



Utilization of freeze thaw process for polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite

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Abstract

Polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel was successfully prepared by freeze thaw process. Without crosslinking agent, hydrogel was formed by using 3, 5 and 7 consecutive cycles of freeze thaw. Hydrogel can be formed by hydrogen bonding formation between OH-group of sodium alginate and polyvinyl alcohol throughout network. Scanning electron microscope reported that microstructure of hydrogel was well packed. The interconnect porosity was also observed. Differential scanning calorimetry exhibited that two exothermic peaks at temperature of 110°C and 225°C were observed due to evaporation of water molecule and melting temperature of hydrogel, respectively. The swelling behavior was rapidly increased within initial stage and then it was dimensionally stable. With low sodium alginate content, tensile strength was slightly superior, whereas low *in vitro* degradation behavior was observed. It was remarkable to note that polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel exhibited outstanding properties for being as a medical material.

1. Introduction

Up to the present time, the use of petrochemical based polymeric material was therefore increased for various sectors of industry. Although it provided significant advantages in terms of efficiency, it was still limited in particular case due to degradability and biocompatibility. With the utilization of petrochemical based polymer, it can create the disaster for ecological system due to difficulty of degradation. Furthermore, the use of petrochemical based polymeric material will be shortage based on the availability of crude oil in the near future. With this regard, numerous bio-based polymeric materials were designed to replace. One effective way to solve this issue was typically related to utilization of eco-friendly material. It provided various advantages such as biodegradability, non-toxicity as well as reduction of environmental pollution. Up to the present time, numerous types of eco-friendly material were developed for various industrial sectors. Among these, medical materials were considered as one of the most important tasks. It can be employed in numerous sectors such as drug delivery system, medical implant, chemical sensor for medical diagnostic and tissue engineering [1]. Moreover, the new research material for the kind of medical applications such as wound dressing and healing, bioseparation, cosmetic, and antibacterial materials are becoming more interesting for biomedical applications [2]. Recently, the design of eco-friendly materials for medical device was therefore favorite. One of the most frequent used medical materials was typically referred to hydrogel. From the fundamental point of

view, hydrogel was defined as a crosslinked polymer chains swollen in water. It was important to note that hydrogel provided many advantages such as high degree of flexibility and moldability. It was biodegradable, biocompatible and injectable. It therefore illustrated the outstanding potential in tissue engineering and drug delivery [3,4]. At the present time, it was notable that hydrogel can be synthesized from both synthetic and natural polymer, which was commonly referred to eco-friendly material. From the fundamental point of view, it was theoretically defined as non-harmful material, whether in its production, the use and dispose were easily recycled. Furthermore, the use of eco-friendly material was strongly encouraged by "Green policy" [5,6]. It was typically referred to the use of product and process with hazardous chemical reagents should be preferably avoided.

To date, the example of eco-friendly material was typically related to polyvinyl alcohol, polycaprolactone, polyethylene oxide, as well as polyacrylic acid. One of the most attractive eco-friendly materials was referred to polyvinyl alcohol. It was structurally considered as a linear hydrophilic synthetic polymer, containing pendent hydroxyl group [7]. It illustrated numerous advantages such as non-toxicity, high biocompatibility, high biodegradability as well as high hydrophilicity. It was commonly employed in numerous sectors of industry such as pharmaceutical and cosmetic products, medical technology and wastewater remediation [8-10].

To use polyvinyl alcohol with higher efficiency, the design of binary blend-based hydrogel was therefore developed. To form hydrogel, sodium alginate was therefore considered as one of the most important materials. From the fundamental point of view, it was structurally noted as a polysaccharide found in brown algae. It was hydrophilic and formed a viscous gum when hydrated. Utilization of sodium alginate was commonly employed due to its low toxicity, biocompatibility and low cost. Therefore, to ameliorate performance of polyvinyl alcohol by addition of sodium alginate was favorable. Recently, in 2018, Jiang *et al* [11] developed polyvinyl alcohol and sodium alginate hydrogel. It can be successfully prepared by freezing/thawing process and soaked in NaCl aqueous solution. It was notable that the chain entanglement between polyvinyl alcohol and sodium alginate chain was increased because of the salting-out effect. Furthermore, hydrogel exhibited tensile strength of 1.32 MPa, elongation at break of 400% and electrical conductivity of 3.62 S·m⁻¹. In 2019, Kong *et al* [12] developed 5-hydroxymethylfurfural-embedded polyvinyl alcohol and sodium alginate-based hydrogels for wound healing application. The presence of 5-hydroxymethylfurfural can be effectively provided the excellent antioxidant properties. It can subsequently induce for cell proliferation in wound healing process. The active molecule can be migrated into human skin fibroblast. In 2021, Bialik-Was *et al* [13] developed aloe vera loaded into sodium alginate and polyvinyl alcohol-based hydrogel for wound dressing application. It was notable that the presence of aloe vera can significantly improve the thermal stability of hydrogel. The position of aloe vera in hydrogel network can therefore provide the active substance delivery properties of hydrogel film.

