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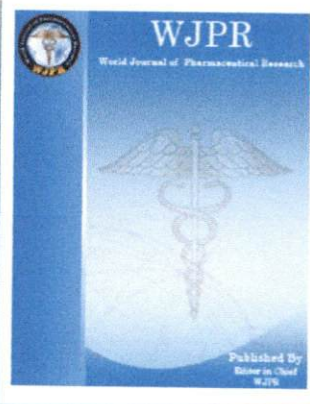
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42	Dr. Abbas Yazdanpanah	abbas_yaz@yahoo.com	Assistant Professor, Department of Healthcare Management, Marvdasht Branch, Islamic Azad University, Marvdasht Iran.	Iran
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46	Dr. M. Prabhakaran	prabhasnc@gmail.com	Assistant Professor in P.G. & Research Department of Botany at Pachaiyappa's College, Chennai – 600 030, India.	India
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88		wazedchaus@gmail.com		India



	Dr. Chauz Wajid Ahmed Nisar Ahmed		Associate Professor & HOD (Pharmaceutics), Dayanand College of Pharmacy, Latur, India	
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100	Dr. N. G. Raghavendra Rao	nraghu@rediffmail.com	Director and Professor, Dept. of Pharmacy, GRD [PG] Institute of Management and Technology, Rajpur Road, Dehradun - 248009, Uttarakhand, India	India
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14	Dr. Alaa H. Abuznait	abuznait@yahoo.com	Department of Pharmaceutical Sciences University of Oklahoma Health Sciences Center 1110 N. Stonewall Ave., Oklahoma City, OK.	Jordan
15	Dr. Muneesh Kumar	manishloves200787@gmail.com		India

			Department of Zoology, University of Jammu, Jammu (J&K) INDIA 180006, India.	
16	Dr. Ajit Singh	ajitsmarty01@gmail.com	Pathologist in charge of routine Hematobiochemical-Profling, Postmortems (domestic, laboratory, wild animals and poultry birds) and Histopathological laboratory at Department of Pathology, College of Veterinary Science and Animal Husbandry, SHIATS.Allaha	India
17	Dr. Neeraj Kumar Patel	neerajkumar.p@himalayawellness.com	Laxmi Niwas, Behind Punjab Bank, Patel Nagar, Suhagi, Jabalpur, Madhya Pradesh 482002, India.	India
18	Dr. Ananda Kumar Konreddy	mrjayapa1007@gmail.com	Post Doctoral Research Associate, College of Pharmacy, University of Georgia, Athens, 30602 Georgia, USA.	USA
19	Dr. Grandhe Usha Rani	ushaindian@yahoo.com	2091, South Millfedge Ave, Apt C60, Athens, Georgia-30605, USA.	USA
20	Dr. Muneesh Kumar	manishloves200767@gmail.com	Department of Zoology, University of Jammu, Jammu (J&K) INDIA 180006, India.	India
21	Dr. Fasalul Rahiman OM	fasaluom@gmail.com	Tutor, Department of Pharmacology, MES Medical College, Perinthalmanna, Malappuram Dt, Kerala- 679338, India.	India
22	Dr. Kiran Mishra	drmishrakiran@gmail.com	Applied Sciences Department, Chandigarh Engineering College, Landran, Mohali (Pb.) India	India
23	Ramesh Chand	rchand@lrri.org	Senior Research Associate, Scientific Core Laboratories, Lovelace Respiratory Research Institute (LRRI), Albuquerque, NM USA	USA
24	Dr. T. Sivapriya	sivaamanick@gmail.com	Assistant Professor and Head, Department of Nutrition, Food Service Management and Dietetics, Prof. Dhanapalan College of Arts and Science, Chennai, India	India
25	Dr. Jessen George	georgejessen@gmail.com	Associate Prof. & Principal, Eben-Ezer Degree College, Bangalore-560077, Karnataka, India	India
26	Dr. Vikas Kumar	vkskumar49@gmail.com	Dept. of Silviculture & Agroforestry, Periyar Hostel, College of Forestry, Vellanikkara, Kerala Agricultural University, Thrissur, Kerala- 680656, India.	India
27	Dr. Pralhad Vinay Rege	pralhad1806@gmail.com	Assistant Professor Dept of Chemistry St. Xaviers College, Mumbai, India.	India
28	Dr. Ali Olfati	a.olfati66@gmail.com	Department of Animal Science, University of Tabriz, Iran.	Iran
29	Dr. Diptendu Sarkar	diptendu81@gmail.com	Assistant Professor, Dept. of Biotechnology Engineering, NHCE, Bangalore, India.	India

