Characterization of cryogenically slightly crosslinked biomedical poly(vinyl alcohol) gels

Jolanta Stasko* a, Liiga Berzina-Cimdina a, and Martins Kalnins b

a Biomaterials Innovation and Development Centre, Riga Technical University, Pulka Street 3/3, Riga, LV-1007, Latvia
b Institute of Polymer Materials, Faculty of Material Science and Applied Chemistry, Riga Technical University, Azenes Street 14/24, Riga, LV-1048, Latvia

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Abstract. Poly(vinyl alcohol) gels, prepared by the freezing/thawing technique, were studied. Poly(vinyl alcohol) water solutions were exposed to 1–3 subsequent cycles of freezing (12 h at –20 °C) followed by thawing (12 h at 20 °C). Water content (weight and volume fraction) and degree of swelling \( \alpha \) at the equilibrium state were determined. Average molecular weights of polymer chains between crosslinks \( M_C \) (using the Flory–Rehner approach) were calculated. Values of \( \alpha \) and \( M_C \) considerably decrease with the growth of the number of freezing/thawing cycles \( n_C \).

The modulus of elasticity \( E \), tensile strength \( \sigma_B \), and elongation at break \( \varepsilon_B \) were determined from experimental stress–strain relationships of swollen gels. The \( E \) and \( \sigma_B \) values considerably increase with \( n_C \): up to 6–8 times for \( E \) and almost by an order for tensile strength \( \sigma_B \). More concentrated water solutions provide almost two times greater \( E \) and \( \sigma_B \) values. Strength-deformation characteristics for gels prepared at \( n_C = 2–3 \) are acceptable for their application in potential drug delivery systems.

To assess the stability of crosslinked structures, gels were subjected to subsequent drying (at 25, 60, and 105 °C) and water sorption (at 25 °C) cycles. Reduction of the swelling degree and respective calculated \( M_C \) values as well as lessening of the initial rate of water sorption after each drying cycle indicate the formation of additional crosslinks.

Key words: poly(vinyl alcohol), gel, cryogenically crosslinked, sorption ability, strength-deformation characteristics.

INTRODUCTION

Water swelling crosslinked poly(vinyl alcohol) (PVA) gels have for many years been a preferred research object, with wide potential practical application mainly in the biomedical area: tissue-engineering, cartilage reconstruction, materials for artificial skin, bioadhesive and mucoadhesive systems, drug delivery systems [1–4].

The freezing/thawing technique [3] as a method of preparation of crosslinked PVA is particularly attractive mainly for the reason that comparatively stable crosslinked structures can be easily obtained without using numerous hazardous ingredients necessary for chemical crosslinking (specific crosslinking agents, organic solvents, emulsifiers, catalysts, and others) [5,6]. The PVA gels prepared by freezing/thawing techniques are considered to have higher elasticity and mechanical strength than chemically crosslinked ones [3,6,7].

The freezing/thawing method is highly suitable for reaching the aim of our work – easy obtaining of stable biomedical gels for drug delivering wound dressing. Except for the main requirement, reliable ability to deliver certain medicine at a predictable rate, these drug delivering gels (DDGs) should protect from infection and external contamination, preserve undamaged epithelium cells as well as be mechanically stable enough [8].

Our previous works [9,10] show that the most favourable molecular weight of PVA, suitable for gel preparation by the freezing/thawing technique, is about \( 130 \times 10^3 \) g/mol. Water solutions of PVA with a higher molecular weight (\( 145 \times 10^3 \) g/mol and more) are too viscous. Poly(vinyl alcohols) with smaller molecular weight (25 × 10^3 to 88 × 10^3) do not form stable gels at
a low number freezing/thawing cycles \((n_c)\). The hydrolysis degree should be great \((\geq 98\%)\). The content of PVA in water solution should be between 15 and 20 wt\%. Less concentrated solutions form a nonuniform crosslinked network, while the viscosity of more concentrated solutions is too high \([9,11]\).