Up to the present time, to develop hydrogel for medical material, utilization of freeze thaw technique was employed. This technique was considered as one of the most attractive strategies for hydrogel formation. The advantage for research as with this freeze thaw technique compared to the conventional technique is not required to use a high temperature or any extra chemicals as crosslinking agent that may cause toxicity [14] but one can resort to the mild, facile and effective method to fabricate physically crosslinked PVA gel [15]. Without the crosslinking agent, hydrogel was successfully synthesized [16,17]. Florez-Castillo *et al* [18] also reported that polyvinyl alcohol based hydrogel prepared by freeze thaw technique presented high elasticity and stability. Because the process was typically involved the freezing conditions such as temperature, number of cycle and polymer ratio. It consequently resulted in properties and application of hydrogel. Due to the use of hydrogel related to medical research area, the use of process without crosslinking agent may be appreciated.

Therefore, the objective of this work is to develop polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite by freeze thaw process, to study the structural, morphological and thermal properties of hydrogel composite and to evaluate the potential of hydrogel for being as a cosmetic material by swelling characteristic, and degradability. With 3, 5 and 7 consecutive cycles of freeze thaw, hydrogel was successfully prepared. Characterization by FTIR, SEM and DSC were conducted. Swelling behavior, degradability and mechanical properties were therefore determined.

2. Experimental

2.1 Chemical reagents

Polyvinyl alcohol (molecular weight 89,000-98,000, 99+% hydrolyzed) and sodium alginate were purchased from Sigma Aldrich Co., Ltd. All chemical reagents were used as received, without further purification.

2.2 Methods

2.2.1 Development of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite

Polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite was prepared by casted onto petri dish. The procedure was conducted based on guideline of previous work reported by Kim *et al* [19]. Briefly, polyvinyl alcohol (10%w/v) was dissolved in deionized water and gently stirred at 80°C for 1 h. In parallel, sodium alginate (2%w/v) was dissolved in deionized water and gently stirred at room temperature for 1 h. To prepare hydrogel, polyvinyl alcohol solution was poured into sodium alginate solution with a mixed ratio of 50:50, 40:60 and 30:70 v/v, respectively. The mixture was casted onto a petri dish, followed by freezing at -20°C for 18 h and thawing at room temperature for 6 h. The experiment was set up for 3, 5 and 7 consecutive cycles, respectively. After that, hydrogel was stored in desiccator to prevent moisture adsorption.

2.2.2 Swelling behavior

The swelling behavior was investigated using a gravimetric technique. Sample was cut into 1 cm² × 1 cm² with the same weight (W_d) and immersed in deionized water (DI) water for 24 h. Sample was removed from the solution, dried using a filter paper to remove excess water and weighed (W_w). Three samples were investigated following equation, and data were reported as statistical average and standard deviation.

$$\text{Swelling (\%)} = \frac{W_w - W_d}{W_d} \times 100$$

where W_w is the of the swollen sample and W_d is the initial weight of the hydrogel.

2.2.3 Degradation behavior

The sample was cut into 1 cm² × 1 cm². Then, it was immersed into 30 mL of deionized water for 1, 3, 5, 7, 14, 21 and 28 days. Sample was removed and dried at 80°C at each time point. The percentage degradation was calculated using following equation. The data was reported as a statistical average and standard deviation.

$$\text{Degradation (\%)} = \frac{W_0 - W_t}{W_0} \times 100$$

where W₀ and W_t are the weights of the sample before and after degradation, respectively.

2.3 Instruments

2.3.1 Fourier transform infrared (FTIR)

The chemical structure was determined using a Fourier transform infrared spectrometer (SPECTRUM ONE, Perkin Elmer, USA). The sample was scanned from 400 cm^{-1} to 4000 cm^{-1} at room temperature in attenuated total reflectance mode at a resolution of 4 cm^{-1} .

