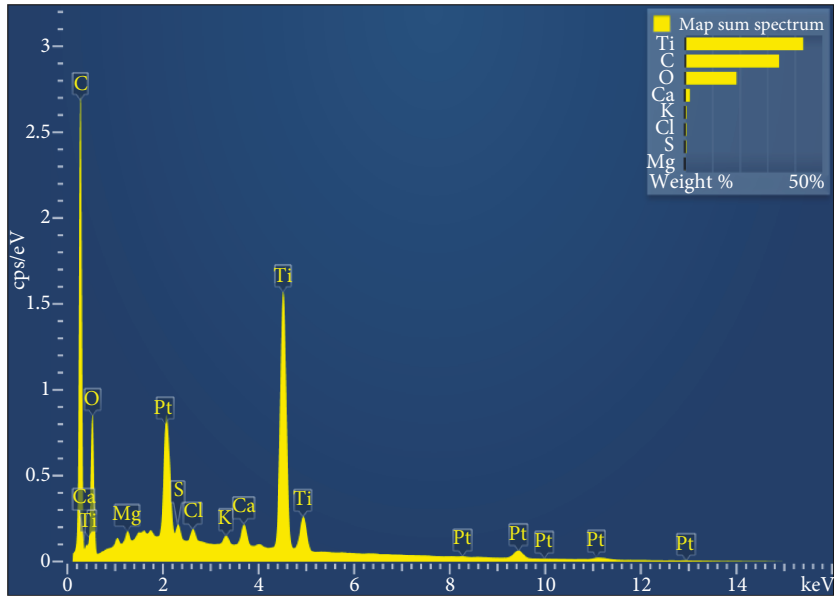
Figure 4: Continued.



(h)

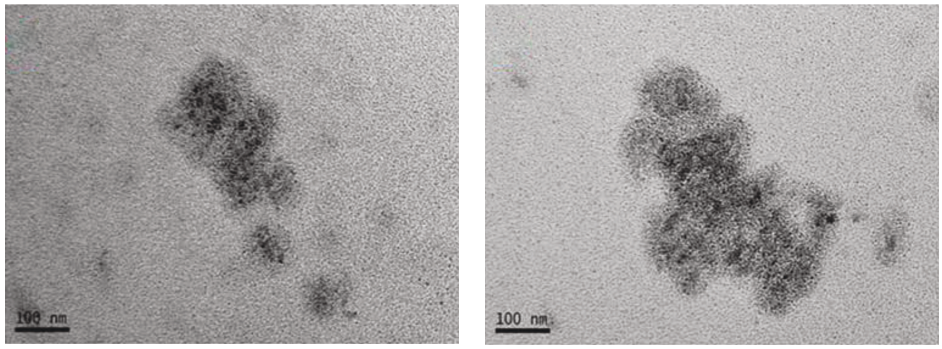


(i) (j) (k)



(l)

Figure 4: SEM-EDX mapping of the element distribution of hydrogel with 4 wt% of β-CD ((b) Ti, (c) O). Similar images of hydrogel with 3 wt% (e–h) and 5 wt% β-CD (i–l).



(a) (b)

Figure 5: TEM images of the cellulose/TiO_2 hydrogel (a) and the cellulose/TiO_2/β-CD hydrogel (b).

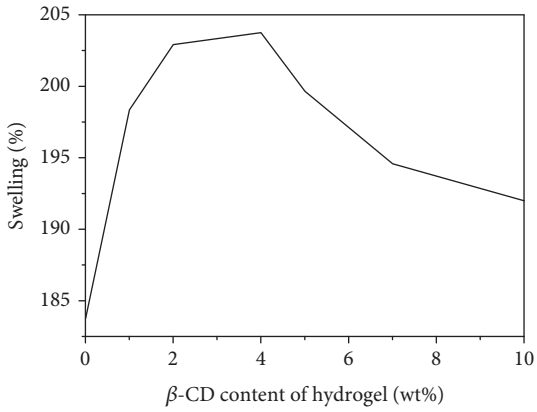


Figure 6: Effect of β-CD content on the swelling behavior of the hydrogel.

with a diameter less than 10 nm, and it is uniformly dispersed in both composite hydrogels without agglomeration. This demonstrates that cellulose, TiO_2, and β-CD were combined very well.

