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

by Widji Soeratri

Submission date: 01-Mar-2019 11:41AM (UTC+0800)
Submission ID: 1085772833
File name: em_Using_Cetyl_Alcohol_As_Lipid_Formulated_In_HPC-H_Gel_Base.pdf (600.28K)
Word count: 2033
Character count: 10396

WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 3, Issue 5, 58-65. Research Article ISSN 2277 – 7105

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[1]*, Widji Soeratri[1], Tristiana Erawati[1], Ayunanda[1], Wakhida Fitriyani[1]

[1]Pharmaceutics Department, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

Article Received on
20 May 2014,

Revised on 14 June 2014,
Accepted on 08 July 2014

***Correspondence for Author**
Noorma Rosita
Pharmaceutics Department, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

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 homogenisatian (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 λ 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 ± 1,33; 48,7949 ± 1,07 and 27,4652 ±0,84 µg/cm2/second-½ , whereas penteration flux were 0,3065 ± 0,1470; 0,1795 ± 0,0634 and 0,2925 ± 0,0996 µg/cm2/second1 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 posibility 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 coalesence 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 toperform 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 antiinflamatory activity. PMCA is a poor soluble drug, which have been tried to be prepared as antiinflamatory 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: KH2PO4 p.a and K3PO4 (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 ± 5°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 emuslifier 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.

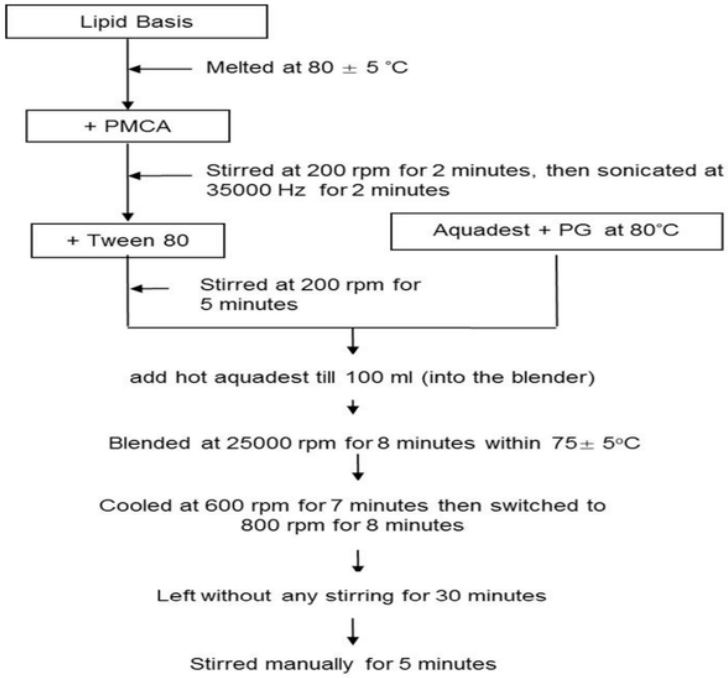

Figure 1. Schematic SLN-PMCA preparation method using high shear homogenisation method

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 spreadabilty.

Release study of PMCA from matrix

Release study of PMCA from matrix were conducted in phosphat buffer medium at pH 7,4±0,05 at 32°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 λ 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±0,05 at 37°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 λ 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).

