Materials Research Express

PAPER

Electrospun $\alpha$-mangosteen–chitosan–poly(ethylene oxide) nanofibers

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Keywords: $\alpha$-mangosteen, chitosan, poly(ethylene oxide), nanofiber, electrospinning

Abstract
In this study, electrospun $\alpha$-mangosteen–chitosan–polyethylene oxide (PEO) nanofibers were produced via electrospinning process. The structure and morphology of nanofibers were evaluated through a field emission scanning electron microscope (FESEM) and Fourier-transform infrared (FTIR) spectroscopy. The FE-SEM demonstrated that the average diameter of electrospun $\alpha$-mangosteen–chitosan–PEO nanofibers were $125.5 \pm 33.6$ nm, $91.8 \pm 27.1$ nm, and $111.7 \pm 39.8$ nm for 0.025, 0.05, and 0.075% (w/v) $\alpha$-mangosteen concentration, respectively, meanwhile the average diameter of electrospun chitosan–PEO nanofibers and electrospun $\alpha$-mangosteen–PEO nanofibers was $124.8 \pm 52.8$ nm and $153.5 \pm 49$ nm, respectively. The FE-SEM image of electrospun $\alpha$-mangosteen–chitosan–PEO nanofibers shows that the higher concentration of PEO resulted in smooth morphology, no beads, and continuous fibers. The morphology of electrospun $\alpha$-mangosteen–chitosan–PEO nanofibers resulted in a better preservative than the morphology of electrospun $\alpha$-mangosteen–PEO nanofibers. The FTIR spectra of the electrospun nanofibers demonstrate the presence of characteristic peaks of $\alpha$-mangosteen, chitosan, and PEO and indicate intermolecular interactions via hydrogen bonds. The average diameter of the electrospun $\alpha$-mangosteen–chitosan–PEO nanofibers are within the size range of the extracellular matrix of the natural structure. Therefore, the electrospun $\alpha$-mangosteen–chitosan–PEO nanofibers are the potential for biomedical applications.

1. Introduction

Mangosteen (Garcinia mangostana L.), commonly known as the ‘queen of fruits’ is a member of the Clusiaceae family mainly cultivated in Southeast Asia (Indonesia, Malaysia, Thailand, etc). The color of the mangosteen fruit is dark purple or reddish and has a juicy white pulp. The main component in mangosteen pericarp is xanthones. The most abundant xanthones in mangosteen pericarp are $\alpha$-mangosteen and $\gamma$-mangosteen, followed by other compounds including $\beta$-mangosteen, gartanin, 8-deoxygartanin, garcinones, mangostinone, 9-hydroxycalabaxanthone, and isomangostin [1]. Several studies have reported that $\alpha$-mangosteen exhibit antioxidant [2–5], antimicrobial [3, 6–8], anti-inflammatory [1, 9, 10], and anticancer [11–13]. $\alpha$-mangosteen have limited aqueous solubility property [14]. Hence, various delivery methods such as solid dispersion [14], microgel [15], microsphere [16], and nanofiber [3] are implemented to improve the bioavailability of $\alpha$-mangosteen.

Nanofibers are one of the nanocarriers that can target the optimum payloads of active agents due to their nano-size and high aspect ratio [17]. Decreasing molecule size to the nanoscale allow high porosity with a large surface area to volume ratio, which increases the release of the active agent through drug diffusion and matrix degradation [18–20]. Electrospinning is the most used processing method for producing continuous nanofiber on a large scale with diameters in the nanometers to the sub-micrometers range [21, 22]. This method involves electrostatic forces to generate uniform nanofibers from polymer solutions. An electrostatic force is applied to the polymer solutions to induce a positive charge between the collector drum and the syringe needle. The
dissolved polymer is extruded from the needle, and the droplets exposed to the electric field begin to form fine fibers. The morphology and size of the electrospun fiber can be adjusted with the applied electric field, flow rate, capillary-collector distance, solution concentration, solvent volatility, and solution conductivity [23]. The nanofibers fabricated by the electrospinning method have an extraordinarily high surface-to-volume ratio and porosity, making them highly attractive in biomedical applications.