3.4. Swelling Properties. The equilibrium swelling degree is an important parameter to evaluate the property of the hydrogel [22]. Figure 6 shows the water uptake curves of the cellulose/TiO_2/β-CD hydrogel investigated with the β-CD content ranging from 1 wt% to 10 wt%; the sample was incubated in water for 24 h before investigating. It was found that as the amount of β-CD increased from 1 wt% to 4 wt%, the swelling percentage gradually increased. In particular, when a content of 4 wt% of β-CD was used in the hydrogel, the optimal swelling percentage is obtained, for which the swelling percentage level reaches the highest value of 203.6% among all investigated samples. This can be ascribed to the structure and properties of β-CD with a hydrophilic exterior. However, the further increase of the β-CD content in the hydrogel leads to the deterioration of their water uptake capacity. It should be due to an increased cross-linking degree upon increasing the dosage of β-CD. Thus, it can be concluded that grafting moderate amounts of β-CD onto the cellulose/TiO_2 hydrogel network may increase its swelling capacity.

3.5. Antibacterial Studies. The antibacterial activity of hydrogels was tested by the inhibition zone method against two representatives clinically relevant bacterial strains, namely *Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative) under natural light irradiation. In agar plate wells, cellulose/TiO_2 hydrogels with 0 wt%, 3 wt%, 4 wt%, and 5 wt% of β-CD were used (Figure 7). The inhibition zones of all the three samples were formed in the test, indicating the good antibacterial activities of hydrogels against *Staphylococcus aureus* and *Escherichia coli*.

The widths of the inhibition rings of the hydrogel with different concentrations of β-CD exposed to natural light are summarized in Table 1. With the increase of β-CD in the hydrogel, the width of the inhibition ring increases; the results indicated that the bacterial growth inhibition capacity of the hydrogels was increased along with the consistency of β-CD, owing to the addition of the hydrophobic inner cavity of β-CD and the acceleration of the charge transfer rate from the photoexcited TiO_2 to the electron acceptors.

Moreover, blank experiments of the cellulose/β-CD (4 wt%) hydrogel without TiO_2 were also carried. As expected, the cellulose/β-CD (4 wt%) hydrogel without TiO_2 did not show any antibacterial activity against either bacteria (Figure 8, 1). The antibacterial activity was increased with the increase of TiO_2 concentration (Figure 8, 2-4). The widths of the inhibition rings of the hydrogel with 1 mL, 2 mL, and 3 mL TiO_2 were 20.32, 22.52, and 24 mm, respectively. These results demonstrate that TiO_2 sol plays a vital role in enhancing the antibacterial activity.

TiO_2 has been reported to be a suitable material for antimicrobial activities and this effect of TiO_2 originates from the generation of reactive oxygen species (ROS) formed with light irradiation [23]. Photocatalytic antibacterial efficiency of TiO_2 is still not high due to the rapid recombination of the electron and hole. β-CD/TiO_2 could show a significant enhancement of the photocatalytic activity mainly because β-CD could trap the photogenerated holes resulting in the lower e^-/h^+ recombination [24]. An illustration of the possible mechanism for the formation of ROS and electron transfers is given in Figure 9.

To test the capability of TiO_2 in generating ROS such as singlet oxygen ($^1O_2$) and hydroxyl radical ($OH^\bullet$) in the cellulose/TiO_2/β-CD hydrogel under natural light irradiation, we used 1,3-diphenylisobenzofuran (DPBF) as a detector [25]. ROS was determined by the decomposition of DPBF correlated to the decay of the absorption at 410 nm

