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POLYMER SCIENCE

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

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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 α 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 α and M_C considerably decrease with the growth of the number of freezing/thawing cycles n_C.

The modulus of elasticity E, tensile strength σ_B, and elongation at brake ε_B were determined from experimental stress–strain relationships of swollen gels. The E and σ_B and values considerably increase with n_C: up to 6–8 times for E and almost by an order for tensile strength σ_B. More concentrated water solutions provide almost two times greater E and σ_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 × 103 g/mol. Water solutions of PVA with a higher molecular weight (145×10^3 g/mol and more) are too viscose. Poly(vinyl alcohols) with smaller molecular weight (25×10^3 to 88×10^3) do not form stable gels at

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a low number freezing/thawing cycles (n_C). The hydrolysis degree should be great (≥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 130×10^3 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):

$$G = \frac{W_D}{W_{PVA}} 100, \quad (1)$$

where
G – gel content,
W_{PVA} – weight of PVA in the gel,
W_D – weight of dry gel.

The weight fraction of water $\psi^{\infty}_{H_2O}$ in the swollen gel at the equilibrium state was calculated as follows:

$$\psi^{\infty}_{H_2O} = \frac{W_S - W_D}{W_S}, \quad (2)$$

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 φ^{∞}_{POL} was calculated according to the expression

$$\varphi^{\infty}_{POL} = (\psi^{\infty}_{POL}/\rho_{POL}) / [(\psi^{\infty}_{POL}/\rho_{POL}) + (\psi^{\infty}_{H_2O}/\rho_{H_2O})], \quad (3)$$

where
ψ^{∞}_{POL} – weight fraction of polymer at the equilibrium state of sorption; $\psi^{\infty}_{POL} = 1 - \psi^{\infty}_{H_2O}$,
ρ_{H_2O} – density of water,
ρ_{POL} – density of polymer (1.28 g/cm^3).

The swelling degree of gel α was calculated as follows:

$$\alpha = \frac{\varphi^{\infty}_{POL} + \varphi^{\infty}_{H_2O}}{\varphi^{\infty}_{POL}} = \frac{1}{\varphi^{\infty}_{POL}}, \quad (4)$$

where
$\varphi^{\infty}_{H_2O}$ – 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]:

$$M_C = -\frac{\rho(1 - 2/\phi)V_1(\varphi^{1/3}_{POL} - 0.5\varphi_{POL})}{\ln(1 - \varphi_{POL}) + \chi\varphi^2_{POL} + \varphi_{POL}}, \quad (5)$$

where
M_C – average molecular weight of polymer chains between crosslinks,
ρ – unswollen polymer density (1.28 g/cm^3),
ϕ – functionality of the crosslinks (in our case $\phi = 3$ [14]),
φ_{POL} – volume fraction of polymer,
V_1 – molar volume of solvent (water),
χ – 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 σ and relative elongation ε 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 σ_B, elongation at break ε_B, efficient modulus of elasticity (calculated by the MathCad program):

$$E_\varepsilon = d\sigma/d\varepsilon, \quad (6)$$

as well as "averaged" modulus

$$\bar{E} = \sigma_B/\varepsilon_B. \quad (7)$$

Three parallel samples were used. The measurement error did not exceed 6% for E and σ_B and 10% for ε_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_{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 ψ_{H_2O} was determined as function of drying/sorption time till respective equilibrium values were reached. The following characteristics were found from $\psi_{H_2O}(t)$ relationships: equilibrium content of water $\psi^{\infty}_{H_2O}$, the initial rate of water sorption v_0:

$$v_0 = \lim[(d(\psi_{H_2O})dt)|_{t\to 0}], \quad (8)$$

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

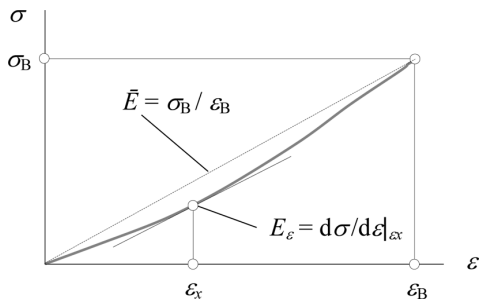

Fig. 1. Schematic depiction of the relationship between typical tensile stress σ and deformation ε of crosslinked PVA gels.

