Synthesis of polyvinylpyrrolidone/mangosteen pericarp extract (MPE) fibered particles using electrospray

Y A Rezeki, N Wahyuni, M M Munir, and K Khairurrijal

1 Department of Physics, Faculty of Mathematics and Natural Sciences, Institut Teknologi Bandung, Jalan Ganesa 10, Bandung 40132, Indonesia
2 Bioscience and Biotechnology Research Center, Institute for Research and Community Services, Institut Teknologi Bandung, Jalan Ganesa 10, Bandung 40132, Indonesia

Email: a miftah@fi.itb.ac.id, b krijal@fi.itb.ac.id

Abstract. The electrospray method was used to produce polyvinylpyrrolidone (PVP)/mangosteen pericarp extract (MPE) solids. The concentrations of PVP/MPE were 3 and 4 wt.% in ethanol solvent with the mass ratios of PVP/MPE of 10:0, 8:2, and 6:4 (w/w). The surface morphology of PVP/MPE solids was investigated by an optical microscope and a scanning electron microscopy (SEM). The PVP/MPE precursor solution with the concentration of 3 wt.% and the mass ratio of 8:2 produced PVP/MPE fibered particles. From its SEM image, the particles and fibers of the PVP/MPE fibered particles had average diameters of 819 and 84 nm, respectively. The FT-IR spectra of the PVP/MPE fibered particles showed that MPE was encapsulated in PVP matrix as the PVP/MPE fibered particles had sharper peaks for the carbonyl, alkene, and amide groups.

1. Introduction
Mangosteen (Garcinia mangostana L.) is a fruit spread in Southeast Asia, including in Indonesia. Beside its delicious taste, the pericarp of a mangosteen can also be useful for human’s health since it contains numerous valuable compounds, one of which is xanthones. Xanthones are phenolic compounds that have strong antioxidant properties [1]. Additionally, xanthones found in a mangosteen pericarp extract (MPE) can also act as antimicrobial, anticancer, and antihistamines [2]. However, these compounds have low solubility in water. Therefore, a carrier is needed to increase the solubility of the MPE. Many studies have been conducted regarding the encapsulation of the extract in polymer nanofibers [3–7]. Synthesis of nanofibers for drug carrier system (DCS) have been carried out using electrospinning method as reported in many previous papers [8–12].

Electrospinning is believed to be the most efficient way to produce fibers since it can produce fibers in a uniform diameter for both organic and inorganic materials. Nanofibers have unique characteristics such as low density, high porosity and very large surface area per unit volume when compared to conventional fibers. Thus, with these characteristics, nanofibers are suitable for use as a media of drug carrier system. Moreover, this apparatus is able to generate particles and the method is called as electrohydrodynamic spraying or electrospray [13]. The main advantage of electrospray over electrospinning method is the ability to produce uniform particles with narrow-size distribution thus obtaining a higher loading efficiency [14, 15]. Compared to other synthesis methods, such as sol-gel, coprecipitation, and self-assembly, electrospray offers another advantage, i.e. the morphology and size.
of the particles can be adjusted relatively easily by controlling process parameters such as the solution flow rate, the magnitude of the applied voltage, and the distance between the needle and the collector. Therefore, the desired morphology and size of the particles can be achieved when using electrospray.

To produce nanoparticles as DCS, some amount of polymer is needed as the carrier for the active ingredient compound. One commonly used polymer for electrospray and electrospinning processes is polyvinylpyrrolidone (PVP). It has been recognized by the Food and Drug Administration (FDA), United States, that PVP is a safe polymer to carry active compounds into a human body. It is also a polymer, which can be dissolved easily in water or, in general, other polar solvents, and is reported to be able to be used as DCS [16]. The purpose of this research was to produce nanoparticles containing MPE using electrospray method. The morphology of PVP/MPE particles was analyzed using an optical microscope and a scanning electron microscopy (SEM) while the existing functional groups of PVP/MPE particles were recognized using a Fourier transform infrared (FT-IR) spectrophotometer.

2. Experimental

Polyvinylpyrrolidone (PVP) was used as the carrier and mangosteen pericarp extract (MPE) acted as the active ingredient. PVP (MW of 1,300,000 g/mol) was purchased from Sigma-Aldrich. The mangosteen was purchased from a local market in Bandung, Indonesia. Ethanol 91 % was purchased from a local distributor of chemical material. Technical grade n-hexane and ethyl acetate (99 %) were used as the solvents for the maceration process and were obtained from BRATACO Chemistry, Bandung, Indonesia.

The extraction of mangosteen pericarp was performed using multi-level maceration method. The simplicia of mangosteen pericarp was macerated in n-hexane and ethyl acetate sequentially for three days each at a dry mass ratio of simplicia with a solvent of 1:8. The paste form of the extract was achieved by filtering the maceration result and then subsequently evaporating it using rotary evaporator (IKA ® Labortechnik) at a temperature of 50 °C to dry up the solvents. The MPE paste used in this research was ethyl acetate fraction paste.

