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Photocrosslinkable tissue adhesive based on dextran

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ABSTRACT

A biodegradable tissue adhesive was prepared from dextran urethane (Dex-U), which could be photocrosslinked under the UV irradiation, and steadily adhere to surface of gelatin and mouse skin, which simulate the human tissue. The structures of above Dex-U were characterized by FTIR, ^{1}H NMR spectroscopy and XRD. The adhesion properties of result products was evaluated by lap-shear test and burst pressure test. The highest adhesion strength and burst pressure could reach to 2.99 MPa and 35 mmHg, respectively. The photopolymerization process of Dex-U was monitored by real time infrared spectroscopy (RTIR), and the surface tension of Dex-U solution was tested by du Nouy Ring method. The cytotoxicity of Dex-U also was evaluated. The relationship between all above properties and degree of substitution of Dex-U was assessed. The adhesive strength of Dex-U is significantly higher than that of fibrin glue. The obtained products present the potential to serve as tissue adhesive in medical area in the future.

1. Introduction

Dextran is a natural polymer of glucose, which consisted of predominantly of linear α-1,6-glucosidic linkage with some degree of branching via 1,3 linkage (Mehvar, 2000). It has good biocompatibility and biodegradability in physical environment. It has been used in the medical and biomedical field for more than 60 years such as plasma volume expansion, antithrombolytic agent, and carrier for drugs and proteins (Lloyd, Kennedy, Methacanon, Paterson, & Knill, 1998; Schmedlen, Masters, & West, 2002; Sun & Chu, 2006; Wondraczek, Elschner, & Heinze, 2011). Recently, dextran was widely used to bioadhesive field (Kim & Chu, 2000).

Tissue adhesives are increasingly applied in the fields of surgeries, trauma and other medical area. They present the potential to replace traditional surgical sutures to become novel traumatic closure method with the advantages of fast closure process, less pain, promotion of wound healing and elimination of suture removal (Lauto et al., 2007). For the purpose of applying in the human body, the tissue adhesives must fulfill some clinical requirements. It could firmly agglutinate the wound of tissue until the wound cicatrized. The adhesive before and after curing, even after degradation, must be biocompatible (Nivasu, Reddy, & Tammishetti, 2003). And it does not cause inflammation or other toxicity issues. Commercially available bioadhesive, such as alkyl cyanoacrylate (Kaplan & Baysal, 2005), glutaraldehyde glues (Hruby et al., 2006) and fibrin glue, often require a choice between adhesion strength and biocompatibility. Cyanoacrylate could firmly conglutinate the tissue, but the products of degradation, formaldehyde and cyanoacetate, could result in serious tissue damages even induce cancers. The fibrin glue was more biocompatible, but inadequately adhered to tissue and introduced a risk of infectious transmission and was difficultly acquired (Ryou & Thompson, 2006; Spotnitz, 2001). The glutaraldehyde glues also induced tissue toxicity and cell damage.

In recent years, there has been a great interest in developing nontoxic, biodegradable and biocompatible tissue adhesives in order to overcome above drawbacks. Karikari, Edwards, Mecham, and Long (2005) has used Star-Shaped Poly(D,L-lactide) reacted with either methacrylic anhydride or 2-isocyanatoethyl methacrylate to yield PDLLA bioadhesive with photocrosslinkable methacrylate end groups. Ferreira, Coelho, and Gil (2008) used low molecular weight hydroxyl end functionalized PCL diol reacted with 2-isocyanatoethyl methacrylate to form a macromer that was crosslinked via UV irradiation. Because of its good biocompatibility, biodegradability in various organs of human body, and a lot of reactive hydroxyl groups in the dextran molecules in favor of many chemical modifications, the dextran was widely applied in the field of bioadhesive system. Artzi, Shazly, Baker, Bon, and Edelman (2009a) and Artzi et al. (2009b) had prepared PEG amine/dextran aldehyde composite, which adhered far better than fibrin glue and had low tissue toxicity. An amine functionalized succinyl chitosan and an oxidized dextran formed a series of hydrogel, which showed excellent haemostatic properties (Liu et al., 2009).

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In this work, we described the preparation of a series of photocrosslinkable adhesive composed of 2-isocyanatoethyl methacrylate (IEMA) chemically modified onto dextran polymer backbone. These dextran urethanes were phtocrosslinked into thin gel samples and their photocrosslinkable kinetics, surface tension, adhesion strength, burst pressure and in vitro biocompatibility were characterized.

2. Methods

2.1. Materials

Dextran ($\overline{M}_w$ 20 kDa) was purchased from Sinopharm Chemical Reagent Co. Ltd. (Shanghai, China). 2-Isocyanatoethyl methacrylate (IEMA) was purchased from Ginray Chemical Reagent Co. Ltd. (Shanghai, China). Dibutyltion dilaurate (DBTL) as catalyst was purchased from Aladdin Reagent Co. (Shanghai, China). Photoinitiator 2-hydroxy-1-[4-(hydroxyethoxy) phenyl]-2-methyl-1-propanone (Darocur 2959) was supplied from Ciba-Geigy Chemical Co. (Tom River, NJ, USA). Sodium chloride and dimethyl sulfoxide (extra dry DMSO, water <50 ppm) were all obtained from Beijing Chemical Agent Co. (Beijing, China).