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 $\psi^{*}_{H_2O}$, volume fraction of polymer φ^{∞}_{POL} in swollen gels as well as the swelling degree of gel α 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 the most important requirements for an efficient DDG. As expected, the value of water weight fraction $\psi^{\infty}_{H_2O}$ 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 α 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 10^4 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 ($n_C \le 9$). Calculated M_C values ranged from 1.1×10^3 to 9.6×10^3 g/mol.

Table 1. Gel content of prepared crosslinked PVA

n_C	Gel content, wt%	
	c_1	c_2
1	71	43
2	69	56
3	73	58

Table 2. Sorption characteristics of prepared gels (*italic* in brackets – ratio of the value to the respective value at $n_C = 3$)

n_C	c_1				c_2				$\alpha(c_1)/\alpha(c_2)$	$M_C(c_1)/M_C(c_2)$
	$\psi^{\infty}_{H_2O}$	φ^{∞}_{POL}	α	$M_C \times 10^{-3}$	$\psi^{\infty}_{H_2O}$	φ^{∞}_{POL}	α	$M_C \times 10^{-3}$		
1	0.96	0.032	32 (*2.0*)	108 (*5.1*)	0.94	0.047	21 (*1.9*)	45 (*4.5*)	1.5	2.4
2	0.93	0.056	18 (*1.1*)	31 (*1.5*)	0.92	0.064	16 (*1.5*)	21 (*2.1*)	1.1	1.5
3	0.92	0.064	16 (*1*)	21 (*1*)	0.89	0.088	11 (*1*)	10 (*1*)	1.5	2.1

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

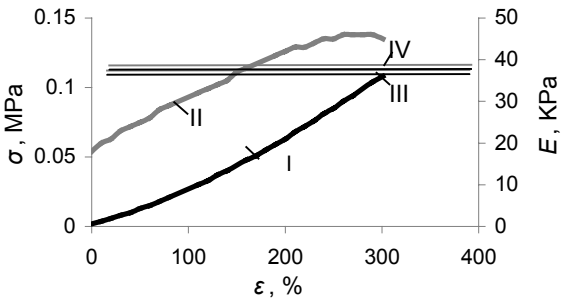

Fig. 3. Tensile $\sigma(\varepsilon)$ relationship of PVA gel ($c_{1,2}$, $n_C = 2$) – I, relationship $E_\varepsilon(\varepsilon)$ – II, values of $\bar{E}$ – III, and $\bar{E}^*$ – IV.