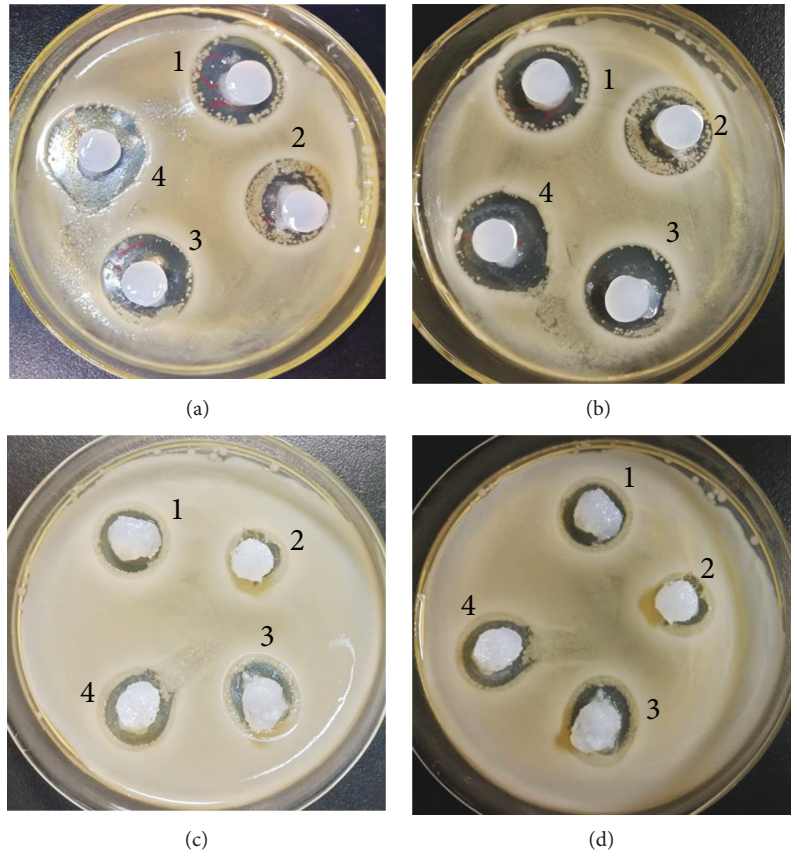


Figure 7: Antibacterial activity against *Staphylococcus aureus* and *Escherichia coli* with visible light illumination (a, b) and without light illumination (c, d). In each picture, 1-4 indicate the contents of β-CD at 0 wt%, 3 wt%, 4 wt%, and 5 wt%, respectively.

Table 1: The widths of the inhibition rings of the hydrogel with different concentrations of β-CD against *Staphylococcus aureus* and *Escherichia coli* exposed to natural light.

Content of β-CD (wt%)	The widths of the inhibition rings of the hydrogel (mm)	
	Staphylococcus aureus	*Escherichia coli*
0	19.48	17.59
3	19.50	18.40
4	21.14	19.52
5	22.59	21.89

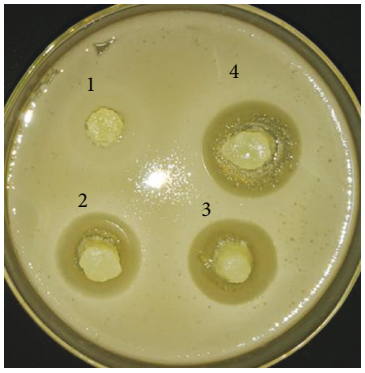


Figure 8: The cellulose/β-CD hydrogel with different concentrations of TiO_2.

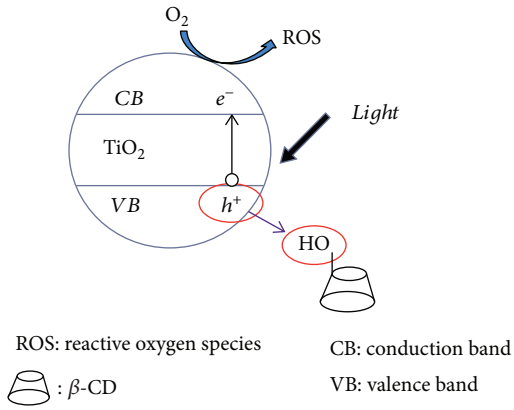


Figure 9: Proposed mechanism for the enhanced photocatalytic activity of β-CD/TiO_2.

(Figures 10(a) and 10(b)). Figure 10(a) plots the ROS output of the cellulose/TiO_2/β-CD hydrogel as a function of irradiation time. About 9.1×10^{-8} mol DPBF was completely decomposed in 2 h, reflecting a very high yield of ROS.