2.3.2 Scanning electron microscope (SEM)

The morphology was monitored by scanning electron microscope (SEM, Quanta 250 microscope, Japan). The specimen was coated with gold using a sputtering device (JEOL, JFC 1200, Japan) prior to the SEM observation. A magnification of 1K and 10K was used.

2.3.3 Differential scanning calorimetry (DSC)

The thermal behavior was investigated using DSC (NETZSCH DSC 204 F1 Phoenix, Germany). The sample was placed in aluminum pans and purged with nitrogen gas at a flow rate of $40\text{ mL}\cdot\text{min}^{-1}$. The temperature was set to 30°C to 250°C , with a flow rate of $10^\circ\text{C}\cdot\text{min}^{-1}$. The data was reported as glass transition temperature, melting temperature, and specific heat capacity.

2.3.4 Tensile testing

The mechanical properties were performed using a universal tensile tester. The hydrogel sheets of 7 cm -length and 1 mm -width were stretched at a tension speed of $30\text{ mm}\cdot\text{min}^{-1}$. For each sample, 7 specimens were tested. The statistical average and standard deviation were then reported.

3. Results and discussion

Polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel was successfully prepared from freeze thaw technique. It presented as a whitish-color. It appeared as reformable shape. Figure 1 illustrates the FTIR spectra of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel prepared by freeze thaw technique. No significant change on functional group of hydrogels was observed based on variation of consecutive cycle in freeze thaw process. The functional group of hydrogels was still similar for all compositions of hydrogel. This was probably due to the fact that FTIR analysis was used to qualitatively analyze the existence of functional group of hydrogels. In Figure 1, the characteristic peak at 3260 cm^{-1} was observed. This was corresponded to the presence of OH stretching group (hydroxyl group). It referred to the existence of polyvinyl alcohol and sodium alginate. This was in agreement with previous work of Ma *et al* [20]. It may imply that hydrogel will be well adsorbed moisture. It can create the hydrogen bonding between OH group of hydrogel and water molecule. At 3445 cm^{-1} , the IR spectra of SA showed typical absorption bands for hydroxyl groups (-OH). It clearly identifies the major peaks related with freeze-thawed PVA [21]. The use of hydrogel should be therefore stored in desiccator. Furthermore, the wavenumbers at 1410 cm^{-1} and 2911 cm^{-1} were existed. These peaks were referred to C-H stretching vibration. The occurrence of wavenumber at 1610 cm^{-1} was also reported

due to the presence of CO stretching (carbonyl group), respectively. The presence of carbonyl group was referred to the sodium alginate [22]. These functional groups can create the hydrogen bonding between polyvinyl alcohol and sodium alginate is reported as a schematic diagram in Figure 2. It can create the hydrogen bonding as an intermolecular and intra-molecular interaction between sodium alginate and poly vinyl alcohol chain. This is in agreement with previous work of Chhatari *et al* [23]. Furthermore, previous studies of PVA absorption band of the PVA/ SA hydrogel composite [24] reported that some changes in the FTIR spectrum caused by hydrogen bonds were observed at approximately 3280 cm^{-1} because of the hydroxyl group's O-H stretching absorption. It should be mentioned that the characteristic peak of O-H stretching absorption of the hydroxyl group (3280 cm^{-1}) shifted from 3280 to 3249 cm^{-1} in PVA/SA, indicating that physical interactions between PVA and SA were generated.