Sufficient strength-deformation characteristics, certain stability in the eventual treatment processes, and most of all high water sorption ability (which would provide the required drug capacity of the gel) can be listed as important features of a potential DDG. Since the growth of crosslinking density with \(n_c\) is a general trend \([12]\), it seems that an efficient DDG may be obtained exactly at a low \(n_c\). It would also benefit from the technology point of view (energy saving).

It is clear that merely slightly crosslinked PVA gels which have not been practically studied can provide a high enough sorption ability. However, there was a concern that such systems may not have sufficient strength and stability, which we aim to find out in this work.

**MATERIALS AND METHODS**

**Preparation of gel systems**

Poly(vinyl alcohol) (the same as in \([9]\)), with molecular weight \(130 \times 10^3\) g/mol, melting temperature \(T_m = 225.8\) °C, glass transition temperature \(T_g = 76.6\) °C, and crystallinity 43%, was used. Poly(vinyl alcohol) aqueous solution of two concentrations, \(c_1 = 15\) wt\% and \(c_2 = 20\) wt\%, were prepared by dissolution of PVA in distilled water (6 h at 80°C). The solutions were poured out on an Al foil mold (110 × 100 mm; the thickness of the solution layer was 5 mm) and put into a polyethylene zip-bag, thus providing constant water content in the sample. Samples of PVA water solutions were exposed to 1–3 subsequent cycles of freezing, immediately followed by thawing. The samples were held in a freezer at –20°C for 12 h, then removed, and kept in a thermostat at 20°C for 12 h. For comparison untreated PVA films were prepared by pouring the PVA solution on glass vessels (thickness of the solution layer 1 mm) and drying at room temperature.

**Determination of sorption characteristics of prepared gels**

The prepared gels were extracted by rinsing to remove sol-fraction. Three parallel samples of gels were placed on pre-weighted glass cloth and rinsed by gently mixing until the equilibrium weight of samples was reached. Finally the samples were dried at 105°C and weighed again.

The content of gel was calculated following formula (1):

\[
G = \frac{W_D}{W_{PVA}} - 100, \tag{1}
\]

where

- \(G\) – gel content,
- \(W_{PVA}\) – weight of PVA in the gel,
- \(W_D\) – weight of dry gel.

The weight fraction of water \(\psi_{H_2O}^-\) in the swollen gel at the equilibrium state was calculated as follows:

\[
\psi_{H_2O}^- = \frac{W_S - W_D}{W_S}, \tag{2}
\]

where

- \(W_S\) – weight of swollen gel,
- \(W_D\) – weight of dry gel.

The volume fraction of polymer in swollen gel at the equilibrium state \(\phi_{POL}^-\) was calculated according to the expression

\[
\phi_{POL}^- = \left(\frac{\rho_{POL}}{\rho_{POL} - \rho_{H_2O}}\right)^{\frac{1}{2}} \left(1 - \psi_{H_2O}^-\right), \tag{3}
\]

where

- \(\rho_{POL}\) – density of polymer (1.28 g/cm³).
- \(\rho_{H_2O}\) – density of poly(vinyl alcohol) aqueous solution (1.28 g/cm³).

The swelling degree of gel \(\alpha\) was calculated as follows:

\[
\alpha = \frac{\phi_{POL}^- + \psi_{H_2O}^-}{\phi_{POL}^-} = \frac{1}{\phi_{POL}^-}, \tag{4}
\]

where

- \(\phi_{H_2O}^-\) – volume fraction of water in swollen gel at the equilibrium state.

