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Fabrication, Characterization and Release Profile of Aloe Vera Extracts/PVA Composite Electrospun Nanofiber

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ABSTRACT

Aloe vera is a well-known remedy that carries many beneficial health effects such as painkiller, anti-inflammatory, promote skin growth and repair. The combination of bioactive natural product of aloe vera as a drug model and polyvinyl alcohol (PVA) as the base material or carrier in the electrospinning process were studied. Smooth straight and continues electrospun fibers were collected with the Field Effect Scanning Electron Microscope (FESEM) images show no formation of bead (defect signed) in the electrospun membrane when the concentration was set at 10% w/w of PVA nanofibre. The morphological structure of the electrospun membranes shows a smooth and longitudinal fiber when aloe vera is mixed with the PVA polymer with percentage ratio of aloe vera over PVA is less than 25%. The Fourier Transform Infrared Spectroscopy (FTIR) shows no reaction between PVA and aloe vera by not showing peaks other than the initial materials. The Differential Scanning Calorimetry (DSC) proves the presence of aloin indicating the presence of aloe vera in nanofiber. The release profile of the electrospun aloe vera in PVA shows a higher initial burst release at the 50% and 70% concentration levels indicating very little control of the release or none at all. These results show the potential of aloe vera – PVA electrospun nanofibers membrane as a promising material for wound dressing and topical drug delivery.

Keywords: Aloe Vera, Concentration, Drug Release, Electrospinning, Polyvinyl Alcohol (PVA)

1. INTRODUCTION

Polyvinyl alcohol (PVA), known as a non-toxic, biodegradable and synthetic polymer, is derived from polymerization of vinyl acetate, followed with the subsequent hydrolysis of the acetate groups into hydroxyl moleties [1]. PVA is a linear polymer having the formula $[CH_2CH(OH)]_n$ with a simple chemical structure of pendant hydroxyl group as shown in Figure 1. PVA is also known as a "green polymer" due to its solubility and degradability. Furthermore, various natural materials can be easily combined with PVA, and it has good compatibility with numerous polymers, further extending the range of its applicability [2]. As one of the properties of PVA is hydrophilic which easily dissolves in aqueous solution, it has also exhibited good chemical and thermal stability. Because of its excellent properties, PVA is widely applied in drug delivery system and dressing for clinicians where it has the ability to create and maintain moist wound environment as to improve the healing process [3].

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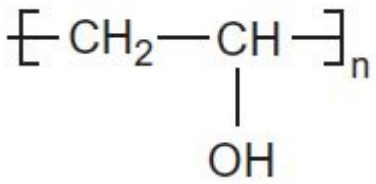

Figure 1. Chemical structure of Polyvinyl Alcohol (PVA).

PVA is a common choice in the preparation of various membranes and hydrogels [4]. Other studies were conducted where both PVA-based cyrogel and hydrogel were successfully fabricated in which PVA cryogel is used for transdermal drug delivery, and PVA/sodium alginate hydrogel is utilized for wound healing applications [5,6]. There were interesting findings by Sirima [7] when investigating the release of aloe vera extract in both electrospun PVA membrane and PVA hydrogel. They found that the swelling degree of PVA nanofiber membrane was higher than PVA hydrogel film which could be due to the fibrous structure of PVA electrospun fibers with higher surface area that are capable of releasing more aloe vera compared to hydrogel film. Saja et al. [8] also reported a highly porous structure of the electrospun PVA membrane that disintegrates promptly which makes it an effective oral fast-dissolving drug delivery. All these findings were further strengthened the validity of electrospun nanofibers which were produced here via electrospinning.

Electrospinning is a well-known method to fabricate polymeric or melt nanofibers with the capability of producing fibers in the range of nano to micrometers. It is a straight forward and effective method that only require some basic equipment including a DC high voltage power supply, a syringe pump together with the syringe and a conductive metal needle. A collector, connected with the counter electrode from the needle, has gain much attention because of its ability to fabricate continuous polymeric ultrafine fibers or fibrous structures. In addition, electrospinning can be recognized as a method that can be further developed for mass production of continuous nanofibers for industrial applications [9]. The electrospinning process is started with electrification of the droplet extruded from the spinneret (syringe). The droplet will soon be deformed into a conical shape (Taylor cone).When the electrostatic forces overcome the surface tension of the droplet, a liquid jet ejects and elongates in a straight line [10,11]. As the jet travels to the collector, it exhibits bending instability, stretching far and elongating to form continuous electrospun nanofibers. The jet that travels would have solidified when it accumulates on the ground collector. In addition, following the whipping and spiral pathway would reduce the fibre diameter, hence became thinner [12]. Electrospun nanofibers can be used as a biomimetic nanofiber with high specific surface area, high porosity, remarkable mechanical and biological properties, which makes them suitable for applications such as tissue engineering, drug delivery, and wound healing [13-15].