We also investigated the ability of the cellulose/β-CD hydrogel to regenerate ROS under the same experimental conditions; no effect of degradation of DPBF was detected even after 24 h. The ROS production measurements with different concentrations of β-CD under irradiation of light for 2 h was also performed (Figure 10(c)). The hydrogel had a

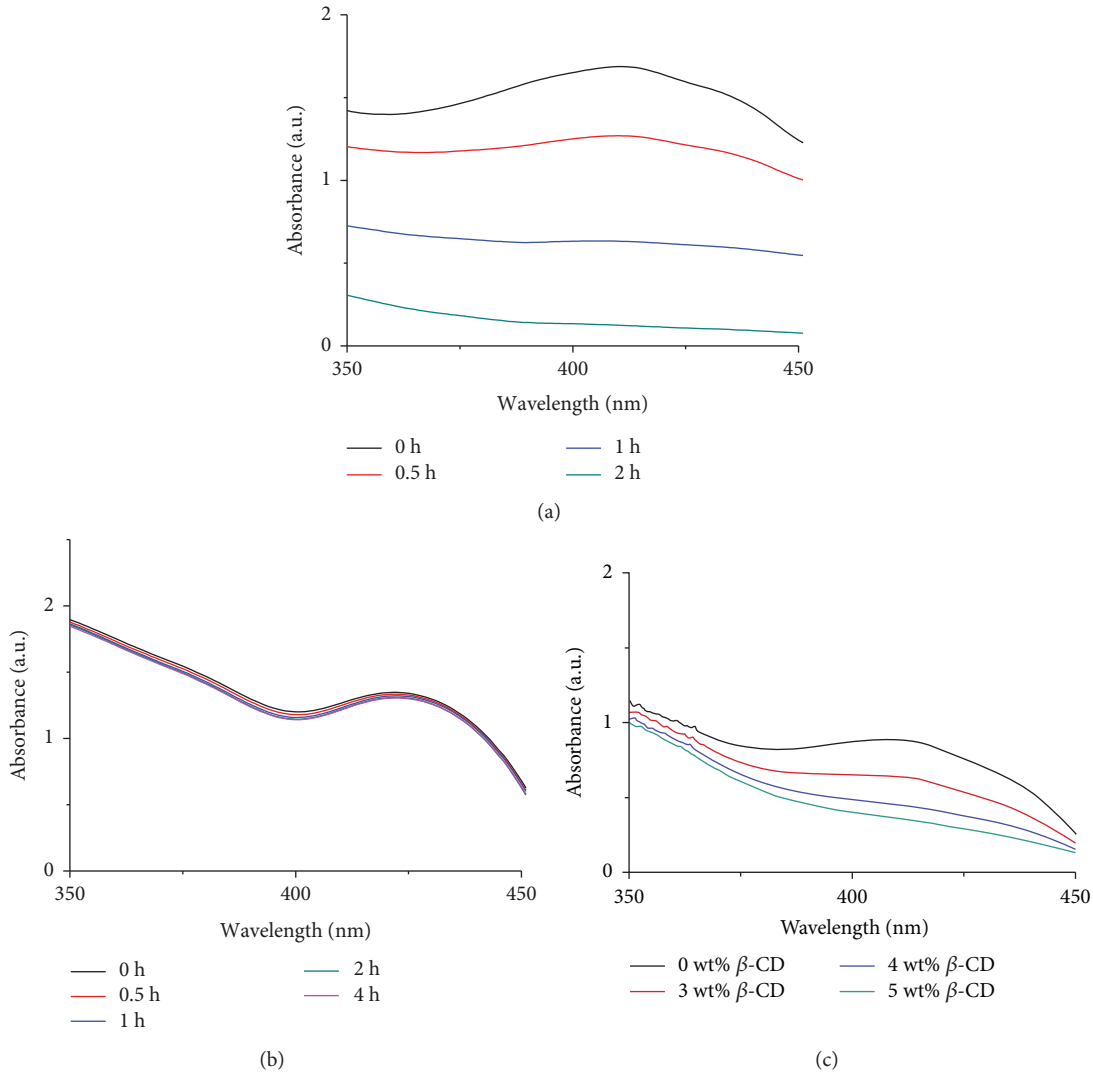


Figure 10: Decomposition of DPBF correlated with the decay of absorption at 410 nm: (a) cellulose/TiO_2/β-CD hydrogel, (b) cellulose/β-CD hydrogel, and (c) cellulose/TiO_2 hydrogel with different concentrations of β-CD under irradiation of light for 2 h.

significant ROS output with 5 wt% β-CD. The ROS output decreased slightly with 4 wt% β-CD and significantly decreased with 3 wt% and 0 wt%. This fact implies that β-CD could evidently increase the antimicrobial activity of the hydrogel.

