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Water absorption by decellularized dermis

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Abstract

Water absorption by decellularized dermis was investigated and compared with biopolymer and synthetic polymer hydrogels (glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogel, respectively). Porcine dermis was decellularized in an aqueous sodium dodecyl sulfate (SDS) solution. Histological evaluation revealed that the SDS-treated dermis has much larger gaps between collagen fibrils than non-treated dermis, and that water absorption depends on these gaps. Decellularized dermis has low water absorptivity and the absorption obeys Fick's second law. During absorption, the water diffusion rate decreases with time and occurs in two steps. The first is rapid absorption into the large gaps, followed by slow absorption by the collagen fiber layer. Because of the gaps, decellularized dermis can absorb more water than native dermis and shows different water absorption behavior to glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels.

Keywords: Bioengineering, Materials science

1. Introduction

Decellularized tissues are widely used as biomaterials as well as scaffolds for tissue engineering and regenerative medicine. Various decellularized tissues have been developed, including dermis, arterial, pericardium, tendon, liver, and cornea [1, 2,

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3, 4, 5, 6]. Although decellularized tissues have been of interest in medical fields for over 20 years, few of their physical or chemical characteristics have been reported [7, 8, 9]. As the application of decellularized tissues is expanded, their basic characterization is becoming important to support their use as medical materials. For instance, the mechanical properties of decellularized tissues have been investigated in the interest of quality assurance for commercial products. Other properties have not been studied in detail until now.

This work focuses on decellularized tissue as a soft biomaterial for use in implants. To date, soft synthetic materials have not been widely used as implants. Some exceptions include artificial blood vessels and anti-adhesion membranes. Hydrogels are believed to have good biocompatibility because of their mechanical properties and hydrated nature, similar to living tissue, which also contains a high proportion of water. Hydrogels have been studied for use in applications including contact lenses, drug delivery and wound dressings for a number of years [10, 11, 12], while decellularized tissues have been widely used for the long-term substitution of living tissue, such as blood vessels, heart valves, and corneas [13, 14, 15, 16]. A comparison of the differences between hydrogels and decellularized tissue is therefore of interest for the development of new hydrogels as implantable biomaterials.

In addition, commercially available decellularized dermis is stored and delivered either dry or wet. Dry dermis can be stored longer than wet dermis, but has to be re-hydrated prior to use [17]. Knowledge of dermis wettability and water absorption during the re-hydration process is valuable for method development.

In this work, to characterize the water content of decellularized tissue, we focus on the rehydration of freeze-dried decellularized tissue. The rehydration behavior of hydrogels has been widely studied [18, 19, 20]; therefore the rehydration of decellularized tissues was studied in parallel with the better-understood hydrogel systems for comparison. Poly(acrylamide) and gelatin gels were used as synthetic and biological hydrogels, respectively.

2. Materials and methods

2.1. Harvest of porcine dermis

Fresh porcine skin was purchased from a local slaughterhouse (Tokyo Shibaura Zouki, Tokyo, Japan). After the epidermal and fat layers were mechanically removed, the dermis was cut into circular samples 12 mm in diameter. The samples were washed in saline and sterilized by washing in Isodine (Meiji Seika, Tokyo, Japan) overnight at 4 °C. They were then washed in gentamicin (Wako Chemical, Tokyo, Japan) overnight at 4 °C and stored in saline at 4 °C.

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2.2. Preparation of decellularized dermis

The dermis samples were washed in 10 mM tris-HCl with 0.1 % ethylenediaminetetraacetate (EDTA) for 24 h at 4 °C, 0.5 % agarose and 1.25 % trypsin for 4 h at 37 °C, and 10 mM tris buffer with 0.1 % EDTA and 0.1% sodium dodecyl sulfate (SDS) for 24 h at room temperature. Samples were then washed with 50 nM tris-HCl buffer with 10 mM $MgCl_2$, 50 μg/ml bovine serum albumin (BSA), 50 U/ml DNase I, and 1 U/ml RNase for 4 h at 37 °C, followed by 0.1 % EDTA in phosphate-buffered saline (PBS) for 72 h at 37 °C (Fig. 1) [21].

2.3. Histological examination

The native and decellularized dermis samples were fixed with 10 % neutral-buffered formalin solution and gradient-dehydrated with ethanol. They were then embedded in paraffin blocks, sliced into 5 μm thick sections, and stained with Mayer's hematoxylin-eosin (H-E).

2.4. Preparation of gelatin hydrogels

Type "a" gelatin (SIGMA-Aldrich Japan, Tokyo, Japan) was used to prepare the biopolymer hydrogels. A 10 % gelatin solution was mixed with 0.1 %, 0.5 %, and 1 % glutaraldehyde (GA), poured into a gel plate, and stored for 12 h at 4 °C. After treating the samples with 100 mM glycine on a shaker for 72 h at 37 °C to terminate

