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CHARACTERISATION OF SOLID LIPID NANOPARTICLES *P-METHOXYCINNAMIC* ACID (SLN-PMCA) FORMULATED WITH DIFFERENT LIPID COMPONENT: STEARIC ACID AND CETYL ALCOHOL

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ABSTRACT

Solid lipid nanoparticles (SLN) had been increasingly investigated as a new drug delivery system. SLN had several benefits as a topical drug carrier. *p*-Methoxycinnamic acid (PMCA) was a hidrolized product of ethyl-p-methoxycinnamic (EPMC), which is the highest component of *Kaempferia Galanga* extract, was proposed to have an antinociceptive activity. The aim of this study is to identify the characteristics of SLN-PMCA formulated through different lipid matrices, such as stearic acid and cetyl alcohol. SLN was prepared using high shear homogenization method at 25000 rpm for 8 minutes. The previous observed formula (Misra, *et al*, 2004) was used as the reference formula with few modifications. SLN-PMCA product were characterized for entrapment efficiency, morphology and particle sized. The result showed cetyl alcohol had higher entrapment efficiency (mean 68,54%) and smaller particle size (mean 119,25 nm) than stearic acid contained formula. The *Transmission Electron Microscope* (TEM) result showed spherical particles for cetyl alcohol while stearic acid was oval-shaped.

Keyword(s) : *p*-Methoxycinnamic acid, Solid lipid nanoparticles, Cetyl alcohol, Stearic acid, High shear homogenization

INTRODUCTION

Solid Lipid Nanoparticle (SLN) as an alternative drug carrier has attracted reseacher's attentions (Muller, 2007). It's because of the SLN advantages, such as: it's lipid ingredient can form "film like" on the skin, therefore increasing skin occlusivity (Wissing, 2003) and decreasing transepidermal water loss (TEWL). Both of them facilitated the absorption and penetration of active ingridient into the skin (Zhai, 2001; Schafer-Korting, 2007). Besides, the entrapment of active ingredients into SLN has controlled release properties. Furthermore, SLN may reduce skin irritation and increase chemical stability of drug over UV degradation, oxidation or hydrolisis reaction (Muller, 2002). PMCA, has an anti-inflamation activities and is formulated into SLN carrier to obtain optimal effects. The quality of SLN, described by: the morfology, size and drug entrapment capability; is influenced by its lipid component character, especially on cristallinity, melting point, and molecular structures. The best size of SLN is 10-1000 nm (Mukherjee, 2009) and drug entrapment more than 50% (Misra, 2004). Stearic

acid and cetyl alcohol are different lipid. It is assumed that it will influence the character of SLN-PMCA formed.

MATERIALS AND METHOD

Material

p-Methoxycinnamic acid (PMCA) was purchased from Sigma, Propileneglycol (PG), Tween 80, lipid components stearic acid and cetyl alcohol was purchased from PT. Brataco. All ingredients of these were pharmaceutical grade. NaOH and KH_2PO_4 as buffer components were obtained Merck and was analytical grade.

Preparation

The SLN systems (table 1) were generated by high shear homogenization method as shown in figure 1. The melted lipid (80±5) °C mixed with PMCA, was stirred at 200 rpm for 2 minutes, and then was sonicated 35000 Hz for 2 minutes. Tween 80 as surfactant was added and stirred again 200 rpm for 5 minutes. Poured the diluted propyleneglycol as co-surfactant into and blended with 25000 rpm velocity. Gradual cooling phase was used by stirring at 600 rpm for 7 minutes and 800 rpm for 8 minutes. After holding for 30 minutes without any stirring, then manualy were stirred for 30 minutes.

Table 1. Formula of the SLN

Ingredient	Function	Concentration in formula:			
		L	T	Blank L	Blank T
PMCA	Active ingredient	1%	1%	-	-
stearic acid	lipid	-	10%	-	10%
cetyl alcohol	lipid	10%	-	10%	-
Tween 80	Emulgator	12%	12%	12%	12%
PG	Co-surfactant	20%	20%	20%	20%
Aquadest	Water phase	ad 100 mL	ad 100 mL	ad 100 mL	ad 100 mL