3.6. Drug Encapsulation Efficiency (DEE). Based on the residual cavities of β-CD in the composite hydrogel, hydrophobic curcumin was chosen as a model drug to study the drug-loading property of the cellulose/TiO_2/β-CD hydrogel. In order to reach the encapsulation capacity saturation of curcumin, curcumin was encapsulated by the hydrogel in the dark for 48 h at room temperature (Table 2). The amount of the curcumin laden in the hydrogel can be determined by a UV-vis spectrophotometer at a wavelength of 440 nm. The curcumin encapsulation efficiency was determined to be 18.79 wt% for the sample of the hydrogel without the addition of β-CD. When the amount of β-CD increased to 5 wt%, the curcumin encapsulation efficiency went up to 22.77%. Hence, this hydrogel has the potential to be a drug carrier.

Table 2: Variation of DEE (%) with respect to change in content of β-CD.

Content of β-CD (wt%)	DEE (%)
0	18.78
1	24.22
2	23.74
3	20.71
4	21.68
5	22.77

The drug encapsulated within the hydrogel gets stabilized by hydrogen bonding between hydroxyl groups of drug molecules and hydroxyl groups of the hydrogel network and by hydrophobic interaction between the respective hydrophobic moieties of the drug and β-CD of the hydrogel. Since cross-linking between the polymeric chains is unfavourable for hydrogen bonding between the drug molecules and the hydrogel network, the hydrogel network without β-CD also

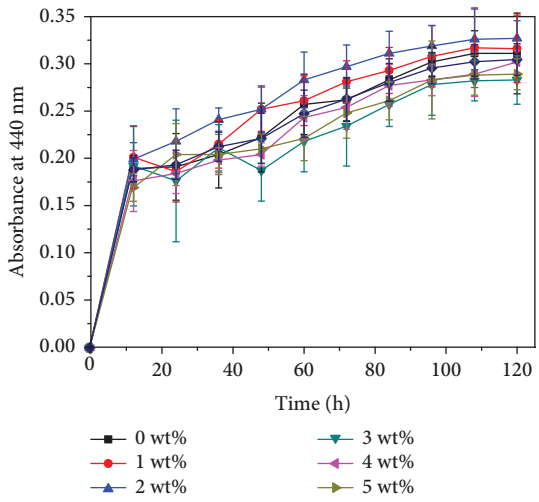


FIGURE 11: Cumulative release of curcumin from the cellulose/TiO_2/β-CD hydrogels at 37°C.

has an appreciable encapsulation capacity. The DEE of the hydrogels increase first with an increase in the β-CD concentration. With a further increase in β-CD concentration, two antagonistic phenomena seem to interplay with an increase in β-CD concentration: (a) an increase in the number of hydrophobic cavities within the hydrogel which support the drug encapsulation and (b) an increase in the potency of ECH-β-CD interactions which decreases the drug-β-CD interactions at the same time [26]. So the curcumin encapsulation efficiency was decreased to 20.71% with 3 wt% β-CD and went up to 22.77% with 5 wt% β-CD.

3.7. Release of Curcumin from Hydrogel. In vitro curcumin release kinetic of the curcumin-loaded cellulose/TiO_2/β-CD composite hydrogels was investigated. Curcumin can be detected by a UV-vis spectrophotometer at a wavelength of 440 nm in PBS buffer solution (pH 7.4). As a control group, curcumin released from the cellulose/TiO_2 hydrogel was also carried out to evaluate the role of β-CD in sustained-release progress.

