

CDD

2016

The 4th

Current Drug Development International Conference 2016

June 1-3, 2016

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



**Proceeding
The 4th Current Drug Development
International Conference 2016 (CDD 2016)**

Editors

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Welcome Address

Dear Colleagues,

It is our great pleasure to welcome you to the fourth Current Drug Development (CDD) International Conference 2016. At the first CDD International Conference in 2010, we heard from speakers and participants who shared their valuable experiences and contributions in drug delivery systems and the development of natural medicines. The second CDD International Conference in 2012, which mainly focused on the development of anticancer agents, had distinguished speakers sharing their expertise in advancing anticancer agent from plants and marine life. During the third CDD International Conference in 2014, which highlighted the importance of pharmaceutical biotechnology, we had a great opportunity to meet and discuss the topic with renowned researchers in the field. We had about 200 local and overseas participants share their experiences throughout this conference.

At the fourth CDD International Conference 2016, we are focusing on “Drugs used in aging-associated diseases” and many interesting perspectives on new drug development. I am very glad to see that there is a wide range of participation from the many different countries that are joining this conference. We hope that this will be not only a great opportunity for scientists and researchers to exchange their ideas and expertise, but also that a productive network can be formed here. I also hope that the conference environment will inspire and motivate our young researchers to further their research interests and produce excellent outcomes.

On behalf of the organizing committee, I would like to thank our keynote speakers and invited speakers, the organizing staff from the Drug Delivery System Excellence Center, the Phytomedicine and Pharmaceutical Biotechnology Excellence Center, and the Faculty of Pharmaceutical Sciences at Prince of Songkla University, and the Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang, and the Drug and Cosmetic Research and Development Unit, School of Pharmacy, Walailak University. Your contribution is recognized. Finally, I hope you enjoy the city and have a memorable stay in Phuket.

Best regards,

Pharkphoom Panichayupakaranant, Ph.D.

Chair of the conference

Organizer Information

Conference Chair

Pharkphoom Panichayupakaranant

Director of Phytomedicine and Pharmaceutical Biotechnology Excellence Center

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- Faculty of Pharmaceutical Sciences, Prince of Songkla University
- Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang
- Drug and Cosmetic Research and Development Unit, School of Pharmacy, Walailak University
- Drug Delivery System Excellence Center, Prince of Songkla University
- Phytomedicine and Pharmaceutical Biotechnology Excellence Center, Prince of Songkla University

Scientific Program

The 4th Current Drug Development International Conference (CDD 2016)

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

Wednesday, June 1, 2016

8.00 - 8.45	Registration
8.45 - 9.00	Opening remark Dean of Faculty of Pharmaceutical Sciences/Prince of Songkla University
Chairperson: Pharkphoom Panichayupakaranant & Jianbo Xiao	
9.00 - 9.45	Keynote Speaker Aerosol Delivery to The Brain: A New Approach for Treatment of Alzheimer's Disease Prof.Dr.Wellington Pham Vanderbilt University, Institute of Imaging Science, USA
9.45-10.15	Alternative Treatment for Elderly from Biomaterials Prof.Dr.Pornanong Aramwit Chulalongkorn University, Thailand
10.15-10.45	Leisure & Break
Chairperson: Teerapol Srichana & Ibrahim Jantan	
10.45-11.15	Edible Bird's Nest Glycoproteins as the Natural Compounds for Anti-aging and Degenerative Diseases Assoc.Prof.Dr.Chua KienHui Universiti Kebangsaan Malaysia, Malaysia
11.15 - 12.00	Keynote Speaker Formulation and Compaction of Orally Dispersible Tablets Assoc.Prof.Dr.Paul W.S. Heng National University of Singapore, Singapore
12.00 - 13.00	Lunch
Chairperson: Kamonthip Wiwattanawongsa & Thipapan Plyduang	
13.00 - 13.30	Bacterial Ribosome Selective Antibiotics Prof.Dr.Dev P. Arya Clemson University, USA
13.30 - 14.00	Research on A Thai Traditional Remedy for Chronic Diseases Assoc.Prof.Dr. Arunporn Itharat Faculty of Medicine Thammasat University, Thailand
14.00 - 14.30	Hair Regeneration by Adipose-derived Stem Cells Assoc.Prof.Dr.Jong Hyuk Sung Yonsei University, Korea
14.30 - 15.00	Rational Design and Synthesis of Polysaccharides Based Nano-Particles for Drug Delivery System Dr.Warayuth Sajomsang National Science and Technology Development Agency, Thailand
15.00 - 15.30	Leisure & Break

