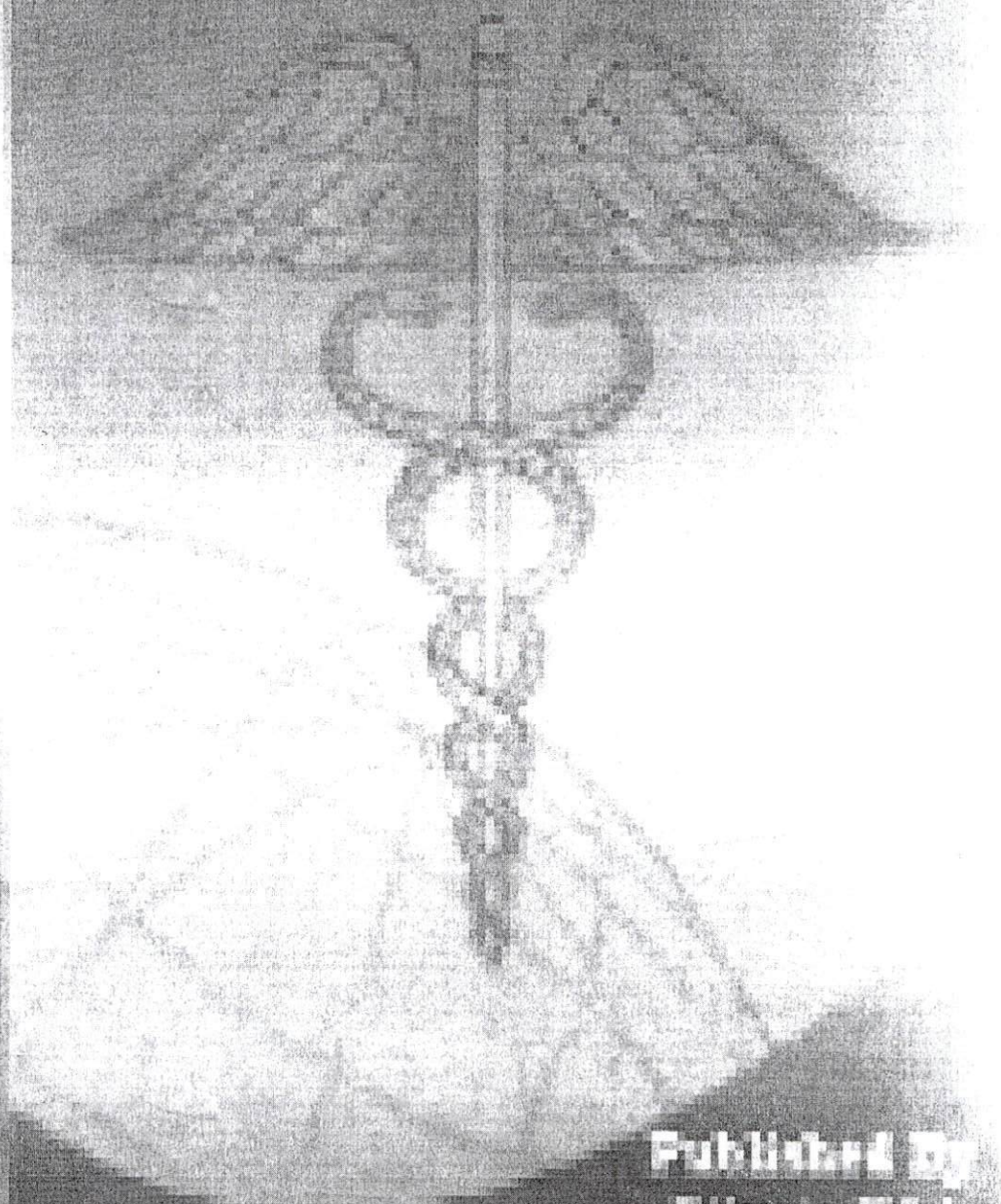


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Research Article

PREVALENCE AND PROPERTIES OF PREGNANT WOMEN WITH LOW PREGNANCY ASSOCIATED PLASMA PROTEIN A (PAPP-A) IN THE FIRST TRIMESTER SCREENING

Zeinab Zamanpur, Mojgan Barati,\*Razieh Mohamad Jafari , Sara Masihi, Najmieh Saadati  
[ABSTRACT] [PDF]