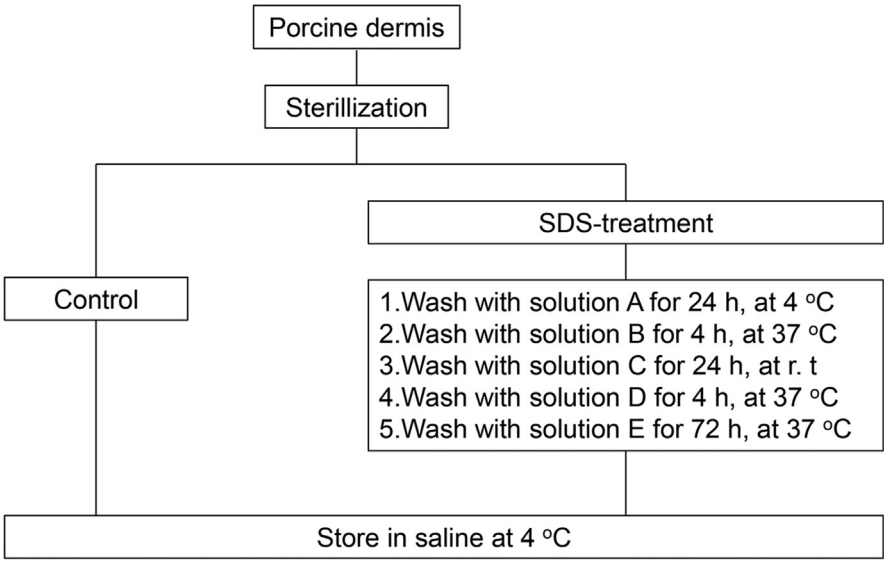

Fig. 1. Preparation of decellularized dermis. Solution A: 10 mM tris-HCl buffer and 0.1 % EDTA in water; Solution B: 0.5 % agarose and 1.25 % trypsin in water; Solution C: 10 mM tris buffer with 0.1 % EDTA and 0.1 % SDS in water; Solution D: 50 mM tris-HCl buffer with 10 mM $MgCl_2$ and 50 μg/ml BSA and 50 U/ml DNase and 1 U/ml RNase in water; Solution E: 0.1 % EDTA in PBS.

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the polymerization, 10 %−0.1 % GA (10−0.1 G gel), 10 %−0.5 % GA (10−0.5 G gel), and 10 %−1 % GA (10-1 G gel) hydrogels were harvested. Finally, 12 mm diameter, 4 mm thick samples were cut and washed with water.

2.5. Preparation of poly(acrylamide) hydrogel

Acrylamide (SIGMA-Aldrich Japan, Tokyo, Japan) was used to prepare the synthetic hydrogels. A 0.5 % acrylamide solution was mixed with 0.5 % ammonium persulfate and 0.5 % N,N,N′,N′-tetramethylethylenediamine, and then poured onto a gel plate. After polymerization to poly(acrylamide) (PA) at room temperature, 5 % (5PA gel), 10 % (10PA gel), 20 % (20PA gel), and 30 % (30PA gel) hydrogels were prepared using the same process. 12 mm diameter, 4 mm thick samples were then cut and washed with water.

2.6. Freeze-drying process

Samples were exchanged with water for 48 h at 4 °C, subjected to rapid freezing with liquid nitrogen, and then dried under reduced pressure for 24 h using a Freeze Dryer (FDU-2000 TOYKO RIKAKIKAI, Tokyo, Japan).

2.7. Water absorption experiments

The dry weight of the samples was established and they were then immersed in water and removed at various time points to be reweighed. As a control, native dermis was also examined. n = 3 measurements were taken for each group. All data are expressed as mean ± standard deviation.

2.8. Determination of the mass transfer coefficient

To describe rehydration, water absorption (Q) was calculated from Eq. (1):

$$Water\ absorption\ (Q) = \frac{W_t - W_0}{W_0} \tag{1}$$

where W_0 is the dry weight of the sample, and W_t is the weight at time "t."

Fick's second law was used to describe the absorption mechanism of the hydrogels [17]. The diffusion exponent *n* of the dermis, gelatin hydrogels and poly(acrylamide) hydrogels was calculated from Eq. (2):

$$\frac{M_t}{M_\infty} = k\, t^n \tag{2}$$

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where M_t is the mass of water absorbed at time "t," M_∞ is the mass of water absorbed at equilibrium (after 48 h), *n* is the diffusion exponent of the dermis, gelatin hydrogels and poly(acrylamide) hydrogels, and k is a characteristic constant of the polymer.

To describe the variation in water diffusion during absorption, the diffusion coefficient *D* was calculated from Eq. (3):

$$\frac{M_t}{M_\infty} = \frac{2}{l}\left(\frac{D}{\pi}\right)^{0.5} t^{0.5} \tag{3}$$

where l is the sample thickness. Measurements were performed up to $M_t/M_\infty < 0.9$ [19, 20, 21, 22, 23].

To investigate the relationship between *D* and the degree of swelling H, Eq. (4) was used to calculate:

$$Log\, D = Log\, D_0 - K\left(\frac{1}{H} - 1\right) \tag{4}$$

Where D_0 is the diffusion coefficient in pure solvent, and K is a characteristic constant [24].

3. Results

3.1. Decellularization of dermis

HE staining was used to evaluate the effects of decellularization on the preservation of tissue structure relative to native dermis (Fig. 2). Cell nuclei (thin arrows in Fig. 2A) were not observed after decellularization (Fig. 2B). Small and large gaps were observed in both native and decellularized dermis, however, large gaps were more prevalent in the latter (thick arrow in Fig. 2B).

3.2. Water absorption

Water absorption by decellularized and native dermis, glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels was investigated by gravimetric analysis (Fig. 3). Decellularized dermis absorbed water quickly in the first 10 min and very little subsequently. Whereas, native dermis absorbed water quickly in the first 20 min, slowed down slightly after that, and then continued gradually until it reached equilibrium after 2 h. At equilibrium, both native and decellularized dermis had absorbed similar amounts of water, which was almost 1.5 times their original weight (Fig. 3A, B).