Chairperson	Athip Sakunphueak & Hazrulrizawati Abd Hamid Session A Dalah 1 Room	Somchai Sawatdee & Attawadee Sae-Yoon Session B Dalah 2 Room
15.30-15.45	Structure-Stability Relationship of Polyphenols in Cell Culture Medium Jianbo Xiao University of Macau, China	Zwitterionic Carbon Nanodots for Simultaneous Nuclear Imaging and Efficient Drug Delivery Yun Kyung Jung Institution Ulsan National Institute of Science and Technology, Korea
15.45 – 16.00	Inhibition of Nitric Oxide Production by <i>Derris scandens</i> (Roxb.) Benth Extract in UVB-Exposed Human Keratinocytes Sumrit Sukhonthasilakun KhonKaen University, Thailand	Characterization of Plaunotol and Plaunotol-Enriched Extract Complexed with Hydroxypropyl- β -Cyclodextrin Wai Mi Aung Prince of Songkla University, Thailand
16.00 – 16.15	Antimicrobial Activity of Commercially Available Curcumin Powder and Ethanol Extract of Turmeric Against Oral Pathogenic Microorganism Mian Waqar Mustafa Prince of Songkla University, Thailand	Molecular interaction studies of amphotericin B formulated with sodium deoxycholate sulfate for inhalation by solid state NMR Faisal Usman Prince of Songkla University, Thailand
16.15 – 16.30	α -Glucosidase Inhibition Activity of Rhinacanthins-rich Extract and Rhinacanthin-C Muhammad Ajmal Shah Prince of Songkla University, Thailand	Microneedle-mediated skin permeation with plasmid DNA complexed transfection reagents Boonnada Pamornpathomkul Silpakorn University, Thailand
16.30 – 17.30	Poster presentation (Odd number)	
18.30	Welcome Party	

Thursday, June 2, 2016

Chairperson: Sukanya Dej-adisai & Apichart Atipairin

8.45 – 9.30	Keynote Speaker
	Effects of standardized extracts of selected medicinal plants and their isolates on modulation of immune functions and inflammation Prof.Dr.Ibrahim Jantan Universiti Kebangsaan Malaysia, Malaysia

9.30 – 10.15	Keynote Speaker Targeting the gut: Methods and effects in the gastrointestinal tract Prof.Dr.med.Karl-Herbert Schäfer University of Applied Sciences Kaiserslautern, Germany
10.15 – 10.45	A search for natural products for erectile dysfunction Assoc.Prof.Dr. Kornkanok Ingkaninan Naresuan University, Thailand
10.45 – 11.00	Leisure & Break
11.00 – 12.00	Poster presentation (Even number)
12.00 – 13.00	Lunch

Chairperson: Chua Kien Hui & Panupong Puttarak

13.00 – 13.30	Development of floating drug delivery systems Assoc.Prof.Dr.Srisagul Sungthongjeen Naresuan University, Thailand
13.30 – 14.00	Chitosan for skeletal drug delivery and tissue engineering Asst.Prof.Dr. Kwunchit Oungbho Prince of Songkla University
14.00 – 14.30	Clinical Drug Development Prof.Dr.Basavaraj K. Nanjwade The Oxford College of Pharmacy, India

Chairperson	Kornkanok Ingkaninan & Juraithip Wungsintaweekul Session A Dalah 1 Room	Chitchamai Ovartharnporn & Namfa Sermkaew Session B Dalah 2 Room
14.40 - 14.55	Antioxidant Capacities of Malayan <i>Murrayakoenigii</i> (Curry Leaves Tree) Rou Chian Ng Universiti Putra Malaysia, Malaysia	Multidimensional Screening Platform for the Simultaneous Targeting of Cancer Pathways Hendrik Luesch University of Florida, USA
14.55 – 15.10	Antioxidant Activity of <i>Etlingeraelator</i> Flower Tea Extracts. Sasiwisa Hosuwan Prince of Songkla University, Thailand	Tamarind seeds polysaccharides (TSP) extracted from <i>Tamarind indica</i> L. as drug delivery system Khanittha Chawananasest Thailand Institute of scientific and Technological Research (TISTR)
15.10 – 15.25	Antioxidant Activity of Synthetic Eugenol-Based Analogues Sudarat Saenset Naresuan University, Thailand	
15.25 – 15.40	Leisure & Break	

