

## High Absorbable Cassava Starch/Poly (vinyl alcohol) Sponge for Medical Applications

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### Abstract

Absorbable cassava starch-based sponges are prepared by freeze-drying method. The mixing solutions of cassava starch, poly (vinyl alcohol) and glycerol with various weight ratios are put in the freeze-dryer machine at -40 °C for 24 h to change to sponge form with interconnecting porosity. The obtained sponge at 50/35-15 weight ratio of CS/PVA-glycerol is soft yet tough, foldable and tolerable to the hands, easy to manipulate and cut into the desired form. The results of porosity and water absorption test reveal high water absorption of the sponge with 67% of total porosity and 522% of water absorption. Iodine test and UV-Vis absorption show no starch dispersion into the medium after sponge immersion in PBS for 7 days. The blood absorbability of the sponge is higher than gauze and cotton pad in the same size. The results demonstrate that the prepared sponge could effectively be used as absorbable for medical applications.

**Keywords:** Cassava starch, Poly (vinyl alcohol), absorbable sponge, medical application  
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### 1. Introduction

Medical materials with porous structures and absorbable property have widely been used for many years and apply for medical applications including an absorbable surgical hemostatic agent [1-4]. As observed, a significant cause of death in trauma patients is unrestrained bleeding [5]. Thus, the priority in emergency medical treatment is to decrease unexpected blood loss. In the past years, numbers of hemostatic materials have been developed aiming to increase the survival rate and reduce bleeding problems in wounded patients [6-10].

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The hemostatic agent is an alternative to usual modalities of hemorrhage control. The required properties of the ideal hemostatic agents are non-toxic, good biocompatibility, ready and easy to use, light, stable, and can rapidly control huge bleeding with low-cost [11, 12]. The numerous natural polymers such as chitosan, cellulose, gelatin, collagen and starch have been examined for hemostatic biomaterial agent development due to their biocompatibility and inherent biological properties has increasingly been utilized in various fields, mostly due to its low cost, readily available, renewable, biocompatible and biodegradable [13, 14]. In the case of medical application, starch has been used as tissue engineering scaffolds, drug delivery devices, absorbing liquid sponges and absorbable hemostatic agents [16-25].

Apart from any other starch, cassava starch (CS) is one of the commonly used as models of eco-friendly biomaterials. CS is easy to process in several forms of medical materials such as film, gel, fibers and sponge. However, the mechanical properties of CS-sponges are usually poor. This can be relieved by blending with other synthetic polymers before a three-dimensional porous structure preparation.

Poly (vinyl alcohol) (PVA) is a non-toxic synthetic polymer produced from poly (vinyl acetate) through hydrolysis. It is an attractive material due to its outstanding characteristics and excellent properties such as biodegradability, biocompatibility, swelling, safety and strength [26-28]. Thus, PVA has found uses in different applications such as adhesives, paper, textile, food, pharmaceutical, biomedical, and commonly used in medical devices [29, 30]. PVA is frequently blended with many types of natural polymers to improve its mechanical properties and stability. CS contains free hydroxyl groups that can interact with PVA. However, the CS and PVA sponges have never been prepared for use as a hemostatic material.

The main purpose of this study is to prepare the CS/PVA sponges by a simple method without using chemical cross-linker to avoid the toxic residue. The CS/PVA solution was homogenized by glycerol addition. Then, the mixing solution was used to form the porous structure sponge using the freeze-drying method to produce a high absorbable anti-bleeding sponge. The effects of PVA and glycerol content on the physical and thermal properties, swelling, stability, porosity, and absorbability of the obtained CS/PVA sponges were also investigated. The potential for a hemostatic agent, blood absorbability of CS/PVA sponges was also studied.

## 2. Materials and Methods

### 2.1 Materials

Cassava starch (CS) was obtained from commercial Thailand cultivation. Poly (vinyl alcohol) (PVA) with the average molecular weight of 85,000-124,000 and 99 % hydrolyzed was purchased from Aldrich Chemical Co., Inc., USA. Glycerol with 86-89 % assay was purchased from Fluka Bio-Chemika, Germany. All chemicals used were analytical grade.