Crosslinking density was adjusted to assess hydrogel water absorption in the gelation hydrogels group. In Fig. 3C, D, the glutaraldehyde-crosslinked gelatin hydrogels absorbed water quickly over the first 10 min. The 10−0.5 G and 10-1 G gels

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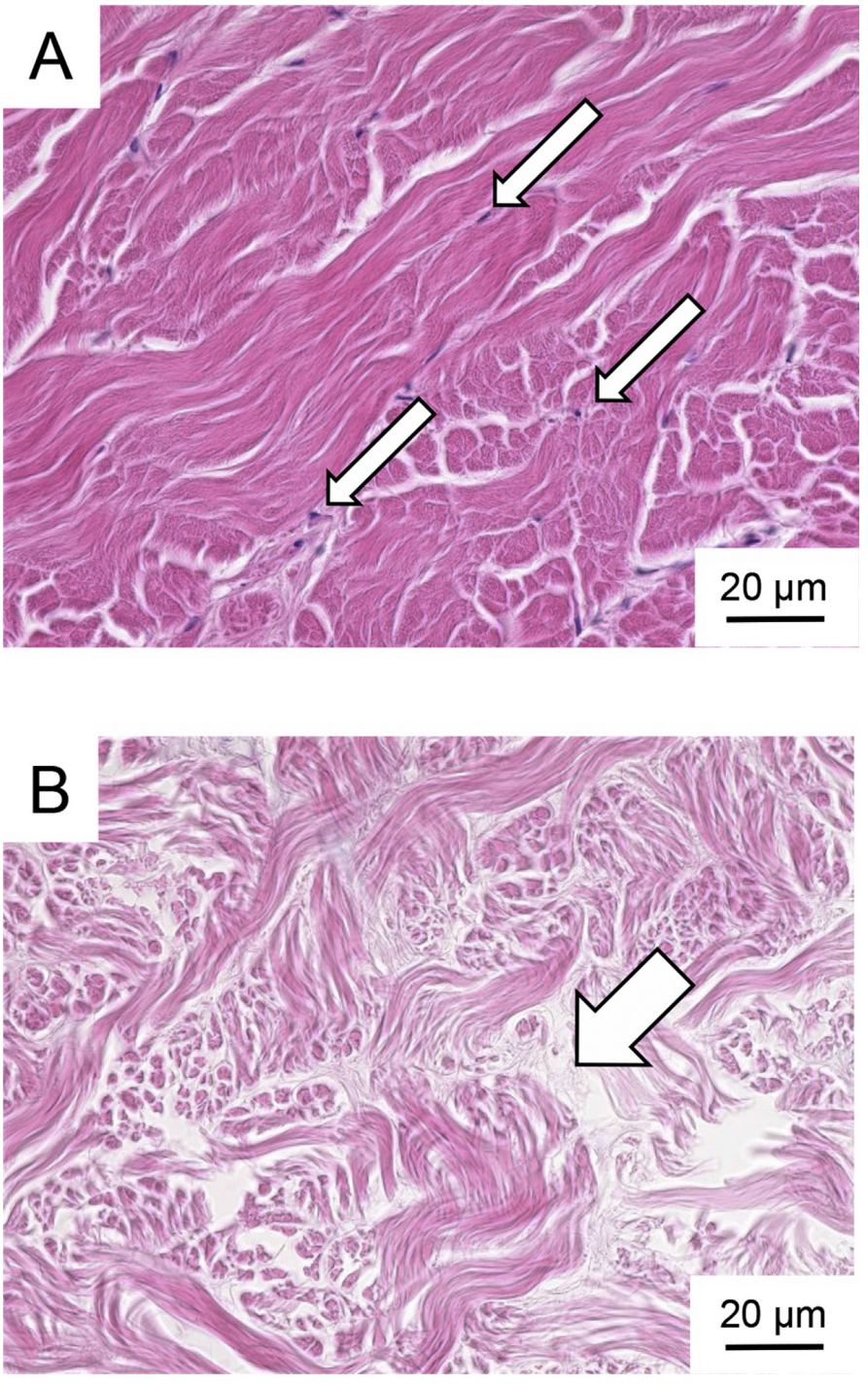

Fig. 2. HE-stained images of A: Native dermis, and B: Decellularized dermis. Thin arrows: nuclei, Thick arrow: large gap.

did not exhibit any absorption after 10 min, while the 10-0.1 G gel had a small increase and plateaued after 60 min (Fig. 3C). Although the 10-0.5 G gel absorbed the most water in the first 10 min, the total volume of water absorbed after reaching equilibrium was similar to that of the 10-0.1 G gel. After 48 h, the 10-0.1 G and 10-0.5 G

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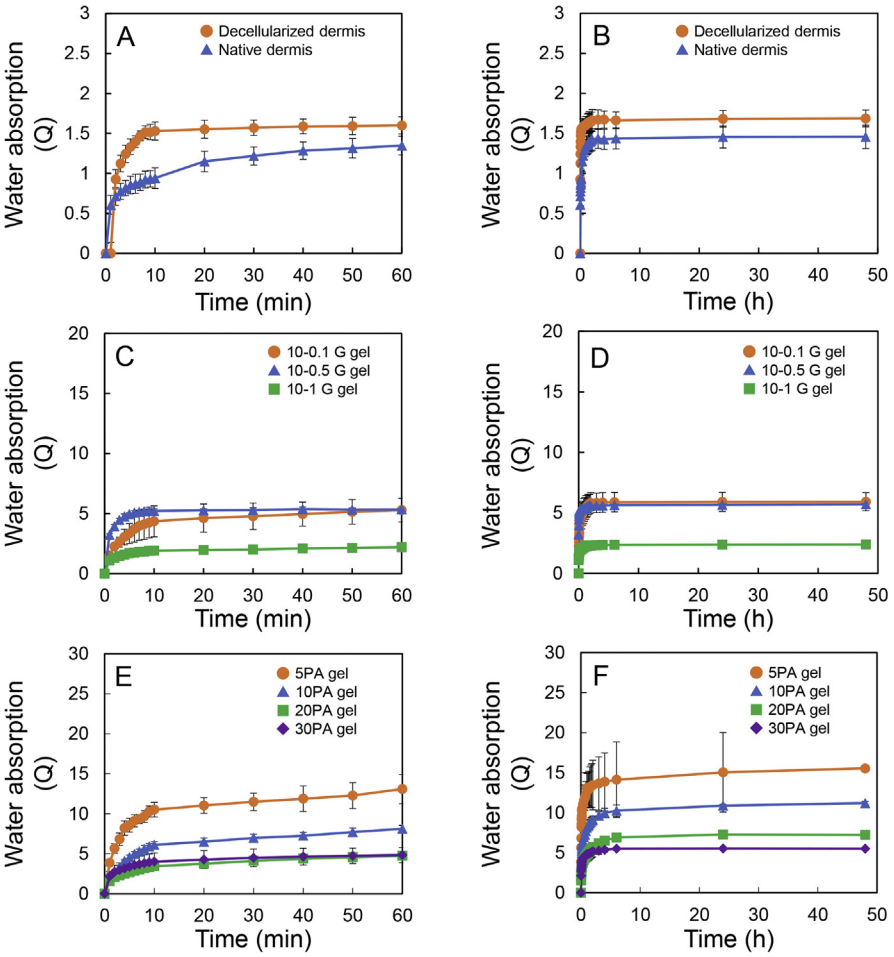