2.2. Preparation of urethane dextran derivatives (Dex-U)

Eight grams of dextran, 0.05 g of DBTL and 250 mL of DMSO was added into a three-necked flack equipped with stirrer, thermometer, and dropping funnel, under 40 °C and nitrogen protection. Then, 7.5 g of IEMA dissolved in 80 mL DMSO was dropped into above mixture within 3 h. The FTIR was used to monitor the progress of reaction, when the absorption peak at 2236 cm^{-1} disappeared in the FTIR spectrum of the reaction solution, which meant that all the –NCO groups of IEMA has already completely reacted with hydroxyl groups of dextran. Then the solution was poured into 800 mL of saturated sodium chloride solution with vigorous stirring. The white precipitate was washed and filtrated with distilled water for three times to remove DMSO and catalyst DBTL. Then the urethane methacrylated dextran was obtained after lyophilization. The different degrees of substitution (DS) of Dex-U could be got by adjusting molar ratio of IEMA to the hydroxyl groups of dextran.

2.3. Preparation of photocrosslinkable gel

The photoinitiator 2959 was added into the Dex-U/DMSO solution. The solution was injected into a round mold consisting of two glass microslides separated by a spacer. The solution was irradiated under UV light source (320–480 nm, EXFOlite, EFOS Corporation, Mississauga, Canada), and the distances between the dip of the light guide and the sample was 44 mm, fixed this distance, the light intensity of UV light source was adjusted to 5, 10, 15, 30 and 50 mW/cm^2. The solution was irradiated for 10 min to form circular samples (diameter 1 cm, thickness 2 mm).

2.4. FTIR spectra measurement

FTIR spectra were recorded on a Nicolet 5700 instrument (Nicolet 5700 instrument, Thermo Company, USA). Samples were prepared as KBr pellet and scanned against a blank KBr pellet background at wavenumber ranging from 4000 to 650 cm^{-1} with resolution of 4.0 cm^{-1}. The polymerization process was monitored by using series real time infrared spectroscopy.

The double bond conversion (DC) of the gels was monitored by real-time near FTIR with the resolution of 4 cm^{-1} (Nicolet 5700, Thermo Electron, USA, equipped with an extended range KBr beam-splitter and an MCT/A detector). A horizontal transmission accessory (HTA) was designed to enable mounting of samples in a horizontal orientation for FTIR measurements. The change of C–H absorbance peak area (C–H, belong double bond) from 6110 to 6210 cm^{-1} in the near-IR range was correlated to the double bond conversion. For each sample, the series FTIR runs were repeated three times, and in most case, the error of double bond conversion was less than 2% (Zhou et al., 2008).

2.5. ^1H NMR

^1H NMR spectra of Dex-U were obtained with a Bruker AV (Bruker, Germany) spectrometer at 600 MHz at room temperature using deuterated DMSO as solvent.

2.6. Solubility test

The solubility of dextran and its derivatives Dex-U were evaluated in different kinds of solvents at the concentration of 5 mg/mL at 25 °C.

2.7. X-ray diffraction (XRD) study

XRD patterns of the samples were recorded on an X-ray diffractometer (D/Max 2500VB2+/Pc, Rigaku, Japan) with Cu Kα characteristic radiation (wavelength 0.154 nm) at a voltage of 40 kV and a current of 50 mA. The scanning rate was 5°/min and the scanning scope of 2θ was from 5° to 50° at room temperature.

2.8. Determination of surface tension

The surface tension of Dex-U solution was measured by du Nouy Ring method. The platinum ring slightly immerged 5 mm below the fluid to be measured. As the ring was slowly raised, the liquid membrane formed in the ring. When the platinum ring get out of liquid membrane, the surface tension of the solution was recorded.

2.9. Measurement of adhesion strength

For simulating the living tissue, 20 wt% gelatin solution was uniformly spread on the surface of glass. The dimension of one piece of glass was 5 mm × 20 mm × 50 mm. After drying at 60 °C for 30 min, there was a homogenous sheet of gelatin on the surface of glass. Then, the pieces of glass were overlapped in 10 mm in which the Dex-U solution was spread and the area of bonding was 10 mm × 20 mm. They were irradiated by UV light under light intensity 30 mW/cm^2 for 10 min. The Dex-U was crosslinked between the gelatin sheets. The glass samples after UV curing were tested by using a universal testing machine (Model 1185, Instron, USA) with a crosshead speed of 5 mm/min at room temperature. Five samples were measured for each experiment, and the average of these values was recorded.

2.10. Measurement of burst pressure

The substrate used for test was circular mouse skin (3 cm diameter), which soaked in the saline in the refrigerator to preserve before test. The mouse skin with a 3 mm diameter in the centre was flat placed on the surface of PTFE sheet, and 0.5 mL of Dex-U solution spread 10 mm diameter circular area to cover the hole in the centre of mouse skin, then Dex-U solution crosslinked under irradiation of UV light. The fixed mouse skin slice was settled between the metal molds, which formed a cavum to charge with compressed air. Compressive air was injected into mold slowly until the adhesion failed. The peak air pressure of fixed mouse skin bore in the whole progress was recorded as the burst strength of the adhesive.