### 2.2 Fabrication of CS-based sponge

An aqueous solution of 3 % w/v CS was prepared by dissolving CS powder in distilled water at 65°C until the starch gelatinized. The 3 % w/v PVA was prepared by dissolving PVA powder in distilled water at 100°C for 60 min. The prepared CS and PVA solutions were mixed with glycerol at 50°C for 60 min to prepare CS/PVA-glycerol solutions with various weight ratios (50/25-25, 50/30-20, 50/35-15, 50/40-10, 50/45-05). Afterwards, the mixed solutions of CS/PVA-glycerol were poured into molds (1.5 cm radius and 1 cm height) and kept in a domestic freezer at -22°C for 24 h. The pre-freeze mixed solutions were lyophilized in a freeze-dryer (CoolSafe 110, Svan Vac

New Zealand) under vacuum at -40°C for 24 h to produce the porous structure sponge. In order to obtain an appropriate CS/PVA-glycerol composition for preparation of CS-based sponge, all obtained CS-based sponges with various weight ratios were composition optimized.

## 2.3 Characterization of CS-based sponges

### 2.3.1 Functional group analysis

The functional groups of samples were analyzed by Attenuated Total Reflectance- Fourier Transform Infrared Spectroscopy (ATR-FTIR). The ATR spectra of sponge samples were recorded with a Spectrum100 (Perkin Elmer Inc.) in the range between 4000 to 600 cm<sup>-1</sup>.

### 2.3.2 Thermal stability

Thermal stability of the sponge samples was characterized using differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). The Perkin-Elmer DSC was used for DSC analysis with a heating rate of 10 °C/min over the temperature range of 40 to 200 °C under a purged nitrogen atmosphere. The TGA instrument used was STA 6000, Perkin-Elmer in non-isothermal mode, heating rate is 10 °C/min under an inert nitrogen atmosphere over the temperature range 50-600 °C.

### 2.3.3 CS-based sponge stability

The essential stabilities of the CS-based sponge were estimated by studying the *in-vitro* release of the carbohydrate from the prepared sponge [31]. The CS-based sponge sheets (1.5×1.5×0.5 cm<sup>3</sup>) were immersed in 20 ml of phosphate buffer saline (PBS), pH 7.4 for 7 days. Then, the released carbohydrate in PBS was studied by pH measurement, iodine test using a UV-Vis spectrophotometer, UV-2401PC (SHIMADZU Corporation). Iodine solution was dropped into the PBS medium after 7 days of sponge sheet immersion and the PBS medium was measured at 580-600 nm by the UV-Vis spectrophotometer [32, 33].

### 2.3.4 CS-based sponge porosity

Percent porosity of the sponges was evaluated by the liquid displacement method [31]. The porosity is defined as total volume of the pores ( $V_i - V_f$ ) divided by total volume of the porous sample ( $V_m - V_f$ ). Sponge samples were immersed in hexane in measuring cylinder and the changed hexane volume was then observed, and the porosity of the sponges ( $\varepsilon$ ) was calculated from equation (1).

$$\varepsilon = \frac{V_i - V_f}{V_m - V_f} \times 100 \quad (1)$$

Where  $V_i$  is an initial hexane volume in a measuring cylinder,  
 $V_m$  is the hexane volume after the sponge immersion for 10 min,  
 $V_f$  is the remaining hexane volume after the removal of the hexane absorbed sample.

### 2.3.5 Water absorption and water equilibrium

All dry sponge samples were weighed and immersed in water at 25 °C. After immersion at different time intervals, the sponges were removed from the medium and instantly weighed after absorbing excess water from the surface. The % water absorption (A) was calculated using equation (2). The

water equilibrium ( $W_{eq}$ ) in the swollen samples was calculated [34] using equation (3).

$$A = \frac{W_r - W_d}{W_d} \times 100 \% \quad (2)$$

$$W_{eq} = \frac{W_s - W_d}{W_d} \times 100 \% \quad (3)$$

Where  $W_d$  is the weight of the dried sponge,  
 $W_r$  is the weight of the water-removed sponge,  
 $W_s$  is the weight of the saturated swollen sponge.

