

# CDD

# 2016

## The 4<sup>th</sup>

# Current Drug Development International Conference 2016

June 1-3, 2016

Phuket Graceland Resort & Spa,  
Patong Beach, Phuket, Thailand



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**CDD2016**

**The 4<sup>th</sup> Current Drug Development  
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**Proceeding**  
**The 4th Current Drug Development**  
**International Conference 2016 (CDD 2016)**

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**First edition 200 copies**

**Price 500 Baht**

**National Library of Thailand Cataloging in Publication Data**

Faculty of Pharmaceutical Sciences  
Proceeding the 4<sup>th</sup> Current Drug Development International Conference (CDD 2016)  
Songkhla • 2016 • 252 pages

**ISBN 978-616-271-303-3**

**Design & Printing**

Neo point  
1/59 Ratuhit Road  
Tambol hatyai Amphur hatyai  
Songkhla 90110 Thailand

**Published by Faculty of Pharmaceutical Sciences , Prince of Songkla University**



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## Increasing of Lycopene's Antioxidant Stability In Solid Lipid Nanoparticle (SLN) and Nanostructure Lipid And Carrier (NLC) in Use As Antiaging

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**Abstract-** Lycopene is known as lipophilic antioxidant are often used as an anti-aging cosmetic active ingredient. Antioxidants is easily degraded so that its activity is reduced. To improve the stability, lycopene was loaded in nanolipid structure, such as: Solid Lipid nanoparticles (SLN) and Nanostructure lipid carrier (NLC). Lycopene loaded in SLN and NLC are made with High Shear homogenisation (HSH) method. An antioxidant stability is determined based on  $IC_{50}$  value changes.  $IC_{50}$  is determined using 1,1-Diphenyl-2-picrylhydrazyl (DPPH) after being kept in controlled conditions on days 1 and 30. Their oclusivity was determined also. The conclusion is the NLC is able to improve the stability of the lycopene antioxidant and have oclusivity greater than the SLN. Oclusivity nature can indicate the ability of the formula to retain skin moisture.

**Keywords:** Lycopene, Solid Lipid Nanoparticles (SLN) and Nanostructure Lipid Carrier (NLC), setil alcohol, oleic acid.

### Background

Lycopene is a lipophilic antioxidant that easily oxidized. It is necessary to improve the stability of lycopene so that it remains effective. One of the delivery system that proper is nanolipid-based systems, such as Solid Lipid Nanoparticles (SLN) and Nanostructure Lipid Carrier (NLC). The emolien effect of lipid can increase skin softness.

This study compared the SLN and NLC ability in maintaining the lycopene antioxidant stability and also on their oclusivity. Solid lipid used was cetyl alcohol, while the liquid lipid used to form the NLC was oleic acid 1.5%. Oleic acid is a fatty acid with the highest content in olive oil and has penetrant enhacher effect. Systems that do not contain liquid lipid referred to SLN. Furthermore lykopene-NLC and lycopene-SLN stability antioxidant were determined on days 1 and 30 by determining of  $IC_{50}$  in controlled conditions. Their oclusivity in vitro was also determined. The oclusivity effect related with the ability of retaining skin moisture.

### Materials and Methods

SLN made of lycopene 10 % , 10 % cetyl alcohol , 1.5 % tween 80 , 20% propilenglikol and acetate buffer pH 4.2 ad 100 % with High Shear homogenization method [ 1 ] with a speed of 24,000 rpm conducted for 8 minutes at 4 cycle. The NLC made by the same methode and formula , but 1.5 % cetyl alcohol was replaced with oleic acid . Furthermore, their lipid characteristic was analysed by their recrystallization index that was calculated based on the enthalpy value was determined by Differential Thermal Analysis ( DTA ) [ 2 ]

$$\% \text{ Crystallinity index} = \frac{\Delta H \text{ formula}}{\Delta H \text{ Lipid phase} \times \text{Lipid Phase Concentration}} \times 100\%$$

The crystal diffraction pattern determined by X Ray Defraktometer. Do also checks pH , morphology , particle size and particle size distribution with Dynamic Light Scattering ( DLS ) . Trapping efficiency is determined by the method of dialysis and determined by spectrophotometry . Stability antioxidants determined in accordance with the method  $IC_{50}$  1,1-Diphenyl - 2 - picrylhydrazyl ( DPPH ) on day 1 dan30 in controlled conditions .  $IC_{50}$  is the concentration of materials to be dampening the free radicals by 50 % . The larger the  $IC_{50}$  , the smaller the antioxidants activity. Percent reduction is calculated by the formula [ 3 ]

$$\% \text{ peredaman} = \left\{ \frac{A_{\text{control}} - A_{\text{sampel}}}{A_{\text{control}}} \right\} \times 100\%$$