PVP was dissolved in ethanol and stirred with a magnetic stirrer for one hour at a temperature of 40 °C. Then, the MPE was added to the PVP solution and stirred for two hours at a temperature of 30 °C until it became homogeneously mixed. The total concentration of PVP with MPE was set at concentrations of 3 and 4 wt.% and varied with the mass ratios (w/w) of 10:0, 8:2, and 6:4.

The solution of PVP/MPE was inserted into a syringe with the needle size 27 G (inner diameter of 0.4 mm). The distance between the needle tip and the drum collector was 10 cm. The drum collector was wrapped with an aluminum foil as the place of particles deposition and was connected to the ground. The syringe was mechanically driven using a syringe pump. The high DC voltage was connected to the tip of the needle. The solution came out from the needle tip formed a Taylor cone and was pulled by the electric force onto the collector. The applied voltage was set at 12 kV with a flow rate of 0.6 mL/h.

The viscosity, the conductivity, and the surface tension of the PVP/MPE solution were measured using a viscometer Fenske-Ostwald (Fisher), a conductometer (Mettler-Toledo), and a du Nuöy tensiometer (Fisher), respectively. The entire measurement processes were carried out at 25 °C.

An optical microscope (National, DC3-163) was used to characterize the morphology of the synthesized PVP/MPE particles during optimization process. The surface morphology and the diameter of PVP/MPE particles were characterized using SEM (Hitachi, SU3500). The particles diameter was determined the SEM images processed using ImageMIF v3.0 software. FT-IR spectral analysis was conducted using a FT-IR spectrometer (Bruker, Alpha Platinum ATR A220/D-01). to determine the existing functional groups of PVP powders, MPE paste, and the synthesized PVP/MPE particles.

3. Results and discussion

3.1. Optical microscope images of synthesized PVP/MPE solids

Electrospraying process have been done to the PVP/MPE precursor solutions with the concentrations of 3 and 4 wt.% with the ratios of PVP:MPE of 10:0, 8:2, and 6:4. The optical microscope images with
a magnification of 1,000 times of the synthesized PVP/MPE are depicted in figure 1. For the PVP/MPE precursor solution with the concentration of 4 wt.% and the mass ratio of 8:2, the synthesized PVP/MPE were beaded fibers as given in figure 1(a). As seen in figure 1(b), there were more fibers formed when using the PVP/MPE precursor solution with the concentration of 4 wt.% and the mass ratio of 6:4. However, the PVP/MPE precursor solution with the concentration of 3 wt.% gives fibers-free particles as shown in figures 1(c) and 1(d). This indicates that less polymer in the precursor solution will result in the formation of fibers. Therefore, larger content of MPE in the precursor solution will result in the formation of fibers since the addition of MPE in the solution will increase the chain entanglement in the precursor solution.

Figure 1. The optical microscope images of PVP/MPE with the concentration of the precursor solutions of (a) 4 wt.% (8:2), (b) 4 wt.% (6:4), (c) 3 wt.% (8:2), and (d) 3 wt.% (6:4)

Shenoy et al. found that there is correlation between the chain entanglement and the fiber formation. The value of chain entanglement can be predicted from the viscosity of the solution [17]. As the entanglement number \((n_e)_{\text{soln}}\) increases until larger than 3.5, the morphology of the sample will be beads-free fibers. On the other hand, if the value of \((n_e)_{\text{soln}}\) is less than two, particles will be formed instead of fibers. When the value of \((n_e)_{\text{soln}}\) is in between 2 and 3.5, there will be a transition from particles to fibers, or also called as beaded fibers. Fibers formation was also influenced by the conductivity of the precursor solution, which is going to be discussed later. Because the goal of this research was to make particles, then any further analysis was only focused on the PVP/MPE precursor solution with the concentration of 3 wt.% since it successfully formed particles under the electrospray process.

3.2. Relationships between conductivity, viscosity, and surface tension of PVP/MPE solutions and morphology of synthesized PVP/MPE solid

The conductivity, viscosity, and surface tension of the PVPV/MPE solution with the concentration of 3 wt.% were measured at different ratios of PVP and MPE as shown in Table 1. It is seen that the conductivity of the PVP/MPE solution increases along with the increase of MPE content in the solution due to the increase in the number of ions contributed by the MPE. This results in the easiness in forming fibers [17] as given in figures 1(c) and 1(d). It is also shown that the surface tension of the PVP/MPE solution gradually decreases with the addition of the MPE. As the surface tension decreases, the formation of fine and beads-free fibers is favored [18] as proven in figures 1(c) and 1(d).

