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Production of Nanocurcumin from *Curcuma Xanthorriza Roxb.* by Homogenization

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Abstract
Curcuma xanthorriza Roxb. contain yellow pigments known as curcuminoids (curcumin, bidesmetoxicurcumin and monodesmetoxicurcumin), protein, phosphorus, potassium, iron and vitamin C, with curcumin as the highest component (50-60%). Curcuma xanthorriza Roxb. has been used widely for treatment of lack of appetite, stomach ulcers, eczema, and acne. Its mainly the effect of curcumin compound. Curcumin has a low bioavailability and poor-water solubility, to enhance it properties, the curcumin convert to nanocurcumin. Nanocurcumins stabilized by Tween 80 were prepared by homogenization. The research was able to produce nanocurcumin with the droplet size less than 100 nm from Curcumin solution, by using a variation of the stirring speed (8,944, 10,822 and 12,879 g), time (20-40 min) and curcumin concentratiom (20 and 30%). The droplet size that lower than 100 nm were using 30% curcumin concentration, stirring speed of 12,879 g for 40 minutes. The nanocurcumin showed increased solubility and bioavailability compared to the extract emulsion.
Keywords: Curcuma xanthorriza Roxb., homogenization, nanocurcumin

1. Introduction

Curcuma xanthorriza Roxb. is a unique spices, the chemical contents of rhizome used for food, industry and medical. The main compound of the rhizome are starch, curcuminoid, and essential oil fraction (Sidik *et al*., 1995). Traditionally the rhizome processes by boiling the minced pieces in water or soaking the extract in hot water. Alhough this process offers a low production cost, it has low extraction of the active compound (Pramono, 1995).

Curcumin is a low water solubility compound, which makes it difficult to incorporate into many food products (Tonnesen, Masson, & Loftsson, 2002), as well as a low bioavailability, which means that its beneficial active compound may not be fully absorbed by the body when it is digested (Maiti, Mukherjee, Gantait, Saha, & Mukherjee, 2007). Therefore, the improvement of the curcumin properties would beneficial to enhance its beneficial usage. One of the method is by reduce the particle size of the active compound in a nano size. The shape and size of particle are similar factors that could increase the affectivity of some compound. This would significantly improve the dissolution, absorbtion and distribution process of the compound. In the medical process, nanomedicine could decrease the dosage that could causing side effect of patients. The treatment by using nanoparticle for the detection and treatment of cell that infected by cancer was more effective than common cancer therapy (Sunderland *et al*., 2006).

Nanoparticle from curcumin made an heterogeneous solution clasify as nanoemulsion. The two immiscible liquids, one of liquid is dispersed in another liquid as droplets with diameter of ten to few hundred nanometers. Nanoemulsions can be prepared by solubilising the lipophilic bioactive components as the oil phase, and then homogenising this phase with an aqueous phase containing a water-soluble emulsifier. The small size of the droplets in nanoemulsion has a different physicochemical and biological properties than in a standard emulsion. Nanoemulsion has better stability to particle aggregation and gravitation separation due to their small droplet sizes (Solans *et al*. 2005; Sonneville-Aubrun *et al.* 2004). Nanoemulsion is optically transparent emulsion system with tiny droplet size (usually in range of 2-500 nm) and it is kinetically stable. Owing to its long-term stability (without flocculation or coallescence), it made nanoemulsion became unique and sometimes refered by “close to termodynamical stability” (Tadros, 2005; Solans, 2003; Fast & Mecozzi, 2009).

The introduction of nanocurcumin in this study is related to enhance it solubility as well as stability especially for medical application. The influence of homogenization conditions and oil phase concentration on the formation of oil-in water emulsion were examined. The droplet size, viscosity, solubility and penetration of nanoemulsion were observed and compared with extract curcumin emulsion.

2. Methods

Materials and Equipment

Materials used were *Curcuma xanthorriza Roxb*., ethanol 98%, maltodextrin, NaOH, aquadest, sodium hydrogen phosphate and Tween 80 as an emulsifier.

The equipments used were disc mill (FFC 15), screen 40 mesh, beaker glass, rotary vacuum evaporator, viscometer, homogenizer (Virtis), digital scale, measurement glass, pH meter, magnetic stirrer, thermometer, and Particle Size Analyzer (Vasco).