Fig. 3. Water absorption by A, B: Biological tissues; C, D: Gelatin hydrogels; and E, F: Crosslinked poly(acrylamide) hydrogels. A, C, E: initial. B, D, F: late stage. n = 3 measurements for each group. Data are mean ± standard deviation.

gels absorbed almost 5.7 times their initial weight, whereas the 10-1 G gel absorbed much less at 2.4 times its initial weight (Fig. 3D).

Polymer concentration was adjusted to assess water absorption of hydrogels in the crosslinked poly(acrylamide) hydrogel group. Fig. 3E, F show that all of the PA gels examined absorbed water quickly during the first 10 min, and continued to absorb gradually after that. Over the full absorption process, the 5PA gel absorbed the most followed by the 10PA gel. After the first 60 min, the 20PA and 30PA gels absorbed a similar amount of water, however, after 48 h, the 20PA gel had absorbed more water than the 30PA gel. After 48 h, the amount of water absorbed by the 5, 10, 20, and 30 PA gels was 15.5, 11.2, 7.2, and 5.5 times their own weight, respectively (Fig. 3F).

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3.3. Dermis and hydrogel diffusion exponents

The diffusion exponent n in Eq. (2) was used to describe the pattern of water absorption by the dermis, glutaraldehyde-crosslinked gelatin hydrogels and crosslinked poly(acrylamide) hydrogels. M_∞ is the mass of water absorbed at equilibrium, $M_t/M_\infty < 0.6$ during the initial absorption, and $0.6 < M_\infty < 0.9$ at the later stage of absorption. For each sample, n is listed in Table 1. All values of n were less than 0.5, and could be divided into two groups; close to 0.5 or less than 0.3. At the initial absorption stage, values of n for the native dermis and for the 10-1 G gel, 20PA gel, and 30PA gel, were less than 0.3; whereas, those of the 10-0.1 G gel, 5PA gel, and 10PA gel were close to 0.5. At later absorption stages, all values were less than 0.3. Decellularized dermis and the 10−0.5 G gel absorbed water too quickly in the initial absorption stage for n to be calculated.

The diffusion exponent *vs*. time was used to evaluate changes in the water absorption patterns over the full 48 h study period (Fig. 4). Native and decellularized dermis did not exhibit changes in gradient (Fig. 4A), however changes were observed for all of the hydrogels examined. The 10-0.5 G gel, 10-1 G gel, 5PA gel, and 10PA gel showed larger changes; while, the 10-0.1 G gel, 20PA gel and 30 PA gel exhibited smaller changes (Fig. 4B, C).

3.4. Water diffusion coefficient of dermis and hydrogels

D calculated from Eq. (3) was used to evaluate water mobility through the matrix. As shown in Fig. 5, decreasing D values were observed for native and decellularized dermis; all glutaraldehyde-crosslinked gelatin hydrogels; and the 30PA gel. No decrease was observed for the 5PA, 10PA, or 20PA gels.

Table 1. Calculated diffusion exponents for water absorption kinetics.

Polymer	Polymer concentration (%)	Cross-linker concentration (%)	$M_t/M_\infty < 0.6$		$0.6 < M_t/M_\infty < 0.9$	
			n	SD	*n*	SD
Native dermis	–	–	0.181	0.042	0.247	0.099
Decellularized dermis	–	–	–	–	0.241	0.052
Glutaraldehyde-crosslinked gelatin hydrogels	10	0.1	0.422	0.156	0.156	0.004
	10	0.5	–	–	0.251	0.025
	10	1	0.259	–	0.112	0.005
Crosslinked poly(acrylamide) hydrogels	5	0.5	0.458	0.158	0.138	0.009
	10	0.5	0.417	0.086	0.181	0.046
	20	0.5	0.262	0.011	0.237	0.019
	30	0.5	0.203	–	0.199	0.056

n = 3.