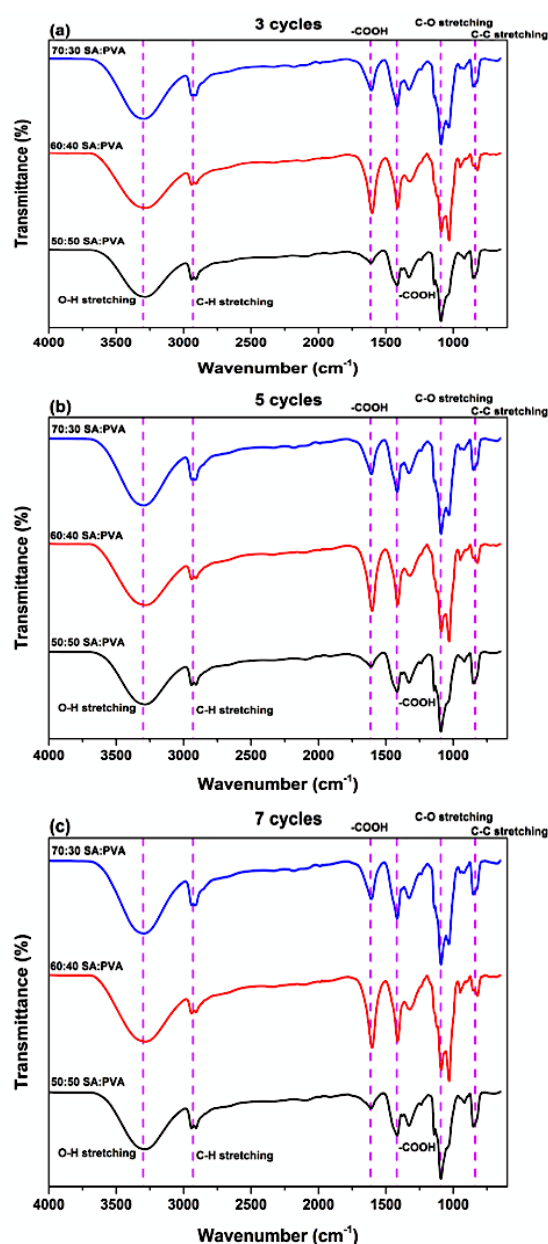


Figure 1. FTIR spectra of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite prepared by freeze thaw process.

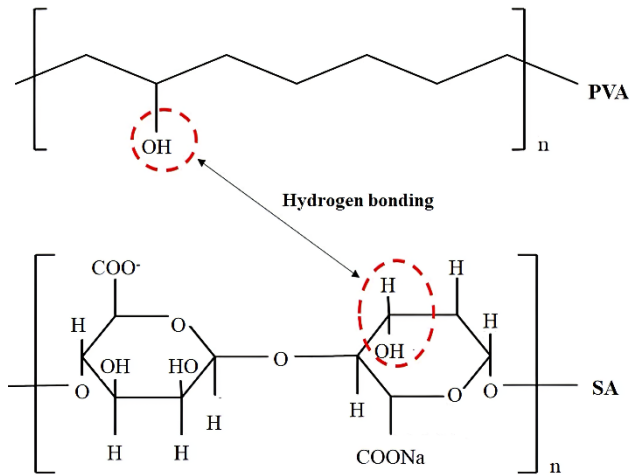


Figure 2. Schematic diagram of chemical bonding between polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel

Figure 3 exhibits the morphological properties of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel prepared by freeze thaw technique.

The cross-sectional view of hydrogel was reported based on magnification of 1K and 10K. With high magnification, it is better to see the porous structure. It was remarkable to note that all microstructural images presented the porous structure. The pores were interconnected and regularly distributed. The pores can create the due to freeze step. Water part in hydrogel structure was then removed. It can be used to confirm the presence of water in hydrogel structure. This result was similar to previous literature of Zhang *et al* [25]. Moreover, with 5 and 7 consecutive cycles, the amount of pore was less compared to 3 consecutive cycles. The surface became smoother. It implied that hydrogel was well packed. With high consecutive cycle of freeze thaw, it can be implied that crosslinking reaction between polyvinyl alcohol and sodium alginate was successfully prepared. As a consequence, it therefore provided the difficulty when hydrogel will be employed as medical materials. On the other side, it was observed that all hydrogels clearly presented porosity. It was implied that the existence of interconnected porous structure significantly provided many benefits. Water molecule can be adhered and it can be considered as a reservoir of any active molecule. It will be therefore excellent if hydrogel will be employed as medical materials.