As can be seen from the curcumin release kinetics (Figure 11), there was a fast release of curcumin at the initial stage, which was ascribed to the quick dissolution of curcumin from the surface of the hydrogel and diffusion out into the PBS medium. As swelling continued, curcumin could be slowly diffused out from the microporous hydrogel, which results in a more smooth release curve of curcumin. About 120 h later, the in vitro drug release reached equilibrium. As the concentration of β-CD was arranged in a sequence from 0 to 5.0 wt%, the drug cumulative release was arranged in the reverse order. At 10 h, about 38% of curcumin was released from the hydrogel with a concentration of 0 wt% β-CD. With an increase of β-CD content in the hydrogel, the cumulative release slowed down. The release of hydrogel-1 wt% (β-CD) after 10 h was 33%, while that of hydrogel-5 wt% (β-CD) was 23%. The increase in time consumption may be ascribed to the hydrophobic forces that played a role in the binding of curcumin and β-CD. This result demonstrates that curcumin encapsulated in the cavities of β-CD in the cellulose/TiO_2/β-CD hydrogel can be released through a long-term mechanism.

4. Conclusions

A novel cellulose/TiO_2/β-CD composite hydrogel with high antimicrobial activity and sustained drug release effect was developed. The as-prepared TiO_2 sol displays good photoantimicrobial ability under natural light irradiation. β-CD in this hydrogel can improve the performance of antibacterial activity and the sustained-release effect. The hydrogel could be used as a biomaterial for some hydrophobic drugs which could complex with β-CD. Hence, the hydrogel composite system has a potential application for biological materials.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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References

[1] X. Y. Qiu and S. W. Hu, ""Smart" materials based on cellulose: a review of the preparations, properties, and applications," *Materials*, vol. 6, no. 3, pp. 738–781, 2013.

[2] N. Sun, T. Wang, and C. Liu, "Preparation, characterization and photocatalytic study of wood-flour/β-cyclodextrin/TiO_2 hybrid composite," *Wood Science and Technology*, vol. 50, no. 6, pp. 1243–1260, 2016.

[3] J. Nie, B. Pei, Z. Wang, and Q. Hu, "Construction of ordered structure in polysaccharide hydrogel: A review," *Carbohydrate Polymers*, vol. 205, pp. 225–235, 2019.

[4] S. P. Lin, H. N. Kung, Y. S. Tsai, T. N. Tseng, K. D. Hsu, and K. C. Cheng, "Novel dextran modified bacterial cellulose hydrogel accelerating cutaneous wound healing," *Cellulose*, vol. 24, no. 11, pp. 4927–4937, 2017.

[5] C. Boyer, L. Figueiredo, R. Pace et al., "Laponite nanoparticle-associated silated hydroxypropylmethyl cellulose as an injectable reinforced interpenetrating network hydrogel for cartilage tissue engineering," *Acta Biomaterialia*, vol. 65, pp. 112–122, 2018.

[6] H. X. Jiang, K. Tovar-Carrillo, and T. Kobayashi, "Ultrasound stimulated release of mimosa medicine from cellulose hydrogel matrix," *Ultrasonics Sonochemistry*, vol. 32, pp. 398–406, 2016.

[7] N. Zainuddin, I. Ahmad, H. Kargarzadeh, and S. Ramli, "Hydrophobic kenaf nanocrystalline cellulose for the binding

of curcumin," *Carbohydrate Polymers*, vol. 163, pp. 261–269, 2017.

[8] L. Zhang, J. Zhou, and L. Zhang, "Structure and properties of β-cyclodextrin/cellulose hydrogels prepared in NaOH/urea aqueous solution," *Carbohydrate Polymers*, vol. 94, no. 1, pp. 386–393, 2013.

[9] L. Gabrielyan, A. Hovhannisyan, V. Gevorgyan, M. Ananyan, and A. Trchounian, "Antibacterial effects of iron oxide (Fe_3O_4) nanoparticles: distinguishing concentration-dependent effects with different bacterial cells growth and membrane-associated mechanisms," *Applied Microbiology and Biotechnology*, vol. 103, no. 6, pp. 2773–2782, 2019.

[10] M. Bhushan, Y. Kumar, L. Periyasamy, and A. K. Viswanath, "Facile synthesis of Fe/Zn oxide nanocomposites and study of their structural, magnetic, thermal, antibacterial and cytotoxic properties," *Materials Chemistry and Physics*, vol. 209, pp. 233–248, 2018.

[11] L. P. Liu, X. N. Yang, L. Ye et al., "Preparation and characterization of a photocatalytic antibacterial material: graphene oxide/TiO_2 bacterial cellulose nanocomposite," *Carbohydrate Polymers*, vol. 174, pp. 1078–1086, 2017.