To assess the crosslinking degree of gels, average molecular weight between crosslinks \(M_c\) was calculated (5) by using the traditional Flory–Rehner approach \([13]\):

\[
M_c = \frac{\rho(1 - 2/\phi)\rho'}{\ln(1 - \phi_{POL}^-) + \chi^2\phi_{POL}^- + \phi_{POL}^-}, \tag{5}
\]

where

- \(M_c\) – average molecular weight of polymer chains between crosslinks,
- \(\rho\) – unswollen polymer density (1.28 g/cm³),
- \(\phi\) – functionality of the crosslinks (in our case \(\phi = 3\) \([14]\)),
- \(\phi_{POL}\) – volume fraction of polymer,
- \(\rho'\) – molar volume of solvent (water),
- \(\chi\) – Flory–Huggins interaction parameter between the polymer (PVA) and the swelling agent (water) (in our case \(\chi = 0.49\) \([15]\)).
Determination of tensile strength-deformation characteristics

Samples in the shape of strips 110 × 20 × 5 mm were cut out from the gel sheet. Both ends of the sample were reinforced for suitable fixing in grips of the test machine. The device Zwick Roell BDO-FB020TN was used to determine the relationships between tensile stress \( \sigma \) and relative elongation \( \varepsilon \) up to the fracture of the sample with the rate of cross-heads motion 50 mm/min at room temperature. Several characteristics were fixed from \( \sigma \varepsilon \) curves (Fig. 1): tensile strength \( \sigma_b \), elongation at break \( \varepsilon_b \), efficient modulus of elasticity (calculated by the MathCad program):

\[
E = \frac{d\sigma}{d\varepsilon},
\]

as well as “averaged” modulus

\[
\bar{E} = \frac{\sigma_b}{\varepsilon_b}.
\]

Three parallel samples were used. The measurement error did not exceed 6% for \( E \) and \( \sigma_b \) and 10% for \( \varepsilon_b \).

Determination of stability PVA gels

To evaluate the stability of PVA crosslinked structures, values of critical temperature and critical time (at 25 °C, 40 °C, and 60 °C) at which samples disintegrate were determined. Three parallel samples (20 × 20 × 2 mm) were placed into separate vessels with distilled water at room temperature. To determine the critical temperature \( T_{\text{CRIT}} \), the vessels were heated at a rate of 2 °C/min. To establish the critical time, the samples were exposed for up to 13 days at certain fixed temperature.

Cyclic drying–water absorption tests of PVA gel samples were also carried out. Poly(vinyl alcohol) gels were dried (at 25 °C, 60 °C, and 105 °C) until constant weight. After each drying the water sorption ability of samples was tested at 25 °C.

Water weight fraction \( \psi_{H_2O} \) was determined as a function of drying/sorption time till respective equilibrium values were reached. The following characteristics were found from \( \psi_{H_2O}^{\infty} \) relationships: equilibrium content of water \( \psi_{H_2O}^{\infty} \), the initial rate of water sorption \( v_0 \):

\[
v_0 = \lim\{d(\psi_{H_2O})/dt\}_{t=0},
\]

as well as water content after the first 15 min and 1 h period of water sorption.

RESULTS AND DISCUSSION

Visually homogeneous gel structure forms already at the first freezing/thawing cycle. Sol is firmly incorporated into gel structure and does not segregate in itself. Gel content, determined by extraction, is comparatively high and almost not affected by \( n_c \) (Table 1). Gel content is somewhat higher for more diluted PVA water solutions (\( c_1 \)).

Sorption characteristics of prepared gels

The values of equilibrium water content \( \psi_{H_2O}^{\infty} \)  volume fraction of polymer \( \bar{\psi}_{\text{pol}} \) in swollen gels as well as the swelling degree of gel \( \alpha \) are summarized in Table 2.

As can be seen, in the swelling equilibrium state gels are able to contain a large amount of water (up to 96 wt%), which is one of the most important requirements for an efficient DDG. As expected, the value of water weight fraction \( \psi_{H_2O}^{\infty} \) in prepared gels decreases with the number freezing/thawing cycles \( n_c \). However, even at \( n_c = 3 \) this value is high enough for practical use. The swelling degree \( \alpha \) essentially decreases with \( n_c \) (up to two times).