One of the essential biomaterials for biomedical applications in recent years is chitosan. Chitosan is produced by alkaline deacetylation of chitin. Chitosan has been desired in the biomaterials field due to its unique characteristics as having antibacterial properties, biocompatible, biodegradable, non-toxic, and activates hemostasis [24, 25]. The most successful approach to fiber formation is blending with synthetic polymers as the matrix material. Synthetic polymers can achieve good structural nanofibers and chemical stability [26]. A water-soluble synthetic polymer such as poly(ethylene oxide) (PEO) is a suitable matrix for electrospun nanofiber with a rapid release. PEO is also widely used as a controlled-releasing carrier and has biocompatible properties of drugs [27], antibiotics [28], and proteins [29, 30] because of its low toxicity.

Some studies have reported the development of electrospun α-mangosteen/polymer nanofibers. For instance, α-mangosteen was spun in a mixture with poly(vinyl alcohol) (PVA) for dermal delivery [31] and was loaded onto chitosan–ethylene diaminetetraacetic acid (EDTA)–PVA for wound healing [3]. α-mangosteen has reached its solubility in DMSO solution [11]. The preparation of electrospun chitosan–PEO nanofibers has been based on the use of acetic acid aqueous solvent [26].

This study intended to prepare α-mangosteen–chitosan–PEO nanofibers utilizing the electrospinning method. It was expected to have a solid structure for biomedical applications. Their morphology and microstructure were investigated using a field emission scanning electron microscope (FE-SEM). The composites were characterized using Fourier-transform infrared (FTIR) spectroscopy.

### 2. Experimental

#### 2.1. Materials

α-mangosteen was provided by Research Center for Advanced Material. Chitosan (≥75% deacetylation degree, low molecular weight) and PEO (Mw ~ 900 kDa) were purchased from Sigma Aldrich (Saint Louis, MO, USA). Acetic acid, ethanol, and dimethyl sulfoxide (DMSO) were purchased from Merck (Darmstadt, Germany).

#### 2.2. Solution preparation

The α-mangosteen solution (0.5% w/v) was prepared by dissolving α-mangosteen in deionized water and DMSO at a weight ratio of 1:1. The chitosan solution (3% w/v) was prepared by dissolving chitosan in 10% (v/v) acetic acid. The PEO solution (6% w/v) was prepared by dissolving PEO in deionized water. Each solution was stirred overnight at RT to obtain homogeneous solutions and bath sonicated for 30 min α-mangosteen, chitosan, and PEO were mixed at various weight ratios with a final solution of 10 ml, as listed in table 1. All the solutions were freshly prepared for the electrospinning process.

#### 2.3. Electrospinning process

The electrospinning setup is shown in figure 1. The vertical electrospinning equipment (Tong Li Tech Co., Ltd, China) consisted of a programmable syringe pump with solution flow rates control, a high DC voltage supply, and a grounded drum collector. Each polymer solution was loaded in a 10 ml syringe with a 21 G blunt-tip needle. The polymer solution was electrospun at a high voltage of 25 kV, the needle tip to the collector distance was fixed at 10 cm, and the solution flow rate was 0.5 ml h⁻¹. During electrospinning, the temperature and the relative humidity (RH) were kept at 30 °C–40 °C and ≥30% RH, respectively.

| Sample | α-mangosteen % (w/v) | Chitosan % (w/v) | PEO % (w/v) |
|--------|---------------------|-----------------|-------------|
| A1     | 0.025               | 0.15            | 5.4         |
| A2     | 0.05                | 0.15            | 5.1         |
| A3     | 0.075               | 0.03            | 5.04        |
| A4     | 0.15                | 0.03            | 4.14        |
| A5     | 0                   | 0.075           | 5.85        |
| A6     | 0.025               | 0               | 5.7         |
| A7     | 0                   | 0               | 6           |

* The fiber could not be produced.
2.4. Characterization

A field emission scanning electron microscope (FE-SEM; JEOL™, JIB-4610F, Japan) was used to observe the nanofiber morphology structures. Priory, the electrospun nanofibers were covered with a gold coating in a sputter coater (E-1045, Hitachi™, Japan) for 1 min. The average diameter of the samples was analyzed by measuring 100 fibers in each FE-SEM image using CAD software.