The usage of electrospun fibers in the field of biomedicine are mainly drug-controlled released, biological dressing and tissue repair. In this project, aloe vera has been chosen to be the natural drug for the study of its delivery properties. Aloe vera or aloe *Barbadensis* is known as the oldest therapeutic herb that can be used to treat burn area on the skin. The health benefits of aloe vera plant have been spread throughout the world and reports of aloe vera's utilization as traditional medicine can be traced back to ancient times, with an initial description dating back to approximately 1500 B.C. As reported by Kumar et al. [16] , aloe vera was used since the ancient civilization for the treatment of many diseases such as wounds treatment, reduce inflammation and mostly known can be used to treat injured tissue. Aloe vera can also be as a bioactive natural product with a lot of medical properties which came from the active functional components of acemannan and glucomannan contained in the gel inside the leaves that can speed up wound healing through activating skin macrophages [17]. Further investigation, done by Teplicki et al.

[18], suggests aloe vera can speed-up wound healing by promoting the proliferation and migration of fibroblast and keratinocytes that can protect from preservative-induced death.

Thus, this paper discusses the aspects of encapsulation of aloe vera through the electrospinning of polymeric nanofibers. Results are presented starting with morphological structures of electrospun nanofibers membrane. The chemical bonds feature in the electrospun PVA-aloe vera composite nanofibers have been identified via FTIR analysis. Thermal analysis has been carried out to analyze nanofibers' crystallinity. On delivery properties, the UV-Vis Spectrometer was used to analyze the samples.

2. EXPERIMENTAL METHOD

2.1 Chemicals and Raw Materials

Polyvinyl Alcohol (PVA) at (Mw: 125 000g/mol) was received from Sigma-Aldrich and Aloe Vera Dry Extract was obtained from A&T Ingredient. Distilled water was used as the solvent to dissolve both the PVA and aloe vera. All chemicals were used as it is with no further processing and modification.

2.2 Samples preparation

2.2.1 Part 1

Sample preparations were started with the polymeric PVA solution. Optimization of the PVA solution concentration as the carrier which will then be mixed with the aloe vera for electrospinning is crucial. Initially PVA powder was first weighted and dissolved into distilled water at 6% w/w and the mixture was stirred while heating up at 80°C. The prepared PVA (6 %w/w) solution was subsequently blended with aloe vera extract powder, commencing with an initial mixture ratio of 5% w/w.

2.2.2 Part 2

The concentration of PVA in distilled water was then changed to 10 % w/w and was mixed with varied aloe vera concentrations as tabulated in Table 1. Each time, the solutions were carefully mixed and stirred until they become homogenous and crystal-clear solution before the electrospinning process.

Table 1: Solution mixture PVA-Aloe Vera in (% percentage)

No	Aloe Vera concentration (%)
1	0
2	5
3	25
4	50
5	75

2.3 Electrospinning Process

Electrospinning setup (Figure 2) consists of a DC high-voltage power supply (Gamma BP series), syringe pump for non-medical which can provide feeding capacity of 0-60 ml/h, a syringe with a blunt tipped needle connected to the positive electrode. A rotating drum acted as collector was covered with aluminum foils and connected to the negative electrode. Several various concentrations of aloe vera in PVA were tested as tabulated in Table 1. The electrospinning process was conducted until fair amount of thick nanofiber mat (membrane) was able to be collected which normally took between 6 to 8 hours. The drum winder collector was fixed at a rotational speed of 50 rpm. Samples were oven dried for more than 12 hours for later stage of characterization and testing.

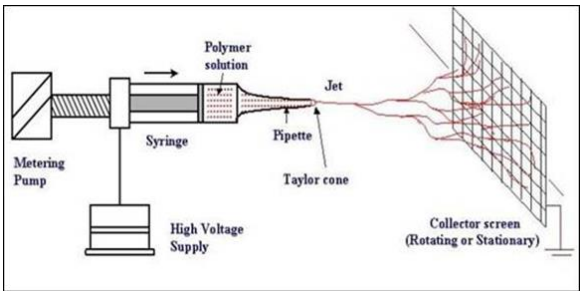

Figure 2. Schematic diagram of the electrospinning setup.