2.11. Cytotoxicity assays

The prepared Dex-U gel samples soaked in the 250 mL phosphate buffered saline (PBS pH 7.4) for 24 h before sterilization with highly compressed steam for 15 min and placed in 24-well culture plate filled with extraction media (RPMI1640) at 37 °C for 48 h. The extraction ratio was 1.25 mg/mL. Then, the samples were removed, and the extractions were obtained for cytotoxicity assays. L-929 cells were seeded in wells of a 96-well plate at a density of 10^3 cells per well. After incubated for another 24 h, the culture medium was removed and replaced with the as-prepared extraction medium, then incubated for another 24, 48 h and 72 h, then 100 μL methylthiazolydiphenyl-tetrazolium bromide (MTT) solution was added to each well. After 4 h incubation at 37 °C, 200 μL of DMSO was added to dissolve the formazan crystals. The dissolved solution was swirled homogeneously about 10 min by the shaker. The optical density of the formazan solution was detected by an ELISA reader (Multiscan MK3, Labsystem Co., Finland) at 490 nm. For the reference purpose, cells were seeded to medium containing 0.64% phenol (positive control) and a fresh culture medium (negative control) with same seeding condition, respectively. Each assay was performed six times.

The prepared circular samples (diameter 1 cm, and thickness 2 mm) soaked in the 250 mL phosphate buffer solution (PBS pH 7.4) for 24 h before sterilization with highly compressed steam for 15 min. Then the samples were transferred to the 24-well plate after being washed with PBS. 1 mL of L929 suspension with 1.5×10^4 cell/mL was seeded on the samples. After 48 h of culture, cellular constructs were harvested, rinsed twice with PBS to remove non-adherent cells. Then the samples were observed by optical microscope (the magnification of 400×).

3. Results and discussion

3.1. Structure analysis of Dex-U

The FTIR spectra of dextran and Dex-U were shown in Fig. 1(a). The broad band at around 3443 cm^{-1} attributed to $-NH_2$ and –OH stretching vibration, and was sharpen along with the DS increasing. New peaks at 1720 cm^{-1} assigned to the C=O, at 1525 cm^{-1} assigned to C–N stretching and N–H bending, and peaks at 1637 and 814 cm^{-1} assigned to C=C double bonds which were brought by the reaction between IEMA and the hydroxyl groups of dextran. With the increase of IEMA amount in the process of Dex-U preparation, the relative absorbance intensities of peaks at 814, 1637 and 1720 cm^{-1} attributed to introduction of IEMA depended upon the degree of substitution (DS) values. The broad peak resulted from hydrogen bond of hydroxyl group at 3443 cm^{-1} was sharpened with the increase of DS, which meant that the introduction of IEMA destroyed the hydrogen bond among hydroxyl groups of dextran molecules. When the DS reached to 3, the sharp peak at 3343 cm^{-1} assigned to N–H indicated that hydrogen bond of hydroxyl group disappeared, which indicated that all hydroxyl groups of dextran had completely reacted with –NCO groups of IEMA. Other prominent peaks at 2920 and 2850 cm^{-1} were assigned to the asymmetrical and symmetrical bending vibrations of methylene groups.

The ^{1}H NMR spectra of the dextran and Dex-U-1 in deuterated DMSO were shown in Fig. 1(b). A singlet at 4.89 ppm assigned to anomeric carbon of the α-1,6 linkages proton (H^1). The typical multiplet peaks range from 3.1 to 3.8 ppm were assigned to the other protons of the glucopyranosyl ring. In the spectrum of Dex-U, new signals at 5.65, 6.05 ppm (H^a, the double bond protons) and 1.87 ppm (H^b, methyl protons) were clearly observed. According the ^{1}H NMR spectra, the DS of Dex-U, which