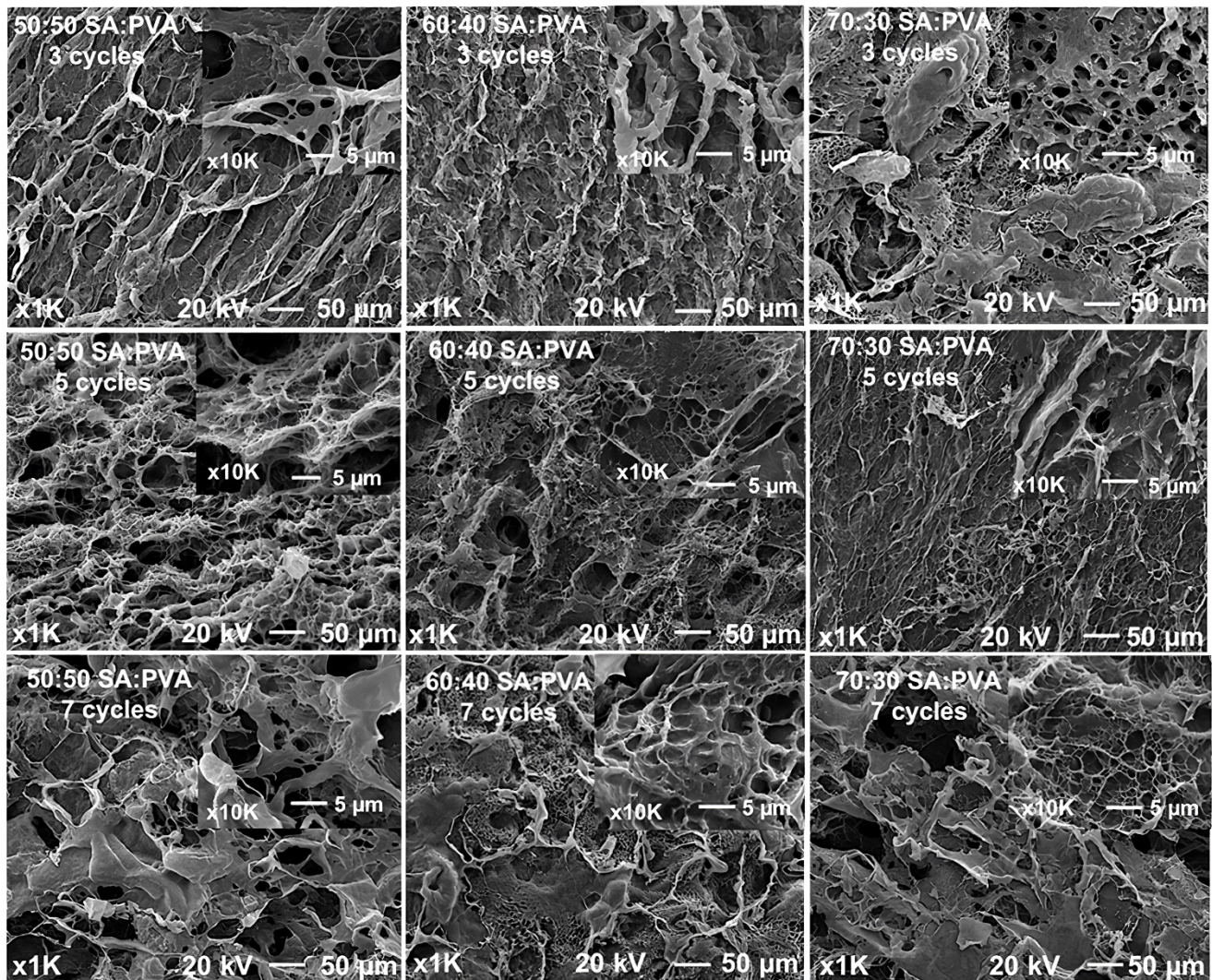


Figure 3. Morphological properties of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite prepared by freeze thaw process.

Differential scanning calorimetry was considered as an effective instrument to evaluate the existence of water molecule in hydrogel network. As for the hydrogel, water was considered as a large portion. This measurement was allowed to imply the water state change in sodium alginate and poly vinyl alcohol-based hydrogel network, as suggested by Jiang *et al* [11]. Figure 4 reports the DSC measurement of polyvinyl alcohol and sodium alginate-based hydrogel prepared by freeze thaw technique. Various compositions of sodium alginate and poly vinyl alcohol were evaluated based on 3, 5 and 7 consecutive cycles of freeze thaw. It was notable that all of curves were presented in the similar form. Two exothermic peaks were presented at 110°C and 225°C. The peak at 110°C may involve the evaporation of water molecule in hydrogel network. This was associated with previous work of Wang *et al* [26]. The strong peak at 225°C was typically