[12] P. Kokila, M. Rameshbabu, and V. Senthil Kumar, "Antibacterial and phitocatalytic activity of pomegranate rind extract doped TIO_2 nanoparticles by sol-gel method," *International Journal of Development Research*, vol. 7, no. 1, pp. 10947–10950, 2017.

[13] I. Willner, Y. Eichen, and B. Willner, "Supramolecular semiconductor receptor assemblies: improved electron transfer at TiO_2-β-cyclodextrin colloid interfaces," *Research on Chemical Intermediates*, vol. 20, no. 7, pp. 681–700, 1994.

[14] K. M. Salleh, S. Zakaria, M. S. Sajab et al., "Chemically cross-linked hydrogel and its driving force towards superabsorbent behaviour," *International Journal of Biological Macromolecules*, vol. 118, pp. 1422–1430, 2018.

[15] I. M. Garnica-Palafox, F. M. Sánchez-Arévalo, C. Velasquillo et al., "Mechanical and structural response of a hybrid hydrogel based on chitosan and poly(vinyl alcohol) cross-linked with epichlorohydrin for potential use in tissue engineering," *Journal of Biomaterials Science, Polymer Edition*, vol. 25, no. 1, pp. 32–50, 2014.

[16] L. Zhang, J. Cai, and J. Zhou, "Novel solvent compounds and its preparation and application," 2005, CN 03128386.1.

[17] T. S. Anirudhan, P. L. Divya, and J. Nima, "Synthesis and characterization of novel drug delivery system using modified chitosan based hydrogel grafted with cyclodextrin," *Chemical Engineering Journal*, vol. 284, pp. 1259–1269, 2016.

[18] Y. M. Wang, J. Wang, Z. Y. Yuan et al., "Chitosan cross-linked poly(acrylic acid) hydrogels: drug release control and mechanism," *Colloids and Surfaces B: Biointerfaces*, vol. 152, pp. 252–259, 2017.

[19] V. S. Ghorpade, A. V. Yadav, and R. J. Dias, "Citric acid cross-linked β-cyclodextrin/carboxymethylcellulose hydrogel films for controlled delivery of poorly soluble drugs," *Carbohydrate Polymers*, vol. 164, pp. 339–348, 2017.

[20] H. Zhang, R. H. Shi, A. J. Xie et al., "Novel TiO_2/PEGDA hybrid hydrogel prepared in situ on tumor cells for effective photodynamic therapy," *ACS Applied Materials & Interfaces*, vol. 5, no. 23, pp. 12317–12322, 2013.

[21] N. Sun, T. Wang, and X. Yan, "Synthesis and investigation of a self-assembled hydrogel based on hydroxyethyl cellulose and its *in vitro* ibuprofen drug release characteristics," *RSC Advances*, vol. 7, no. 16, pp. 9500–9511, 2017.

[22] X. L. Hu, C. Sun, B. Peng et al., "Swelling property of PVA hydrogels with different concentration and specifications and its influencing factors," *International Journal of Clinical and Experimental Medicine*, vol. 9, no. 2, pp. 708–716, 2016.

[23] D. Yang, G. X. Yang, Q. Q. Sun et al., "Carbon-dot-decorated TiO_2nanotubes toward photodynamic therapy based on water-splitting mechanism," *Advanced Healthcare Materials*, vol. 7, no. 10, article 1800042, 2018.

[24] P. Sakthivel and P. Velusamy, "Modification of the photocatalytic performance of various metal oxides by the addition of β-cyclodextrin under visible light irradiation," *Journal of Water Process Engineering*, vol. 16, pp. 329–337, 2017.

[25] J. Y. Zhang, S. Chen, P. Wang et al., "$NaYbF_4$ nanoparticles as near infrared light excited inorganic photosensitizers for deep penetration in photodynamic therapy," *Nanoscale*, vol. 9, no. 8, pp. 2706–2710, 2017.

[26] M. Maswal, O. A. Chat, and A. A. Dar, "Rheological characterization of multi-component hydrogel based on carboxymethyl cellulose: insight into its encapsulation capacity and release kinetics towards ibuprofen," *Colloid & Polymer Science*, vol. 293, no. 6, pp. 1723–1735, 2015.