15.40 – 15.55	Production and Characterization of Monoclonal Antibodies against the Isoflavone Glycoside Daidzin Gorawit Yusakul Kyushu University, Japan	Isolation and Chemical Profile Confirmation of <i>Tinosporacrispa</i> Extract by UPLC/QToF MS for their antidiabetic potential Hazrulrizawati Abd Hamid Universiti Malaysia Pahang, Malaysia
15.55 – 16.10	An In Vitro Study of Wound Healing Effect of Okra Extract as Evidenced by Enhanced Cell Proliferation and Cell Migration Sirikhwan Manee Prince of Songkla University, Thailand	Comparison of Electroporation and Iontophoresis effects on Magnesium Ascorbyl Phosphate Permeation through Skin Model Soawaluk Poldech Srinakharinwirot University, Thailand
16.10 – 16.25	Heparan Sulfate and Heparin Oligosaccharides as Versatile Molecules for Biological Approaches: Their Structural Heterogeneity and Diversities Challenges Nina SuhaityAzmi Universiti Malaysia Pahang, Malaysia	Amino Acids and Peptide-Based Molecular Imprinted Polymers Sreenu Madhumanchi Prince of Songkla University, Thailand
16.25 – 16.40	Antibacterial and Effect on Bacterial Growth of Crude Ethyl Acetate Extract of <i>Actinomyces</i> strain PN51B-4-1 Jirarat Surinta Mahidol University, Thailand	
17.00	Closing Ceremony	

Friday, June 3, 2016

8.00 – 17.00 Excursion 1 & 2

Poster Presentation

Session A: Pharmaceutical Biotechnology and Herbal Medicines & Dietary Supplements

Paper Code	Paper name	Name	Surname
Pharmaceutical Biotechnology			
PA001	Biotransformation of dehydroepiandrosterone by <i>Aspergillus candidus</i>	Ali	Kuru
PA002	Functional consequences of BARD1 missense mutations on ubiquitin ligase activity	Apichart	Atipairin
PA003	Antioxidant Effect of Imperatorin against Ultraviolet B Irradiation -induced ROS in Human Keratinocytes	Kanuengnit	Choochuay
PA004	Differential mRNA expression of homologous recombination-related genes in breast cancer cells treated with cisplatin	Khwanjira	Hongthong
PA005	Anthraquinone variation in <i>Cassia tora</i> plantlet	Maseetoh	Haling
PA006	Construction of Genomic Library of <i>Streptomyces</i> sp. KBI	Nuttapon	Songnaka
PA007	Synergistic effects of combined olaparib and RAPTA-EA1 in <i>BRCA1</i> -associated breast cancer cell lines	Pornvichai	Temboot
PA008	Effect of Dilution Susceptibility Testing Methods on Antibacterial Activity of Chitosan	Supreedee	Sungkarak
Herbal Medicines & Dietary Supplements			
PA009	Screening of anti-breast cancer activity from Thai and Indian medicinal plants extract	Aisah	Yusoh
PA010	Formulation Development and Evaluation of Multifunctional Cosmetic Cream	Attawadee	Sae-Yoon
PA011	Simultaneous HPLC Quantitative Analysis of Phenolic Compounds in <i>Pluchea indica</i> Leaf Extract	Boonyadist	Vongsak
PA012	Cytotoxic Effect of Thai Medicinal Herbal Extracts on Human Cancer Cell Lines	Juthathip	Poofery
PA013	Antimicrobial activity of endophytic fungi isolated from <i>Eurycoma longifolia</i> Jack.	Kusuma	Jitsaeng