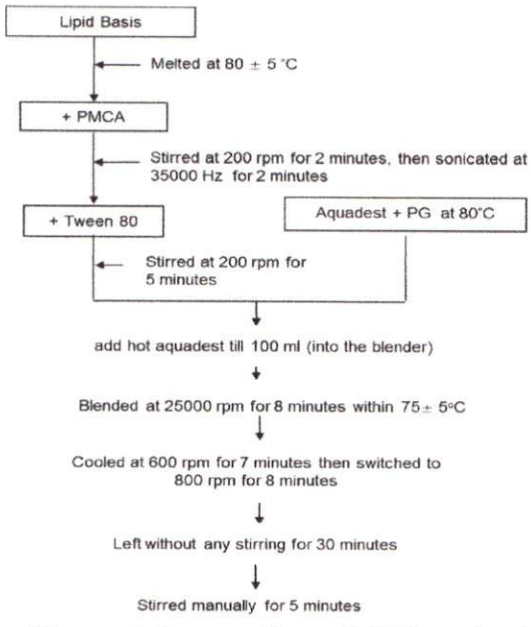

Figure 1. Process flow of SLN production

Evaluation of SLN

Morphological observation

SLN stearic acid and cetyl alcohol were dried and then restituted for TEM analysis.

Particles size determination

The particles size of each SLN was obtained from TEM image and were manually measured then scaled into their actual size.

Entrapment efficiency determination

The amount of active ingredients entrapped inside the SLN system was determined by dialysis method using dialysis bag with phospate buffer pH 7,4±0,5 and was expressed into percent drug entrapped

RESULTS AND DISCUSSION

Stearic acid SLN are more liquid than Cetyl alcohol SLN, it is considered that the amount of carbon atoms in stearic acid is greater than in cetyl alcohol. Furthermore, the internal hydrogen bonding of carboxylic group within stearic acid molecules are stronger than the hydrogen bonding with water molecules.

Based on TEM result, it is observed the morphology of SLN, the stearic acid SLN have oval shape while Cetyl alcohol SLN have spherical shape (Figure 2 and 3).

The particle size of Stearic acid SLN is significantly and statistically different compare with Cetyl alcohol SLN. Stearic acid SLN particles size are ranged 575—2107 nm while cetyl alcohol SLN particles are ranged from 26—665 nm.

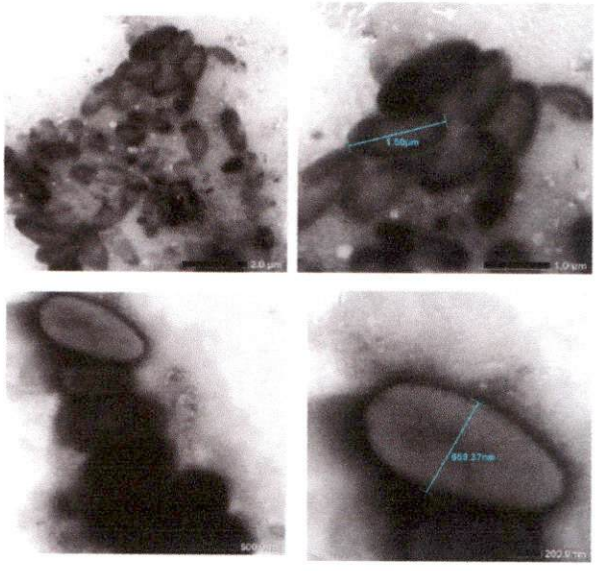

Figure 2. Morphology of stearic acid SLN

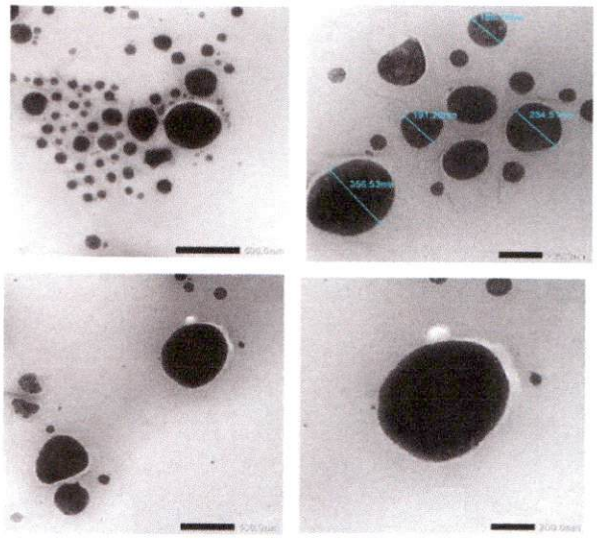

Figure 3. Morphology of cetyl alcohol SLN

The particle size of stearic acid SLN is bigger than cetyl alcohol SLN (Figure 4 and 5). This phenomena probably because of the number of carbon atoms of stearic acid are greater than cetyl alcohol.