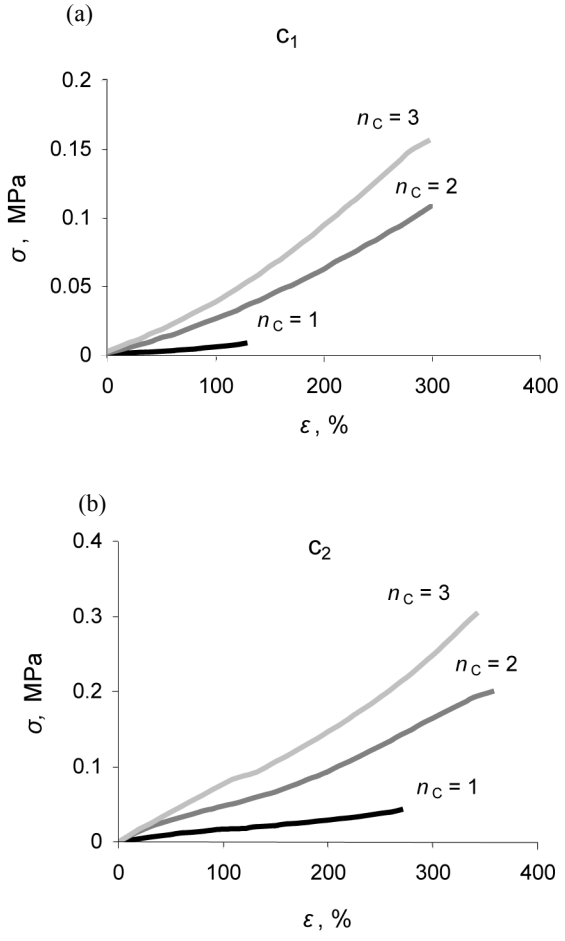

Fig. 2. Tensile $\sigma(\varepsilon)$ relationships of prepared gels: c_1 (a) and c_2 (b).

The values of modulus $\bar{E}$, tensile strength σ_B, and elongation at break ε_B of gels versus the number of freezing/thawing cycles n_C are shown in Fig. 4.

The $\bar{E}$, σ_B, and ε_B 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 $\bar{E}$ and σ_B 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 $\bar{E}$ and σ_B values.

The average σ_B value of prepared gels is about 0.1 MPa. Thus the average specific strength σ_B/ρ (ρ – density of gel), expressed as self-support length, is comparatively high – approximately 10^2 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

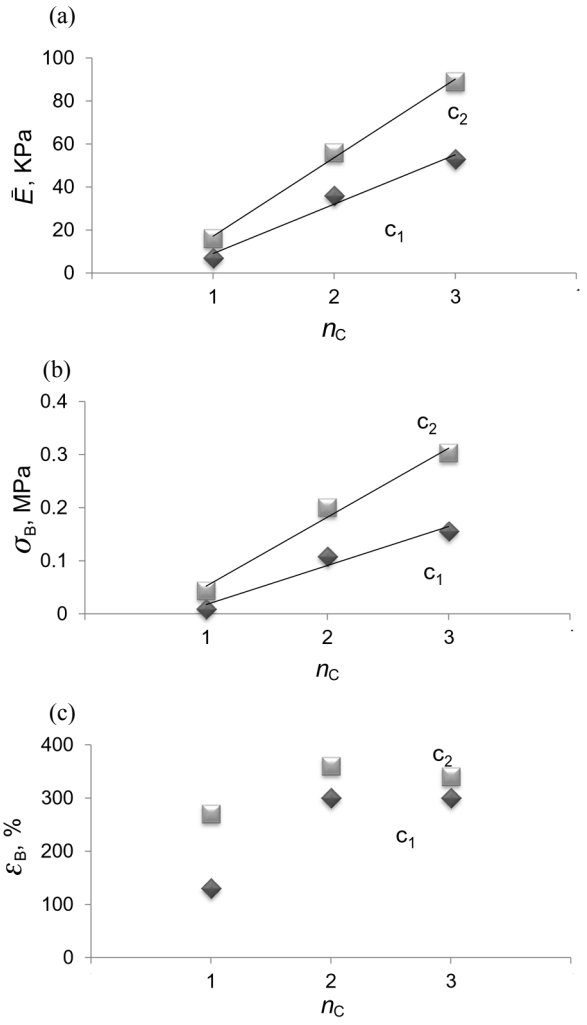

Fig. 4. Tensile modulus $\bar{E}$ (a), strength σ_B (b), and elongation at break ε_B (c) of PVA gels depending on the number of freezing/thawing cycles n_C.

the values of elastic modulus. Let us denote it by M_C^*. The relationship (derived from rubber elasticity theory [18,19] showing inverse proportionality of M_C^* to E value was used:

$$M_C^* = \frac{3\rho RT}{\bar{E}}, \qquad (9)$$

where

M_C^* – average molecular weight of polymer chains between crosslinks,
ρ – density,
R – universal gas constant,
T – absolute temperature,
$\bar{E}$ – average modulus.

In a similar way M_C^* was calculated for crosslinked epoxy oligomers [20], protein-based hydrogels [21], xantan-konjac glucomannan hydrogels [22], etc.