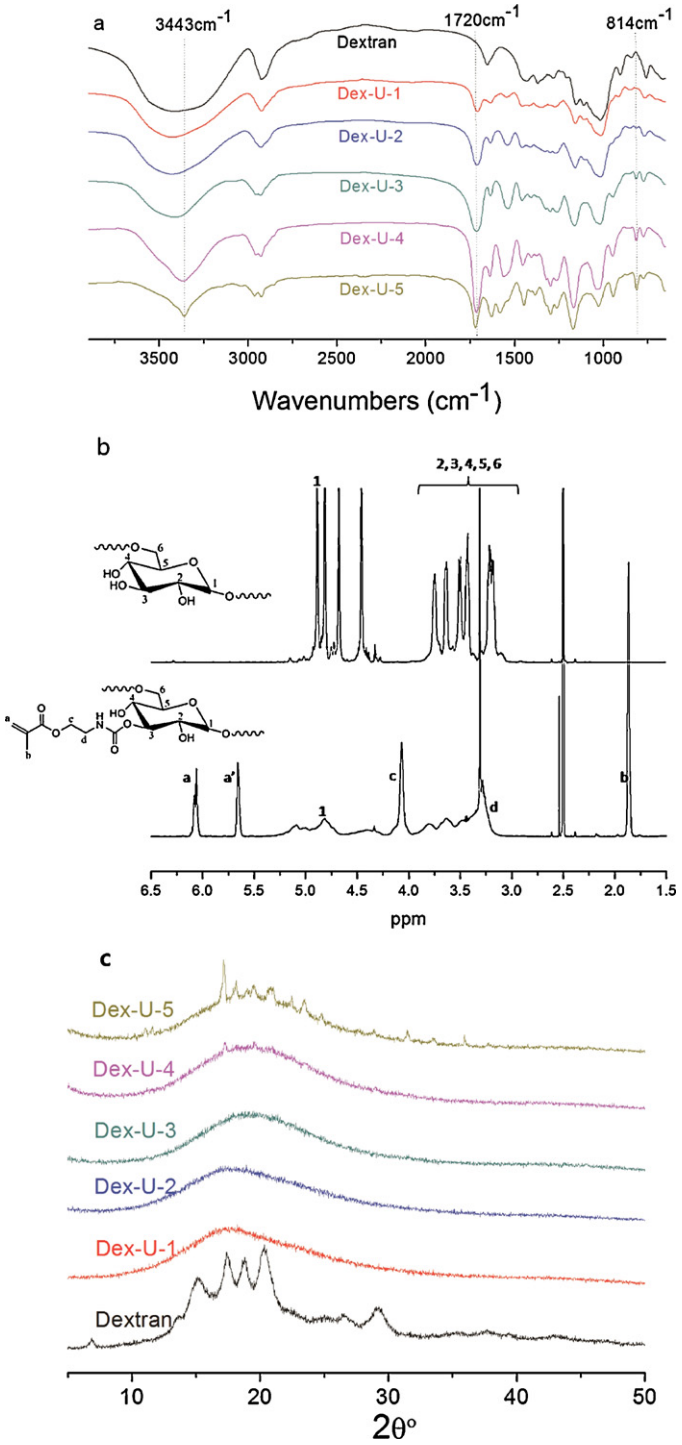

Fig. 1. (a) The FTIR spectra of dextran and Dex-U; (b) ^{1}H NMR spectra of dextran and Dex-U; (c) XRD patterns of dextran and Dex-U with different DS.

was adjusted by molar ratio of IEMA to the hydroxyl groups of dextran, was calculated as A_1/A_a, in which A_a was the area of proton of double bond (H^a), and A_1 was the average area of proton of anomeric carbon of the α-1,6 linkages proton (H^1) (Yin, Wang, Han, & Nie, 2010). The Dex-U with five different DS was obtained as shown in Table 1.

The XRD pattern evaluated the crystalline degree of dextran and Dex-U with different DS (Fig. 1(c)). The dextran showed a series characteristic peaks at 2θ regions of 15.1, 17.5, 18.8, 20.5 and 29.5°, which indicated that the dextran has a high crystalline degree. The

Table 1
Degree of substitution of Dex-U.

	Dex-U-1	Dex-U-2	Dex-U-3	Dex-U-4	Dex-U-5
Molar ratio of –NCO of IEMA:–OH of dextran	0.2	0.6	1.3	2.3	3.2
A_a/A_1	1/8.7	1/2.08	1/0.93	1/0.47	1/0.33
DS	0.1	0.5	1.1	2.1	3.0

XRD patterns of Dex-U were significantly different from the neat dextran. The characteristic peaks of dextran disappeared as the dextran reacted with IEMA. The Dex-U with DS range from 0.1 to 1.1 was almost amorphous, which illuminated the crystalline structure of dextran were completely destroyed. The introduction of IEMA hindered the formation of inter- and intra-molecular hydrogen bonds after isocyanate groups reacted with hydroxyl groups. As the degree of substitution increased to 3, the arrangement of Dex-U molecule chains was improved, and the new peaks were formed at regions from 17.1 to 24.8°, which indicated that the new crystalline structure of Dex-U was formed.

3.2. Solubility analysis

Table 2 listed the solubility of dextran and Dex-U with different DS in different solvents. Dextran only dissolved in water and DMSO, and the Dex-U could dissolve in many solvents such as methanol, acetone and chloroform. When the DS of Dex-U was changed, the variety of solvents also changed. This attributed to the introduction of hydrophobic groups and long carbon chain of IEMA and reduction of hydrophilic hydroxyl groups of dextran. Dex-U-5 even could be dissolved in methylene chloride.

3.3. Photocrosslinking of Dex-U

When the Dex-U solution was crosslinked by UV irradiation, the unsaturated C=C double bonds of Dex-U stared to polymerize. In the FTIR spectra, the area of absorption peak at 6110–6210 cm^{-1} attributed to C=C bond of methacrylate rapidly decreased. The effect of Dex-U concentration on the polymerization kinetics was shown in Fig. 2(a). The max conversion rate and eventual conversion of methacylate double bonds decreased with the increase of concentration for Dex-U-3. This may be due to the high concentration of Dex-U-3 could increase the density of methacylate double bonds and viscosity of the solution, which could hinder the dispersion of unreacted double bonds. The effect of concentration of photoinitiator D-2959 was performed in Fig. 2(b). When the concentration of photoinitiator D-2959 was raised from 0.5 wt% to 2 wt%, both the max conversion rate and eventual conversion of methacylate double bonds was improved, which resulted from the more free radicals by D-2959 under UV light. But the further increase of the concentration of photoinitiator made the max conversion rate and eventual conversion reached to be constant. This may be attributed to light shielding effect, which was induced by combination termination of excessive free radicals produced by D-2959. As shown in Fig. 2(c), both the max conversion rate and eventual conversion of methacylate double bonds increased with the increase of UV light intensity from 5 mW/cm^2 to 50 mW/cm^2, which resulted from the more free radicals by D-2959 under higher UV light intensity. But the high light intensity could bring on cell damage of bioadhesive, light intensity of 30 mW/cm^2 was selected to insure the rapid polymerization and low cytotoxicity. Considered all above factors, the best phtocrosslinkage conditions were set 50 wt% of Dex-U concentration, 2 wt% of photoinitiator D-2959 and 30 mW/cm^2 of light intensity.