EXPERIMENTAL CHRONIC TUBERCULO-TYPHOID EXPOSURE IN A LAPIAN IMMUNE EVALUATION MODEL II: CUMULATED EFFECT

Dr. Ibrahim M.S. Shnawa, Dr. Zainab Khudhur Ahmed Al-Mahdi  
[ABSTRACT] [PDF]



THE EVALUATION OF DRUG RELATED PROBLEMS (DRPs) OF THE TUBERCULOSIS (TB) PATIENTS AT THE LUNG DISEASE WARD IN THE INSTALLATION OF STAYED CARING OF CENTRAL GENERAL HOSPITAL PERSAHABATAN (RSUP PERSAHABATAN)

\*Diana Laila Ramatillah, Siti Suhartini, Noviani Nongkang, Syahrul Tuba, Candra Junaedi, Mumar, Aprilita Rinayanti  
[ABSTRACT] [PDF]



DRUG RELATED PROBLEMS IN THE TUBERCULOSIS PATIENT AT THE PERSAHABATAN HOSPITAL (RSUP PERSAHABATAN)

\*Diana Laila Ramatillah, Siti Suhartini, Aprilita Rinayanti  
[ABSTRACT] [PDF]



IMPACT OF SUB-INHIBITORY CONCENTRATIONS OF AMOXICILLIN ON HELICOBACTER PYLORI VIRULENCE FACTORS

Fabiana C Donofrio,\* , Maria Stella G Raddi, Iracilda Z Carlos, Elaine T Miranda, Danielle C G Maia, Jenifer Ferrezini , Mariana Fioramonte , Emanuel Carrilho, Fábio C Gozzo  
[ABSTRACT] [PDF]



STUDY ON RAMADAN FASTING TOWARDS LIPID PROFILES AND TOTAL ANTIOXIDANT STATUS (TAS) AMONG HIGHER INSTITUTION LEARNING CENTRE STAFFS

\*Mohd Adzim Khalili, R., Zetty Hulwany, M.Z., Norhayati, A.H Mohd Nasir, M.N, Muralidara, D.V and Intan Suhana Munira, M.A  
[ABSTRACT] [PDF]



IN VITRO EFFECTIVITY PARA METHOXY CINNAMATE ACID (PMCA) IN SOLID LIPID NANOSTRUCTURE (SLN) SYSTEM USING CETYL ALCOHOL AS LIPID FORMULATED IN HPC-H GEL BASE

Noorma Rosita\*, Widji Soeratri, Tristiana Erawati, Ayunanda, Wakhida Fitriyani  
[ABSTRACT] [PDF]



DRUG RELATED PROBLEM ASSOCIATED WITH THE TREATMENT FOR CONGESTIVE HEART FAILURE (CHF) AND ACUTE MIOCARDIAL INFARCTION IN PGI CIKINI HOSPITAL

\*Aprilita Rina Yanti, Muhammad Ashar Muslimin and Diana Laila  
[ABSTRACT] [PDF]



**IN VITRO EFFECTIVITY PARA METHOXY CINNAMATE ACID (PMCA) IN SOLID LIPID NANOSTRUCTURE (SLN) SYSTEM USING CETYL ALCOHOL AS LIPID FORMULATED IN HPC-H GEL BASE**

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**ABSTRACT**

**Introduction:** In vitro effectivity of solid lipid nanostructure (SLN) as carrier system has been studied on para methoxy cinnamate acid (PMCA) as a means of releasing PMCA and penetrating to prolong antiinflamasi preparation. **Methods:** SLN was made using cetyl alcohol as lipid and Tween 80 as stabilizer, produced by high shear homogenisation (HPH) method. SLN was then formulated in HPC-H 3% gel base. Release study were conducted in phosphat buffer medium pH 7,4±0,05 at 32°C and stirred at 100 rpm using apparatus type 5-paddle overdisk. Penetration study were investigated in same medium at 37°C by using Wistar male rat skin 2-3 month age and weight 115-