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 $\bar{E}$ should be much higher than the values determined experimentally[1]. 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 $n_C = 3$)

n_C	c_1		c_2		$M_C^*(c_1)/M_C^*(c_2)$
	$\bar{E}$, KPa	$M_C^* \times 10^{-4}$, g/mol	$\bar{E}$, KPa	$M_C^* \times 10^{-4}$, g/mol	
1	7	130 (*7.2*)	16	59 (*5.9*)	2.2
2	36	26 (*1.4*)	56	17 (*1.7*)	1.5
3	53	18 (*1*)	89	10 (*1*)	1.8

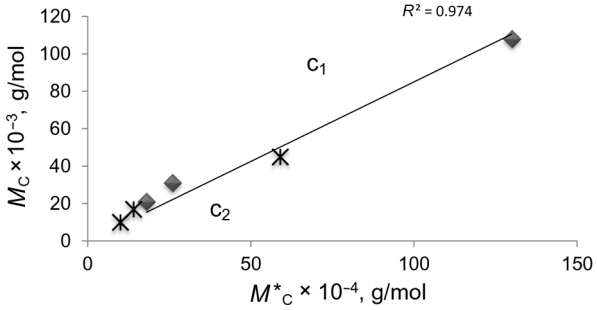

Fig. 5. Correlation of M_C and M_C^* values; c_1 – rhombs, c_2 – stars.

[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_{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_{CRIT} values of each phenomenon somewhat increase with n_C. Though, the difference between T_{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 ψ_{H_2O} as function of drying/sorption time was determined.

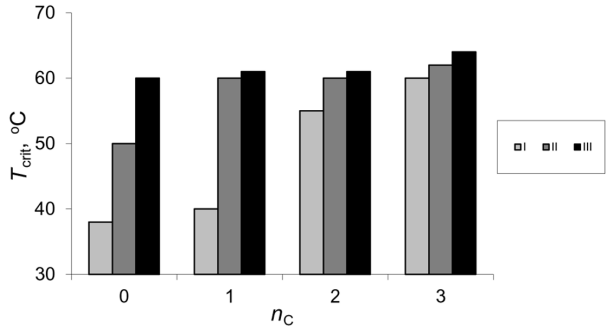

Fig. 6. Values of critical temperature of gel samples (c_1) at which: sample gets transparent (I), loses shape (II), and dissolves/disintegrates (III).

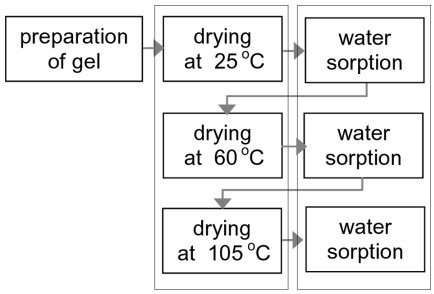

Fig. 7. Scheme of cyclic drying–soaking (absorption) tests.

The equilibrium water content $\psi^{\infty}_{H_2O}$ which is reached after respective drying decreases from cycle to cycle (Table 4). After drying at 25 °C the $\psi^{\infty}_{H_2O}$ 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 $\psi^{\infty}_{H_2O}$ 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 α and M_C values (calculated from the respective $\psi^{\infty}_{H_2O}$ 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 $v_0 = \lim(\mathrm{d}\psi_{H_2O}/\mathrm{d}t)|_{t\to 0}$. 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 crosslinking 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

n_C	Initial gel	Drying at 25 °C	Sorption after drying	Drying at 60 °C	Sorption after drying	Drying at 105 °C	Sorption after drying
1	0.96	0.13	0.78 (*81*)	0.04	0.73 (*76*)	0	0.62 (*65*)
2	0.93	0.13	0.76 (*81*)	0.05	0.71 (*76*)	0	0.59 (*63*)
3	0.92	0.14	0.74 (*80*)	0.05	0.69 (*71*)	0	0.56 (*61*)