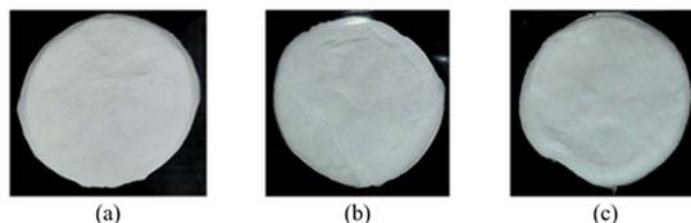
### 2.3.6 Blood absorption capability

To compare the blood absorption capacity of the CS-based sponges with gauze and cotton pad, their absorption capacity was studied to estimate surgical blood loss as mentioned by Kristen *et al.* [35] with some modifications [36]. Each of the sponge, gauze and cotton pad samples in the same size ( $3 \times 5 \times 0.5 \text{ cm}^3$ ) was placed in Petri-dishes, the Petri-dishes were consecutively filled with 0.5 ml of collective amounts of fresh pig blood ranging from 0.5-5 ml. The saturation was defined as the point at which no dry sample was evident or felt.

## 3. Results and Discussion

### 3.1 Fabrication of CS-based sponge

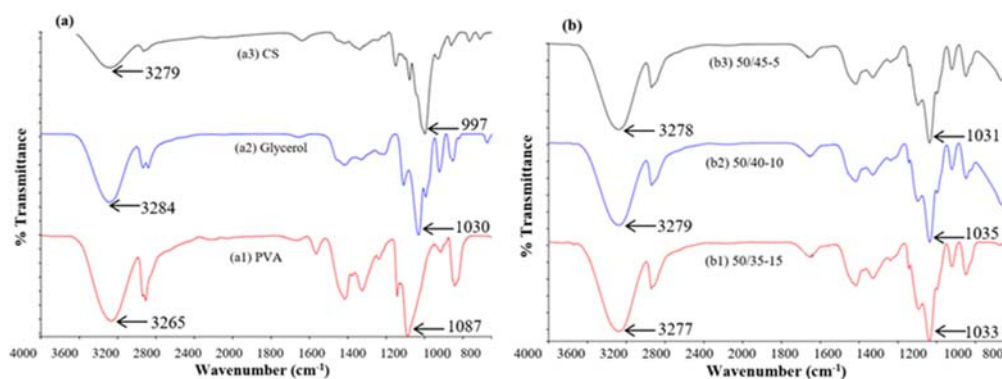
As cassava starch (CS) is a renewable biopolymer, the obtained sponges are expected to contain higher CS content and can still be prepared to sponge form with good properties. Therefore, the CS/PVA-glycerol sponges with various weight ratios at 50/25-25, 50/30-20, 50/35-15, 50/40-10 and 50/45-05 were prepared. However, only the polymer blended solution with PVA content equivalent to or higher than 35 weight ratio and glycerol content equivalent to or lower than 15 weight ratio can be fabricated to the sponge form. This is because the polymer blended solution with PVA content lower than 35 makes the sponge break and brittle while a polymer blended solution with glycerol content higher than 15 makes the sponge unstable. This suggested that the addition of PVA and glycerol can help to form the CS-based sponges. The obtained sponges with various weight ratios of CS/PVA-glycerol were shown in Figure 1. The fabrication process intrinsically generated the porous structure of CS-based sponges. The moisture formed in the blended solution during the homogenization, after solvent evaporation by freeze-drying methods, promoted the formation of pores structure. The sponges at 50/35-15, 50/40-10 and 50/45-05 weight ratio of CS/PVA-glycerol were smooth, soft, tough, foldable and can simply be made into the desired shape. Therefore, the CS-base sponge with these three compositions was selected for more characterization.