30	Dr. G. Swathi	swathi.gun@gmail.com	Govt. Degree and PG College for Women, Srikalahasthi, India.	India
31	Dr. Tajamul Islam	taju.zoology@gmail.com	Contractual Lecturer in Deptt. of Zoology at Govt Degree College for Women Baramulla, India.	India
32	Dr. Mohanraj Rathinavelu	moley4u@rediffmail.com	Assistant Professor, Dept. of Pharmacy Practice, Raghavendra Institute of Pharmaceutical Education and Research (RIPER), Andhra Pradesh, India.	India
33	Dr. Anuj Singh Parihar	dr.anujparihar@gmail.com	Assistant Professor, Vyas Dental Collage and Hospital, Jodhpur, Rajsthan, India.	India
34	Dr. Islam Mostafa Abdo Bayomi Elbaz	islam_mostafa_elbaz@yahoo.com	Lecturer of Pharmacognosy Faculty of Pharmacy, Zagazig University, 44519- Zagazig, Egypt.	Egypt
35	Dr. Gopinath Shankar Khansole	gopinathskhansole@gmail.com	Assistant Professor, Department of Chemistry, D.A.B.N. Arts and Science College, Chikhali, Sangli, Maharashtra-415408, India.	India
36	Dr. Namrata Singh	namrata.singhms@gmail.com	Asst. Professor in P. Cognosy Dept. Shreeyash Institute of Pharmaceutical Education and Research, Aurangabad (MS) India.	India
37	Dr. Anoop Narayanan V.	anoopvn84@gmail.com	Assistant Professor, NGSM Institute of Pharmaceutical Sciences, NITTE University, Mangalore- 575018, India.	India
38	Dr. Maheshkumar Prakash Patil	maheshprakashpatil1984@gmail.com	Lab of Cell Signaling, Department of Microbiology, Pukyong National University, Busan, Korea.	Korea
39	Dr. Abhinandan Ghosh	abhinandan.vu@gmail.com	Dept. of BMLSM Vidyasagar University, Midnapore- 721102 West Bengal, India.	India
40	Dr. Jagdish Labhubhai Kakadiya	jagdishkakadiya@gmail.com	Assistant Professor, Department of Pharmacology, Indubhai Patel College of Pharmacy and Research Centre, Petlad-Khambhat Road, Dharmaj-388430, Anand, Gujarat, India.	India
41	Dr. Kunal Kishor	kunal_biotech@yahoo.co.in	Head Department of Microbiology SGRRTS Patel Nagar Dehradun, India.	India
42	Dr. Kishor R. Chudasama	krchudasama84@gmail.com	Assistant Professor Department of Shalakyia IPGT and RA Jamnagar- 361008, Gujarat, India.	India
43	Dr. Myle Akshay Kiran	myleakshaykiran@gmail.com	Doctor of Pharmacy (pharm. D), JNTUH UNIVERSITY, Pratista Institute of Pharmaceutical Science, Durjipaly, Chevimala Mandalam, Suryapeta, Telangana State, India.	India
44	Dr. Prakash S. Goudanavar	pgoudanavar01@gmail.com	Professor and Head Department of Pharmaceutics Sri Adichunchenagiri College of Pharmacy B.G.Nagar-571448	India