Preparation of Nanoemulsion

Oil-water nanoemulsions, containing extract curcumin dissolved into an aqueous emulsifier solution. The emulsifier solution contains 10 % (v/v) Tween 80 (based on the oil phase) and maltodextrin (4% and 10%) that dissolved in phosphat buffer solution (PBS) at pH 7 and stirring for at least 15 minutes to ensure complete hydration. The homogenisation process using a variation of ratio extract curcumin and emulsifier solution i.e 20:80 and 30:70 percent, stirred for 20, 30 and 40 min with the stirring speed of 20,000, 22,000 and 24,000 rpm (8,944, 10,822 and 12,879 g).

Nanocurcumin Measurement

- The droplet sizes were measured by using Particle Size Analyzer.
- Solubility
  Nanocurcumin mixed with solvent in the ratio 1:1, the solvents were hexane, ethyl acetate, acetone, ethanol, methanol and water. The solution well mixed and allowed to stand for 6 hours before observed
- Bioavailability
  The bioavailibilty tested by using Franz diffusion cells, it measured the amount of curcumin that transfer via a membrane during a specific time interval. The membrane used in the testing is a goat intestines. Phosphat buffer solution (pH 7.4) was used in the compartment receptor side and stirred using magnetic stirrer at 300 rpm to homogenized the active compound that dissolved in compartment receptor. Temperature of solution in the compartment receptor is maintained at 37 ± 0.5^{o}C (appropriate body temperature). Membrane was placed between the receptor and donor compartment. Samplings were analyzed after 120 minutes. The absorbance of samples were measured by using spectrofotometer at 530 nm wavelength .

3. Results and Discussion

3.1. Nanocurcumin size

The stability of nanocurcumin depend on droplet size, type of emulsifier (surfactant) and ratio of oil in solution. The physical observations showed that the nanocurcumins obtained were clear and transparent (Figure. 1). The analysis of variance by DNMRT (Duncan's Multiple Range Test) at 5% significance level showed that the homogenization stirring speed and time have effected the droplet size of nanocurcumins. However, the use of low strirring speed was fail to produce a homogenous emulsions (Lachman *et al.* 1994). By using a stirring speed of 8,944 g, the size of droplet significantly differ with the application of stirring speed 10,822 and 12,879 g, as well as the application of variation of stirring time (Figure 2 and 3). Increasing the stirring speed and time result in a lower droplet size, the stirring speed of 12,879 g for 40 minutes result in the smallest droplet size. This may cause by the increased of interfacial tension by the used of high homogenization energy input. The decrease of droplet size with the increasing homogenizer stirring speed was reported due to an increase in the disruptive energy by the homogenizer at higher stirring speed (Tan & Nakajima, 2005). Others reported that increasing stirring speed and time will strengthen the collision intensity between molecules hence produce smallest nanocurcumin droplets (Muller-Fischer *et al.* 2006; Hanselmann 1996). This observed in the application of same amount energy input to the lower oil phase concentration that significantly resulted in the smallest droplet size. For curcumin nanocurcumin, smaller droplet size could be produced at 20% compared to 30% oil phase concentration, with the average size 74 nm and 130 nm consequently.

3.2 Viscosity of Nanocurcumin

Nanocurcumin behaves as a non-Newtonian fluid, as the viscosity increase with higher stirring speed or shear rate as as shown in Figure 3. This rheology characteristic of nanocurcumin classified as a dilatant. The highest viscosity 3.9 cP was obtained when using 30% oil mixed at stirring speed 12,879 g for 40 min. The treatment of higher oil concentration produce higher viscosity as shown in Figure 3, the comparison of oil 30% and 20%. Prolong the stirring time would also significantly raise the viscosity for all stirring spped applied (Figure 4). This indicates that more energy input by extends the time may break the cell and produce lower droplet size. However smallest droplet size would effect the higher viscosity. According to Koocheki and Kadkhodaee (2011), the droplets with small diameter will increase surface's area and hence the viscosity. The increase of the stirring speed and time may enhance the interaction of droplets that produce lower droplet size.

3.3 Solubility

The characteristic of nanocurcumin is differed from curcumin extract has been shown by its dissolved phenomenon Figure 5). The curcumin extract can not dissolved in water and hexane but dissolved in lower alcohol such as ethanol and methanol, ethyl acetate and acetone. This agree with the experiment done by Parthasarathy (2008) which shown curcumin dissolves in ethyl acetate, acetone and ethanol. However, the nanocurcumin solutions behave as as a different solution as it can dissolve in totally in hexane and 90% in water, but in ethyl acetate only 50% dissolved. This indicates the characteristic alteration was occured between curcumin and nanocurcumin.

