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Effects of Formulation Parameters on Particle Size and Polydispersity Index of *Orthosiphon Stamineus* Loaded Nanostructured Lipid Carrier

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Abstract – *This study was conducted to investigate the effect of particle size and polydispersity index (PDI) by changing the concentration of active ingredient and solid lipid in the Orthosiphon stamineus (O. stamineus) loaded nanostructured lipid carrier (NLC) formulation. O. stamineus extract was prepared by maceration method. From the HPLC analysis, the O. stamineus extract contains 38% sinensetin and 62% rosmarinic acid. The method used to prepare the formulation of O. Stamineus loaded NLC is melt emulsification homogenization technique. Solid and liquid lipid used were glyceryl monostearate and triglyceride respectively. It was found that the size of particles increased as increasing in concentration of active and solid lipid in the formulation. The best range for concentration of active and solid lipid are 1-4% and 1-3% respectively since the particle size and PDI needed are below 200 d.nm and 0.2. Collectively, based on particle size and PDI results show that the NLC system is highly potential to be a carrier of transdermal delivery for O. stamineus.*

Keywords: *Orthosiphon stamineus*, Nanostructured lipid carrier, Solid lipid

1.0 INTRODUCTION

O. stamineus belongs to Lamiace or Labiate family. This plant is also known as misai kucing (Malaysia), kumis kucing (Indonesia) and java tea (Europe). *O. stamineus* is extensively used for syphilis, rheumatoid disease, hypertension, diabetes, epilepsy, tonsillitis, menstrual disorder, jaundice, edema, gonorrhea, renal calculus, eruptive fever, hepatitis and influenza [1]. Three phytochemical compounds found in different extract of *O. stamineus* are polymethoxylated flavonoids, phenylpropanoids and terpenoids. Besides, its leaves have been established in Europe and Japan as health tea. Combination of *O. stamineus* powder with green tea has been utilized for an anti-obesity effect. In addition, it was found that *O. stamineus* reduced visceral fat mass and food intake [2].

NLC is first introduced to overcome the limitations imposed by solid lipid nanoparticle (SLN) such as drug expulsion during storage and high water content of SLN dispersion. Besides, NLC shows a higher loading capacity compared to SLN due to the perfect crystal produced by SLN. In addition, highly organized crystalline lipid may cause pharmaceutical expulsion [3]. The combination of solid and liquid lipid deforms the perfect crystal. Thus the particle matrix

contains imperfections, allocating space to fit the drug molecules in the amorphous cluster [4]. Furthermore, NLC is suitable for carrying both lipophilic and hydrophilic drug, hence making it easy to scale up and more affordable.

2.0 METHODOLOGY

2.1 Materials

Glyceryl monostearate, triglyceride, Tween 80, soy lecithin distilled and deionized water.

2.2 Preparation of Nanostructured Lipid Carrier

Preparation of *O. stamineus* loaded into NLC was conducted according to Rosli *et al.* [5] method. The preparation of NLC loaded into *O. stamineus* was conducted using melt emulsification homogenization technique. Lipid and aqueous phase were prepared separately. Lipid phase was made up from solid lipid (glyceryl monostearate) and liquid lipid (triglyceride) while aqueous phase involved water and surfactant (Tween 80 and soy lecithin). Both phases were heated individually as well. Next, aqueous phase was added to lipid phase and mixed well. After that, active ingredient (*O. stamineus*) was added into the mixture. The mixture was homogenized using IKA Ultra Turrax® Homogenizer at 11 000 rpm for one minute. The acquired pre-emulsion was ultasonicated using probe sonicator for 20 minutes. Lastly, the NLC was cooled in iced water bath.

2.3 Determination of Particle Size and Polydispersity Index

Particle size determination and polydispersity index measurement were performed using Malvern Zetasizer Nano S (Malvern instrument, UK). All samples were diluted using deionized water at ratio of 1:9. The purpose of dilution was to prevent back-scattering phenomena [6]. Each measurement will be done in triplicate.

3.0 RESULTS AND DISCUSSION

Table 1 shows the composition of active ingredient, solid lipid and liquid lipid. Based on the preliminary study, it was found that 5% of lipid composition resulted in smallest particle size and PDI. Therefore, in this research, the total amount of lipid was fixed to be 5% while the ratio of solid and liquid lipid was varied to investigate their effect on particle size and PDI.

Particle size is a crucial factor in producing nano sized particles. It described the stability of the formulation. In addition, composition of formulation such as surfactant added, drug incorporated and properties of lipid affected the particle size.

In this research, it was found that an increase in drug concentration contributed to larger particle size. This finding are indeed in agreement with Dingler *et al.* [7] who found that higher drug concentration (%) increased the particle size of nanoparticles. Also, Emami *et al.* [8] disclosed that altering the concentration of the drug from 5 to 10 percent increased the particle size.