The influence of DS of Dex-U on photocrosslinking process was showed in Fig. 2(d), it could be observed that the higher max conversion rate of methacylate double bonds of Dex-U-3 and Dex-U-4 than that of Dex-U-5. This may be attributed to autoacceleration induced by lower viscosity of Dex-U-3 and Dex-U-4 than that of Dex-U-5. All eventual conversion of Dex-U/DMSO solution reached around 80% within 5 min. But the eventual conversion of Dex-U-5 was slightly higher than that of Dex-U-3 and Dex-U-4. The higher density of crosslinkage hindered the movement of residual methacylate double bonds in late stage of photocrosslinkage, which decreased the eventual of methacylate double bonds. Because of the low density of double bond in the solution, it was hardly detected the peak near 6110–6210 cm^{-1} of the Dex-U-1and Dex-U-2.

3.4. Determination of surface tension

When adhesive adhered to some substrate, one of the most important parameters was surface tension of adhesive, which could affect the dispersion of adherend and steady performance after crosslinking. The surface tension of adhesive must be equal to or less than the one of adherend. Then, the adhesive could spread and

Table 2
Solubility of dextran and Dex-U in various solvents.

	Water	DMSO	Ethylene glycol	Methanol	Ethanol	DMF	Acetone	Dioxane
Dextran	√	√	×	×	×	×	×	×
Dex-U-1	√	√	√	×	×	√	×	×
Dex-U-2	√	√	√	×	×	√	×	×
Dex-U-3	×	√	√	√	×	√	×	√
Dex-U-4	×	√	√	√	×	√	√	√
Dex-U-5	×	√	×	√	×	√	√	×
	Chloroform	*i*-Propanol	Ethyl acetate	Tetrahydrofuran	Methylene chloride	Toluene	Cyclohexane	Petroleum ether
Dextran	×	×	×	×	×	×	×	×
Dex-U-1	×	×	×	×	×	×	×	×
Dex-U-2	×	×	×	×	×	×	×	×
Dex-U-3	×	×	×	√	×	×	×	×
Dex-U-4	√	×	×	√	×	×	×	×
Dex-U-5	√	×	×	√	√	×	×	×

√: Soluble.
×: Unsoluble.