2.4 Samples characterization

Morphological structures of the electrospun PVA and PVA-Aloe Vera nanofibre were scanned using the Field Effect Scanning Electron Microscope (FESEM) by Zeiss with working voltage of 2 kV. All samples undergone gold-coating evaporator treatment to avoid any charging effect for 3 minutes before the FESEM imaging process. The average diameter was measured via Image J software.

2.5 Release of Aloe Vera

The electrospun membranes can be separated-off from the aluminum foil that covered the drum winder collector, and cut into certain sizes, then weighted on electronic balance. Roughly about 0.03 g of each sample was measured. For the start, each sample was immersed in 40 ml of distilled water with magnetic stirrer at 300 rpm in ambient temperature of 37 ^{0}C. When the membrane had been dissolved completely in the solution, a small amount of it was taken out to determine the presence of aloe vera using UV-Vis spectrometer at an optical length of 299 nm. About 5 ml was withdrawn at a given time intervals and subsequently replaced with similar amount of fresh water in order to maintain the constant sink condition. These procedures were repeated for each of four samples.

3. RESULTS AND DISCUSSION

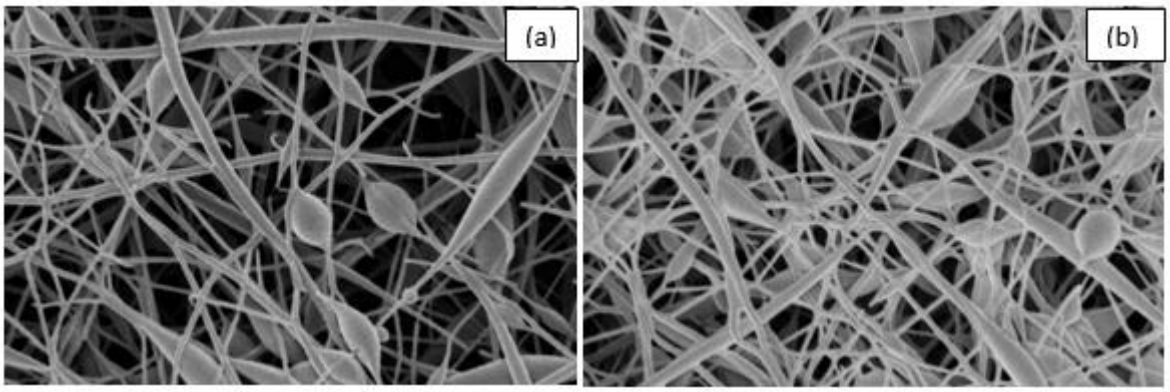

Figure 3. (a) As spun 6% PVA (b) Composite 6% PVA – 5% Aloe Vera

As discussed earlier, finding optimum conditions for electrospinning such as solutions mixture of PVA – water to be mixed with aloe vera were carried out. Figures 3 (a) and (b) show the SEM images of the as-spun nanofiber at 6% of PVA-water, and the 6% PVA-water solution mixed with 5% w/w aloe vera, respectively. In this preliminary experimental work, the important variables that can affect the resulted morphology of the electrospun fibers such as the applied voltage, nozzle-collector distance and feed rate were set here as; 12.2 kV, 20 cm and 0.13 ml/h, respectively. The resulted electrospun morphological structures for both solutions show the formation of beads which was a sign of weaknesses and not a favorable structure for biomedical applications. However, the average size (diameter) of these beads decreased from 542 nm to 430 nm when aloe vera extract powder was added. The fiber density also increased which indicates that the presence of aloe vera is somehow has improved the electrospun fibers yielding. The viscosity and conductivity of the solution were thought to be the reason behind the overall improvement. Higher concentration of aloe vera will result in the increasing of the ionization capacity of the aloe vera-PVA solution which also responsible in lifting the electrical conductivity. It is a well-known fact that high electrical conductivity in the solution will ease up the drawing of jet stream in the electric field.