The calculated values of \( M_c \) decrease up to five times with the growth of \( n_c \). For more concentrated PVA water solutions (\( c_2 \)) \( M_c \) values are roughly two times smaller. Calculated \( M_c \) values are comparatively large and no less than 10^3 g/mol for the most crosslinked samples (\( n_c = 3 \)). So, the obtained gels should be recognized as slightly crosslinked.

Similarly average molecular weight between crosslink values was determined in [5,15] for considerably more crosslinked PVA gels (\( n_c \leq 9 \)). Calculated \( M_c \) values ranged from \( 1.1 \times 10^3 \) to \( 9.6 \times 10^3 \) g/mol.

Table 1. Gel content of prepared crosslinked PVA

<table>
<thead>
<tr>
<th>( n_c )</th>
<th>Gel content, wt%</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( c_1 )</td>
<td>( c_2 )</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>71</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>69</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>73</td>
<td>58</td>
<td></td>
</tr>
</tbody>
</table>
### Table 2. Sorption characteristics of prepared gels (italic in brackets – ratio of the value to the respective value at $n_C = 3$)

<table>
<thead>
<tr>
<th>$n_C$</th>
<th>$\psi_{H_2O}$</th>
<th>$\varphi_{POL}$</th>
<th>$\alpha$</th>
<th>$M_c \times 10^{-3}$</th>
<th>$\psi_{H_2O}$</th>
<th>$\varphi_{POL}$</th>
<th>$\alpha$</th>
<th>$M_c \times 10^{-3}$</th>
<th>$\alpha(c_1)/\alpha(c_2)$</th>
<th>$M_c(c_1)/M_c(c_2)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.96</td>
<td>0.032</td>
<td>32 (20)</td>
<td>108 (5.1)</td>
<td>0.94</td>
<td>0.047</td>
<td>21 (1.9)</td>
<td>45 (4.5)</td>
<td>1.5</td>
<td>2.4</td>
</tr>
<tr>
<td>2</td>
<td>0.93</td>
<td>0.056</td>
<td>18 (1.1)</td>
<td>31 (1.5)</td>
<td>0.92</td>
<td>0.064</td>
<td>16 (1.5)</td>
<td>21 (2.1)</td>
<td>1.1</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>0.92</td>
<td>0.064</td>
<td>16 (1)</td>
<td>21 (1)</td>
<td>0.89</td>
<td>0.088</td>
<td>11 (1)</td>
<td>10 (1)</td>
<td>1.5</td>
<td>2.1</td>
</tr>
</tbody>
</table>

### Strength-deformation characteristics

Experimental $\sigma(\varepsilon)$ curves are shown in Fig. 2. The curves are concave, which is typical of moderately crosslinked polymers in a high-elastic state (elastomers) [16].

The relationship $E_p(\varepsilon)$ for one individual gel sample together with $\sigma(\varepsilon)$ relationship, as an example, is shown in Fig. 3.

Considering certain instability of $\sigma(\varepsilon)$ and $E_p(\varepsilon)$ relationships (Figs 2 and 3) (caused by uneven stress distribution in heterogeneous gel structure), instead of the initial modulus of elasticity $E = \lim(\text{d} \sigma/\text{d}\varepsilon)_{\varepsilon \to 0}$ [17], the elastic behaviour of gels was characterized by moduli $E$ and $E^*$. Both characteristics take into account the whole range of $\varepsilon$ values (up to $\varepsilon_n$), thus allowing averaging structural inhomogeneities of gels. The values of both moduli are quite close (for crosslinked PVA with $c_1$, $E = 36$ KPa and $E^* = 35$ KPa).

The values of modulus $E$, tensile strength $\sigma_n$, and elongation at break $\varepsilon_n$ of gels versus the number of freezing/thawing cycles $n_c$ are shown in Fig. 4.

