EFFECT OF SOLID LIPID NANOPARTICLE (SLN) AND NANO STRUCTURE LIPID CARRTER (NLC) SYSTEM ON ANTIOXIDANT STABILITY OF TOMATO EXTRACT (LIPID: CETYL ALCOHOL AND ISOPROPYL MYRISTATE)

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INTRODUCTION

Tomato extract was known contains many antioxidants (Chauhan *et al.*, 2010), such as lycopene, that are easily degraded by UV-B rays. The mechanism lycopene as an antiaging is to reduce skin regeneration and increase the thickness of the epidermis (Sahasrabuddhe, 2011). As an antioxidant, lycopene easily degraded when exposed to light, heat, and oxygen (Chauhan et al., 2011). Drug delivery system based on nanolipid carrier system, such as: Solid Lipid Nanoparticles (SLN) was appropriate to stabilize lycopene, as lipophilic substance (Wissing and Muller, 2003; Helgason et al., 2009; and Okonogi dan Riangjanapatee, 2014).

One of the limitations of SLN is the drug molecule that has been trapped expulsed easily during storage. It is caused of the orderdness of lattice lipid crystal. Replacement part of solid lipid using liquid lipid (called as nanostructure lipid carriers or NLC) can reduce the orderdness of lattice lipid crystall and it will repaired it (Kaur et al, 2015).

In this research have been tried to be compared the ability of SLN and NLC to improve the stability of antioxidant tomato extract. Using 20% total amount of lipid, extract tomato-SLN made from cetyl alcohol as solid lipid and extract tomato-NLC made from difference ratio between cetyl alcohol and isopropyl myristate (IPM) such as: 9:1 and 7:3. Tween 80 and Kollipor were used as surfactant and co-surfactant. IPM was choose because of its enhancer and emollient effect so easily to apply to the skin (Vadgama et al, 2015).

MATERIALS AND METHODS

Material:

Tomato extract, contain of 20% lykopene (CN Lab Nutrition, Asian Group),, DPPH (Sigma Aldrich), cetyl Alcohol (PT.Bratachem), Isopropyl Myristate (Sigma Aldrich), Kolliphor® (Sigma Aldrich), Tween 80 (Sigma Aldrich), Metanol (Sigma Aldrich), Aquadest,

Instrument:

Ultra Turax IKA T-25, Hot-plate stirer , pH meter SCHOTT CG-842, cone and plate viscometer Brookefield, *Spectrophotometer* Shimadzu UV-1800, *X-ray Diffractometry* (XRD), , Delsa™ Nano *Submicron Particle Size.*

METHOD:

Determination of Tomato Extracts IC_{50} Value by 1,1-Diphenyl-2-Picrylhydrazyl (DPPH) and Spectrophotometry Methode (Muller, 2011). IC_{50} is the concentration of sample that can inhibite 50% free radical activity, further more call as antioxidant power. Various concentration of workong standard tomato extract solution were reacted with 0.004% DPPH solution The free radical inhibition concentarion determined from the absorbance spectrophotometer, absorbance measurements were taken at three wavelengths, namely 505 nm, 515 nm, 525 nm. Next percent inhibition be calculated by :

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

IC_{50} was obtainded from correlation regression curves between percent free radical inhibition and concentration of extract solution, that indicate 50% inhibition of free radical activity.

Preparation of SLN and NLC tomato extract. SLN tomato extract was made of 0,25% tomato extraxt that contain of 20% lycopene (CN Lab Nutrition, Asian Group), 20 % cetyl alcohol as solid lipid, 5 % tween 80, and 5% kollipor and aquadest ad 100 % as aqueous phase. NLC tomato extract had same compotition with SLN, but there were cetyl alcohol replacement with IPM, with two different ratio, such as: 9:1 and 7:3. SLN and NLC tomato extract were made by High Shear Homogenization (HPH) method with a speed of 24,000 rpm conducted for 8 minutes at 4 cycle with Ultra Turax T-25.

Characterisation of sample. Furthermore, sample were characterized such as: pH, viscosity, particle size and its distrbution were measured by pH meter, cone and plate viscosimeter and Delsanano™ particle size analyzer respectively. Characterization be held before and after UV-B exposure.

Measurement antioxidant stability. Each sample were exposed with 32.400 Joule/hour UV-B radiation for 2, 5, 9, 15, and 21 hours. After reacting with DPPH solution, the aborbance was observed by spectrophotometer and were calculated the percent inhibition of free radical activity using equation 1. Furthermore the stability of antioxidant were interpreted based on constanta of percent scavenging activity decreasing in antioxidant power (*k* value) on the appropriate reaction order.