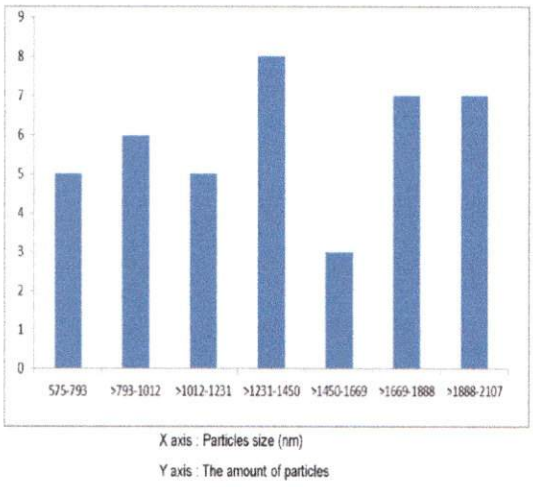

Figure 4. Stearic acid SLN particles size distribution

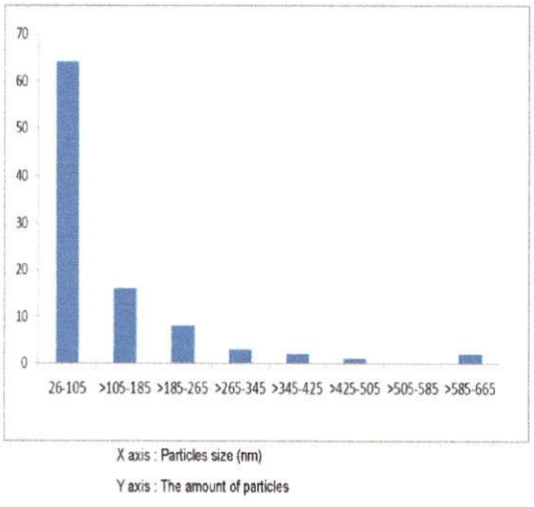

Figure 5. Cetyl alcohol SLN particles size distribution

Another reason is internal hydrogen bonding of carboxylic group within stearic acid molecules are stronger than cetyl alcohol hydrogen bonding of the alcoholic group.

The entrapment efficiency of stearic acid SLN is 58.8% (CV 3.46%) while cetyl alcohol is 68.54% (CV 4.02%). Based on %CV data, it is known that SLN is homogen, the active ingredients is distributed evenly into the the system. The PMCA Entrapment Efficiency (EE) in Stearic acid SLN is lower than Cetyl alcohol. Westesen (1997) explained by the experiment using tristearic gliseryl which is gliseryl ester form of stearic acid, showed the low entrapment effisiency. It was because of the formation of more regular β-crystal within its crystal structure which expulsed the drug out from the systems.

Based on thermogram (Figure 6 and 7), it is known there are two exothermal peak in physical mixture lipid with PMCA. The peak of PMCA in physical mixture is smoother than PMCA thermogram itself, that is considered any interaction between PMCA with either tween 80 or propyleneglycol or both.