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

n_C	Initial gel		Sorption after drying					
			at 25 °C		at 60 °C		at 105 °C	
	α	$M_C \times 10^{-3}$	α	$M_C \times 10^{-3}$	α	$M_C \times 10^{-2}$	α	$M_C \times 10^{-2}$
1	32	108	5.1	1.1	4.5	7.6	3.1	2.5
2	18	31	5.0	1.2	4.1	6.1	2.8	1.9
3	16	21	5.0	1.2	3.8	4.9	2.6	1.5

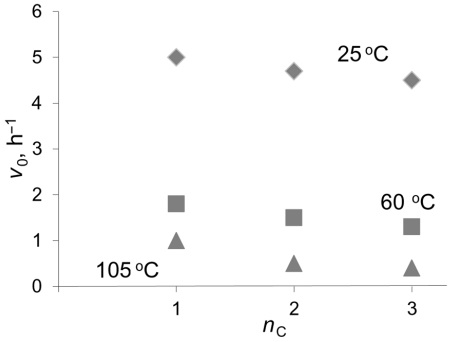

Fig. 8. Initial rate of water uptake v_0 for PVA gels.

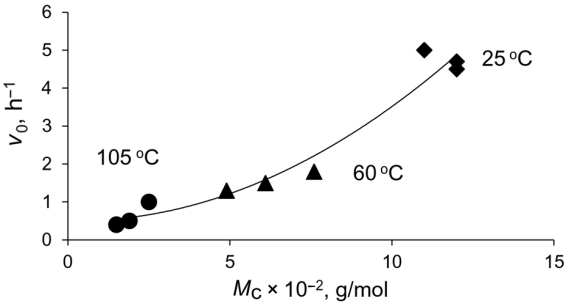

Fig. 9. Relationship between v_0 and M_C values.

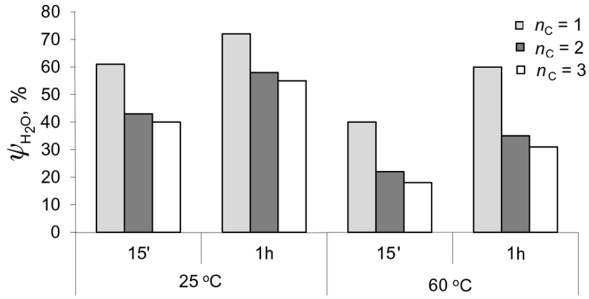

Fig. 10. Water content ψ_{H_2O} in gel at defined time of water sorption (drying temperatures 25 °C and 60 °C).

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 α, 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 10^4 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 σ_B. A more concentrated water solution provides almost two times greater E and σ_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

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Uuriti külmutamis-sulatamistehnikaga valmistatud polüvinüülalkoholi (PVA) geele. PVA vesilahuseid hoiti 12 h –20 °C ja 12 h +20 °C juures 1–3 tsüklit. Määrati veesisaldused (mahu- ja massiprotsentides) ning pundumisastmed α tasakaaluolekus. Flory-Rehneri metoodikaga arvutati ristsildadevaheliste ahelalõikude keskmine molekulmass M_C. Külmumis-sulamistsüklite arvu kasvuga vähenevad α ja M_C oluliselt. Pundunud geelide eksperimentaalsetest pinge-deformatsioonikõveratest määrati elastsusmoodul, tõmbetugevus ja pikenemine purunemisel. Külmumistsüklite arvu suurenedes kasvavad mooduli ja tõmbetugevuse väärtused oluliselt: moodul kasvab 6–8 korda ning tõmbetugevus umbes suurusjärgu, kontsentreeritumate vesilahuste korral on mooduli ja tõmbetugevuse väärtused peaaegu kaks korda suuremad. Kaks-kolm külmumistsüklit annavad sobiva geeli ravimi kohaletoimetamiseks kehas. Ristsillatud struktuuride stabiilsuse hindamiseks lasti geelidel tsükliliselt kuivada (25, 60 ja 105 °C juures) ning niiskust imada (25 °C). Pundumisastme vähenemine ja sellest arvutatud M_C väärtused, samuti veeimavuse vähenemine pärast iga kuivamistsüklit annavad tunnistust täiendavate ristsildade tekkimisest.