To test further on the precursor solution, the concentration of PVA solution mixed with aloe vera powder was slightly increased from 6% w/w to 10% w/w. After testing the range of possible variables, the optimum conditions are set as followed: voltage at 15 kV, feed rate at 0.5 ml/h and distance needle – collector at 15 cm. Figure 4 shows the SEM micrographs of the electrospun aloe vera-PVA composite nanofibers with different mixture ratio. Smooth and bead-less electrospun nanofibers were successfully collected when the PVA-water solution concentration was changed from 6% w/w to 10% w/w. Polymeric solution concentration is one of the most critical processing parameters where generally higher concentrations will produce larger fibers diameters.

The shape of the fibers is also depending on the processing parameter where variety of shape such as round fibers, flat ribbons fibers, bead fibers etc. can be produced by an electrospinning process. Figure 4 also shows that by changing the ratio of PVA-aloe vera, several shapes starting from round shape and flat ribbons, followed with beaded fibers, were observed. Branched fibers and split fibers were among shapes that can be spotted in almost all concentration ratios. Beads and pores are common features found in electrospun fibers. Beads are normally appeared at the higher solution viscosity (concentration), and in our case it starts to appear when the solution ratio between PVA-aloe vera is at (25%-75% w/w) level. Beaded fibers also become dominant once the ratio of the aloe vera surpass the 25% mark. The solution viscosity, which in our case

was proportional with content of aloe vera, was varied to find the optimum concentration for producing smooth and straight fibers. The disruption of the equilibrium between electrostatic forces and surface tension in the solution, which typically yields smooth and straight fibers, led to the formation of beaded fibers.