			Nagamangala Taluk Mandya Dist. Kamataka, India.	
45	Dr. Somil Dubey	somildubey11@gmail.com	Associate Professor Rasa Shastra and Bhaishajya Kaipana to Govt. College Burhanpur, M.P., India.	India
46	Dr. Naga Rathna Supriya G.	rathna.supriya@utu.ac.in	Assistant Professor C.G. Bhakta Institute of Biotechnology Uka Tarsadia University Maliba Campus, Gopal Vidyanagar, Bardoli- Mahuva Road, Ta. Mahuva, Dist. Surat-394350, Gujarat, India.	India
47	Dr. Dhivya Ravichandran	dhivya6@hotmail.com	Ph.D Biotechnology, Vels University India.	India
48	Dr. Sachin Kumar	sachin.amroha@gmail.com	DST-SERB National Post Doctoral Fellow in the Dept. Animal Science, M.J.P.Rohilkhand University, Bareilly, U.P., India.	India
49	Dr. Pravin Kendrekar	kkpravin@gmail.com	Department of Health Sciences, Faculty of Health and Environmental Sciences Central University of Technology (CUT) Bloemfontein 9300, Free State, South Africa.	South Africa
50	Dr. S. Sathish	sathishamg88@gmail.com	Assistant Professor and Head in Department of Automobile Engineering, Vels University, Chennai, India.	India
51	Dr. Sanjay Kumar Bharti	drskbharti24@gmail.com	Assistant Professor-cum- Junior Scientist, Department of Veterinary Anatomy, Bihar Veterinary College, Patna- 800014, India.	India
52	Dr. Anurag Kutehreshtha	anuragpt@iitr.ac.in	Faculty-Packaging Technology Ph.D., D.I.H., FICC Indian Institute of Technology, Roorkee Saharanpur Campus Saharanpur, India.	India
53	Dr. Nilesh Wagh	waghnk@gmail.com	Principal Scientist R&D at Radiomedix Inc, USA.	USA
54	Dr. Pradeep Kumar Soni	pradeepsoni@gmail.com	Faculty of Chemistry, Institute of Engineering, Jiwaji University, Gwalior (M.P.), India.	India
55	Dr. Siddharth	dr.siddharthevatia@gmail.com	Master of Dental Surgery (M.D.S) Periodontology & Oral Implantology ITS-CDSR, Muradnagar, Ghaziabad, Uttar Pradesh, Ch. Charan Singh University, Meerut, India.	India
56	Dr. Tina Singhal	drtinasinghal@gmail.com	Assistant Professor, Deptt. of Rachana Sharir Govt. Ayurvedic College & Hospital, Varanasi, India.	India
57	Dr. Mridul Malakar	mridulmalakar1@gmail.com	District Microbiologist, IDSP I/C District Public Health Laboratory District Hospital, Sonapur, Kamrup (M), Assam, India	India
58	Dr. Dheeraj Nagore	nagoredheeraj@gmail.com	Senior Manager- Research and Development Center, Ari	India

			Healthcare Pvt. Ltd., Pune, Maharashtra, India	
59	Dr. Tushita Thakur	dr_tushita@yahoo.co.in	Consultant (Homoeopathy), AYUSH Wellness Clinic, Rashtrapati Bhavan, New Delhi-110004, India.	India
60	Vd. Rohit Mehta	rohitayu04@yahoo.com	Senior Medical Officer - Panchakarma; Vivekanand Medical Research Trust; Kayakalp (Himalayan Research Institute for Naturopathy & Yoga), Palampur, Kangra, Himachal Pradesh, India.	India
61	Dr. Sunita Verma	vermas.bot@gmail.com	Assistant Professor, Department of Botany, Rakesh P.G. College, Pilani (Raj.) India	India
62	Dr. Sujith Abraham	sujithabraham1@gmail.com	Professor & Principal, St John's College of Pharmaceutical Sciences & Research, Kattappana South (PO), Idukki Dist., Kerala- 685515, India	India
63	Dr. R. Mary Suja	rmsuja.83@gmail.com	Director William Research Centre at Nagercoil, India	India
64	Dr. Silpa Somavarapu	silpasomavarapu.1981@gmail.com	Faculty in Vikrama Simhapuri University, Andhra Pradesh, India	India
65	Dr. Teresa May B. Bandiola	bandiolateresamayb@gmail.com	Instructor A, School of Pharmacy, Far Eastern University- Dr. Nicanor Reyes Memorial Foundation, Quezon City, Philippines	Philippines
66	Dr. Janki B. Patel	janki0410pharma@gmail.com	Associate Professor, B.Pharmacy College Rampura, Kakanpur Godhra, Gujarat, India	India
67	Dr. Prasanna B. Ranade	prasannaranade@yahoo.com	Assistant Professor, Department of Chemistry, Vivekanand Education Society's Arts, Science and Commerce College, Sindhi Society, Chembur Mumbai 400071, India.	India
68	Dr. Md. Elias-Al-Mamun	elias_0276@yahoo.com	Associate Professor, Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Dhaka, Dhaka-1000, Bangladesh.	Bangladesh
69	Dr. Harika Vemula	vharikashetty@gmail.com	Senior Scientist, Upstream R&D Millipore Sigma, Kansas, USA	USA
70	Dr. J. Sai Chandra	jsaichandra@gmail.com	Academic Assistant in Chemistry, Jawaharlal Nehru Technological University, Hyderabad- Sultanpur, Sangareddy Dist. - 502273, India.	India
71	Dr. Farah Naaz	farah.ali07@gmail.com	Research Associate Under Swasthya Rakshan/ Pankshan Programme of Ministry of AYUSH, Government of India	India
72	Dr. Rajendra H. M.	ayurrajhm@gmail.com	Assistant Professor (Reader) in Dravyaguna Vigyan in Sri Jayendrasaraswathi Ayurveda College & Hospital, Chennai, India	India
73		javeedh3@gmail.com		India