The Fourier-transform infrared (FTIR) absorption spectra were recorded at a wavelength from 4500 to 500 cm\(^{-1}\) wavenumbers on a Nicolet iS10 instrument (Thermo Scientific™, USA) with the Attenuated Total Reflection (ATR) mode.

3. Results and discussion

3.1. Morphological structure studies

Figure 2 shows FE-SEM micrographs of the electrospun chitosan–PEO, α-mangosteen–PEO, and PEO nanofibers, confirming that the fiber structures have been successfully formed. FE-SEM micrographs of A7 exhibit that the PEO produced fibers without beads. The formation of fibers is correlated with the ideal concentration of PEO solution used in the electrospinning process being 4%–8% (w/v) [32]. FE-SEM micrographs of A5 and A6 show continuous fibers without forming beads. The continuous fibers revealed that adding PEO facilitates the formation of electrospun chitosan and α-mangosteen nanofibers via the formation of hydrogen bonding, confirmed by Fourier-transform infrared (FTIR) spectra (figure 4). For the A7 nanofiber, the diameter was distributed from 50 to 500 nm, with the average diameter (\(D_{\text{average}}\)) of 175 nm and the standard deviation (SD) of 83.6 nm. The range, \(D_{\text{average}}\) and SD of the A5 nanofiber were 53 to 287 nm, 124.8 nm, and 52.8 nm, respectively. The range, \(D_{\text{average}}\) and SD of the A6 nanofiber were 74 to 326 nm, 153.5 nm, and 49 nm, respectively. The fiber diameter of the A6 nanofiber was greater than the A5 nanofiber. The difference in fiber diameter size can be influenced by the conductivity of each solution. Solutions with high conductivity will have a higher charge density in the polymer jet, resulting in a stronger elongation force in an electric field and thinner fibers with smaller diameters [21]. Furthermore, the fiber diameter of the A7 nanofiber was greater than the A5 nanofiber. The increasing fiber diameter reveals that the viscosity of the blended solutions also affects the diameter of the nanofiber. The solution is too concentrated, and it is hard to create smooth fibers due to its high viscosity, making it challenging to regulate the flow rate of the solution via the capillary [21].

The morphology of A1, A2, A3, and A4 nanofibers is shown in figure 3. The smooth nanofibers were observed in A1 and A2, whereas a small number of broken strands of fibers were found in A3 nanofiber. The A4 nanofiber could not be produced by the electrospinning process, showing that the concentration of α-mangosteen was high enough to tie PEO and chitosan chains. The presence of α-mangosteen with a different mass concentration in chitosan–PEO affects their morphologies. Along with the increasing concentration of...
polymer α-mangosteen to 0.15%, solution drops were obtained. It has been proven in the viscoelastic jet breakup theory that the formation of fibers is related to the viscoelasticity of the solution. In the electrospinning process, viscoelastic force permits the continuous and uniform elongation of the jet into fibers. As the fiber travels to the collector, it becomes thinner as it elongates. In a solution with low viscosity, polymer chain entanglement is restricted, and the process of fiber thinning leads to fiber break-up, formation of beads, and solution droplets [23, 33, 34]. By adding highly extensible polymers, such as PEO polymers, a high viscoelastic characteristic can be created. Therefore, when the PEO concentration in the solution increased, bead-free fibers were successfully produced. The morphology of A1 nanofibers is more uniform and smoother than the morphology of A6 nanofibers, even though it has a lower concentration of PEO. The difference in the morphology of these nanofibers is in the chitosan concentration. The presence of 0.15% (w/v) chitosan can maintain the fiber structure, which has semi-rigid molecular chains.