Table 1. The conductivity, viscosity, and surface tension of the precursor solution

| Ratio of PVP to MPE | Conductivity (μS/cm) | Viscosity (cPoise) | Surface Tension (dyne/cm) |
|---------------------|----------------------|--------------------|--------------------------|
| 10:0                | 3.80                 | 54.89              | 28.2                     |
| 8:2                 | 5.33                 | 47.99              | 27.9                     |
| 6:4                 | 5.89                 | 27.68              | 27.3                     |
| 0:10                | 4.20                 | 0.87               | 28.1                     |

3.3. SEM images of synthesized PVP/MPE solids
As the image resolution of the optical microscope is low, a scanning electron microscope was also employed. The SEM images of the synthesized PVP/MPE produced from the precursor solution with the concentration of 3 wt.% and the ratio of 8:2 are shown in figure 2. The SEM images with magnifications of 5,000 and 10,000 times were used to obtain the average particles diameter and its standard deviation. To determine the homogeneity of the particles, a property called geometric standard deviation is used, in which uniform particles have less than or equal 1.22, otherwise they are non-uniform [19]. Moreover, to determine the homogeneity of the fibers, a coefficient of variance (CV) is used. CV is basically the ratio of the standard deviation of fibers diameter over the average fiber diameter, in which uniform fibers have CV smaller than 0.3 otherwise the fibers are uniform [20].

![Figure 2](image-url)  
**Figure 2.** SEM characterization results and sample size distribution curve PVP/MPE 8:2 with magnification of (a) 5,000 times and (b) 10,000 times

The images indicated that there were spherical particles formed with geometric average diameter ($d^*$) and geometric standard deviation ($\sigma^*$) of 819 nm and 1.43, respectively. It can be concluded that the particles produced are not uniform. However, the synthesized PVP/MPE did not only form pure particles but also fibers with an average diameter ($d$) and CV of 84±20 nm and 0.24, respectively. With the value of the CV, the fibers can be said to be uniform. The formation of fibered particles corresponds to the viscoelasticity of the precursor solution. The viscoelastic force causes a continuous elongation during the transformation of the liquid jet into fiber. If the viscosity is low, the elongation process of the solution will be restricted since the entanglement of the polymer chain is weak. Therefore, at some time during the travel of the solution towards the collector, the inertial force of the liquid, which tends to form beads, is greater than the viscous force of the liquid as the main reason of the formation of fibers. The fibers will be rebuilt from the beads after some relaxation time and then the elongation and thinning of the fiber will reoccur [16].

The formation of fibers was also due to the high molecular weight of PVP (1,300,000 g/mol). As described previously, increasing the concentration of MPE will increase the chain entanglement in the solution. Therefore, greater concentration of MPE in the solution will likely lead to the formation of fibers (figure 1). Munir et al. have reported that the use of PVP at constant concentration in solution will eventually form fibers as the molecular weight of PVP increases [11].

### 3.4. FT-IR spectra of synthesized PVP/MPE solids

The FT-IR spectra of the PVP/MPE fibered particles obtained from the PVP/MPE precursor solution with the concentration of 3 wt.% and the mass ratio of 8:2, MPE paste, and PVP powder are demonstrated in figure 3. All FT-IR spectra showed the peaks at the wavenumber ranges of 3405-3424 cm$^{-1}$, 2912-2950 cm$^{-1}$, 1608-1650 cm$^{-1}$, 1422-1460 cm$^{-1}$, and 1276-1285 cm$^{-1}$ representing O-H bond strain in hydroxyl group, C-H strain in methyl group, C=O strain in carbonyl group, C-H bond in alkene group, and C-N strain in amide group, respectively [16,21]. The peak at 1050 cm$^{-1}$ of the FT-IR spectrum of the MPE paste represented the C-O stretching [16]. In the FT-IR spectra of the MPE paste and PVP/MPE fibered particles, there were peaks at wavenumbers of 811-843 cm$^{-1}$ and 571-585 cm$^{-1}$, which represented the symmetric stretching vibration of C-O-O [22] and in plane N-C=O bending, respectively [5]. These results showed that there was MPE in the PVP/MPE fibered particles.
In the FT-IR spectrum of PVP/MPE fibered particles, the peak of O-H group shifting towards smaller wavenumbers indicated that the O-H group in the PVP/MPE fibered particles dominantly came from the MPE paste as evidenced by the peak of O-H group that was more akin to the MPE paste. A similar case also took place for the wavenumber shift in the peak of C-H group. Moreover, the PVP/MPE fibered particles had sharper peaks intensity for the carbonyl group, alkene group, and amide group when compared to the peaks of the PVP powders.

4. Conclusions
The synthesis of PVP/MPE fibered particles from the mixture of the PVP solution and mangosteen pericarp extract (MPE) paste has successfully been done by employing the electrospray method. The PVP/MPE precursor solution with the concentration of 3 wt.% and the mass ratio of PVP to MPE of 8:2 has obtained the PVP/MPE fibered particles with the average particles diameter of 819 and the average fibers diameter of 84 nm as shown by the SEM image. The FT-IR spectrum have proved that MPE could be encapsulated in PVP matrix as shown by the peaks at wavenumbers of 811-843 cm\(^{-1}\) and 571-585 cm\(^{-1}\) representing the symmetric stretching vibration of C-O-O and in plane N-C=O bending, respectively.

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