	Dr. Javeed Ahmad Tantray		Assistant Professor in Department of Zoology, Centre for Biodiversity and Biotechnology, Baba Ghulam Shah Badshah University, Rajouri J. & K., India	
74	Dr. M. Selvendran	selvendran008@gmail.com	Assistant Professor, Dept. of Microbiology, Sardar Raja College of Arts and Science, Vadakkankulam, Thirunelveli Dist. Tanil Nadu, India	India
75	Dr. S. Krishnamoorthy	drkrishna83@gmail.com	Assistant Professor, Department of Biotechnology, The Madura College, Madurai-625011, India	India
76	Dr. Kinage Pradip Ravindra	drkinagepradeep@gmail.com	Asst. Professor, Parul Institute of Ayurveda and Research, Parul University Gujarat, India	India
77	Dr. Chandra Mohan	gurgaonmohan@yahoo.co.in	Assistant Professor in Chemistry, SBAS, K. R. Mangalam University, Sohna Road, Gurgaon-122103, Haryana, India	India

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



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

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**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**



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**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**



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Nausheen H Siddiqui, Arshad Arain, Zafar .S.Saify, Iqbal Azher, Shazia Haider and Zafar A Mahmood\*

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COMPARISON OF INVITRO ANTIMICROBIAL ACTIVITY OF DIFFERENT CRUDE PAKISTANI HONEY SAMPLES AND COMMERCIALS ANTIBIOTICS AGAINST CLINICAL PATHOGENS



\*Samiyah Tasleem, Syed Baqir Shyum.Naqvi

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\*S. Sujatha and Briska Renuga

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METHOD DEVELOPMENT AND VALIDATION FOR SIMULTANEOUS ESTIMATION OF OFLOXACIN AND DEXAMETHASONE SODIUM PHOSPHATE BY RP-HPLC

G.N.Renukadevi\*, M.Sri lakshmi, V.Prathyusha, SK.Sharmila, K.Shantha Kumari



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Nageshwara Rao Chilumula, Blessi Priyanka K\*, Ravi J\*, Kusuma B,Kalyani T., Gade Dayakar



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DEVELOPMENT AND EVALUATION OF ANTIMICROBIAL OINTMENT FORMULATION CONTAINING EXTRACTS OF OCIMUM SANCTUM, ANTHOCEPHALUS CADAMBA, ALLIUM SATIVUM AND ORIGANUM VULGARE



T. Rajesh\* Anup Kumar Roy, V.N.Raju Erumalla, Divakar Goli , Syed Jalaluddin Basha

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STUDIES ON MEDICINAL PLANTS OF A.V.V.M SRI PUSHPAM COLLEGE CAMPUS THANJAVUR DISTRICT OF TAMIL NADU, SOUTHERN INDIA

\*D.Rekha, A.Panneerselvam and N.Thajuddin

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FORMULATION AND EVALUATION OF CEPHALEXIN MONOHYDRATE RECONSTITUTIONAL ORAL SUSPENSION WITH PIPERINE AND THEIR ANTIBACTERIALACTIVITY

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#### FORMULATION AND EVALUATION OF LIPOSOMES CONTAINING FAMOTIDINE

Biresh K Sarkar\*, Maddi Ramaiah, Manish Devgan, Y.Ankamma chowdary

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#### FORMULATION, IN-VITRO EVALUATION AND ANALYTICAL QUANTIFICATION OF ZALTOPROFEN MICROCAPSULES

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#### GC, GC/MS CHARACTERIZATION OF THE ENICOSTEMA LITTORALE

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**DERIVATIVES OF CYCLOPROPYL AMINES AS AN INHIBITOR FOR HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR)**

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**SAFETY MARGIN OF COSMETICS: A REVIEW**

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**PREPARATION AND EVALUATION OF TASTE MASKING COMPLEX OF CIPROFLOXACIN HYDROCHLORIDE BY USING INCLUSION COMPLEXATION APPROACH**