The diameters of A1, A2, A3, and A4 nanofibers are 50 to 287 nm. The $D_{\text{ave}}$ of these nanofibers were 125.5, 91.8, and 111.7 nm, respectively. The $D_{\text{ave}}$ of electrospun nanofibers decreased with the increase of α-mangosteen concentration (A1 with A2 nanofiber). The decrease in fiber diameter might be due to the higher conductivity of the solution. However, the A3 nanofiber has $D_{\text{ave}}$ greater than the A1 and A2 nanofiber. A possible reason is decreasing the solution’s viscosity, where the polymer chains tend to interact with the solvent rather than trapping the solute, resulting in larger fibers.

The coefficient of variation (CV) is the ratio of the SD of the fiber diameter to the $D_{\text{ave}}$. The fiber distribution is considered uniform (smooth) if the CV ratio is less than 0.30 [35]. The A1, A2, A3, A5, A6, and A7 nanofibers with the CV ratio of 0.26, 0.29, 0.35, 0.42, 0.31, 0.47, respectively, were less uniformly distributed. The less uniformly distributed fibers are because of the imbalance of the charged polymer’s attraction from the needle to the collector [23]. The 25-kV applied voltage lead to one or more jets forming in fibers’ production. Nevertheless, the diameters of electrospun nanofiber remain within the extracellular matrix (ECM) size ranges of the native structure (50–500 nm).

### 3.2. FTIR spectroscopy

FTIR analysis was conducted to identify characteristic functional groups. Figure 4 shows the FTIR spectra of α-mangosteen–chitosan–PEO nanofiber, chitosan–PEO nanofiber, and α-mangosteen–PEO nanofiber. The
Figure 3. Field Emission Scanning electron microscope images and fiber diameter distribution of the electrospun α-mangosteen–chitosan–PEO nanofibers.

Figure 4. FTIR spectra of the (a) α-mangosteen–chitosan–PEO nanofiber; (b) chitosan–PEO nanofiber; (c) α-mangosteen–PEO nanofiber.
Figure 5. Hydrogen bonding between α-mangosteen, chitosan, and PEO in nanofiber.

| Sample                           | Wavenumber (cm$^{-1}$) | Functional Group                  |
|----------------------------------|------------------------|-----------------------------------|
| α-mangosteen–chitosan–PEO nanofiber | 3485                   | –OH, –NH$_2$                       |
|                                  | 2886                   | –CH$_3$, –CH$_2$                  |
|                                  | 1870, 1659             | –C=O                              |
|                                  | 1570                   | –NH$_2$                           |
|                                  | 1466, 1370, 950, 865   | –CH$_2$                           |
|                                  | 1279, 1241, 1097       | –C–O–C                           |
| chitosan–PEO nanofiber           | 3487                   | –OH, –NH$_2$                       |
|                                  | 2885                   | –CH$_3$, –CH$_2$                  |
|                                  | 1870, 1654             | –C=O                              |
|                                  | 1570                   | –NH$_2$                           |
|                                  | 1466, 1370, 950, 865   | –CH$_2$                           |
|                                  | 1279, 1241, 1097       | –C–O–C                           |
| α-mangosteen–PEO nanofiber       | 3520                   | –OH, –NH$_2$                       |
|                                  | 2879                   | –CH$_3$, –CH$_2$                  |
|                                  | 1870, 1812, 1647       | –C=O                              |
|                                  | 1466, 1370, 950, 865   | –CH$_2$                           |
|                                  | 1279, 1241, 1097       | –C–O–C                           |
recorded spectra of the samples are summarized in table 2. FTIR spectra of \( \alpha \)-mangosteen–chitosan–PEO nanofiber were identified at 3485 cm\(^{-1} \) corresponding to N–H and O–H stretching; the peak at 2886 cm\(^{-1} \) corresponding to C–H stretching and CH\(_2\) stretching; the peaks at 1870 and 1659 cm\(^{-1} \) corresponding to C=O stretching; the peaks at 1570 cm\(^{-1} \) corresponding to –NH\(_2\); the peaks at 1466, 1370, 950, 865 cm\(^{-1} \) corresponding to CH deformation of the methyl group; the peaks at 1279, 1241, 1097 cm\(^{-1} \) corresponding to C–O–C stretching. FTIR spectra of chitosan–PEO nanofiber were observed at 3487 cm\(^{-1} \) assigned to N–H and O–H stretching; the peak at 2885 cm\(^{-1} \) assigned to C–H stretching and CH\(_2\) stretching; the peaks at 1870 and 1654 cm\(^{-1} \) assigned to C=O stretching; the peaks at 1570 cm\(^{-1} \) assigned to –NH\(_2\); the peaks at 1466, 1370, 950, 865 cm\(^{-1} \) assigned to CH deformation of the methyl group; the peaks at 1279, 1241, 1097 cm\(^{-1} \) assigned to C–O–C stretching. FTIR spectra of \( \alpha \)-mangosteen–PEO nanofiber were found at 3520 cm\(^{-1} \) attributed to O–H stretching; the peak at 2879 cm\(^{-1} \) attributed to C–H stretching and CH\(_2\) stretching; the peaks at 1870, 1812, and 1647 cm\(^{-1} \) attributed to C–O stretching; the peaks at 1466, 1370, 950, 865 cm\(^{-1} \) attributed to CH deformation of the methyl group; the peaks at 1279, 1241, 1097 cm\(^{-1} \) attributed to C–O–C stretching. The FTIR spectra of the \( \alpha \)-mangosteen.