3.4 Bioaccesibility

The absorption and bioavailability of the hydrophobic active compound in the body would enhance by reduce the size of the molecule. Therefore, rapid penetration of the small size medicine occurs and raise the efficiency of the medicine (Devarajan and Raichandran, 2011). Acosta (2009) reported that the bioavailability of lipophilic components is greater in nanocurcumins than conventional emulsions. This experiment carried out the *in vitro* penetration of nanocurcumin with the molecular size lower than 100 nm and compared to the curcumin extract with the size approximately 6 µm.

The penetration of the curcumin extract across the membrane cell was 13.7% whereas the nanocurcumins penetrated 20.7 %. This indicated a greater penetration of nanocurcumin compare to the curcumin extract, and proved that the smaller molecular size would enhance the penetration across the cell in the body. The experiment of transport cell through skin also observed the application of small size droplet would intensify a transport of the active molecule to the skin (Sharma and Sarangdevot 2012). According to He *et al*. (2011) the nanocurcumins in a drug would provide a large interfacial surface area for drug absorption. Li and McClements 2010 and Lundin and Golding 2009 observed that small droplet size would attribute to increase in the surface area of the lipid phase exposed to the aqueous phase therefore enhance the diffusivity of the cell.

4. Conclusion

The nanocurcumin can be produced by homogenization using low concentration of curcumin extract (20-30%) and an adjustment of homogenization conditions, i.e. time and stirring speed. The Nanocurcumin with the size lower than 100 nm was achieved by using higher stirring speed and optimized at 40 min due to an increase in the disruptive energy by the homogenizer at higher stirring speed. The addition of high concentrations of curcumin oil phase prior to homogenization would reduce the droplet sizes, this may be related to dilatant rheology properties of the solution. The nanocurcumin performed better properties as it dissolved in water and increased absorption to membrane cell.

Acknowledgement

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References

Acosta, E. (2009). Bioavailability of nanoparticles in nutrient and nutraceutical delivery. Current Opinion in Colloid & Interface Science, 14(1),3e15.

Derajavan V., Ravichandran V. 2011. Nanoemulsions : as Modified Drug Delivery Tool. *International Journal of Comprehensive Pharmacy*.

Fast, J. P. & Mecozzi, S. 2009. *Nanoemulsions for Intravenous Drug Delivery.* In Villiers, M.M. de., Aramwit, P., & Kwon, G. S. (Ed.). *Nanotechnology in Drug Delivery.* New York: American Association of Pharmaceutical Scientist, 461, 463-465. December 20, 2010. http://books.google.co.id.

He wei, Tan Y, Tian Z. 2011. Food Protein-Stabilized Nanoemulsions as Potensial Delivery System for Poorly Water-Soluble Drugs: Preparation, In Vitro Characterization and Pharmacokinetics in Rats.International Journal of Nanomedicine 2011:6 521-533.

Koocheki, A., Kadkhodaee, R. (2011). Effect of Alyssum Homolocarpum Seed Gum, Tween 80 and NaCl on Droplets Characteristics, Flow Properties and Physical Stability of Ultrasonically Prepared Corn Oil-in-Water Emulsions. *Food Hydrocolloids* 25, 1149-1157.

Lachman, L., H.A. Lieberman and Kanig. 1994. Teori dan Praktek Farmasi Industri. Penerjemah S. Suyatmi. Jakarta : UI-Press.

Li, Y., & McClements, D. J. (2010). New mathematical model for interpreting pH-Stat digestion profiles: impact of lipid droplet characteristics on in vitro digestibility. Journal of Agricultural and Food Chemistry, 58(13), 8085-8092.

Pramono S. (1995). Kontrol Efektifitas Berbagai Cara Pembuatan Ekstrak Temulawak Dilihat Dari Kandungan Kurkumin Dan Minyak Atsirinya. Abstrak. Fakultas Farmasi UGM. Yogyakarta.