The $E$, $\sigma_n$, and $\varepsilon_n$ values grow considerably with the number of cycles and are higher for gels formed from a more concentrated solution ($c_2$). Taking into account essential growth of the crosslinking degree (Table 2) judged from water sorption data, sharp increase in both $E$ and $\sigma_n$ values (up to 6 times) with the number of freezing/thawing cycles $n_c$ is no surprise (Fig. 4). As a consequence of the greater crosslinking degree, gels prepared from a more concentrated PVA water solution $c_2$ show several times larger $E$ and $\sigma_n$ values.

The average $\sigma_n$ value of prepared gels is about 0.1 MPa. Thus the average specific strength $\sigma_n/\rho$ ($\rho$ – density of gel), expressed as self-support length, is comparatively high – approximately 10 m. Therefore certain swollen gel wares can be reliably handled in practical application. It seems that strength-deformation characteristics of PVA gels, prepared with $n_c = 2–3$, are quite acceptable for drug delivery use.

It was of special interest to estimate the value of the average molecular weight between crosslinks also from...
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Fig. 4. Tensile modulus \(E\) (a), strength \(\sigma\) (b), and elongation at break \(\varepsilon\) (c) of PVA gels depending on the number of freezing/thawing cycles \(n_c\).

The calculated \(M_c^*\) values (Table 3), compared to respective \(M_c\) values obtained from sorption data (Table 2), are roughly one order higher and do not seem quite credible. The most likely explanation is as follows. Because of the porous (spongy) structure of gels [23], actual values of modulus \(E\) should be much higher than the values determined experimentally. Taking inverse proportionality of \(M_c\) to \(E\) into account, the actual value of \(M_c^*\) could be smaller.

Nevertheless, relative values of both types of moduli differ little (Tables 2 and 3), and absolute modulus values correlate almost linearly (Fig. 5). Thereby \(M_c^*\) may by used as a comparative characteristic of the crosslinking degree.

In particular, the concept of average molecular weight “between links” for PVA gels is rather conditional. According to the prevailing view [5], crosslinks are small crystallites, gradually arising in freezing/thawing cycles. The density of intermolecular bonds (mainly hydrogen bonds) within crystallites is large. On the other hand, it is also argued [24] that in freezing/thawing cycles simple increase in the density of intermolecular bonds occurs without sufficient changes in three-dimensional order. Anyway, \(M_c\) may be used for relative evaluation of the crosslinking degree.

Table 3. Elastic characteristics of prepared gels (*italic* in brackets – ratio of the \(M_c\) value to the respective value at \(n_c = 3\))

<table>
<thead>
<tr>
<th>(n_c)</th>
<th>(c_1)</th>
<th>(c_2)</th>
<th>(\frac{M_c^<em>(c_1)}{M_c^</em>(c_2)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>130 (7.2)</td>
<td>59 (3.9)</td>
<td>2.2</td>
</tr>
<tr>
<td>2</td>
<td>26 (1.4)</td>
<td>17 (1.7)</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>18 (1)</td>
<td>10 (1)</td>
<td>1.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(M_c^*)</th>
<th>(E), KPa</th>
<th>(M_c^*)</th>
<th>(E), KPa</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\times 10^{-4})</td>
<td>(\times 10^{-3})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>130 (7.2)</td>
<td>59 (3.9)</td>
<td>2.2</td>
</tr>
<tr>
<td>2</td>
<td>26 (1.4)</td>
<td>17 (1.7)</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>18 (1)</td>
<td>10 (1)</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Fig. 5. Correlation of \(M_c\) and \(M_c^*\) values; \(c_1\) – rhombs, \(c_2\) – stars.

1 Our numerous SEM studies of brittle fractured gel samples show that the actual load-bearing cross section often does not exceed half of the imaginary one.
Characteristic of the stability of crosslinked structures

Application of gels as components of drug delivery systems often requires their treatment (forming, sterilization, etc.) at temperature above room temperature. Thus adequate thermal resistance of gels becomes crucial. There is a reason to believe that crosslinks, which develop in a course of freezing/thawing cycles, are the same intermolecular bonds which link together macromolecules of untreated PVA. That is why swollen untreated PVA samples were included in the thermal stability test.