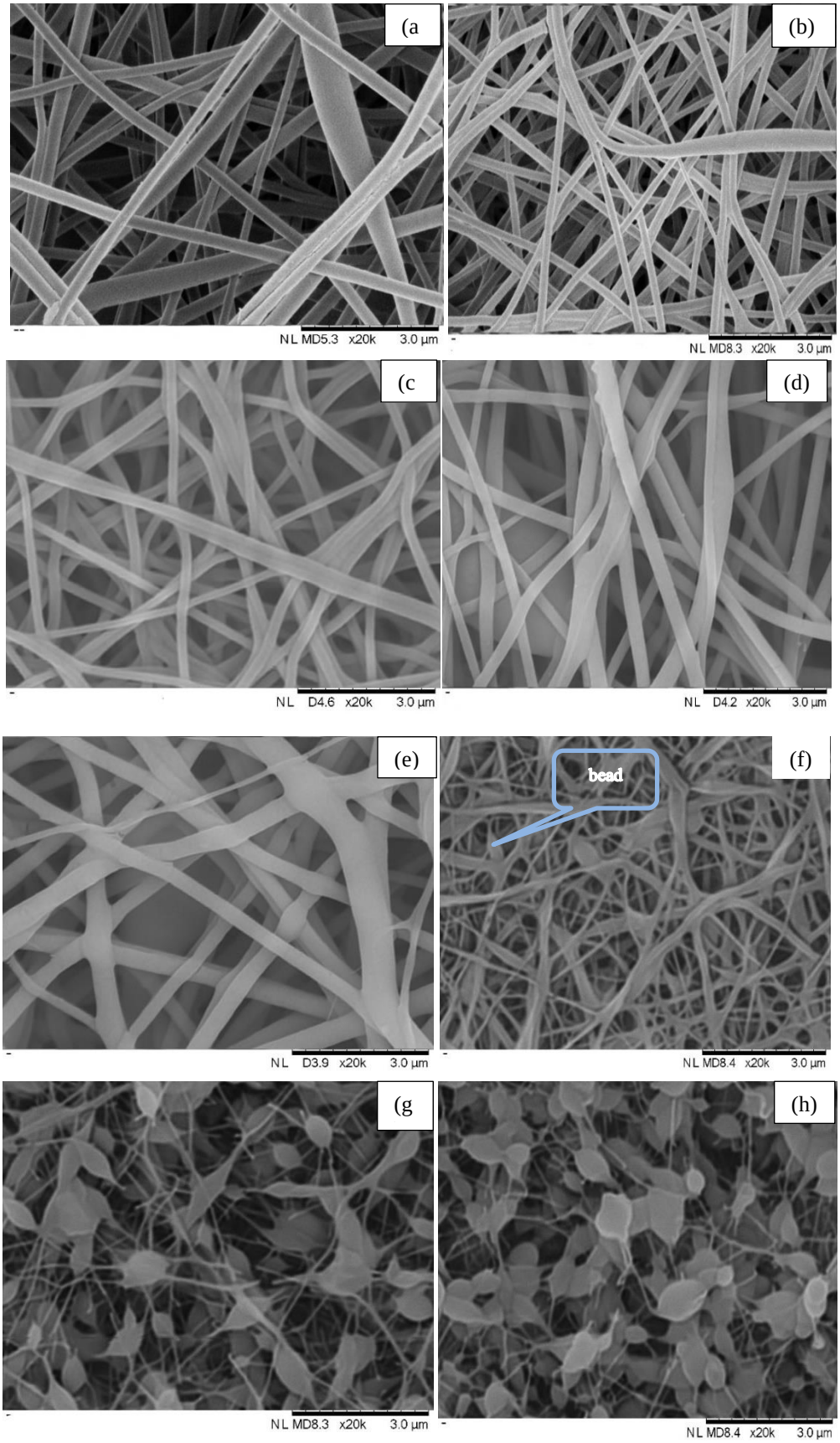

Figure 4. SEM micrograph of the electrospun aloe vera (AV)-PVA composite nanofibers; a) AV 0% w/w, b) AV 5% w/w, c) AV 10 %w/w, d) AV 15 %w/w, e) AV 20% w/w, f) AV 25% w/w, g) AV 50 % w/w and h) AV 75% w/w .

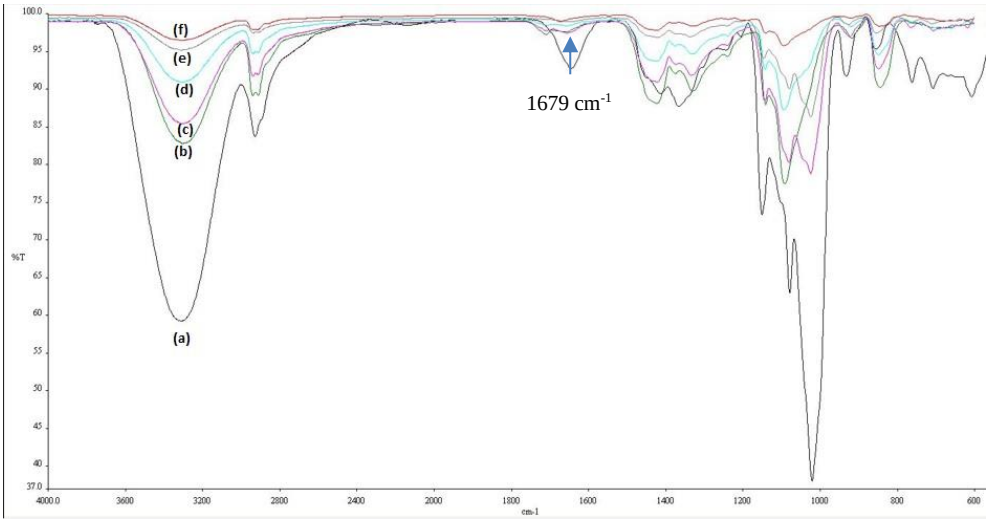

Figure 5. FTIR spectrum for (a) aloe vera extract powder; aloe vera's content in the electrospun fibers (b) AV 0% w/w, (c) AV 5% w/w, (d) AV 25% w/w, (e) AV 50% w/w, (f) AV 75% w/w

The FTIR spectra in Figure 5 shows the aloe vera (powder) and PVA-aloe vera composite electrospun fibers chemical composition. Strong and broad intensity band appeared at 3480 cm-1 in aloe vera powder indicates phenolic-Oh group in aloe vera [19]. The peak also appeared at 3400 cm^{-1} – 3380 cm^{-1} in both PVA and PVA-aloe vera where it shows the majority characteristic of their respective assignment which represents hydroxyl group in the membrane. It is due to the properties of PVA and aloe vera that both contain hydroxyl group. Such appearance also been recorded by Li et al. [8], where there is a presence of water absorbed ($-CH_3$) stretching by PVA molecular chain. Apart from that, Peresin et al. [20] and Zaman et al. [21] also recorded major peak that related to hydroxyl group and acetate group which responding to neat PVA. The presence of the hydroxyl group in both the polymer and the drug resulted in the appearance of a peak at 2780 cm^{-1}, indicative of hydroxyl group stretching. This situation has also been studied by Azabayjian et al. [22] where hydrogen abstraction occurred in between the mixture of PVA and T_4 which slightly changes the characteristic of the polymer due to intermolecular interaction between the hydrogen group with carbonyl in both PVA chains and aloe vera. These can be seen when the peak at Figure 5 (c) shifts from 1679 cm-1 to 1690 cm-1. According to Akhagari et al. [23] and Awanthi et al. [24], there was no any significant change while combining the polymer and drug either in ionic and hydrogenic even irradiation to promote the presence of the drug which assumes the good prominent method of network formation. However, the distinction of the peak in the PVA-AV does not affect the efficiency as drug carrier, as most of the characteristics remained unchanged.