RESULT AND DISCUSSION

IC50 of tomato extract. The regression equation obtained was y = 637,23x + 7.7944 with a correlation coefficient was r = 0.9973. IC_{50} values can be obtained from the regression equation by entering a value of y = 50% to obtain the value of x, namely the concentration of tomato extract, which can inhibite 50% free radical activity of DPPH. IC_{50} value of tomato extract obtained is equal to 0.0662%.

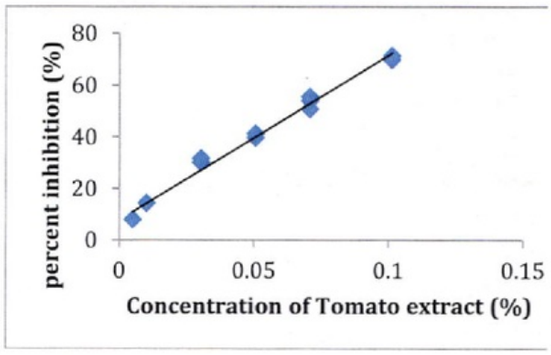

Figure 1. Calculation curve of percent inhibition of free radical activity

Further more, preparation SLN-tomato extract and NLC-tomato extract using extract tomato concentration at least twice to its IC_{50}.

Character of SLN-tomato extract and NLC-tomato extract.

All character of sample presented in table1. All sample had pH in between skin pH range . It was mean all sample did not have potential iritation for skin. There were no significan change of pH relatively after 21 hour UV-B exposure.

Table 1. Character of tomato extract-SLN and tomato extract-NLC

Sample		Mean pH ± SD (%KV)	Mean diameter (nm) ± SD (%KV)	mean PI ± SD (%KV)	Mean Viskositas (cPs) ± SD (%KV)
Without UV-B exposure	SLN	5,73 ± 0,20 (3,49)	274.17 ± 8,38 (3,06)	0,47 ± 0,02 (3,34)	7733,33 ± 1419,72 (18,36)
	NLC 9:1	5,82 ± 0.07 (1,21)	203,54 ± 5,64 (2,77)	0,29 ± 0,01 (4,14)	1916,33 ± 152,67 (7,97)
	NLC 7:3	5,87 ± 0,14 (2,46)	187.8 ± 31.15 (1,66)	0,20 ± 0,10 (4,78)	1231,00 ± 331,39 (26,92)
After UV-B exposure for 21 hours	SLN	5,68 ± 0,28 (4,93)	411,27 ± 11,24 (2,73)	0,33 ± 0,10 (29,59)	6845,33 ± 1003,23 (14,66)
	NLC 9:1	5,64 ± 0.09 (1,60)	229,72 ± 13,75 (5.98)	0,30 ± 0,01 (2,76)	1232,56 ± 300,,24 (24,36)
	NLC 7:3	5,83 ± 012 (2,06)	235,92 ± 8,78 (3,72)	0,24 ± 0,01 (5,31)	906,12 ± 171,14 (18,89)

NLC had viscosity lower than SLN. Viscosity NLC with ratio cetyl alcohol : IPM 7:3 lower than 9:1. It was consequence of solid lipid replacement by liquid lipid.. This phenomena were the same with the particle size.

UV-B exposured for 21 hours decreased the viscosity but increased particle size. Based on Stokes law, viscosity invers relate with floculation rate of droplet emulsion. Therefore the particle size of NLC with ratio cetyl alcohol : IPM 7:3 increased significant compare with others after UV-B radiation exposure, but indicated more homogen in size.

Diffraction Pattern Determination of Lipid Cetyl alcohol and in the system SLN, NLC (9:1) and NLC (7:3) . From diffractogram (fig. 2 and table 2) were known that declining intensity of the crystal lattice cetyl alcohol after made to be SLN. It was effect of adding surfactant in the lipid. Furthermore the intencity more decline once created NLC.