A group of samples was placed in water and were heated from 20 °C at a rate of 2 °C/min. The critical temperature $T_{\text{CRIT}}$ at which certain changes in the sample become visible was fixed: the sample gets more transparent, loses shape, and finally dissolves/disintegrates.

As seen from Fig. 6, the $T_{\text{CRIT}}$ values of each phenomenon somewhat increase with $n_c$. Though, the difference between $T_{\text{CRIT}}$ at which untreated PVA dissolves ($n_c = 0$) and more crosslinked gel disintegrates ($n_c = 3$) does not exceed 4 °C.

For another group of samples the time interval was determined in which the samples dissolve/disintegrate at different temperatures: 25 °C, 40 °C, and 60 °C. Untreated PVA dissolves within 2–5 h, less crosslinked gel ($n_c = 1$) withstand 20–30 h at 25 °C, 15–18 h at 40 °C, and 8–12 h at 60 °C. More crosslinked gels resist more than ten days at 60 °C without any visible changes.

It is important to find out whether gels, which are intended to be used as DDGs, should be kept in a swollen state or may be stored in dried form, with water soaking just before use. For that purpose cyclic drying–soaking (absorption) tests were carried out. Poly(vinyl alcohol) gels were successively dried (at 25 °C, 60 °C, and 105 °C) until constant weight. After each drying, the water sorption ability of gels was tested at 25 °C (Fig. 7). The water content in the gel $\psi_{\text{H}_2\text{O}}$ as function of drying/sorption time was determined.

![Fig. 6. Values of critical temperature of gel samples ($c_i$) at which: sample gets transparent (I), loses shape (II), and dissolves/disintegrates (III).](image)

The equilibrium water content $\psi_{\text{H}_2\text{O}}^\infty$ which is reached after respective drying decreases from cycle to cycle (Table 4). After drying at 25 °C the $\psi_{\text{H}_2\text{O}}^\infty$ value exceeds 80% of the initial water content in gel, after 60 °C ~ 75%, and after 105 °C ~ about 60%. At the same temperatures the $\psi_{\text{H}_2\text{O}}^\infty$ values slightly decrease with growth of $n_c$.

After drying at 60 °C the gel contains merely 5% water. Considering that the water content reachable in subsequent sorption is high enough (swollen gel contains more than 70% water), it is reasonable to conclude that, if necessary, gels dried at up to 60 °C can be used as DDGs.

The swelling degree $\alpha$ and $M^*_c$ values (calculated from the respective $\psi_{\text{H}_2\text{O}}^\infty$ values) reduce from cycle to cycle (Table 5). This suggests that not only the initial crosslinks (that have emerged in freezing/thawing cycles) remain but also stable additional links arise in consecutive drying procedures.

Resistance of the gel network to water diffusion can be characterized by the initial rate of water uptake $v_0 = \lim (d\psi_{\text{H}_2\text{O}}/dt)_{t \to 0}$. The higher the drying temperature, the higher is the resistance of gel to water diffusion: respective $v_0$ values decrease considerably (Fig. 8). Values of $v_0$ are determined by the cross-linking degree of gel (Fig. 9).

Dried gels absorb water rapidly enough (Fig. 10). This feature is particularly important for practical use, when it is necessary to prepare swollen gel for drug delivery systems by soaking with water or drug water solution.