**Figure 1.** CS-based sponge with various weight ratios of CS/PVA-glycerol, (a) 50/35-15, (b) 50/40-10 and (c) 50/45-5

### 3.2 Functional group analysis

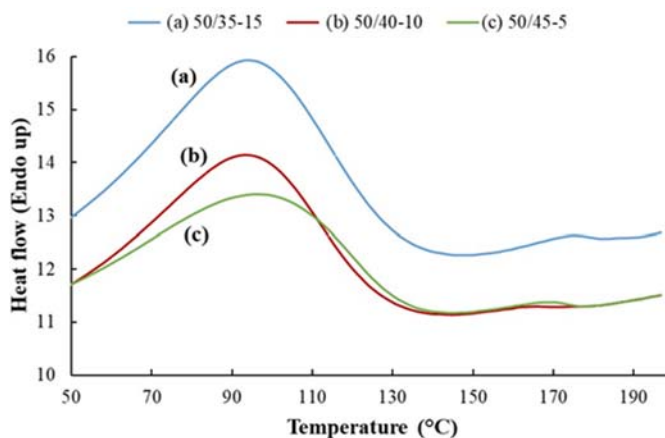
The CS-based sponge was prepared from CS, PVA and glycerol. The functional groups of the starting materials (Figure 2a) and the prepared samples with different proportions (Figure 2b) were confirmed by FTIR spectroscopy. All peaks emerged in CS, PVA and glycerol had also appeared in the CS-based sponge with a slight chemical shift value. In Figure 2b, there were the absorption peaks at  $3277\text{ cm}^{-1}$ ,  $3279\text{ cm}^{-1}$  and  $3278\text{ cm}^{-1}$ , which were corresponded to O-H stretching vibration of 50/35-15, 50/40-10 and 50/45-5 weight ratio of CS/PVA-glycerol, respectively. The absorption peaks at  $1033\text{ cm}^{-1}$ ,  $1035\text{ cm}^{-1}$  and  $1031\text{ cm}^{-1}$  corresponded to C-O stretching of the CS/PVA-glycerol sponges with the weight ratio of 50/35-15, 50/40-10 and 50/45-5, respectively. Comparing with CS, the O-H stretching and C-O stretching showed the absorption peaks at  $3279\text{ cm}^{-1}$  and  $997\text{ cm}^{-1}$ , respectively. In the CS/PVA-glycerol sponges, the peaks of O-H stretching showed stronger absorption peak, while C-O stretching shifted to higher wave number and became more intense, which indicated that the H-bonding increased. The FTIR results indicated that CS and PVA were blended by intermolecular force (H-bond), and the H-bonding density depended on the sponge composition. Moreover, the glycerol addition can improve the compatibility of CS and PVA due to the increase of H-bonding by more polymer chains motion.



**Figure 2.** FTIR spectra of (a) starting materials (a1: PVA, a2: glycerol, a3: CS) and (b) CS-based sponge with various weight ratios of CS/PVA-glycerol (b1: 50/35-15, b2: 50/40-10, b3: 50/45-5)

### 3.3 Differential scanning calorimetry

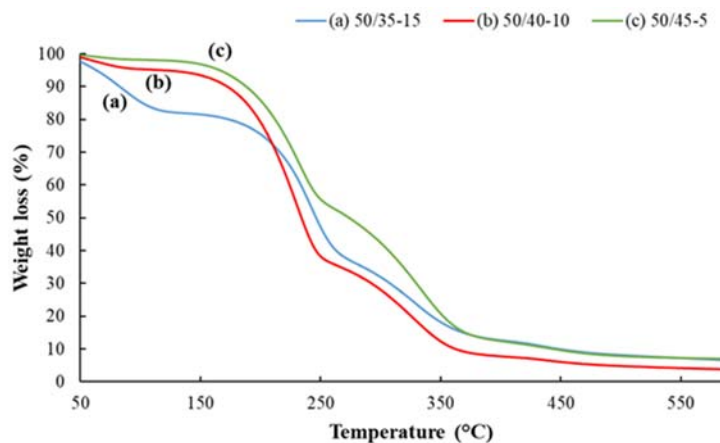
Normally, the first heating run of starch DSC thermograms shows a broad endothermic peak at about 100 °C. The crystalline melting temperature in native starch was previously studied and reported. For example, in the case of the amylopectin part in sago starch, the melting temperature peak is between 50 and 150 °C [37] while some study revealed that the starch chains interacted with the remaining water by H-bonding which showed the endothermic peak at 126.9 °C due to the crystalline melting [38]. Moreover, there is a report presuming that it may be because of water adsorption occurring above room temperature during the heating scan [39]. At this moment, there is no conclusion for these descriptions but all native starch shows this peak [40]. As the discussion, in Figure 3, there is the broad peak at 93 °C, 94 °C and 96 °C on DSC thermogram of CS-based sponges at 50/35-15, 50/40-10 and 50/45-5 weight ratio of CS/PVA-glycerol, respectively. The CS-based sponge with higher glycerol content showed the lower temperature of the broad peak because glycerol functioned as the plasticizer which can increase the mobility of polymer chains and decrease the crystallinity of the sponge.