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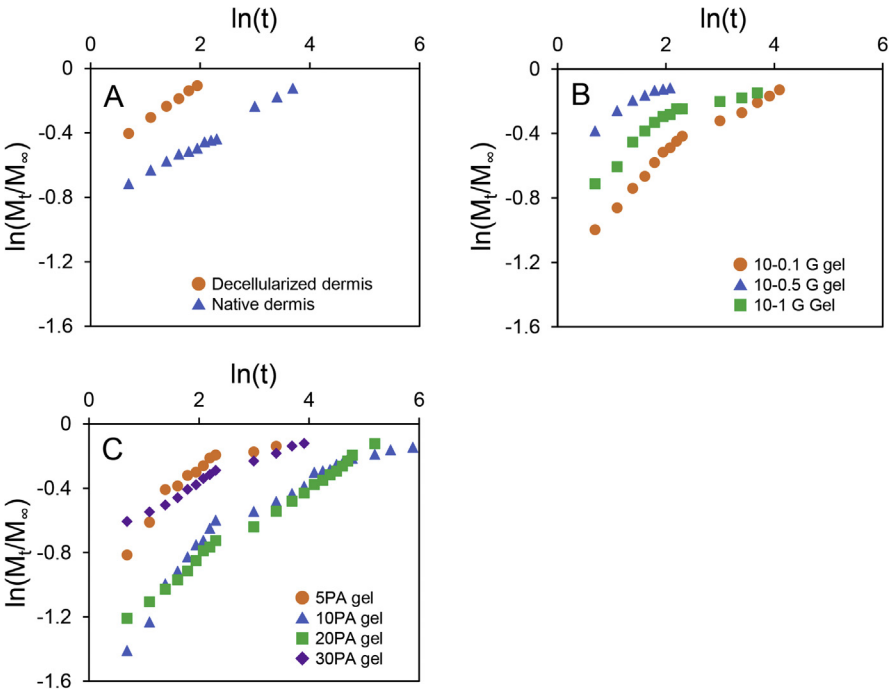

Fig. 4. Relationship between M_t/M_∞ and time for A: Biological tissues; B: Glutaraldehyde-crosslinked gelatin hydrogels; and C: Crosslinked poly(acrylamide) hydrogels.

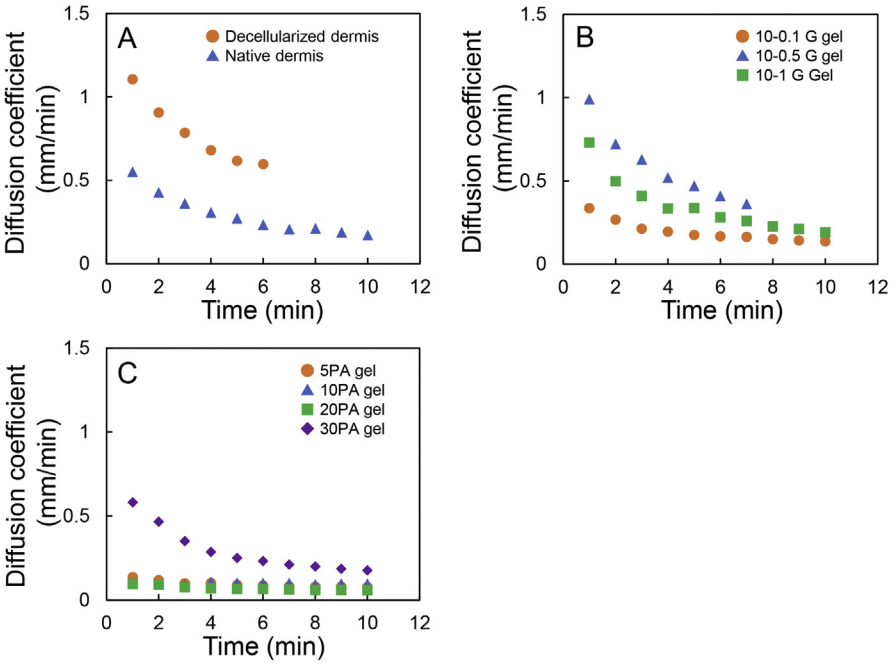

Fig. 5. Relationship between diffusion coefficients and time for A: Biological tissues; B: Glutaraldehyde-crosslinked gelatin hydrogels; and C: Crosslinked poly(acrylamide) hydrogels.

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3.5. Relationship between diffusion coefficient and degree of swelling

Fig. 6 shows Log *D* *vs*. 1/H for each sample, as calculated from Eq. (4). This demonstrates that Log *D* and 1/H had a linear relationship.

4. Discussion

Various decellularization methods such as high hydrostatic pressure (HHP), sodium deoxycholate (SDC), SDS, Triton X-100, and trypsin treatments have been developed to remove cell nuclei from tissue [3, 25]. SDS was used in this work because it is readily available and has been used on various tissues [26, 27, 28]. After decellularization of the porcine dermis, the nuclei were removed, resulting in much larger gaps between the collagen fibrils (Fig. 2). This indicates that SDS also removes extracellular components from the dermis.

Hydrogels can hold large quantities of water in their three-dimensional networks, and have been shown to be highly biocompatible in drug delivery, cell encapsulation, and tissue repair applications. Hydrogel parameters such as water absorption, diffusion, and re-hydration have been widely characterized [29, 30]. In this work, the water absorption behavior of decellularized dermis was compared with