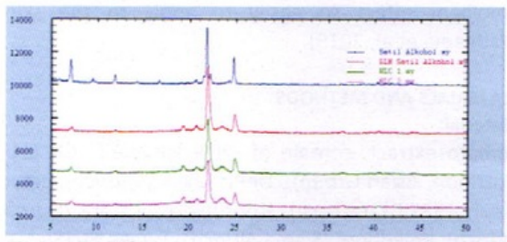

Figure 2. Difractogram cetyl alcohol, cetyl alcohol in SLN, NLC (9:1) and NLC (7:3)

The addition liquid lipid (IPM) reduce the orderdness of lattice lipid crystal. According to Jenning (2000) the orderdness of lattice crystal corresponds to the capability of lipid to entrap the drug. The drug was more difficult to be inserted in the particle lipid that have ordered lattice crystal and was easier to expelled from the carrier

Table 2. The main diffraction peak intensity of the diffraction pattern of the sample

Sample	Angle 2θ		
	7,06°	21,76°	24,70°
Cetyl Alcohol(CA)	1523,72	3459,99	1668,71
CA in SLN	211,33	3415,49	1068,65
CA in NLC (9:1)	237,02	3257,35	833,49
CA in NLC (7:3)	190,32	2449,97	737,46

Antioxidan Stability Test. From the result of the reaction order determination of changes percent free radical activuty inhibition on each exposure time of each sample was known that the reaction according to first order. Furthermore, the constanta of percent scavenging activity decreasing in antioxidant power (k value) every sample was calculated by making the regretion curve plot time versus log percent inhibition (fig.3). Using the equation for the first order can be calculated the value of *k*, as presented in the table 3.

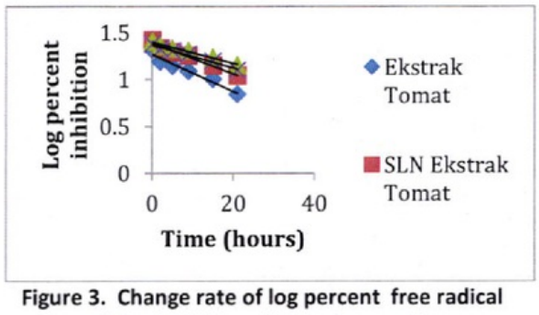

Figure 3. Change rate of log percent free radical activity inhibition of sample over time

First orde reaction means that the change was occurring exponentially with time (Martin et al., 2008). In this case that means decreasing antioxidant power depends only on the concentation of ingridient in tomato extract that has antioxidant power. The greater the value of *k* indicates that the rate of change of percent inhibition faster, or the sample was unstable. It was known that constanta of percent inhibition free radical activity decreasing of tomato extract was $4{,}58 \times 10^{-2} \pm 0{,}0045$/ hour faster than SLN and NLC. This was due to the lipophilic antioxidants ingredients in tomato extract, exposed to the conditions that could degrade the material. Meanwhile, when they were made in nanolipid such as SLN and NLC, the materials were encapsulated in the system.

Table 3. Mean constanta of change rate of percent free radical activity inhibition of sample over time (based in orde 1 reaction)

Sample	Mean constanta (*k*) of change rate of percent inhibition between time (/hour) ± SD* (%KV)
Tomato Extract (TE)	$4{,}58 \times 10^{-2} \pm 0{,}0045$ (9,87)
TE - SLN	$3{,}82 \times 10^{-2} \pm 0{,}0019$ (4,93)
TE – NLC 9:1	$2{,}59 \times 10^{-2} \pm 0{,}0011$ (4,19)
TE - NLC 7:3	$2{,}83 \times 10^{-2} \pm 0{,}0006$ (2,05)

The antioxidant power tomato extract in the NLC was more stable than in the SLN form. It was seen from the smaller of *k* value. It was the impact of reducing of lattice lipid crystal orderdness (fig. 2). Therefore the active ingredient was not easily expulsed out. In this case, the more IPM addition in the system by changing the ratio of cetyl alcohol: IPM from 9: 1 to 7: 3 was not very meaningfull in stability effect. Decreasing orderdness of lipid crystal lattice was not necessarily improve the drug entrapment. There were need optimal conditions that produce optimal trapping anyway.

CONCLUSION

The conclussion of this research were:

1. Antioxidant stability of tomato extract increased in nanolipid system carrier with total amount of lipid cetyl alcohol 20%
2. Replacing part of solid lipid (cetyl alcohol) to liquid lipid (isopropyl myristate/IPM) to be NLC system in ratio 9:1 and 7:3 could increased antioxidan stability of tomato extract.
3. Increasing isopropyl myristate ratio in NLC system from 9:1 to be 7:3 did not increase antioxidan stability of tomato extract meaningfuly

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