**Figure 3.** DSC thermogram of CS-based sponge with various weight ratios of CS/PVA-glycerol, (a) 50/35-15, (b) 50/40-10 and (c) 50/45-5

### 3.4 Thermogravimetric analysis

Figure 4 shows the weight remains against temperature as measured by TGA for various CS-based sponges. The TGA thermograms of CS-based sponges with various weight ratios of CS/PVA-glycerol showed three similar main stages of degradation process as discussed previously [41, 42]. The sponges presented an initial drop between 50 to 200 °C which corresponds to a mass loss of absorbed moisture and possibly, glycerol (boiling point of glycerol is about 198 °C). It should be noted that all sponges were dried at 50 °C before the TGA analysis, thus, most of the moisture was already removed, resulting in smaller mass loss of glycerol that relates with the amount of added glycerol into each composition of approximately 15%, 10% and 5% of 50/35-15, 50/40-10 and 50/45-5 weight ratio of CS/PVA-glycerol, respectively. The second stage (200-500 °C) is the main stage of decomposition and it can be attributed to CS and PVA depolymerization [43]. And the final



**Figure 4.** TGA thermogram of CS-based sponge with various weight ratios of CS/PVA-glycerol, (a) 50/35-15, (b) 50/40-10 and (c) 50/45-5

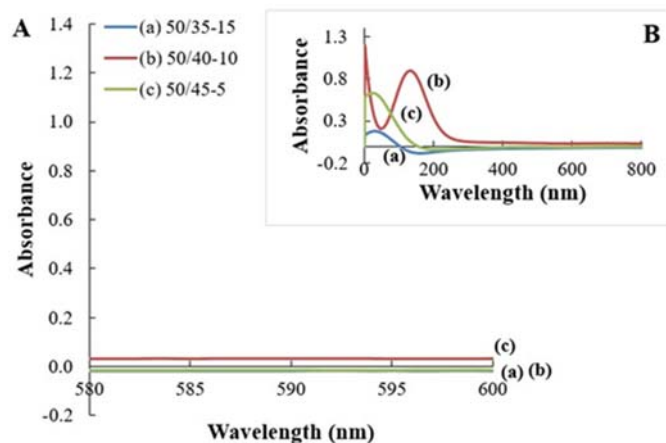
stage of weight loss above 500 °C is generally carbonization stage with slow degradation rate. Furthermore, CS-based sponges showed very little ash (less than 5%) after thermal degradation. The results concluded that the thermal stability of the prepared CS-based sponge was appropriate to meet the necessities for fabrication, storage, sterilization, and use as absorbable material.