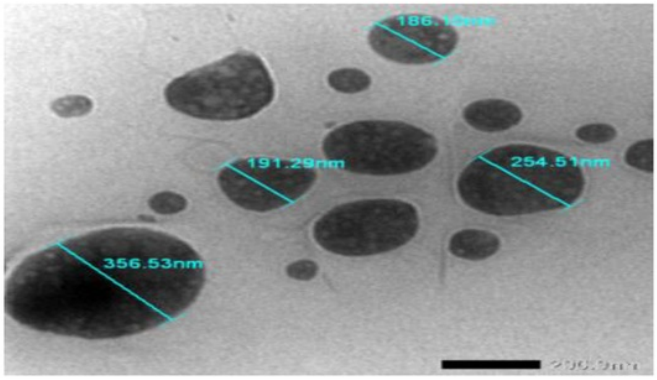

Figure 2. TEM picture of SLN-PMCA

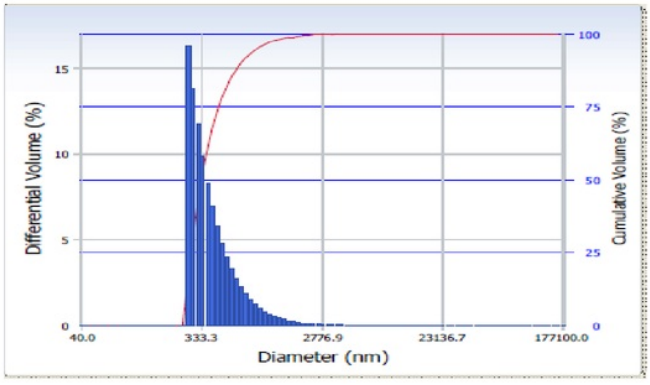

Figure 3. Particle distribution of SLN-MPCA

Centrifugation method showed that PMCA was entraped 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 iritation potential effect.

Table 2. pH of PMCA gel

Formula	Mean pH ±SD
F I	3,89±0,02
F II	3,86±0,08
F III	3,79±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. Spreadibilty of PMCA gel

Formula	Spreadability (cm/gram)
F I	0,0360 ± 0,0009
F II	0,0409 ± 0,0030
F III	0,0477 ± 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).

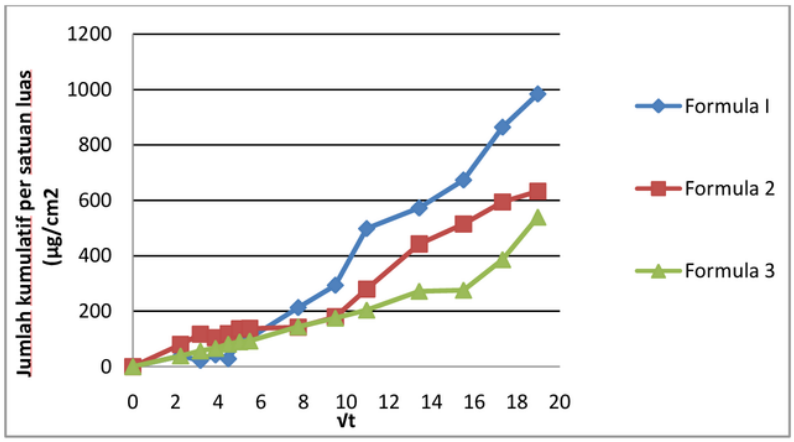

Figure 4. Released profile of PMCA

Table 4. Flux release of PMCA

Formula	Flux release mean of PMCA (µg/cm2/menit1/2)
Formula I	62,6969 ± 1,33
Formula II	48,7949 ± 1,07
Formula III	27,4652 ±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).

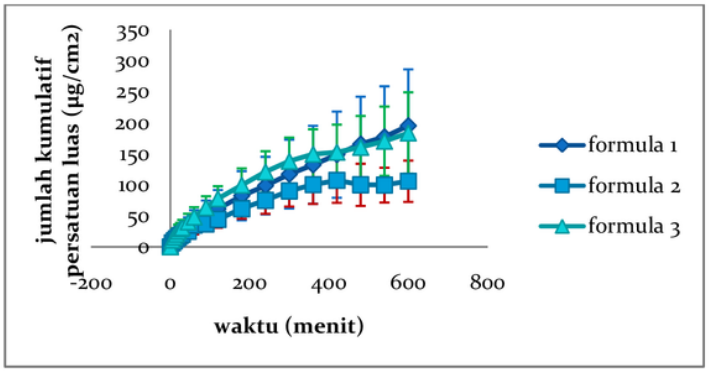

Figure 5. In Vitro penetration profile of PMCA through skin rat membrane

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

Formula	Fluks Penetration Mean of PMCA through rat skin membrane ± SD (%KV)
I	0,3065 ± 0,1470 (47,96)
II	0,1795 ± 0,0634 (35,34)
III	0,2925 ± 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 oclusive 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.