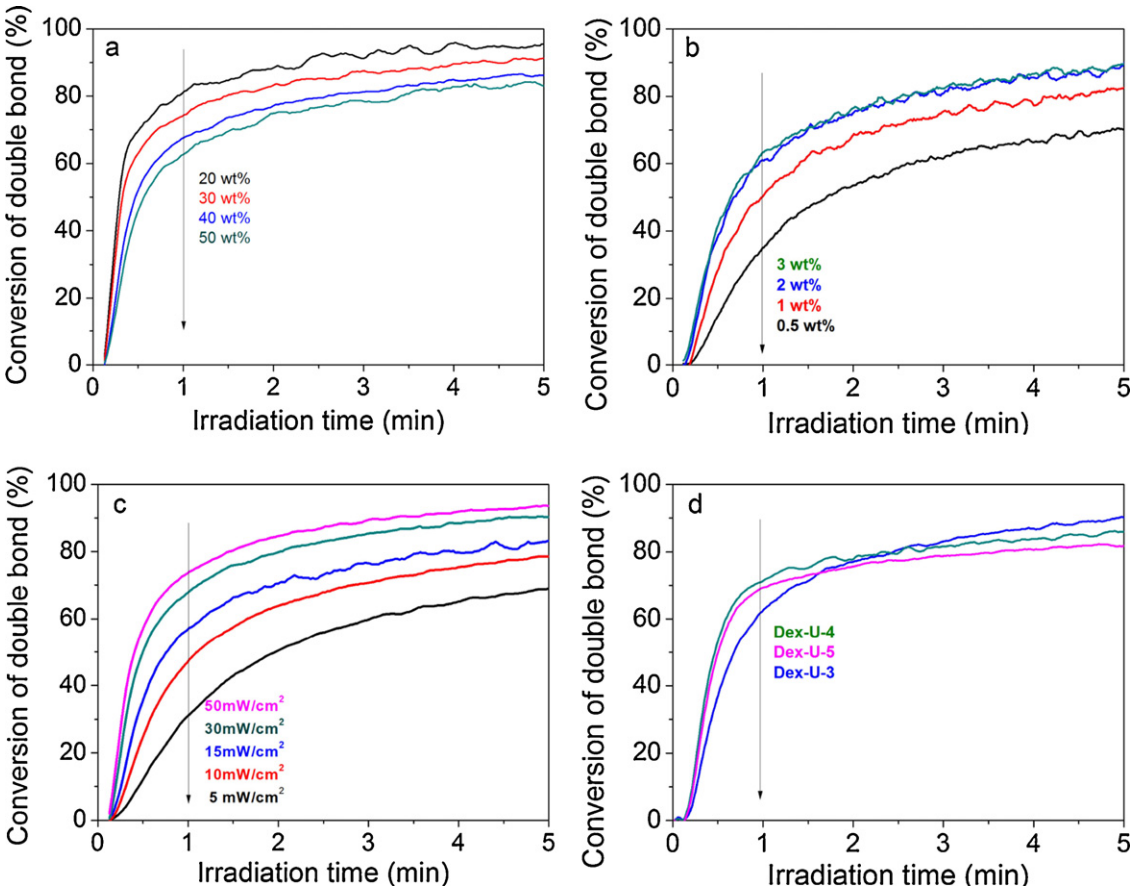

Fig. 2. Photocrosslinking kinetics of Dex-U in DMSO solution under different conditions: (a) different concentration of Dex-U-3; (b) different concentration of photoinitiator D-2959 in Dex-U-3/DMSO solution; (c) different light intensity in Dex-U-3/DMSO solution; (d) different DS of Dex-U.

wet the surface of the adherend. The surface energy of skin varied from 38 to 56 mN/m under different temperature and relative humidity (Venkatraman & Gale, 1998). The surface tension of blood was 47.5 mN/m by the sessile drop method at 37 °C (Agathopoulos & Nikolopoulos, 1995).

Dextran was a polar substance due to a lot of hydroxyl groups in its molecules. When IEMA reacted with the dextran, the nonpolar side chains were introduced into the backbone to form amphiphilic structure. When Dex-U with higher DS solved in the DMSO, the more nonpolar side chains were excluded from DMSO to air, and tendered to accumulate on the surface of solution, which reduced the surface tension of solution. As shown in Fig. 3, the value of surface tension of Dex-U solution decreased from 56.6 to 37.7 mN/m with the increase of DS of Dex-U, and these values were close to the surface tension of skin and blood, which indicated that the Dex-U solution could easily spread on the surface of human tissue before gelation.

3.5. Evaluation of adhesion strength

Adhesive performance of the Dex-U gel was evaluated by lap-shear test and burst strength adhesion test. The samples for lap-shear test was prepared as Fig. 4(a) and executed as Fig. 4(b). The adhesive strength was improved with the increase of the DS of Dex-U from 0.1 to 2.1 in Fig. 4(c). When the DS of Dex-U reached to 2.1. The highest fracture strength obtained was 2.99 MPa, but exhibited no further increase when the DS exceeded 2.1. These results indicated that the adhesive strength depended upon the DS of Dex-U.

This might be due to higher DS of Dex-U resulted in the more introductions of urethane groups and methacrylate groups. The more urethane groups enhanced the interaction of interface between gelatin and Dex-U. The more methacrylate groups could improve the cohesive force of adhesive according to increase the density of crosslinkage inside the Dex-U. They both enhanced the adhesion strength of Dex-U after photocrosslinking. So the adhesion strength was improved along with the increase of DS from 0.5 to 2.1. However, as all of hydroxyl groups of the

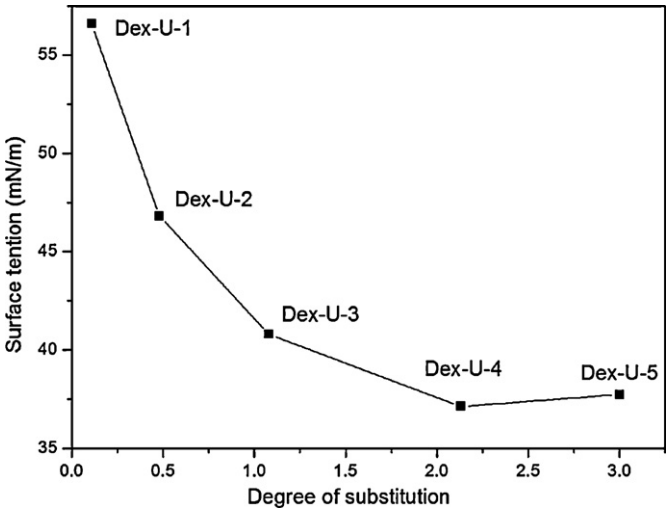

Fig. 3. Surface tension of Dex-U with different DS solution.