Sharma S. and Sarangdevot K. 2012. Nanoemulsion For Cosmetics. International Journal of Advanced Research

in Pharmaceutical & Bio Sciences, 2012 Vol. 1 (3):408-415.
Sidik, Moelyono MW., Muhtadi A.. 1995. Temulawak (*Curcuma xanthoriza*). Yayasan Pengembangan Obat Bahan Alam Phyto Medica. 200 hal.
Solans, Conxita. 2003. *Nanoemulsions Formation, Properties and Application*. In Mittal, K. L.
Solans C, Izquierdo P, Nolla J, Azemar N and Garcia-Celma M J. 2005. Nano-emulsions Curr. Opin. Colloid Interface Sci.
Tadros, Tharwat F. (Ed.). (2005). *Applied Surfactants: Surfactans in Nanoemulsions*. Weinheim: Wiley-VCH, 285-286. December 20, 2010. http://books.google.co.id.
Tonnesen, H. H., Masson, M., & Loftsson, T. (2002). Studies of curcumin and curcuminoids. XXVII. Cyclodextrin complexation: Solubility, chemical and photochemical stability. International Journal of Pharmaceutics, 244(1–2), 127–135.

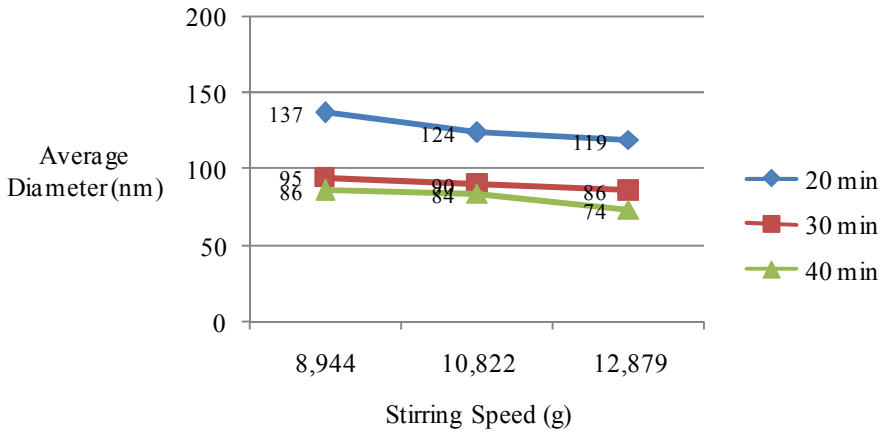

Figure 1. Diameter size of nanocurcumin at various stirring speed and time using extract concentration 30%.

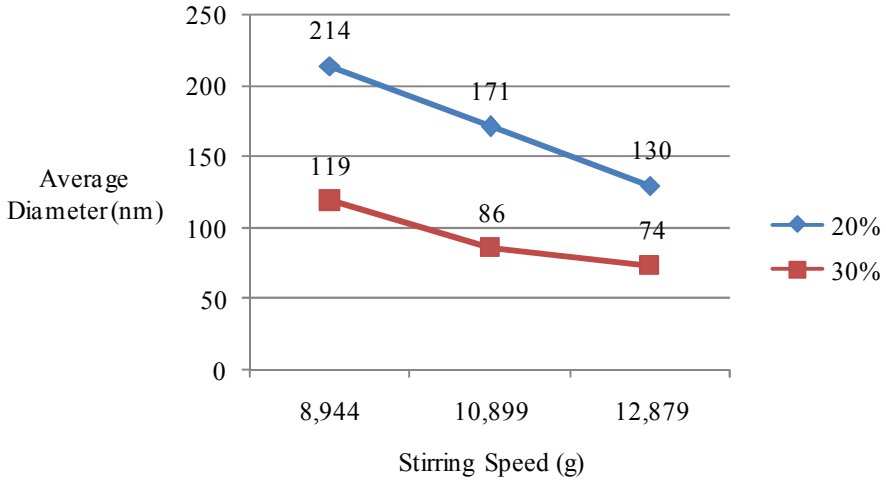

Figure 2. Diameter of nanocurcumin at various stirring speeds and extract concentrations after mixed for 40 min.