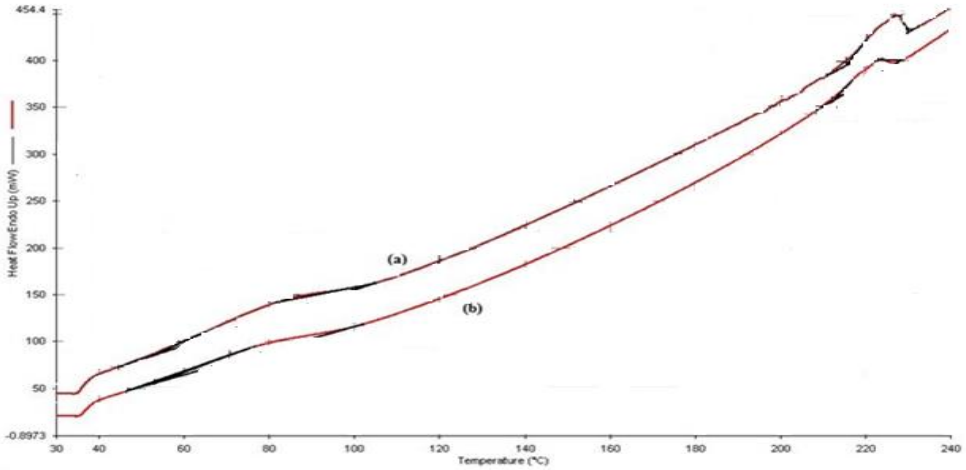

Figure 6. DSC thermograms for nanofibre of (a) electrospun PVA 100% and (b) electrospun PVA- aloe vera

Figure 6 illustrate the differential scanning calorimetry (DSC) thermograms for both the pristine PVA fibers and the PVA-aloe vera fibers. The electrospun PVA fibers exhibit the loss of moisture ranging from 60 ˚C to 100 ˚C as it shows the peak at 81 ˚C of glass transition. It started to melt when reaching 222 ˚C, then possibly thermal degrades between 240 ˚C to 300 ˚C. The alignment and semi-crystallizations of polymer chain in individual PVA fibres had demonstrated the high sheer stress during electrospinning. For comparison, when aloe vera was mixed with the PVA polymer, the electrospun fibers began to lose their moistures earlier at 76 ˚C. This was possibly because of the presence of aloin in aloe vera [25]. The presence of aloe vera might affect the crystallinity of neat PVA polymer which converts into amorphous structure that easier to degrade as reported by Khanzada [35]. Combination of aloe vera and PVA shows a good miscibility which also signaling the lacking of crystallinity [26]. The melting point was also decrease from 226 ˚C to 222 ˚C which is another strong evident of amorphous structure. Consequently, the increase of macromolecules mobility subject to polymeric chain due to the present of aloe vera has previously demonstrated [27,28] where single endothermic response was found probably due to the amorphous state. The result of the thermogram had elucidated as well that aloe vera-PVA electrospun fiber was successfully fabricated which can be a promising material for wound dressing and topical drug delivery.