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**A.Santosh Kumar Sreevatsav\*, A.K.Hareesh babu, P.Vamsi reddy, K.Radhika, Shravani Boguda, N.Mamatha.**

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**SIMPLE AND RAPID METHOD FOR THE QUANTIFICATION OF IMATINIB MESYLATE AND DESMETHYL IMATINIB IN HUMAN PLASMA USING LC-MS/MS AND ITS APPLICATION TO ROUTINE THERAPEUTIC DRUG MONITORING**

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## 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<sup>1\*</sup>, Widji Soeratri<sup>1</sup>, Tristiana Erawati<sup>1</sup>, Ayunanda<sup>1</sup>, Wakhida Fitriyani<sup>1</sup>

<sup>1</sup>Pharmaceutics Department, Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

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**\*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 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 al, 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 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 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

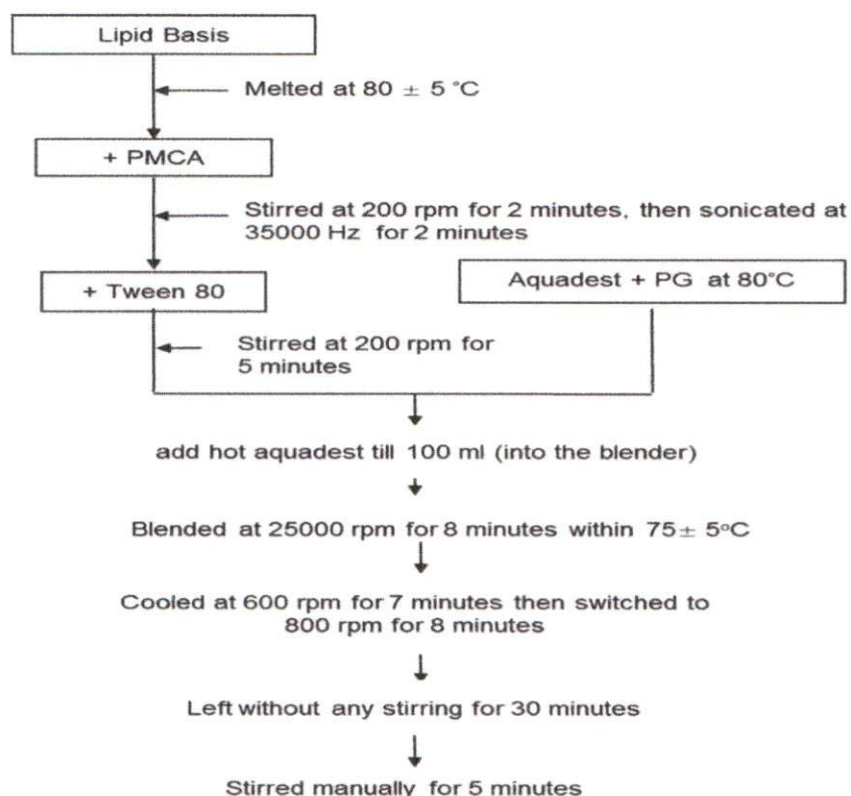
There were three PMCA formulas in gel 3%HPC-H: PMCA enriched in 3% HPC-H directly (Formula I), PMCA in 3% HPC-H with all components of SLN (Formula II) and PMCA-SLN incorporated in 3% gel HPC-H (Formula III). SLN was composed by cetyl alcohol 10% as lipid carrier, tween 80% as surfactant and propylene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