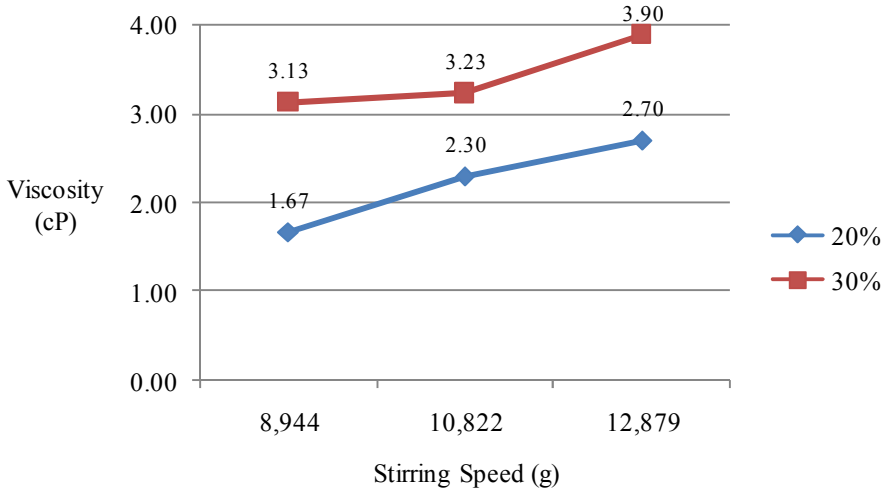

Figure 3. Viscosity of nanocurcumin at various stirring speeds and extract concentrations after mixed for 40 min.

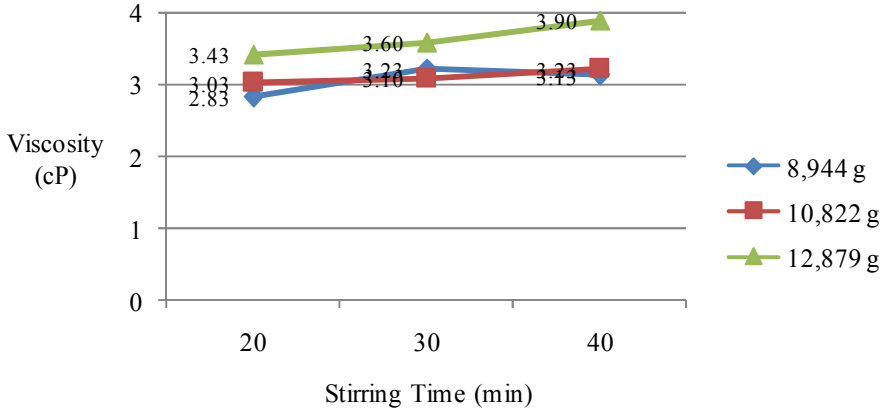

Figure 4. Viscosity of nanocurcumin at various stirring times and speeds

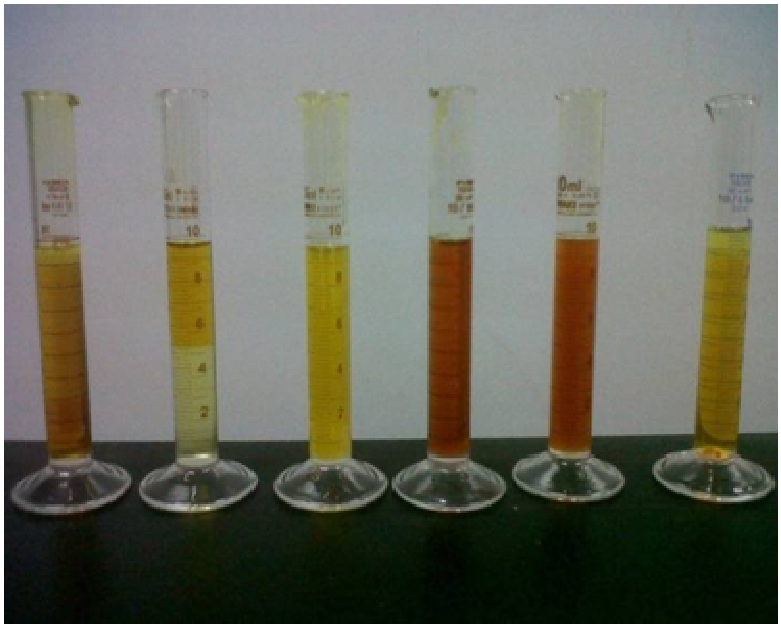

Figure 5. Solubility of nanocurcumin in hexane, ethyl acetate, acetone, ethanol, methanol and water (from left to right) after dissolved for 6 hrs.

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