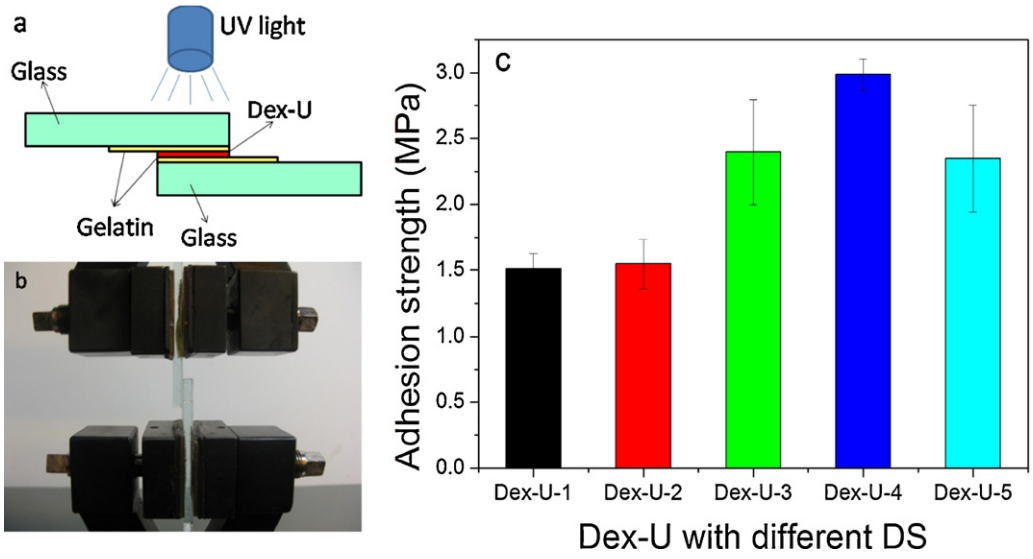

Fig. 4. Adhesion strength test of Dex-U/DMSO solution: (a) the schematic of preparation of lap-shear sample; (b) the device of lap-shear test; (c) the adhesion strength of Dex-U with different DS.

glucopyranosyl ring were substituted by the IEMA, the methacrylate groups among the adjacent rings in one molecule chain tended to polymerize, which resulted in decline of the density of crosslinkage. Finally, the adhesion strength of Dex-U decreased at the maximum of DS.

The adhesive properties of the DEX-U gel were compared to commercial available bioadhesives Tisseel (a fibrin adhesive). The Dex-U-4 gel exhibited the highest adhesion strength. For example, Dex-U-4 gel (2.99 ± 0.12 MPa) and Dex-U-5 gel (2.35 ± 0.40 MPa) which were 47 times higher than that of Tisseel (0.05 MPa) (Alston, Solen, and Broderick (2007)).

3.6. Measurement of burst pressure

The burst pressure of tissue adhesive is an important parameter of properties evaluation. The sample for burst pressure test was prepared in Fig. 5(a). When a amount of compressive air was charged into sample, the adhesive failure was at the tissue–material interface, which indicated that the interface force between adhesive and substrate rather than cohesive force of adhesive significantly affected the burst pressure. As shown in Fig. 5(b), the increase of DS has apparent effect on the capacity of Dex-U to adhere to the mouse skin. The increase of the DS resulted in the more introductions of urethane groups into the dextran, and enhanced the interface force between adhesive and mouse skin. When DS increased to 3, the burst pressure reached to 35 mmHg, and was greater than the reported capillary blood pressure (25 mmHg) (Prior, Wallace, Harner, & Powers, 1999). It was suitable for tissue sealant applications.

3.7. Cytotoxicity assays

An ideal bioadhesive should not release toxic products or produce adverse reactions, which could be evaluated through in vitro cytotoxic tests, such as MTT assay. In this evaluation, mouse fibroblast cells (L929) were used. Fig. 6-1 showed that the absorbance illustrating the viability of L929 cells that were cultured with the extraction medium from various types of Dex-U gels. Although that statistically significant differences ($p < 0.05$) were also observed in the cell activity of L929 culture for 24 h, 48 h, and 72 h in the presence of Dex-U gel extracts in comparison with negative control, and the average absorbance values were lower than that of the negative control, but the viability of the cell still reached above 80% of that

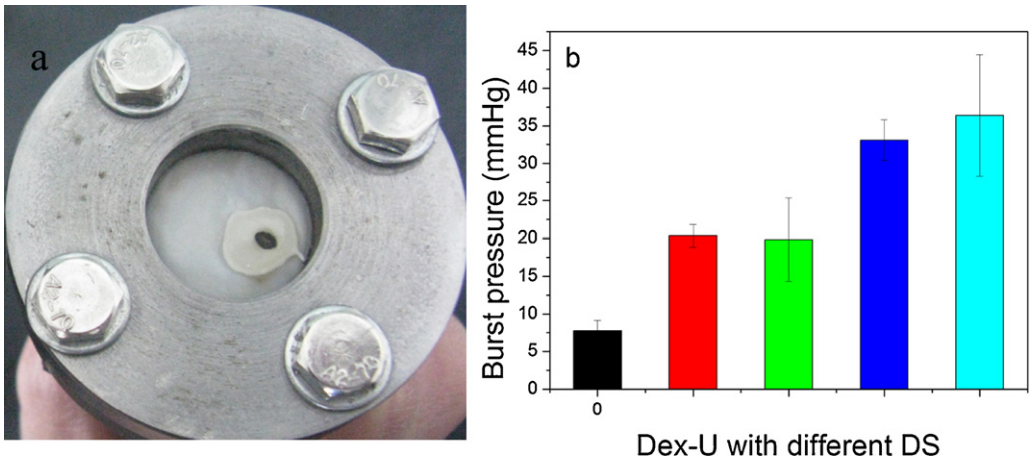

Fig. 5. Burst pressure test of Dex-U/DMSO solution: (a) sample for burst pressure test and (b) burst pressure of Dex-U with different DS.