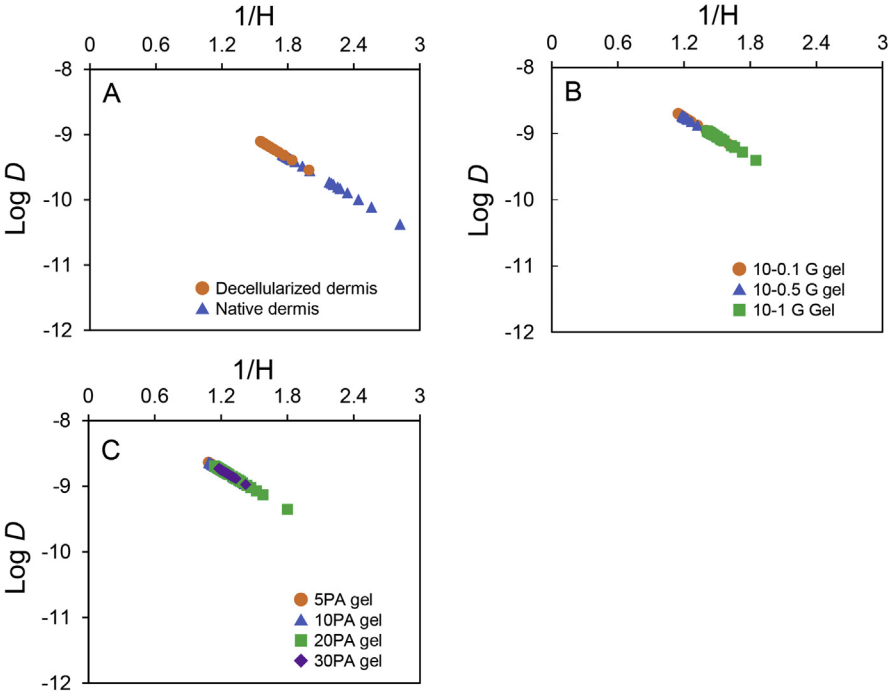

Fig. 6. Relationship between degree of hydration and water diffusion coefficients. A: Dermis; B: Glutaraldehyde-crosslinked gelatin hydrogels; C: Crosslinked poly(acrylamide) hydrogels.

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biological hydrogels (glutaraldehyde-crosslinked gelatin gels) and synthetic hydrogels (crosslinked poly(acrylamide) gels).

Crosslinking density and polymer concentration were adjusted to assess the water absorption of glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels, respectively. Fig. 3 shows that all of the examined hydrogels absorbed water slowly until equilibrium was reached. Hydrogels with low crosslinking densities and concentrations were able to absorb greater quantities of water than those with high crosslinking densities and concentrations because they allow greater expansion of the gel network, thus accommodating higher water absorption. Decellularized dermis slowly absorbs water before reaching equilibrium, similar to glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels, but in comparison with the hydrogels absorbs a relatively small amount of water. Decellularized dermis reaches equilibrium much faster and absorbs a larger amount of water than native dermis because of the large gaps formed by SDS treatment (Fig. 2), allowing water to easily penetrate the matrix.

Ritger and Peppas reported that the value of n depends on the diffusion mechanism. The transport is less Fickian when $n < 0.5$, Fickian diffusion when $n = 0.5$, and non-Fickian when $n > 0.5$ [19, 20, 22, 23]. As discussed above and shown in Table 1, $n < 0.5$ in all cases, which indicates that water diffuses into dermal tissue, glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels by Fickian diffusion. It is also evident that n is markedly lower for hydrogels with low crosslinking density (10−0.1 G gel) and low polymer concentration (5PA and 10PA gels). For dermis tissue, high crosslinking hydrogels (10-1 G gel), and high concentration hydrogels (20PA and 30PA gels) n values were closer to 0.5. Furthermore, the hydrogels with low polymer concentrations and crosslinking densities showed significant swelling, while dermal tissue and hydrogels with high concentrations and crosslinking densities showed only slight swelling (Table 1, Fig. 3) [16]. This suggests that, during the water absorption process, the ability of the glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels to swell influences their water absorption behavior. Water absorption behavior changed from initial absorption to later absorption in low crosslinking and low concentration glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels, however the change was not marked. This indicates that even within Fickian diffusion, there are two different water absorption behaviors for hydrogels.

In this study, freeze-dried samples were used to investigate water absorption behavior, therefore, the samples can be discussed macroscopically as solid polymer, with the results being explained by free-volume theory. In polymers, molecular diffusion occurs through gaps between the polymer molecules (free volume) [24,

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31, 32, 33]. Thus, the free volume in tissues, glutaraldehyde-crosslinked gelatin, and crosslinked poly(acrylamide) hydrogels, enables Fickian water diffusion. In glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels, the internal free volume decreases with increasing polymer concentration and crosslinking density. Hence, water absorption was lower for hydrogels with high crosslinking densities and polymer concentrations relative to those with low crosslinking densities and polymer concentrations (Fig. 3C–F). Many tissue components such as cells, polysaccharides, and proteins were removed during decellularization, thereby increasing the free volume, and allowing more water to be absorbed relative to the native dermis (Fig. 3A, B).

The mobility of water in the samples can be estimated from the diffusion coefficient (D) (Eq. (3)). During the water absorption process, water was absorbed from the surface to the interior, it can therefore be considered continuous membrane absorption. According to the free-volume theory of diffusion, when a solute diffuses into a swelling film, and the interaction between the solute and polymer chain can be ignored, then D and degree of swelling H conform to Eq. (4). Fig. 6 shows that Log D *vs* 1/H was linear for all samples. This suggests that the interaction between water and polymer can be ignored, and that the degree of swelling dominates diffusion.

It is evident from Fig. 5, that during absorption, the diffusion rate decreases in dermis tissue and in highly swollen glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels (n unchanged), while it does not decrease in less swollen glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels (n decreased). To understand this, the relationships between the swelling rate, n, and D values were examined. Because hydrogels with low crosslinking densities and low polymer concentrations swell easily, swelling occurred immediately following immersion in water. As a result, the voids involved in water penetration became narrow, and D values did not change appreciably. In contrast, when the effect of swelling was greater, n decreased (Fig. 7A). The glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels with high crosslinking densities and high polymer concentrations showed very little swelling. As a result, when these hydrogels were immersed in water, swelling occurred slowly and voids involved in water penetration narrowed gradually, decreasing D values. When the swelling was low, n did not change (Fig. 7B). The decellularized dermis initially had both large gaps and voids that between collagen fiber bundles, allowing water to penetrate into the large gaps, followed by the voids between the collagen fiber bundles, which resulted in decreasing D values. However, because the decellularized dermis took time to absorb water, the swelling did not occur during water absorption; therefore, n did not change (Fig. 7C) [18, 34].