Oclusivity test performed with in vitro methods . Calculated based on the percentage of water that evaporates in a vial covered with a membrane that is smeared preparations and which are not . Membrane used is a membrane filter (cellulose filter with pores 0.45 mm , Whatman no. 4) . Observations were made during a week . The oclusivity ( F ) is calculated by the following formula [ 4 ] :



microplate analyzer [6]. The results of the assay were expressed as  $IC_{50}$ . For SBP extraction, the results were expressed as %inhibition. The free radical scavenging activity was assessed using equation 1:

$$\% \text{ Inhibition} = [(A_{\text{control } 520 \text{ nm}} - A_{\text{sample } 520 \text{ nm}}) / A_{\text{control } 520 \text{ nm}}] \times 100 \quad (1)$$

where  $A_{\text{sample } 520 \text{ nm}}$  is the absorbance in the presence of the extracts and  $A_{\text{control } 520 \text{ nm}}$  is the absorbance of the control.

**Table 1** The formulation of SBP mouthwashes with various concentration of SBP extract

Ingredients	Formulation			
	1	2	3	4
SBP extract	0.0125%	0.025%	0.05%	-
Ethanol	10.0%	10.0%	10.0%	10.0%
Glycerin	25.0%	25.0%	25.0%	25.0%
TWEEN 80	1.0%	1.0%	1.0%	1.0%
Sodium benzoate	0.1%	0.1%	0.1%	0.1%
Sodium saccharin	0.03%	0.03%	0.03%	0.03%
Peppermint oil	0.2%	0.2%	0.2%	0.2%
Water to	100%	100%	100%	100%

### Results and discussion

After extraction, the content of  $\alpha$ -mangostin in the stingless bees' propolis extracts was  $5.59 \pm 0.4$  % w/w. For the antioxidant activity, SBP extract exhibited the DPPH radical scavenging activity with the  $IC_{50}$  value of 124.5  $\mu\text{g/ml}$ . This result corresponding with a previous study, the DPPH radicals scavenging activity of extract from the stingless bees' propolis (*Tetragonula pagdeni*) showed the  $IC_{50}$  value of 122.7  $\mu\text{g/ml}$  [2]. SBP extract was loaded into mouthwashes with 0.0125, 0.025 and 0.05% of the SBP extract. The SBP mouthwashes were yellow clear. The color of mouthwash was deeper when the concentration of SBP extract increased. The pH value of 0, 0.0125, 0.025 and 0.05% SBP mouthwashes were 6.24, 6.35, 6.31 and 6.23, respectively. The % label amount of 0.0125, 0.025 and 0.05% SBP mouthwashes were 95.2, 95.6 and 95.9%, respectively. These results indicated that SBP extract did not affect the pH of the mouthwashes and was not lost during the production.

The antioxidant activity of SBP mouthwashes was evaluated by DPPH method compared with C-20<sup>®</sup>, a commercial 0.2% chlorhexidine solution. Table 2 shows the %inhibition of SBP mouthwashes and C-20<sup>®</sup> with various concentration. The formulation 1 to 3, that contained SBP extract exhibited antioxidant activity more than C-20<sup>®</sup>. The % inhibition of the SBP mouthwash formulation 1, 2 and 3 were 40.7, 56.6 and 62.7%, respectively. The antioxidant activity directly depended on the concentration of SBP extract. This result suggested that SBP mouthwashes have been successfully formulated with an antioxidant activity. Furthermore, this study needs to investigate the antibacterial activity against *Streptococcus mutans* in the future.