### 3.5 CS-based sponge stability

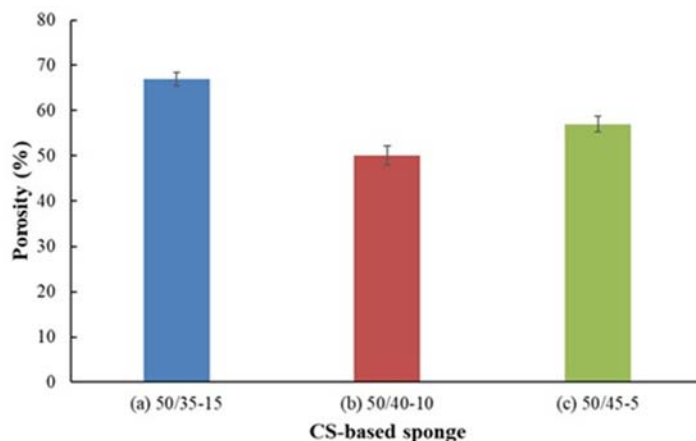
This study was carried out to estimate the stability of the sponges. If the samples are to be operated successfully and stable, the main components as CS should not leach out from the sample. Accordingly, *in-vitro* carbohydrate releases from CS- based sponges were evaluated by pH measurement, iodine test, and UV-Vis absorption at 580-600 nm.

The leaching of carbohydrate from all CS-base sponges was observed after 7 days of sponge immersion, after that, there was not much change in pH value. Moreover, the iodine test, which was investigated by UV- Vis absorption at 580- 600 nm (Figure 5), indicated that the CS-based sponge was almost unchanged and the leached-out fraction is negligible after 7 days. This behavior can conclude that the sponge can be used in the PBS medium up to 7 days.

From Figure 6, the percent porosity of the CS-based sponges drastically decreases with the decrease of glycerol content up to 10 % weight ratio, then it increases afterward due to the glycerol and PVA contents. This is because glycerol performed as a plasticizer which usually inserts between the CS and PVA chains to expand the free volume of the polymer chain. Moreover, increasing of PVA content leads to the sponges with lower porosities. However, the porosity of CS/PVA-glycerol sponge at 50/45-5 weight ratio increases possibly because this composition with a small amount of glycerol which is not enough for function as a plasticizer can help the CS and PVA chains more compatible.



**Figure 5.** UV-Vis absorption of PBS medium after 7 days of CS-based sponge immersion (A) at 580-600 nm and (B) at 0-800 nm



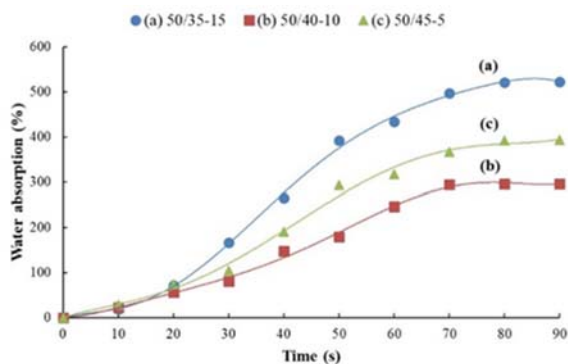
**Figure 6.** Percent porosity of CS-based sponge with various weight ratios of CS/PVA-glycerol, (a) 50/35-15, (b) 50/40-10 and (c) 50/45-5

### 3.6 Water absorption and water equilibrium

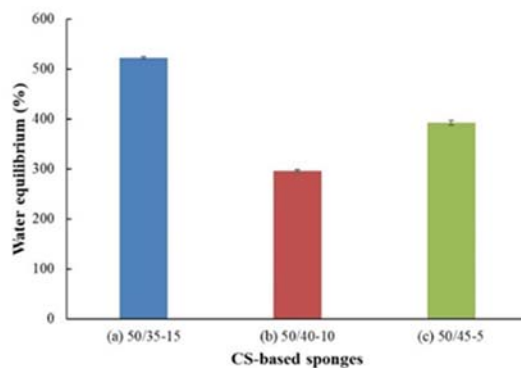
One of the important functions of the medical absorbable sponge is good liquid absorbing capability [44, 45]. The water absorption of CS-based sponges was presented in Figure 7. Three different ratios of CS-based sponges could absorb 3-5 times of their own dry weight in 80 s. Since the water absorption of the sponges is related to its porosity, thus water can be more easily absorbed in the sponges due to both porous structure and the absorbing of CS and PVA. This water uptake is higher than the reported value for porous materials [46-50] which demonstrated a usual water absorption of 10 - 200%. Moreover, the absorption rate increased continuously with time until its equilibrium at about 80 s.