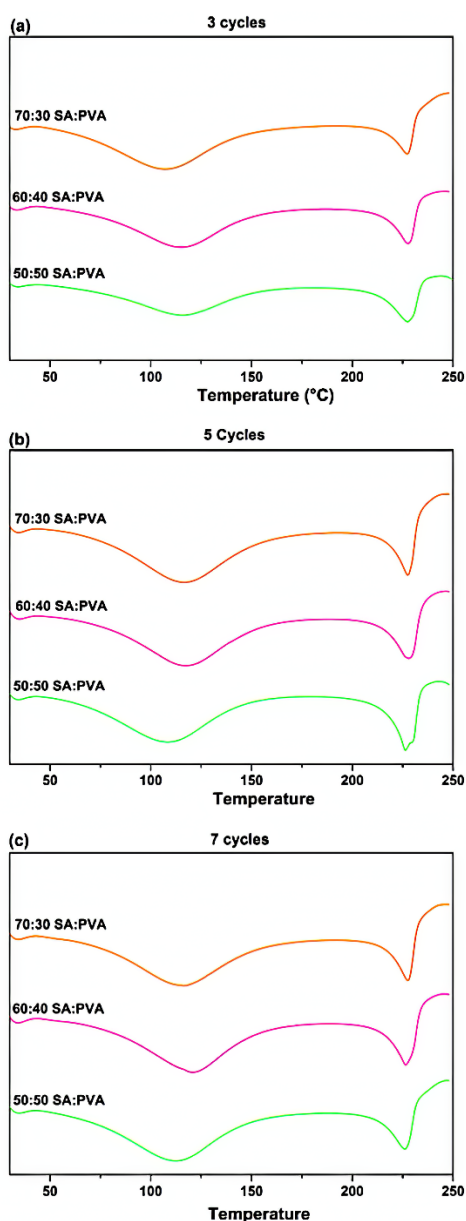


Figure 4. Thermal properties of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite prepared by freeze thaw process.

related to melting temperature of sodium alginate and poly vinyl alcohol. Furthermore, it was remarkable to note that the melting temperature was slightly increased respect to increment of sodium alginate content. It was slightly shifted to 230°C for 3, 5 and 7 consecutive cycles. The existence of sodium alginate may enhance the compactness of hydrogel by freeze thaw process. This discussion was similar to previous literature of Lutfi *et al* [27].

Figure 5 represents the swelling characteristic of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite. The swelling ratio was highly observed within 200 min for all hydrogel structure. After that, the swelling ratio was steady. It can be explained that swelling behavior was occurred due to two reasons. First, it was typically related to hydrophilicity of sodium alginate located inside hydrogel network. It can adsorb water molecule in the system. Second, the swelling behavior was associated with interconnected porous structure in hydrogel network, as suggested by Yu *et al* [28]. This discussion is in agreement with SEM analysis. Furthermore, it was notable that with high sodium alginate content, the swelling behavior was significantly superior. It can be noted that sodium alginate has high water adsorption [29]. Besides, the swelling (%) was increased as the number of cycles increased up to the 7 cycles. At a higher number of cycles of 7 cycles, the swelling (%) was rapidly increased within 20 min and reached equilibrium in about 50 min [24]. The swelling behavior of hydrogels increased and subsequently decreased, and the initial increase in swelling could be attributed to an increase in hydrophilicity and the formation of an optimum pore size network. It is believed that this is due to the blockage of active sites on polymer chains, which results in a decrease in hydrophilic groups [30].

To use hydrogel as a medical material, mechanical properties were therefore determined. Figure 6 exhibits the tensile strength of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite. Five measurements for each sample were tested and the data was reported as statistical average and standard deviation. Uniform dispersion of poly vinyl alcohol in sodium alginate was prepared, as suggested in Figure 2. It can create the interfacial adhesion in between, similar to previous work of Hu *et al* [31]. The level of tensile strength for all hydrogels was in the region of 0.25 MPa to 1 MPa. It can be indicated that polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite can be prepared by freeze thaw technique. No presence of crosslinking agent is necessary. From the result, it was remarkable to note that with high amount of poly vinyl alcohol, tensile strength was slightly high. It can be observed for sodium alginate and poly vinyl alcohol of 50:50 weight ratio for 3, 5 and 7 consecutive cycles. However, with low amount of polyvinyl alcohol content, tensile strength were slightly decreased. It can be implied that poly vinyl alcohol exhibited high dimensional stability. Furthermore, it can be explained that due to the existence of -OH group in both sodium alginate and poly vinyl alcohol, it can effectively create the intermolecular and intramolecular interaction throughout hydrogel network. This is in agreement with previous literature of Mousa *et al* [32]. No agglomeration was observed. It can be therefore transfer load when external force will be applied [33].