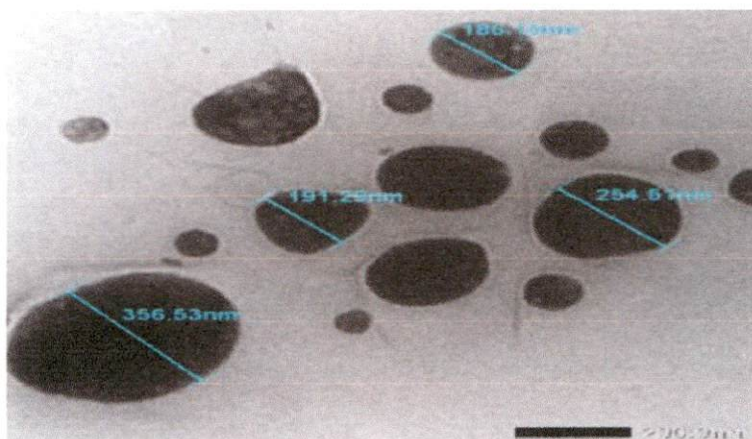


Figure 2. TEM picture of SLN-PMCA

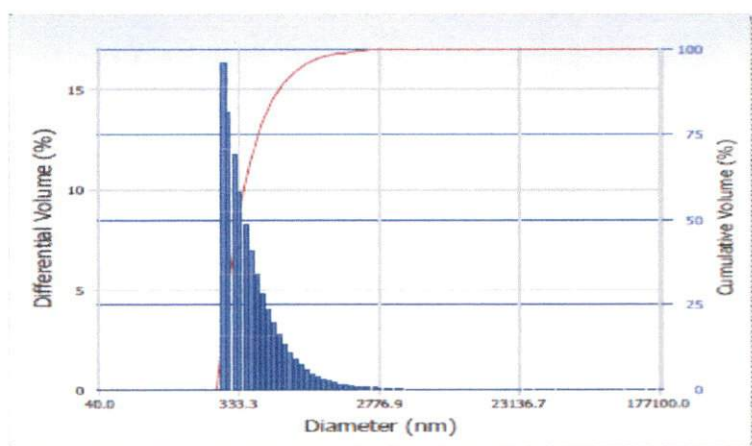


Figure 3. Particle distribution of SLN-MPCA

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**

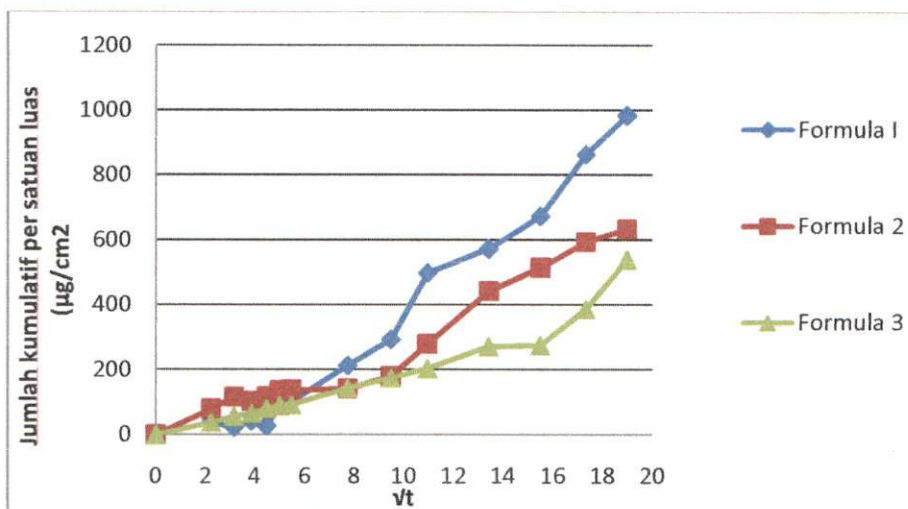
Formula	Mean pH $\pm$ SD
F I	3,89 $\pm$ 0,02
F II	3,86 $\pm$ 0,08
F III	3,79 $\pm$ 0,005

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).

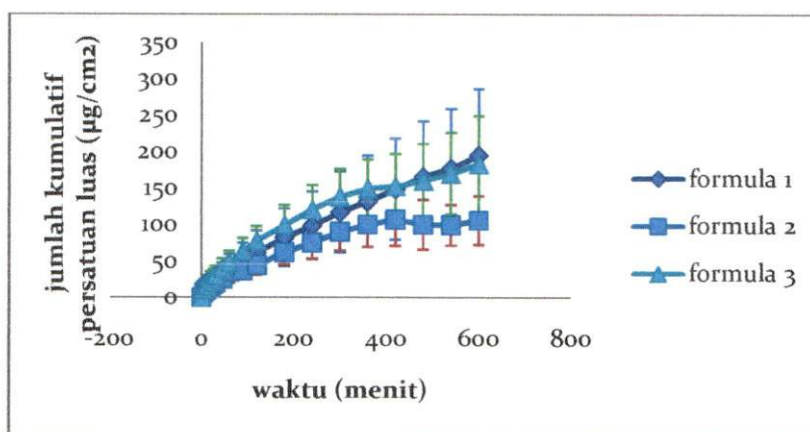


Figure 5. In Vitro penetration profile of PMCA through skin rat membrane

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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