Paper Code	Paper name	Name Surname	
PA014	Antibacterial Potential of Singawalang (<i>Petiveria Alliacea</i>) Against <i>Mycobacterium Tuberculosis</i> H37Rv	Mulyani	Yani
PA015	Effects of carbazole alkaloid from <i>Murraya Koenigii</i> on proliferation and MMP-13 mRNA expression in PC3 cell line and HUVECs	Nurdina	Charong
PA016	Green extraction method for <i>Garcinia cowa</i> leaf extracts containing chamuangone	Pirunrat	Sae-Lim
PA017	Efficacy Evaluation of a Multifunctional Cosmetic Cream	Pisit	Rakkong
PA018	Anti-oxidative Activity of <i>Clerodendrum inerme</i> (L.) Gaertn. Extracts	Poonsit	Hiransai
PA019	In Vitro Bioactivities Study of <i>Portulaca oleracea</i> Linn. Extract in HaCaT cell	Pornsawan	Juntong
PA020	Inhibition of Lipopolysaccharide-Induced Nitric Oxide production By Isolated Compounds from <i>Chromolaena odorata</i> (L.) in RAW 264.7 Macrophages	Rana	Dhar
PA021	Cytotoxic effect of <i>Piper cubeba</i> Linn extract for breast cancer treatment.	Saowanee	Muangchanburi
PA022	Preliminary study on the effect of a topical alcohol free curcumin preparation on a modified acetic acid-induced buccal mucosal ulcer in hamster model	Sineenat	Kuadkaew
PA023	Stability-indicating HPLC Method for Determination of Berberine Hydrochloride in <i>Arcangelisia flava</i> Extract	Sirinan	Khongphan
PA024	Nitric oxide inhibitory activity of topical gel containing an aqueous noni fruit extract	Sonsawan	Kongpuckdee
PA025	Inhibition of Nitric Oxide Production by <i>Derris scandens</i> (Roxb.) Benth Extract in UVB-Exposed Human Keratinocytes	Sumrit	Sukhonthasilakun
PA026	Enzymes inhibitory activity of isolated phytoconstituents from <i>Euphorbia hirta</i> for treatment and management of metabolic syndrome	Sunil	Kumar
PA027	Antioxidant activity of <i>Bauhinia aureifolia</i> K. & S.S. Larsen (stems) extract	Supat	Langyanai

Paper Code	Paper name	Name	Surname
PA028	Study on antioxidant activity of Thai medicinal plants in Songkhla Rajabhat University	Supat	Langyanai
PA029	Study on Culture Condition of the Mycelial Growth of <i>Schizophyllum commune</i>	Surachai	Techaoei
PA030	ROS Scavenging Effect of Isolated Interruptins from <i>Cyclosorus terminans</i>	Suriya	Chaiwong
PA031	Increased multidrug transporter activity in human oral squamous cell carcinoma cells is associated with cisplatin resistance	Warangkana	Chunglok

Session B: Pharmaceutical Chemistry, Pharmaceutical Technology & Drug Delivery System and Biopharmaceutics

Paper Code	Paper name	Name Surname
Pharmaceutical Chemistry		
PB001	Carbon Dioxide Supercritical Fluid Extraction of <i>t</i> -Resveratrol from <i>Arachis hypogaea</i> Using Central Composite Design	Amornrut Chaidedgumjorn
PB002	Phytochemicals and cytotoxicity studies of <i>Smithatris supraneeanae</i> W.J. Kress & K.Larsen	Khanittha Chawanorasest
PB003	Simultaneous Quantitative HPLC Method for Determination of <i>trans</i> -Resveratrol and Its Glucoside in Thai Beverages	Malai Satiraphan
PB004	Development of <i>in vitro</i> assay for the detection of fetal hemoglobin inducers	Patamaporn Pruksakorn
PB005	Synthesis of Benzhydrol and Its Acetamido Analogues as Antituberculosis Agents	Pitikan Kanjanapruk
PB006	Synthesis of Some Biologically Important Thiazolidinone Compounds	Sedat Sevmezler
PB007	Antiproliferative compound of <i>Dipterocarpus obtusifolius</i> root	Woranan Chancherdha
Pharmaceutical Technology & Drug Delivery System		
PB008	Analytical Method Validation for Determination of Quinine Sulfate in Extemporaneous Oral Suspension	Aitsara Mitchuayrod
PB009	Development of Lidocaine Mucoadhesive Films	Araya Raiwa
PB010	Influence of hydrophobicity or hydrophilicity of nano silica in flow property of cohesive API in a powder mixing: a comparative evaluation	Bappaditya Chatterjee
PB011	Water Absorption and Mucoadhesive Properties of <i>Scaphium macropodium</i> Beaum. (Malva Nut)	Benjabhorn Sethabouppha