From Figure 8, the water equilibrium of 50/35-15, 50/40-10 and 50/45-5 exhibited as 522%, 296% and 392%, respectively, that related to their porosity, thus water can be more easily absorbed in the porous sponge due to the openness of the sponge structure. In the case of the 50/35-15 weight ratio of CS/PVA-glycerol with 522 % water absorption at equilibrium, which was probably attributed to high absorbability sponge that could be used for medical absorbable materials.



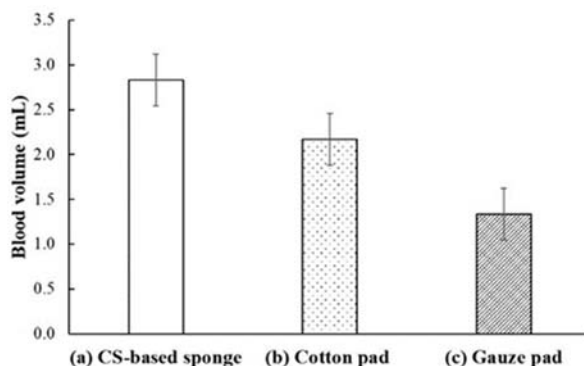
**Figure 7.** Water absorption of CS-based sponge with various weight ratios of CS/PVA-glycerol, (a) 50/35-15, (b) 50/40-10 and (c) 50/45-5 at various time intervals



**Figure 8.** Water equilibrium of CS-based sponge with various weight ratios of CS/PVA-glycerol, (a) 50/35-15, (b) 50/40-10 and (c) 50/45-5

### 3.7 Blood capability

The comparison of viscosity, surface tension and relative density between fresh human blood and fresh and aged pig blood showed a notable similarity between the human and pig bloods, even when the pig blood is up to two weeks old, provided it has been incubated at 4°C for that period. This means that it is valid to use pig blood instead of human blood for educational purposes [51]. This blood capacity test of the CS-based sponge, the pig blood was used as a model blood. To study the blood capacity of the CS-based sponge, the 50/35-15 weight ratio of CS/PVA-glycerol was selected to study due to its highest water absorption. As shown in Figure 9, it revealed that the 50/35-15 of



**Figure 9.** Blood absorption capacity of (a) CS/PVA-glycerol sponge at 50/35-15 weight ratio, (b) Cotton pad and (c) Gauze pad samples in the same size

CS/PVS-glycerol sponge completely absorbed a maximum of about 3 ml of the pig blood. The blood absorption capacity of the sponge is higher than gauze and cotton pad in the same size. Moreover, the CS-based sponge showed no sticking problem with skin due to its smooth surface and stability. These again suggested that the porous CS-based sponge could be used as an absorbable sponge for medical applications.

#### 4. Conclusions

The absorbable CS-based sponge composite was successfully fabricated by using the freeze-drying method. The FTIR results indicated that the polymer compositions were blended by hydrogen bonding. The CS, PVA and glycerol contents affect the sponge properties and the water absorption of the sponge is also related to its porosity. The sponge at the 50/35-15 weight ratio of CS/PVA-glycerol was soft and easy to blend into the desired shape. Moreover, its absorption increased continuously with time and reached 522 % water absorption at 80 s. Iodine test and UV-Vis absorption showed that the CS-based sponge was almost unchanged and the leached-out fraction was negligible after sponge immersion in PBS for 7 days. Moreover, TGA result revealed that the thermal stability of the CS-based sponge was appropriate to meet the necessities for sterilization and its ash less than 5% after thermal degradation at 600 °C. Furthermore, blood absorption capacity of the 3×5 cm<sup>2</sup> sponge was about 3 ml, and the capacity can increase with the larger sponge size. As conclusion, the results demonstrated that the prepared sponge could be acceptable for use as absorbable material in biomedical applications.

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