Studies on kinetic of drug release from slightly crosslinked PVA gels cryogenically prepared from PVA water and ethanol solutions containing a wide spectra of plant product extracts (e.g. calendula, St.-John’s-wort) and conventional medicine (e.g. *Viride nitens* and methylene blue) are in our focus and underway right now. Current data show that the release rate of certain drugs can be efficiently controlled by the number of freezing/thawing cycles and concentration of PVA–drug solutions.
Table 4. Changes in the equilibrium weight fraction of water $\psi^\infty_{H_2O}$ and percentage of initial gel water content (italic, in brackets) of PVA gels ($c_1$) in successive water sorption–drying cycles

<table>
<thead>
<tr>
<th>$n_C$</th>
<th>Initial gel</th>
<th>Drying at 25 °C</th>
<th>Sorption after drying</th>
<th>Drying at 60 °C</th>
<th>Sorption after drying</th>
<th>Drying at 105 °C</th>
<th>Sorption after drying</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.96</td>
<td>0.13</td>
<td>0.78 (81)</td>
<td>0.04</td>
<td>0.73 (76)</td>
<td>0</td>
<td>0.62 (63)</td>
</tr>
<tr>
<td>2</td>
<td>0.93</td>
<td>0.13</td>
<td>0.76 (81)</td>
<td>0.05</td>
<td>0.71 (76)</td>
<td>0</td>
<td>0.59 (63)</td>
</tr>
<tr>
<td>3</td>
<td>0.92</td>
<td>0.14</td>
<td>0.74 (80)</td>
<td>0.05</td>
<td>0.69 (71)</td>
<td>0</td>
<td>0.56 (61)</td>
</tr>
</tbody>
</table>

Table 5. Changes in the swelling degree $\alpha$ and $M_C$ values (calculated from $\alpha$) of gels ($c_1$) in successive water sorption–drying cycles

<table>
<thead>
<tr>
<th>$n_C$</th>
<th>Initial gel</th>
<th>Sorption after drying</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>at 25 °C</td>
<td>at 60 °C</td>
</tr>
<tr>
<td></td>
<td>$\alpha$</td>
<td>$M_C \times 10^3$</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>108</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>21</td>
</tr>
</tbody>
</table>

Fig. 8. Initial rate of water uptake $v_u$ for PVA gels.

Fig. 9. Relationship between $v_u$ and $M_C$ values.

Fig. 10. Water content $\psi^\infty_{H_2O}$ in gel at defined time of water sorption (drying temperatures 25 °C and 60 °C).

CONCLUSIONS

Poly(vinyl alcohol) (PVA) gels, prepared by cyclic freezing/thawing of PVA water solutions (number of cycles $n_C \leq 3$), are able to comprise a high amount of water (up to 96 wt%) in the swelling equilibrium state. It is one of the most significant requirements for gels intended to be used for drug delivery.

The equilibrium swelling degree $\alpha$, as well as respective calculated average molecular weight of polymer chains between crosslinks $M_C$, substantially decrease with the number of freezing/thawing cycles $n_C$ up to 2 and 5 times, respectively. Gels prepared from
more concentrated water solutions are more densely crosslinked. Calculated $M_C$ values are comparatively large and not less than $10^5$ for most of the crosslinked samples. Thus the obtained gels should be recognized as slightly crosslinked.

Strength-deformation characteristics increase with $n_C$: up to 6–8 times for the tensile elasticity modulus $E$ and almost by an order for tensile strength $\sigma_B$. A more concentrated water solution provides almost two times greater $E$ and $\sigma_B$ values. These characteristics for gels prepared at $n_C = 2–3$ are acceptable for use in potential drug delivery systems.

The stability of crosslinked structures was evaluated by exposure of gels to subsequent drying–water sorption cycles. Gradual reduction of the swelling degree and respective calculated $M_C$ values, as well as lessening of the initial rate of water sorption after each drying cycle, result from the formation of additional crosslinks. The sorption ability of gels remains on the level which is suitable for biomedical application.

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Krüogeensel teel osaliselt ristsillatud biomeditsiinilise polüvinüülalkoholi geeli iseloomustamine

Jolanta Stasko, Līga Berzina-Cimdina ja Martins Kalnins