180 gram, as a membrane. **Results:** Both PMCA released and penetrated PMCA concentration was measured spectrophotometrically at 286 nm as  $\lambda$  max. Spherical SLN-APMS with particle size of 26-265 nm and 64.86% drug entrapment were produced. PMCA-SLN had pH 3,79±0,05 in HPC-H gel. In vitro release and penetration study were investigated using PMCA only (F-I), PMCA in macroemulsion (F-II) and PMCA-SLN (F-III) which was formulated in gel HPC-H. PMCA which was dispersed in gel had largest release and higher penetration, followed by PMCA in macroemulsion and lastly PMCA-SLN. Release flux for formula PMCA only, PMCA in Macroemulsion and PMCA-SLN were  $62,6969 \pm 1,33$ ;  $48,7949 \pm 1,07$  and  $27,4652 \pm 0,84$   $\mu\text{g}/\text{cm}^2/\text{second}^{-1/2}$ , whereas penteration flux were  $0,3065 \pm 0,1470$ ;  $0,1795 \pm 0,0634$  and  $0,2925 \pm 0,0996$   $\mu\text{g}/\text{cm}^2/\text{second}^1$  for formula I, II and III respectively. **Conclusion:** SLN system has been able to retard released and penetrated PMCA.

**KEY WORDS:** Para methoxy cinnamate acid (PMCA), solid lipid nanostructure (SLN), cetyl alcohol, release, penetration

## INTRODUCTION

Colloidal carrier system have been receiving growing interest in the field of drug delivery system because they can offer several advantages in this area for example possibility to formulate poorly water soluble drug substances in aqueous system, protection of drug against degradation or alteration. Many particulate can be used as carrier in colloidal delivery system eg: polymeric nanoparticles, fat emulsion and liposome (Bujes Heike, 2011, Jores Katja et all, 2004). Since a high degree of physiological compatibility is expected for lipid excipients, several types of colloidal lipid based carrier systems have been develop (Bujes Heike, 2011).

Solid lipid nanoparticles (SLN) is colloidal system based on nanotechnology which have been proposed as an alternative colloidal drug delivery system (Schubert, MA and Muller CC, 2005). Compared to liposome and emulsion, solid particles possess some advantages, e.g. protection of incorporated active compounds against chemical degradation and more flexibility in modulating the release of the compound (Muller R.H., Radtke M, Wissing SA, 2002). Another advantages are biodegradable, non toxic, stable against coalescence and drug leakage (Bunjes Heike, Westesen Kirsten and Koch Michel, 1996) and no need to use higher surfactant concentrations, therefore able to avoid potential necessity to perform a tolerability excipient compound (Muller R.H., Radtke M, Wissing SA, 2002). Standard manufacturing procedure is dissolving or dispersing the drug in the molten lipid prior to high pressure or high shear homogenisation (Schubert, MA and Muller CC, 2005).

Para-methoxycinnamic acid (PMCA) is a hydrolyzed product of ethyl-p-methoxycinnamic (EPMC), which is the highest component of Kaempferia Galanga extract, was proposed to have an antiinflammatory activity. PMCA is a poor soluble drug, which have been tried to be prepared as antiinflammatory topical using SLN as carrier system.

The aim of this study is (1) to identify characteristics of SLN-APMS with cetyl alcohol as lipid carrier produced by high shear homogenisation methode, (2) to study effect of SLN system enriched in 3% gel HPC-H on released of PMCA from matrix, and (3) to study effect of SLN system enriched in 3% gel HPC-H on the penetration of PMCA-SLN through rat skin membrane, SLN system composed with cetyl alcohol as lipid (10%), Tween 80 (12%) as emulsifier and propylene glycol 1% as co-surfactant.

## MATERIAL AND METHODE

### Materials

p-metoksisinamat acid (PMCA) from Sigma, HPC-H (PTShin Etsu), cetyl alcohol, tween 80, (PT. Bratako). Dapar component: KH<sub>2</sub>PO<sub>4</sub> p.a and K<sub>3</sub>PO<sub>4</sub> (E. Merck) , aquadest (PT. Jawisesa). Rat male wistar strain

### Method

There were three PMCA formulas in gel 3%HPC-H: PMCA enriched in 3% HPC-H directly (Formula I), PMCA in 3% HPC-H with all components of SLN (Formula II) and PMCA-SLN incorporated in 3% gel HPC-H (Formula III). SLN was composed by cetyl alcohol 10% as lipid carrier, tween 80% as surfactant and propylene glycol 1% as co-surfactant. SLN was prepared by high shear homogenisation method.