The ratio between solid and liquid lipid plays an important role in determining the particle size. Particle size of formulation increased as the composition of solid lipid increased. Higher lipid concentration produced higher viscosity of the sample. Khalil *et al.* [9] stated that high

viscosity contributed to larger particles size. In addition, less dispersion energy available per unit lipid in high concentration of solid lipid caused the particle size to increase.

Polydispersity index (PDI) indicated the width of particle size distribution. The PDI value ranged from 0 to 1. As PDI value became closer to zero, the particles became more homogeneous. The outcome of increasing both amount of active and solid lipid was a higher PDI value.

Table 1 Composition (%) of *O. Stamineus*, solid and liquid lipid and their respective respond

Formulation	Composition (%)			Respond	
	O. stamineus	Solid lipid (GMS)	Liquid lipid (Triglyceride)	Particle size (nm±SD)	PDI
NLC_1	1	2.5	2.5	127.8±6.24	0.159±0.02
NLC_2	2	2.5	2.5	158.2±12.02	0.178±0.01
NLC_3	3	2.5	2.5	135.5±17.08	0.187±0.01
NLC_4	4	2.5	2.5	144.3±22.75	0.195±0.01
NLC_5	5	2.5	2.5	268.0±18.74	0.329±0.02
NLC_6	1	1	4	107.4±2.65	0.143±0.01
NLC_7	1	2	3	93.96±1.53	0.168±0.02
NLC_8	1	3	2	117.5±7.71	0.178±0.01
NLC_9	1	4	1	158.8±7.52	0.203±0.01
NLC_{10}	1	4.5	0.5	197.1±4.66	0.223±0.01

4.0 CONCLUSSION

Therefore, it can be concluded that concentration of active and solid lipid in the formulation affect the particle size and PDI. Particle size is a crucial factor in transdermal drug delivery as it needs to overcome the stratum corneum. Besides, both particle size and PDI play important roles in determining the stability of NLC.

REFERENCES

[1] O.Z. Ameer, I.M. Salman, Z.M. Asmawi, Z.O. Ibraheem, M.F. Yam, *Orthosiphon stamineus:* traditional uses, phytochemistry, pharmacology, and toxicology: A review, Journal of Medicinal Food 15 (2012) 1-13.

[2] J.Y. Son, Orthosiphon stamineus reduces appetite and visceral fat in rats, Journal of the Korean Society for Applied Biological Chemistry 54 (2011) 200–205.

[3] S. Selvamuthukumar, R. Velmurugan, Nanostructured lipid carriers: A potential drug carrier for cancer chemotherapy, Lipids in Health and Disease 11 (2012) 1-8.

[4] C.L. Fang, S.A. Al-Suwayeh, J.Y. Fang, Nanostructured lipid carriers (NLCs) for drug delivery and targeting, Recent Patents on Nanotechnology 7 (2013) 41–55.

[5] N.A. Rosli, N.M. Noor, R.A. Aziz, A.A. Aziz, R. Hasham, Formulation and characterization of [6]-gingerol loaded nanostructured lipid carrier (NLC), International Science Postgraduate Conference, Faculty of Science, Universiti Teknologi Malaysia, 2014, 1412-1422.

[6] W.K. Ng, L. Saiful Yazan, L.H. Yap, W.A.G. Wan Nor Hafiza, C.W. How, R. Abdullah, Thymoquinone-loaded nanostructured lipid carrier exhibited cytotoxicity towards breast cancer cell lines (MDA-MB-231 and MCF-7) and cervical cancer cell lines (HeLa and SiHa), BioMed Research International 2015 (2015) 263131.

[7] A. Dingler, R.P. Blum, H. Niehus, R.H. Mulle, S. Gohla, Solid lipid nanoparticles (SLNTM/LipopearlsTM) — a pharmaceutical and cosmetic carrier for the application of vitamin E in dermal products, Journal of Microencapsul 16 (1999) 751–767.

[8] J. Emami, M. Rezazadeh, J. Varshosaz, M. Tabbakhian, A. Aslani, Formulation of LDL targeted nanostructured lipid carriers loaded with paclitaxel: a detailed study of preparation, freeze drying condition, and in vivo cyototoxicity, Journal of Nanomaterials 12 (2012) 1-10.

[9] R.M. Khalil, A.A. El-Bary, M.A. Kassem, M.M. Ghorab, M.B. Ahmed, Solid lipid nanoparticles for topical delivery of meloxicam: development and in vitro characterization, 1st Annual International Interdisciplinary Conference, 2013, 779-798.