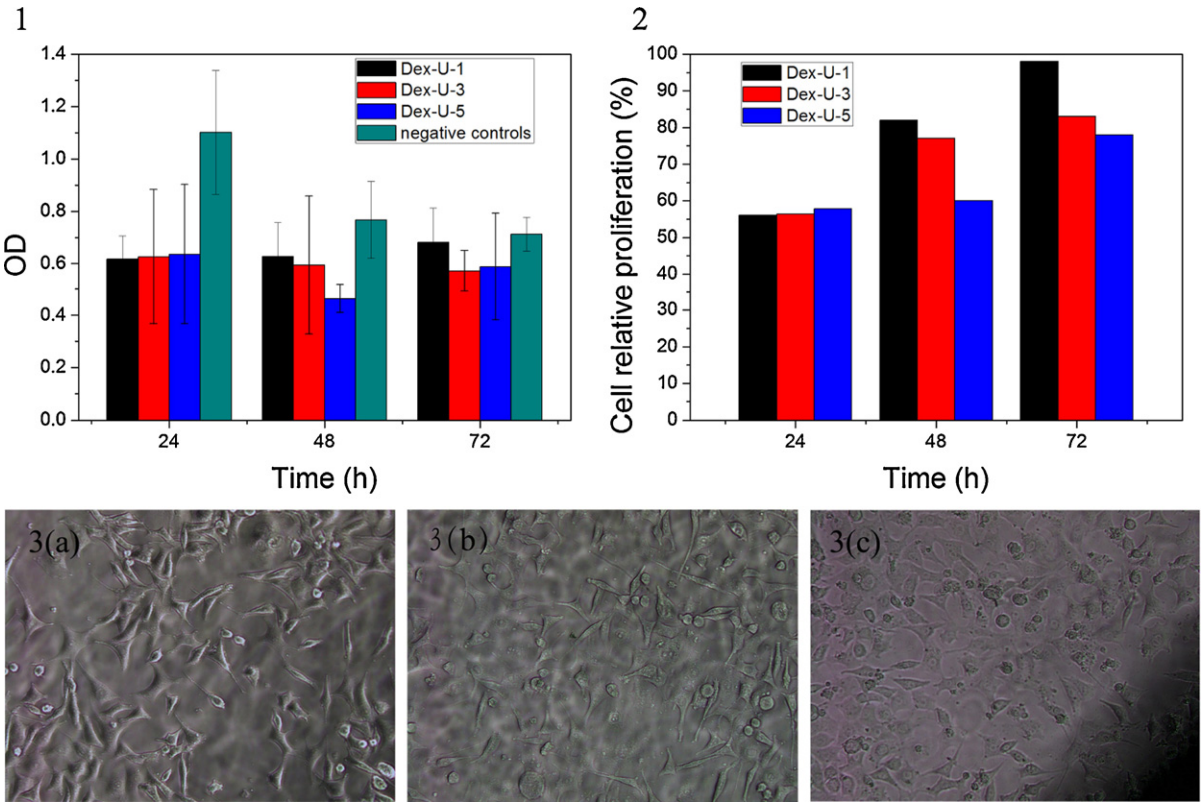

Fig. 6. Cytotoxicity test of Dex-U gels: (1) MTT test of Dex-U gels with positive and negative controls, $^{*}p < 0.05$ predicated statistically significant differences when compared to the negative control of indirect cytotoxicity. The data represented mean and standard deviations of six samples; (2) Cell relative proliferation; (3) Optical microscope images of L929 cell seeded on the adhesive gels (400× magnification), (a) Dex-U-1; (b) Dex-U-3; (c) Dex-U-5.

of the negative control at 72 h in Fig. 6-2. This indicates that the Dex-U were less toxic to L929 cells.

The interaction between bioadhesive and tissue cells was observed by optical microscopy (Fig. 6-3), which exhibited the L929 cells distribution on the surface of Dex-U gel after 48 h culture. According to the optical microscope images, there was no obvious difference among the Dex-U samples with different DS. The cells appeared to attach and distribute well on the surface of Dex-U samples with three different DS, and exhibited normal cell morphology. It indicated that L929 cells can attach well and suggest good cell viability on the Dex-U gel surface.

4. Conclusion

The drawbacks of commercially available bioadhesives have raised the need for the development of new materials that could meet the needs of both strength and biocompatibility. We developed an attractive photocrosslinkable bioadhesive system consisting of dextran derivatives (Dex-U) prepared from commercially available dextran and IEMA. The degree of substitution of Dex-U, as an important factor, was related to the product properties, including solubility, crystalline degree, photocrosslinking rate, wettability, adhesion strength and burst pressure. The DS of Dex-U could be readily manipulated by adjusting the molar ratio of dextran and IEMA. The Dex-U bioadhesive demonstrated adhesive strength that significantly superior to the commercially available fibrin based adhesives, but it has a lower bonding strength than cyanoacrylate. Therefore, investigations to increase its bonding strength are now warranted.

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