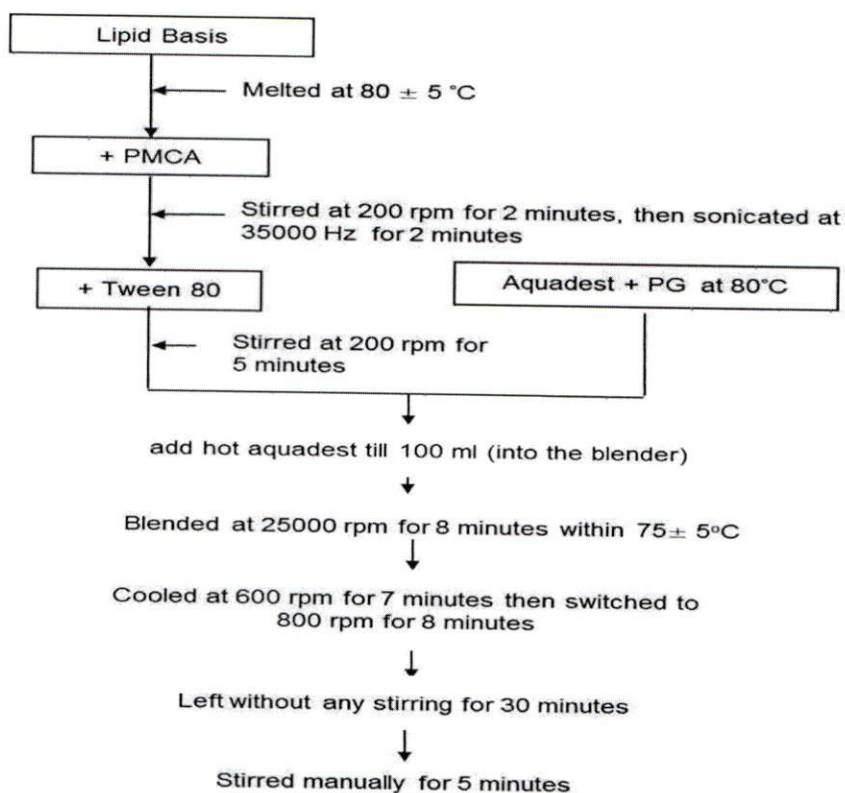
**Tabel 1. Formula samples**

Ingridients	Function	Concentration		
		FI (g)	FII (g)	FIII (g)
PMCA	Active Ingredient	0,0068	0,0068	
PMCA-SLN	Active Ingredient in SLN system			6,8 g (~ 0,068 g APMS)
Cetyl alcohol	Lipid component of SLN		0,680	
Tween 80	Emulsifier (SLN component )		0,816	
Aquadest	Component of SLN		5,3 mL	
Basis gel HPC - H	Basis	ad 20 g	ad 20 g	ad 20 g

### Preparation of PMCA-SLN,

SLN-PMCA was prepared by melting cetyl alcohol at  $80 \pm 5^{\circ}\text{C}$ , above cetyl alcohol melting temperature. Then PMCA was dissolved in the melted lipid. The hot lipid phase was added to an aqueous solution of 12% tween 80 as emulsifier and propylene glycol 1% as co-surfactant at the same temperature and was stirred at 200 rpm for 5 min in beaker glass to make primary emulsion followed by stirring at 25000 rpm using blender Madato®. The hot dispersion were cooled kept in stirring at gradual reduced speed.





**Figure 1. Schematic SLN-PMCA preparation method using high shear homogenisation method**

### Characterisation of SLN

The shape of SLN was observed with Thermal Electron Microscope (TEM) and the particle size measurements were analysed by photon correlation spectroscopy (PCS). Drug entrapment of PMCA was measured by centrifugation method.

### Preparation of Gel Formula.

HPC-H was used as gel bases with propylene glycol as humectant. Either PMCA or SLN-PMCA was prepared by dispersing into HPC-H gel directly to produce formula I and formula III., whereas formula II was prepared by component producing SLN with low stirring speed.

### Characterisation of PMCA Gel

PMCA gel was characterized in terms of pH and spreadability.