**Table 2** The antioxidant activity of the SBP mouthwashes with various concentration of mouthwash

% concentration of mouthwash	%Inhibition				
	Formulation 1	Formulation 2	Formulation 3	Formulation 4	C-20 <sup>®</sup>
10	9.4 $\pm$ 2.7	11.0 $\pm$ 0.3	13.3 $\pm$ 1.9	3.5 $\pm$ 2.6	17.8 $\pm$ 2.6
20	14.6 $\pm$ 2.6	21.0 $\pm$ 1.4	28.7 $\pm$ 1.3	2.7 $\pm$ 0.7	18.4 $\pm$ 3.6
40	26.8 $\pm$ 0.2	33.5 $\pm$ 1.6	38.6 $\pm$ 1.4	7.7 $\pm$ 1.2	25.5 $\pm$ 1.9
60	31.3 $\pm$ 5.2	40.8 $\pm$ 3.5	43.3 $\pm$ 2.1	12.7 $\pm$ 2.3	25.7 $\pm$ 1.5
80	35.7 $\pm$ 0.6	46.0 $\pm$ 1.7	51.3 $\pm$ 0.9	13.8 $\pm$ 0.4	28.4 $\pm$ 3.5
100	40.7 $\pm$ 1.7	56.6 $\pm$ 2.5	62.7 $\pm$ 4.4	14.8 $\pm$ 1.7	30.1 $\pm$ 1.9

### Acknowledgement

This work was financially supported by the Research Grant of Burapha University through National Research Council of Thailand (Grant no. 09/2559).

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$$F = \left( \frac{A-B}{A} \right) \times 100$$

Information :

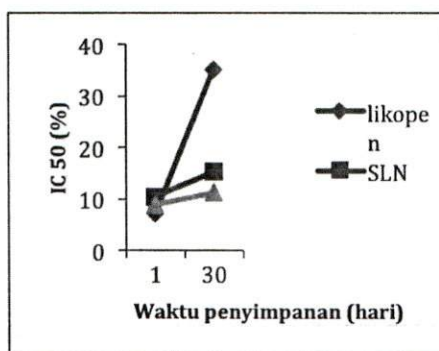
A = The amount of water lost in the control

B = The amount of lost water in the sample

### Results and Discussion

Based on the data DTA thermogram single cetyl alcohol, base SLN and NLC base note that due to the addition of oleic acid peak calorimetry be more gentle. It shows become more amorphous. Based on calculations, percent recrystallization index, NLC is lower than the SLN, respectively: 0.32% dan 1,01%. It stretcher in accordance with the stated Hu et.al (2005) [5] that the decline in the degree of crystallinity of a material due to a lower order of the crystal lattice. The fall in the regularity of the crystal lattice has resulted in active ingredients more easily trapped and not easily terekspulsi out during storage. This makes the NLC able to trap larger lycopene ( $75.52 \pm 2.75\%$ ) than the SLN ( $57.30 \pm 5.10\%$ ). The presence of lipid liquid, in this case oleic acid, significantly decreased the size of the particles. SLN particle size of  $226.67 \pm 22.72$  nm while NLC  $134.03 \pm 19.01$  nm. Neither the particle size distribution of  $0.63 \pm 0.03\%$  of SLN and NLC  $0.48 \pm 0.06\%$ .

Stability is expressed based on changes in antioxidant power IC50. The smaller the IC50, the greater the antioxidant activity. From Figure 1 it appears that at the initial antioxidants activity determination, lycopene has antioxidant power greater than when lycopene is made either SLN or NLC. This caused by lycopene was trapped in the SLN and NLC lipid matrix. After storing for 30 days, the opposite happens that pure lycopene antioxidant activity declined sharply. While the antioxidant activity of lycopene in SLN lower than in NLC. It shows that the NLC system was better able to maintain the stability of lycopene antioxidant compared with SLN. It was related to lycopene trapping efficiency of the system. Lycopene efficiency entrapment of NLC was  $75.52 \pm 2.75\%$ , while in the SLN:  $57.30 \pm 5.10\%$ . That made the lycopene had better protected from environmental influences that can accelerate degradation.



**Figure 1** Diagram IC50 of lycopene , lycopene in the lycopene in the SLN and NLC on the 1st and 30<sup>th</sup>

The result of NLC oclusivity NLC was  $40.33 \pm 2.08\%$ , higher than the SLN ( $34.67 \pm 2.51\%$ ). This can be due to the smaller size of lycopene NLC particle there for no gaps between the particles . Oclusivity effect of nano-sized particles larger than micro-sized particles on the skin. It leads to reduced transcellular evaporation water lost . That's why the nano-sized cosmetic preparation can maintain skin moistur .

**Conclusion.** The conclusion of this study were: 1) SLN and NLC system were able to improve the stability of the lycopene antioxidant. 2) . The NLC delivery system ( with oleic acid as a liquid lipid ) better to improve the stability of the lycopene antioxidant than the SLN .

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