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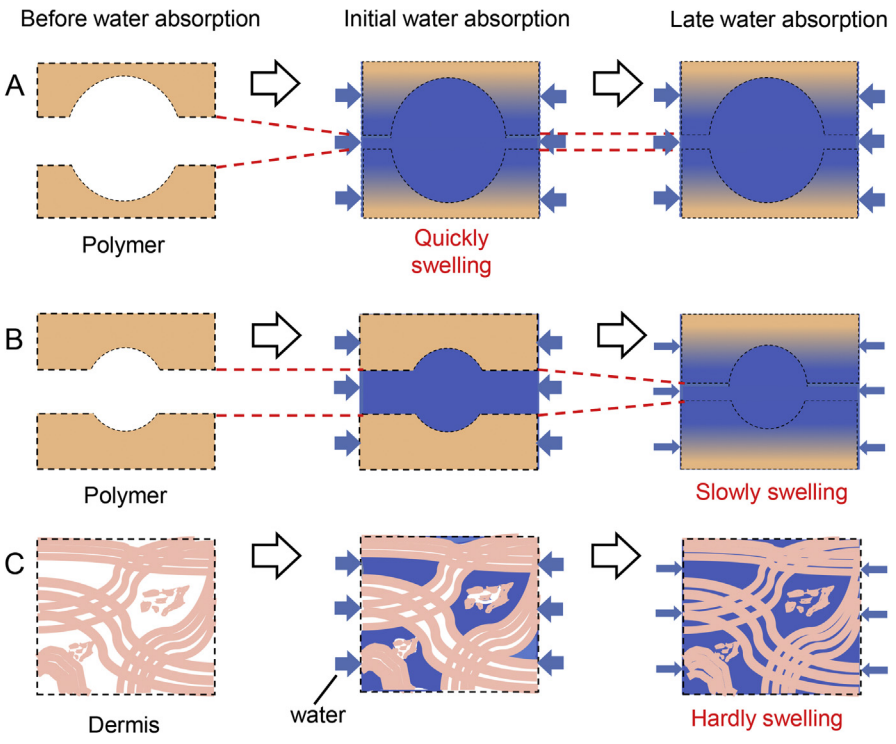

Fig. 7. Water absorption A: low crosslinking, low concentration glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels, B: High crosslinking, high concentration glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels, and C: Dermis.

5. Conclusion

The mechanism of water absorption by decellularized porcine dermis was investigated and compared with those of glutaraldehyde-crosslinked gelatin and crosslinked poly(acrylamide) hydrogels. The process obeyed Fick's second law. Decellularized dermis was found to be a low-water-absorption material. Gaps in the tissue structure effect water absorption, and there was almost no swelling in the fiber layer during water absorption. These results provide an improved understanding of dermis water absorption and may lead to possible applications of decellularized dermis and the development of new hydrogels.

Declarations

Author contribution statement

Y. Zhang: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

T. Iwata, K. Nam, T. Kimura, P. Wu, N. Nakamura, Y. Hashimoto, A. Kishida: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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References

[1] P.M. Crapo, T.W. Gilbert, S.F. Badylak, An overview of tissue and whole organ decellularization processes, Biomaterials 32 (12) (2011) 3233–3243.

[2] J.J. Song, H.C. Ott, Organ engineering based on decellularized matrix scaffolds, Trends Mol. Med. 17 (8) (2011) 424–432.

[3] C.R. Deeken, A.K. White, S.L. Bachman, B.J. Ramshaw, D.S. Cleveland, T.S. Loy, S.A. Grant, Method of preparing a decellularized porcine tendon using tributyl phosphate, J. Biomed. Mater. Res. Part B Appl. Biomater. 96 (2) (2011) 199–206.

[4] H. Bannasch, G.B. Stark, F. Knam, R.E. Horch, M. Föhn, Decellularized dermis in combination with cultivated keratinocytes in a short-and long-term animal experimental investigation, J. Eur. Acad. Dermatol. Venereol. 22 (1) (2008) 41–49.

[5] S.P. Márquez, V. Sáez Martínez, W.M. Ambrose, J. Wang, N.G. Gantxegui, O. Schein, J. Elisseeff, Decellularization of bovine corneas for tissue engineering applications, Acta Biomater. 5 (2009) 1839–1847.

[6] S. Funamoto, K. Nam, T. Kimura, A. Murakoshi, Y. Hashimoto, K. Niwaya, S. Kitamura, T. Fujisato, A. Kishida, The use of high-hydrostatic pressure treatment to decellularize blood vessels, Biomaterials 31 (13) (2010) 3590–3595.

https://doi.org/10.1016/j.heliyon.2018.e00600

[7] P. Wu, T. Kimura, H. Tadokoro, K. Nam, T. Fujisato, A. Kishida, Relation between the tissue structure and protein permeability of decellularized porcine aorta, Mater. Sci. Eng. C 43 (2014) 465−471.

[8] S.B. Lumpkins, N. Pierre, P.S. McFetridge, A mechanical evaluation of three decellularization methods in the design of a xenogeneic scaffold for tissue engineering the temporomandibular joint disc, Acta Biomater. 4 (4) (2008) 808−816.

[9] C. Williams, J. Liao, E.M. Joyce, B. Wang, J.B. Leach, M.S. Sacks, J.Y. Wong, Altered structural and mechanical properties in decellularized rabbit carotid arteries, Acta Biomater. 5 (4) (2009) 993−1005.

[10] E. Caló, V.V. Khutoryanskiy, Biomedical applications of hydrogels: a review of patents and commercial products, Eur. Polym. J. 65 (2015) 252−267.

[11] Y. Qiu, K. Park, Environment-sensitive hydrogels for drug delivery, Adv. Drug Deliv. Rev. 53 (2001) 321−339.