### Release study of PMCA from matrix

Release study of PMCA from matrix were conducted in phosphat buffer medium at pH  $7.4 \pm 0.05$  at  $32^\circ\text{C}$  and stirred at 100 rpm and used apparatus type 5-paddle overdisk. Medium

in reseptor chamber was sampled on 5, 10, 15, 20, 25, 30, 60, 90, 120, 180, 240, 300 and 360 minute and then was measured spectrophotometrically at 286 nm as  $\lambda$  max.

### Penetration of PMCA through rat skin membrane

Penetration study of PMCA through abdomen rat skin membrane were conducted in phosphate buffer medium at pH  $7.4 \pm 0.05$  at  $37^\circ\text{C}$  and stirred at 100 rpm and used apparatus type 5-paddle overdisk. Medium in reseptor chamber sampled on 5, 10, 15, 20, 25, 30, 60, 90, 120, 180, 240, 300 and 360 minute and then was measured spectrophotometrically at 286 nm as  $\lambda$  max.

## RESULT AND DISCUSSION

SLN-PMCA had spherical shape (fig 2) and average of particle size was 437,3 nm with Polydispersity Index (PI) was 1,138 ( $>0.3$ ) it means that SLN-PMCA was not homogenous (fig 3).

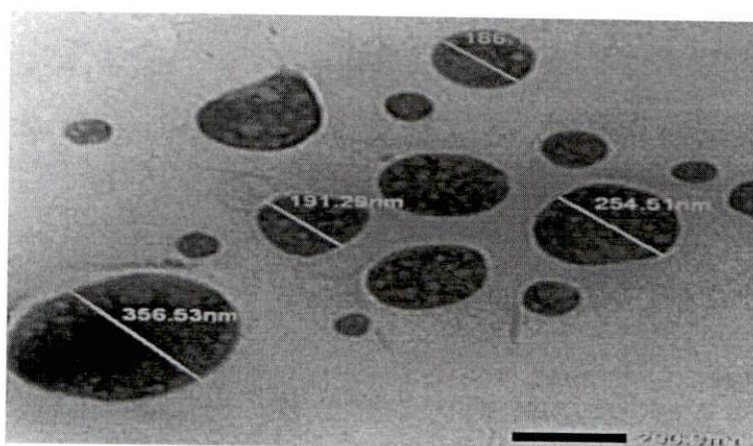


Figure 2. TEM picture of SLN-PMCA

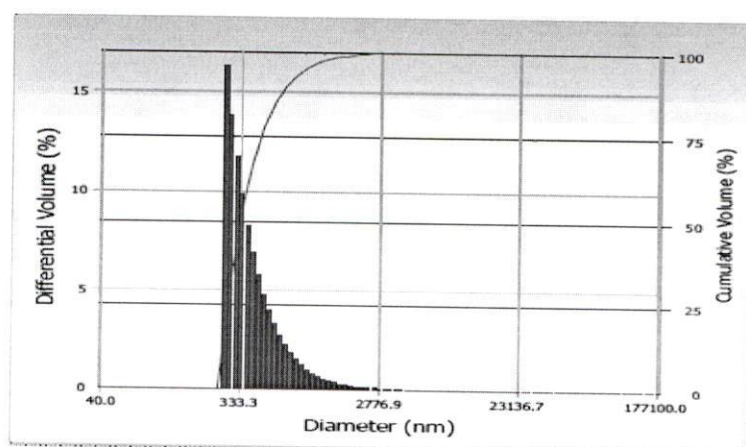


Figure 3. Particle distribution of SLN-MPCA

Centrifugation method showed that PMCA was entrapped of about 64,86% in lipid matrix as carrier of SLN. All pH of PMCA gel showed pH at below skin pH as illustrated in table 2, that might be had irritation potential effect.