The FTIR spectra of the \( \alpha \)-mangosteen–chitosan–PEO nanofiber and \( \alpha \)-mangosteen–PEO nanofiber had the O–H stretching peaks, C–H stretching, C=O stretching, and C–O–C stretching, which is confirm the presence of polyphenol in \( \alpha \)-mangosteen, methyl group, carbonyl group, and methoxy group, respectively. These peaks are characteristic peaks of the \( \alpha \)-mangosteen [11]. The typical peaks of the chitosan are amide I (C=O stretching) and amide II (the amine –NH\(_2\)) [30], which are noticed in \( \alpha \)-mangosteen–chitosan–PEO nanofiber and chitosan–PEO nanofiber. The presence of CH\(_2\) stretching and C–O–C stretching in the \( \alpha \)-mangosteen–chitosan–PEO nanofiber, chitosan–PEO nanofiber, and \( \alpha \)-mangosteen–PEO nanofiber were indicated as characteristic peaks of the PEO [30]. The FTIR analysis of \( \alpha \)-mangosteen–chitosan–PEO nanofiber showed intermolecular hydrogen bonding between the ether groups of PEO and the amine groups of chitosan and OH groups of \( \alpha \)-mangosteen, as shown in figure 5.

### 4. Conclusion

Electrospun nanofibers were successfully prepared from solutions containing \( \alpha \)-mangosteen–chitosan–PEO, chitosan–PEO, and \( \alpha \)-mangosteen–PEO using an electrospinning process. FE-SEM analysis confirms the formation and the nanoscale diameter of electrospun nanofibers. Continuous and bead-free fibers could be obtained by a maximum concentration of 0.05% (w/v) \( \alpha \)-mangosteen and 0.15% (w/v) chitosan, which suggested good spinnability and suitable polymer concentration. The fiber formation of the \( \alpha \)-mangosteen polymer was more uniform in chitosan–PEO nanofiber than in PEO nanofiber. Additionally, the average diameters of the electrospun \( \alpha \)-mangosteen–chitosan–PEO nanofibers mimic the natural ECM. FTIR analysis suggested hydrogen-bond formation between \( \alpha \)-mangosteen, chitosan, and PEO. Findings of an advantageous characteristic implied that the electrospun \( \alpha \)-mangosteen–chitosan–PEO nanofibers could be potential in the biomedical field.

### Acknowledgments

We acknowledge the characterization support from Advanced Characterization Laboratories Serpong, National Research and Innovation Agency (BRIN) through E-Layanan Sains (ELSA).

### Data availability statement

All data that support the findings of this study are included within the article (and any supplementary files).

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