[12] J.S. Boateng, K.H. Matthews, H.N.E. Stevens, G.M. Eccleston, Wound healing dressings and drug delivery systems: a review, J. Pharmaceut. Sci. 97 (8) (2008) 2892−2923.

[13] S.L.M. Dahl, J. Koh, V. Prabhakar, L.E. Niklason, Decellularized native and engineered arterial scaffolds for transplantation, Cell Transplant. 12 (2003) 659−666.

[14] B.S. Conklin, E.R. Richter, K.L. Kreutziger, D.S. Zhong, C. Chen, Development and evaluation of a novel decellularized vascular xenograft, Med. Eng. Phys. 24 (2002) 173−183.

[15] H.C. Ott, T.S. Matthiesen, S.K. Goh, L.D. Black, S.M. Kren, T.I. Netoff, D.A. Taylor, Perfusion-decellularized matrix: using nature's platform to engineer a bioartificial heart, Nat. Med. 14 (2) (2008) 213−221.

[16] Y. Hashimoto, S. Funamoto, S. Sasaki, T. Honda, S. Hattori, K. Nam, T. Kimura, M. Mochizuki, T. Fujisato, H. Kobayashi, A. Kishida, Preparation and characterization of decellularized cornea using high-hydrostatic pressurization for corneal tissue engineering, Biomaterials 31 (14) (2010) 3941−3948.

[17] S.F. Adylak, D.O. Freytes, T.W. Gilbert, Reprint of: extracellular matrix as a biological scaffold material: structure and function, Acta Biomater. 23 (2015) S17−S26.

[18] F. Ganji, F.S. Vasheghani, F.E. Vasheghani, Theoretical description of hydrogel swelling: a review, Iran. Polym. J. 19 (5) (2010) 375−398.

 https://doi.org/10.1016/j.heliyon.2018.e00600

[19] J.R. Witono, I.W. Noordergraaf, H.J. Heeresb, L.P.B.M. Janssen, Water absorption, retention and the swelling characteristics of cassava starch grafted with polyacrylic acid, Carbohydr. Polym. 103 (2014) 325−332.

[20] J. Wang, W. Wu, Z. Lin, Kinetics and thermodynamics of the water sorption of 2-hydroxyethyl methacrylate/styrene copolymer hydrogels, J. Appl. Polym. Sci. 109 (2008) 3018−3023.

[21] S.A. Korossis, H.E. Wilcox, K.G. Watterson, J.N. Kearney, E. Ingham, J. Fisher, In-vitro assessment of the functional performance of the decellularized intact porcine aortic root, J. Heart Valve Dis. 14 (3) (2005) 408−421.

[22] P.L. Ritger, N.A. Peppas, A simple equation for description of solute release I. Fickian and non-fickian release from non-swellable devices in the form of slabs, spheres, cylinders or discs, J. Contr. Release 5 (1987) 23−36.

[23] A.K. Bajpai, J. Bajpai, S. Shukla, Water sorption through a semi-interpenetrating polymer network (IPN) with hydrophilic and hydrophobic chains, React. Funct. Polym. 50 (1) (2002) 9−21.

[24] H. Yasuda, C.E. Lamaze, L.D. Ikenberry, Permeability of solutes through hydrated polymer membranes part I. Diffusion of sodium chloride, Makromol. Chem. 118 (1968) 19−35.

[25] T.W. Gilbert, T.L. Sellaro, S.F. Badylak, Decellularization of tissues and organs, Biomaterials 27 (2006) 3675−3683.

[26] P.H. Liem, N. Morimoto, R. Ito, K. Kawai, S. Suzuki, Autologous skin reconstruction by combining epidermis and acellular dermal matrix tissue derived from the skin of giant congenital melanocytic nevi, J. Artif. Organs 16 (2013) 332−342.

[27] J. Liao, E.M. Joyce, M.S. Sacks, Effects of decellularization on the mechanical and structural properties of the porcine aortic valve leaflet, Biomaterials 29 (2008) 1065−1074.

[28] R.W. Grauss, M.G. Hazekamp, S. van Vliet, A.C. Gittenberger-de Groot, M.C. DeRuiter, Decellularization of rat aortic valve allografts reduces leaflet destruction and extracellular matrix remodeling, J. Thorac. Cardiovasc. Surg. 126 (2003) 2003−2010.

[29] E.M. Ahmed, Hydrogel: preparation, characterization, and applications: a review, J. Adv. Res. 6 (2015) 105−121.

[30] D.A. Young, D.O. Ibrahim, D. Hu, K.L. Christman, Injectable hydrogel scaffold from decellularized human lipoaspirate, Acta Biomater. 7 (2011) 1040−1049.

 https://doi.org/10.1016/j.heliyon.2018.e00600

[31] K. Ishihara, N. Hamada, S. Kato, I. Shinohara, Photoresponse of the release behavior of an organic compound by an azoaromatic polymer device, J. Polym. Sci. Polym. Chem. Ed. 22 (3) (1984) 881−884.

[32] K. Ishihara, N. Muramoto, I. Shinohara, Controlled release of organic substances using polymer membrane with responsive function for amino compounds, J. Appl. Polym. Sci. 29 (1) (1984) 211−217.

[33] K. Ishihara, M. Kobayashi, N. Ishimaru, I. Shinohara, Glucose induced permeation control of insulin through a complex membrane consisting of immobilized glucose oxidase and a poly (amine), Polym. J. 16 (8) (1984) 625−631.

[34] J. Chen, K. Park, Superporous, hydrogels: fast responsive hydrogel systems, J. Macromol. Sci. Part A Pure Appl. Chem. 36 (1999) 917−930.

https://doi.org/10.1016/j.heliyon.2018.e00600