To use hydrogel as a medical material, *in vitro* degradation test was observed. The data was reported as a statistical average of weight loss of immersed hydrogel into DI water. This was considered as an important key to determine the degradation behavior of hydrogel.

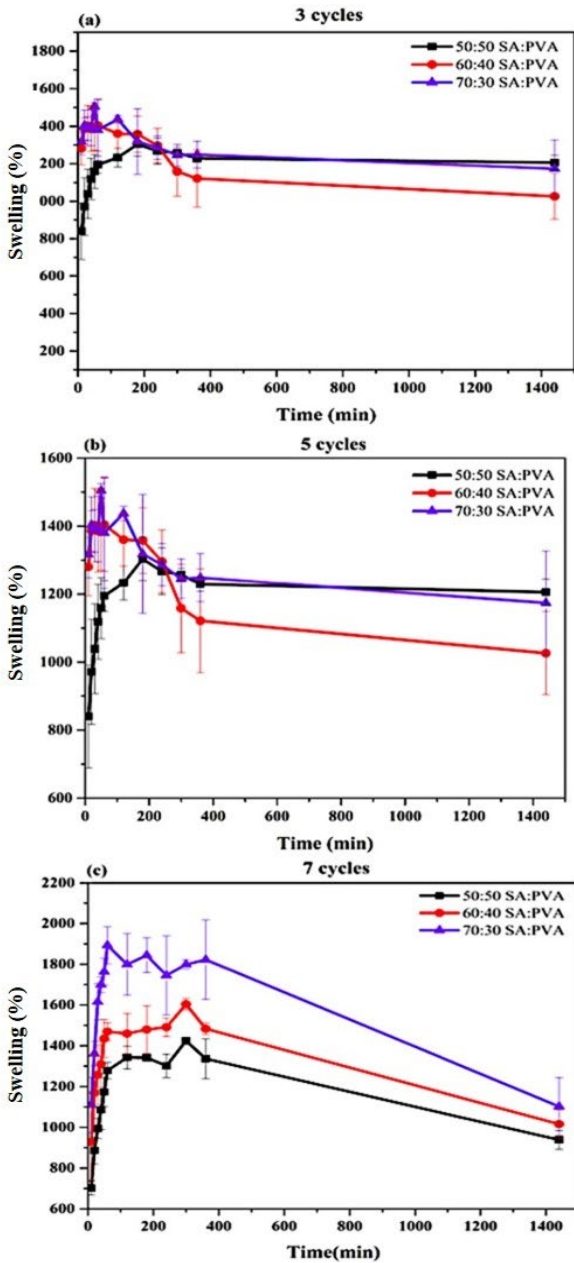


Figure 5. Swelling behavior of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite prepared by freeze thaw process

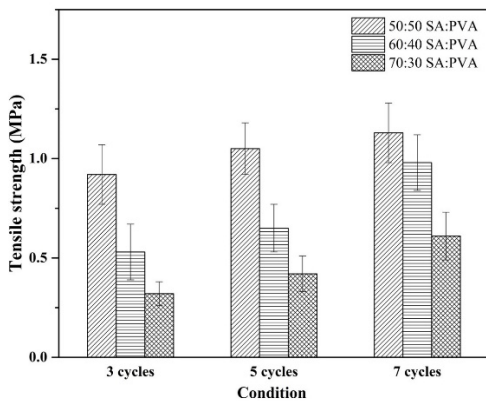


Figure 6. Tensile strength of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite prepared by freeze thaw process