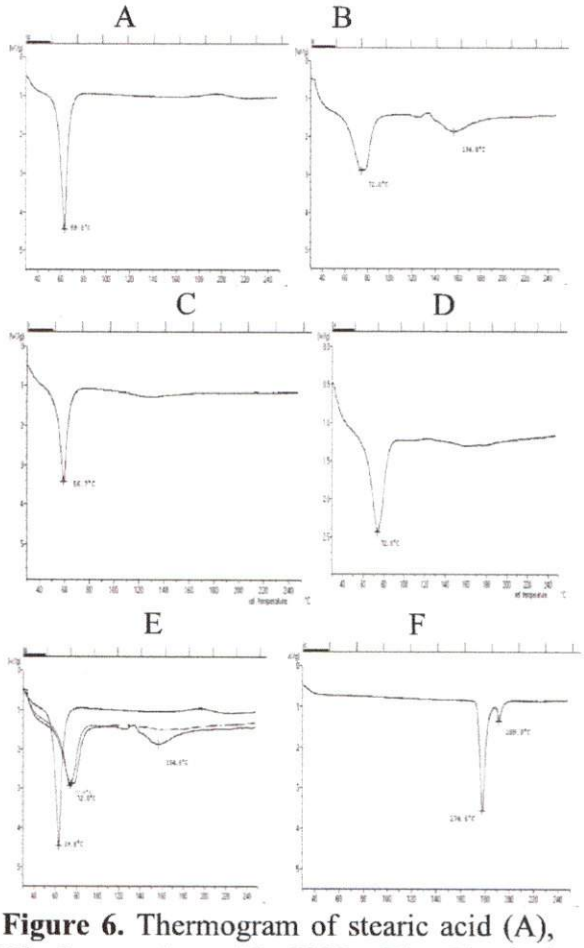

Figure 6. Thermogram of stearic acid (A), Blank stearic acid SLN (B), Physical mixture of stearic acid + PMCA (C), Stearic acid SLN (D), Overlay of A,B,C,D (E) and PMCA (F)

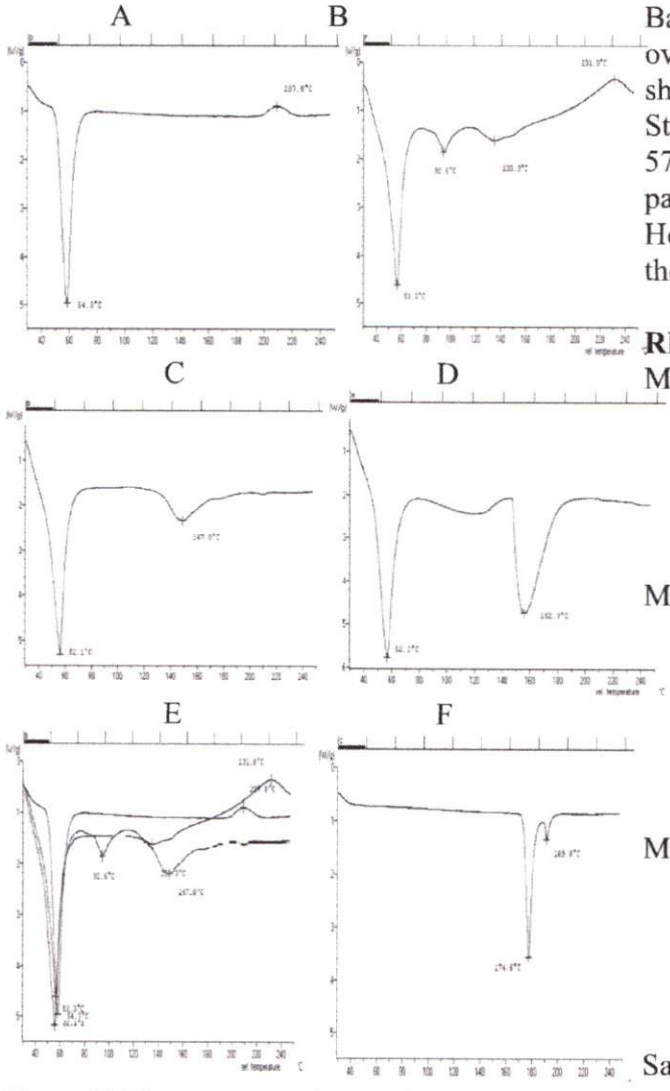

Figure 7. Thermogram of cetyl alcohol (A), Blank cetyl alcohol SLN (B), Physical mixture of cetyl alcohol + PMCA (C), Cetyl alcohol SLN (D), Overlay of A,B,C,D (E) and PMCA (F)

There is no PMCA peak in thermogram of SLN system. It proves that APMS has been dispersed moleculary in lipid .

Cetyl alcohol did not show any altering of its melting point within SLN systems while the melting point of stearic acid SLN is increase. It showed there is any formation of more stabil crystal modification with higher regularity than the initial stearic acid.

CONCLUSIONS

Basis differences influence SLN formation. Based on TEM result, stearic acid SLN has oval shape while cetyl alcohol have spherical shape and also influence SLN particles size. Stearic acid SLN particles are ranged from 575—2107 nm while cetyl alcohol SLN particles are ranged from 26—665 nm. However, basis differences do not influence the entrapment efficiency.

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