**Table 2. pH of PMCA gel**

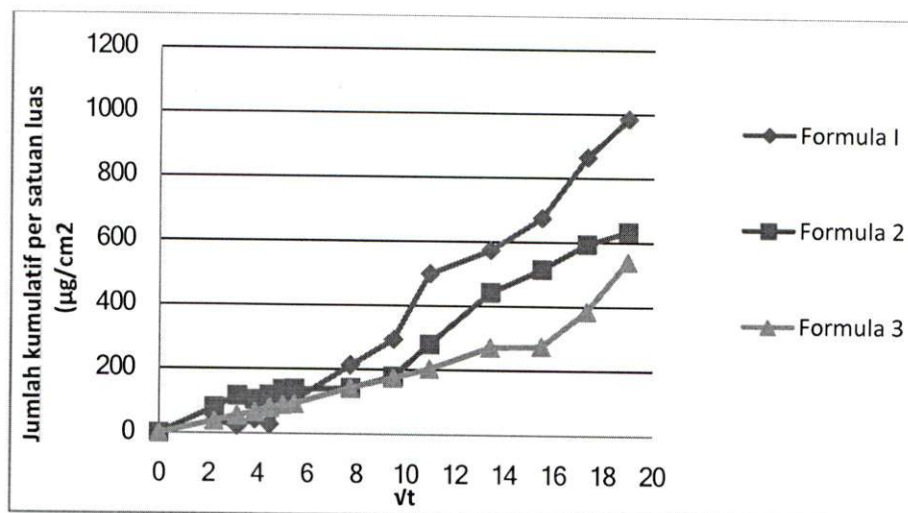
Formula	Mean pH $\pm$ SD
F I	3,89 $\pm$ 0,02
F II	3,86 $\pm$ 0,08
F III	3,79 $\pm$ 0,005

Spreadibility of formula III was higher than others (table 3), it could because of nano size of lipid as carrier SLN. Smallest particle can increased occlusivity (Muller R.H., Radtke M, Wissing SA, 2002) and it could be a reason why formula III had the best spreadibility.

**Table 3. Spreadibility of PMCA gel**

Formula	Spreadability (cm/gram)
F I	0,0360 $\pm$ 0,0009
F II	0,0409 $\pm$ 0,0030
F III	0,0477 $\pm$ 0,0010

Release study we showed that formula III had slowest release; it can be seen from its flux release (fig 4 and table 4).



**Figure 4. Released profile of PMCA**

Table 4. Flux release of PMCA

Formula	Flux release mean of PMCA ( $\mu\text{g}/\text{cm}^2/\text{menit}1/2$ )
Formula I	$62,6969 \pm 1,33$
Formula II	$48,7949 \pm 1,07$
Formula III	$27,4652 \pm 0,84$

About 64,86% PMCA was entrapped in lipid matrix, therefore it caused retardation of PMCA to released. Trend differences of PMCA flux release between formulas were not showed in the penetration PMCA study (fig 5 and table 5).

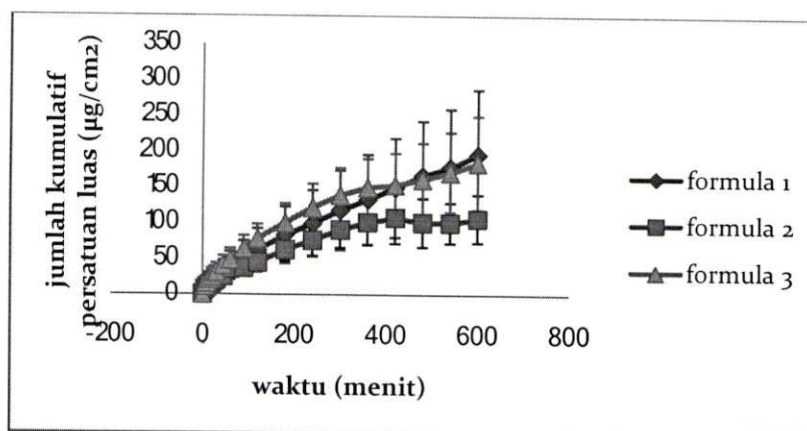


Figure 5. In Vitro penetration profile of PMCA through skin rat membrane

Table 5. Flux Penetration Mean of PMCA through skin rat membrane

Formula	Fluks Penetration Mean of PMCA through rat skin membrane $\pm$ SD (%KV)
I	$0,3065 \pm 0,1470$ (47,96)
II	$0,1795 \pm 0,0634$ (35,34)
III	$0,2925 \pm 0,0996$ (34,05)

There were no significantly differences between formulas. Eventhough SLN system PMCA showed slowest release, but another mechanisms helped it to alter the penetration rate. The smallest particle of solid lipid can increase the occlusive effect, this due to its ability to increase stratum corneum hydration that help drug penetration. Another reasoning was the smallest particle of solid lipid entrapping dissolved PMCA can penetrated not only through transcelluler pathway.

## CONCLUSION

SLN system has been able to retard release and penetrated PMCA.

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