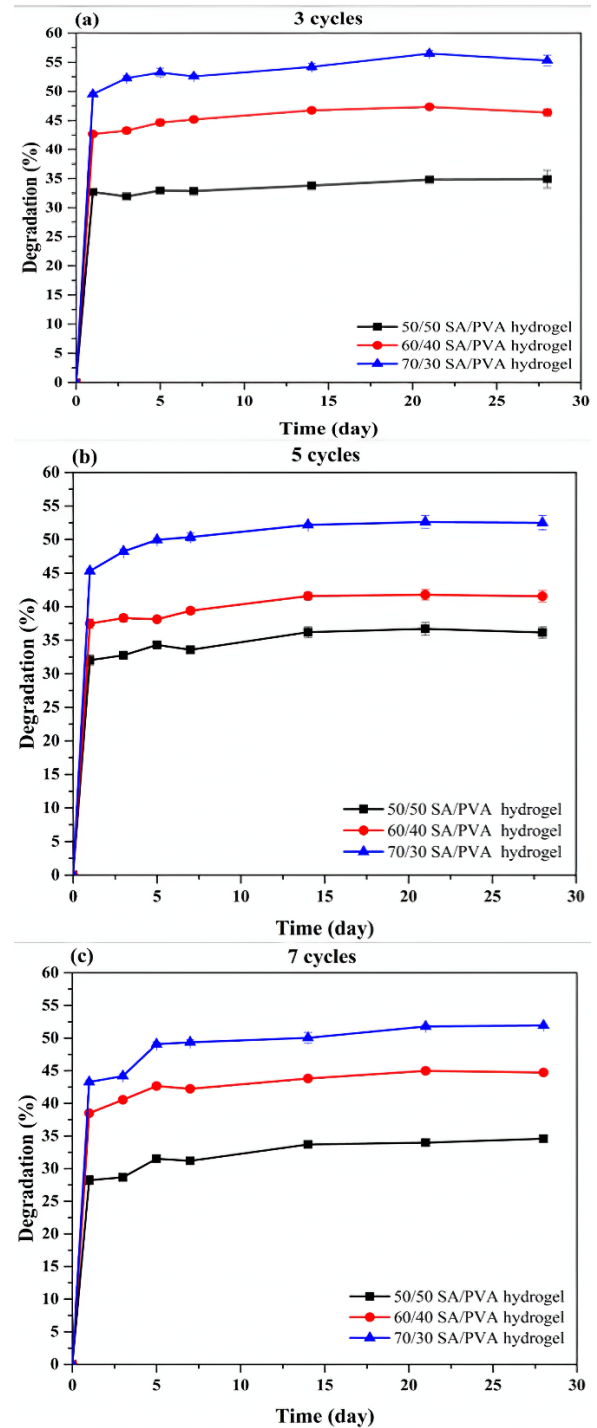


Figure 7. *In vitro* degradation behavior of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel composite prepared by freeze thaw process.

Figure 7 reports the percentage of weight loss of polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel versus incubation time. The experiment was conducted at ambient temperature for 28 days. The degradation characteristic of hydrogel was evaluated by mass loss, internal structure transformation and mechanical disintegration, similar to previous work of Zhang *et al* [34]. Before 3 days, hydrogel can keep its dimensional stability. After that, it initially changes the shape. The results were also typically presented in the similar feature for 3, 5 and 7 consecutive cycles of freeze thaw. No significant change of percentage of composition between sodium alginate and poly vinyl

alcohol was observed based on variation of consecutive cycles. It was remarkable to note that with high content of sodium alginate, the percentage of degradation behavior is superior. Sodium alginate has high solubility in water, as suggested by previous literature of Wardhani *et al* [35]. This is also in agreement with swelling behavior reported in Figure 5. The degradation mechanism was typically involved high water solubility of sodium alginate. It can dissolve into DI water and thus the hydrogen bonding with polyvinyl alcohol was then disintegrated. Therefore, the range of degradation percent was estimated to be 27% to 35%, 35% to 45% and 45% to 55% for the composition ratio of sodium alginate and poly vinyl alcohol of 50:50, 60:40 and 70:30, respectively. For measurements on swollen hydrogel samples, corresponding to an increase in absorbed water related to a decrease in cross-linking density, associated mostly to the occurrence of a hydrolysis process, although we cannot exclude some material loss because of disentanglements of non-crosslinked chains [36]. The increase of degradation (%) refer to measurements on dried samples after swelling, indicating a mass loss because of both network dissipation of free PVA chains and degradation (hydrolysis).

4. Conclusions

In this study, polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel was successfully prepared by freeze thaw technique. Only 3 consecutive cycles of freeze thaw were optimal for hydrogel formation. Fourier transform infrared confirmed that hydrogen bonding was formed throughout hydrogel network by OH group of sodium alginate and poly vinyl alcohol. The 60:40 composition ratio between sodium alginate and poly vinyl alcohol was optimal. Scanning electron microscope exhibited microstructure of hydrogel. It presented as a porous network. The swelling behavior is relatively high at the initial stage of incubation time. With low content of sodium alginate, tensile strength was slightly enhanced, whereas low *in vitro* degradation behavior was relatively occurred. Polyvinyl alcohol/sodium alginate (PVA/SA) hydrogel remarkably illustrated extraordinary properties for being as a medical material.

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