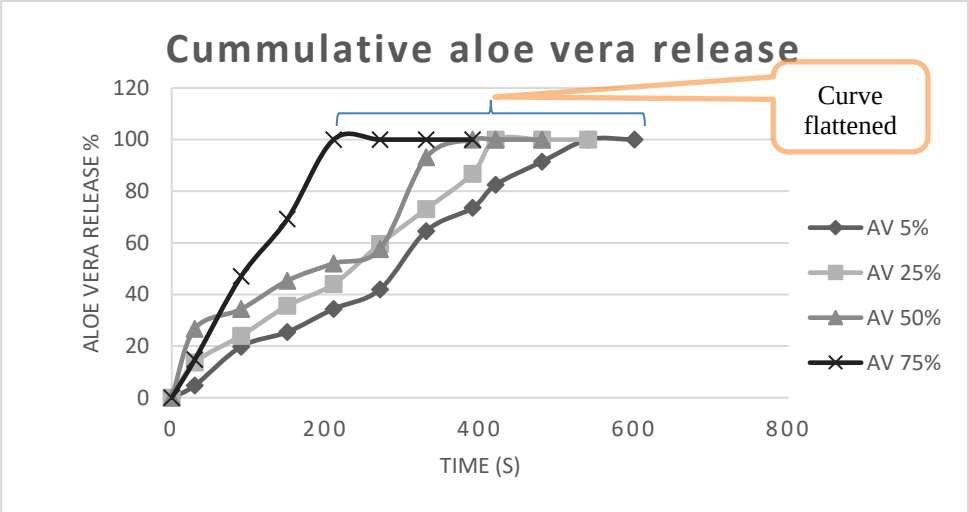

Figure 7. Percentages delivery rate of aloe vera from the PVA electrospun nanofibers nanofibers matrix

Figure 7 displays the release percentage of the aloe vera from PVA electrospun nanofibers matrixes were tested using the UV-Vis spectrometer. At 60 s, the percentage of aloe vera reached around 30% to 40% and increased steadily until 70% at 150 s which suggests the immediate release of drug had occurred during degradation from PVA membrane [29]. The fastest release of aloe vera from the PVA electrospun nanofiber matrix was the 75% aloe vera content where after just 240 s, almost the entire content was released. At 75%, the electrospun aloe vera- PVA membrane had not offered any signs of controlled where burst released was occurred soon after it was exposed to water. At a 50% concentration, intriguing results were observed, with a noticeable influence on the release of aloe vera. Flat curves were evident at approximately 80 seconds and 200 seconds, respectively. This pattern of controlled release was consistently maintained for the remaining ratios. The immediate release of aloe vera probably because of the hydrophilic property which is very soluble in the water since the experiment was using water as the medium transport. Moreover, high surface area and porosity obtained through small diameter of as-spun nanofibre also promote fast release of the drug. In addition, the excellent wettability in nanoporous structure remarked the rapid penetration of water, thus shortened the release time [30]. Taepaiboon et al. [31] stated that the highly porous structure of as-spun nanofibre had

contributed to immediate release of drug whereas according to Lee et al. [32], releasing rate of PDGF-BB from heparin conjugated polycaprolactone (PCL) /gelatin scaffolds was proportional with fiber diameter whereby smaller diameter fibers showed faster release. Initially, the immediate release of aloe vera provides a quick onset of action at specific site but according to R.Imani et al. [34], sharp increase of drug concentration potentially increase the toxic levels of drug at initial drug administration which probably causes high therapeutic effect that might slowdown the healing process. However, at 5% of aloe vera content, the drug was steadily released on time taken which suggested that it was released on controlled manner thus reduced the toxic level on the surface of targeted cell. In addition, formation of beads at 50% and 75% of aloe vera content also gives an initial burst release as both of composite membranes show the fastest release in Figure 7. The drug release behaviour of beads had also been studied extensively by T.Li et al [33] where it concluded that electrospun bead-on-string could potentially be used to attenuate the drug initial burst release. Nonetheless, both of aloe vera content at 50% and 75% were not suitable candidates because of high percentage of drug release on short period of time that might cause high therapeutic effect on specific target area on cell.

4. CONCLUSION

This paper aims to fabricate the electropun PVA and PVA-Aloe Vera nanofibre as polymer-drug carrier, and it is successfully achieved. The morphological structure of electrospun PVA nanofibre shows smoother and non-beaded nanofibers when the concentration was increased from 6% to 10%. Both FTIR and DSC displayed the presence of aloe vera as an evident to prove the encapsulation of drug in polymer membrane. Aloe vera release profiles have shown very encouraging results whereby smooth and non-beaded fibers demonstrate an ability for controlling release of aloe vera from PVA matrixes. Electrospun fibers of Aloe Vera-PVA with concentration of 50% and 75% have shown burst released with no flat curve detected especially for 75% sample which indicated only a very minimum control of release is required (or maybe not required at all). Both 50% and 75% samples morphologically are beaded fibers with some small fractions of fibers which suggest the importance of fine and smooth electrospun nanofibers to limit the burst release that can cause an increase in toxic level on the target surface,causing therapeutic effect that might slowdown the healing process.

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