REFFERENCE

1. Bujes Heike, 2011, Structural Properties of Solid Lipid Based Colloidal Drug Delivery Systems, Journal homepage: www.elsevir.com/ locate/cocis, Current Opinion in Colloidal & Interface Sciences 16: 405-411
2. Bunjes Heike, Westesen Kirsten and Koch Michel, 1996, Crystallization Tendency and PolymorphicTransitions in Triglyceride Nanoparticles, International Journal of Pharmaceutics 129: 159-173
3. Jores Katja, et all, 2004, Investigations on the Structure of Solid Lipid Nanoparticles (SLN) and Oil-Loaded Solid Lipid Nanoparticles by Photon Correlation Spectroscopy , Fiel-Flow Fracti0nation and Transmission Electron Microscopy, Journal of Controlled Release 95: 217-227
4. Muller R.H., Radtke M, Wissing SA, 2002, Solid Lipid Nanoparticles (SLN) and Nanostructures Lipid Carriers (NLC) in Cosmetic and Dermatological Preparations, Advanced Drug Delivery Reviews 54 Suppl. 1, S.131-S.155
5. Schubert M.A. and Muller-Goymann C.C, 2005, Characterisation of Surface-Modified Solid Lipid Nanoparticles (SLN): Influence of Lecithin and Nonionic Emulsifier, Europian Journal of Pharmaceutics and Biopharmaceutics 61: 77-86

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

ORIGINALITY REPORT

14%	12%	10%	0%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	www.ijppsjournal.com Internet Source	4%
2	journal.unair.ac.id Internet Source	2%
3	Paolo Blasi, Aurélie Schoubben, Stefano Giovagnoli, Carlo Rossi, Maurizio Ricci. "Solid Lipid Nanoparticles to Improve Brain Drug Delivery", Wiley, 2012 Publication	2%
4	eprints.nottingham.ac.uk Internet Source	2%
5	Juan M. Irache, Irene Esparza, Carlos Gamazo, Maite Agüeros, Socorro Espuelas. "Nanomedicine: Novel approaches in human and veterinary therapeutics", Veterinary Parasitology, 2011 Publication	1%
	epublication.cheme.utm.my	

6	Internet Source	1%
7	Jores, K.. "Investigations on the structure of solid lipid nanoparticles (SLN) and oil-loaded solid lipid nanoparticles by photon correlation spectroscopy, field-flow fractionation and transmission electron microscopy", Journal of Controlled Release, 20040305 Publication	<1%
8	Arıca Yegin, Betül, Jean-Pierre Benoît, and Alf Lamprecht. "Paclitaxel-Loaded Lipid Nanoparticles Prepared by Solvent Injection or Ultrasound Emulsification", Drug Development and Industrial Pharmacy, 2006. Publication	<1%
9	T. Helgason. "Influence of Polymorphic Transformations on Gelation of Tripalmitin Solid Lipid Nanoparticle Suspensions", Journal of the American Oil Chemists Society, 06/2008 Publication	<1%
10	Anthony A., Mumuni A., Philip F.. "Chapter 5 Lipid Nanoparticulate Drug Delivery Systems: A Revolution in Dosage Form Design and Development", InTech, 2012 Publication	<1%
11	Schubert, M.A.. "Structural investigations on lipid nanoparticles containing high amounts of	<1%

lecithin", European Journal of Pharmaceutical Sciences, 200602
Publication

12	Roberto Solaro, Federica Chiellini, Antonella Battisti. "Targeted Delivery of Protein Drugs by Nanocarriers", Materials, 2010 Publication	<1%

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	On		

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

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6

PAGE 7

PAGE 8