Paper Code	Paper name	Name	Surname
PB012	Effect Of Incubation Time On Protein Loading And Encapsulation Efficiency Of Ovalbumin-Alginate Microspheres	Dewi Melani	Hariyadi
PB013	Activity of Ciprofloxacin from implant with cross link agent genipin in composites to <i>Staphylococcus aureus</i> ATCC25923 dan <i>Escherichia coli</i> ATCC 25922	Esti	Hendradi
PB014	Preparation and Characterization of Chlortetracycline Hydrochloride Solid Dispersions	Jenjira	Apiwongngam
PB015	Screening of Cytotoxic and Antioxidant Activities of <i>Jatropha curcas</i> Linn Latex Extracts	kittiya	Tinpun
PB016	Formulation Development of Mucoadhesive Microspheres from Extract of <i>Piper betle</i>	Namfa	Sermkaew
PB017	Antimicrobial Effect of <i>Piper betle</i> Leaf Extract for Foot Anti-malodor	Natamon	Dorkbuakaew
PB018	In vitro Antioxidant Activity of Mouthwash Containing Stingless Bee's Propolis Extract	Natthan	Charernsriwilaiwat
PB019	Increasing of Lycopene's Antioxidant Stability In Solid Lipid Nanoparticle (SLN) and Nanostructure Lipid And Carrier (NLC) in Use As Antiaging	Noorma	Rosita
PB020	Development of Pluronic Lecithin Organogel loaded <i>Kaempferia parviflora</i> Extract for Transdermal Delivery	Paisit	Wattanasri
PB021	Effect of skin penetration enhancers containing liposome on ATRA loading capacity	Ponwanit	Charoenputtakun
PB022	Effect of Tween on transport function of organic cation transporter 2	Sirima	Soodvilai
PB023	<i>In vitro</i> release kinetic of sildenafil dry foam tablets	Somchai	Sawatdee
PB024	Development of Dong quai extracts-loaded solid lipid nanoparticles cream and its preliminary characterization	Somkamon	Manchun

Paper Code	Paper name	Name Surname
PB025	Formulation and Characterization of Capsaicin-loaded Microemulsions for Transdermal Drug Delivery: Trial and Error Method vs Response Surface Method	Sureewan Duangjit
PB026	Formulation and Evaluation of Topical Antimicrobial Tea Tree Oil Gels	Suwannee Panomsuk
PB027	Fabrication of clotrimazole-microemulsion nanofibers for oral candidiasis application	Teeratas Kansom
PB028	Selection of Stabilizers for Preparation of Alpha-mangostin Nanosuspension	Tharahpi Aung
PB029	Development and Evaluation of Hydrogel Formulation of Gac Fruit Extract	Thipapun Plyduang
PB030	Bioactivity and safety studies of nanofilm from povidone-iodine spray <i>in vitro</i>	Titpawan Nakpheng
PB031	Effect of different types and amount of fatty acid content in corn oil and virgin coconut oil (VCO) on the characteristic, release rate, penetration and effectiveness of para methoxycinnamic acid (PMCA) in nanoemulsion	Tristiana Erawati M.
PB032	Advanced Characterization of Ethanolic Nano Lipid Vesicles Loaded with Raloxifene HCl for Transdermal Drug Delivery	Uttam Kumar Mandal
PB033	Preparation and characterization of silymarin-loaded amphiphilic chitosans micelles	Wajee Tipparos
PB034	The physicochemical properties of indomethacin topical spray	Wilaiporn Buatong
PB035	Impact of Foam Powder Level and PEO Grade on Properties of Floating Matrix Tablet Prepared by Hot Melt Extrusion	Worawut Kriangkrai
Biopharmaceutics		
PB036	The Study of Suitable Conditions for Effective Use of Insulin Human Reference Standard	Chanida Kampracha
PB037	Liquid chromatography-tandem mass spectrometry with electrospray ionization method for quantitation of donepezil in human plasma and its application to a bioequivalence study	Ekawan Yoosakul

Paper Code	Paper name	Name Surname
PB038	Valproic acid attenuates MPP ⁺ -mediated toxicity in human neuroblastoma SH-SY5Y cells involve Erk pathway	Jakkapong Muangsab
PB039	Antibacterial and Effect on Bacterial Growth of Crude Ethyl Acetate Extract of Actinomycetes strain PN51B-4-1	Jirarat Surinta
PB040	Rapid and simple LC-MS/MS method for the determination of atorvastatin in human plasma	Nattawut Sukkhum
PB041	Biopharmaceutics Classification System (BCS)-based Biowaiver for Immediate Release Solid Oral Dosage Forms of Pregabalin 75 and 150 mg Capsules (Pregabalin GPO)	Nawaphon Saelim
PB042	Pharmacokinetic Modeling to Predict the Phenytoin Level in Blood by Using STELLA Program	Pattarawit Rukthong
PB043	Evaluation of Survival Rate of Encapsulated <i>Lactobacillus fermentum</i> LF026 in Yoghurt	Sirima Suvarnakuta Jantama
PB044	Synergistic Effect of Diterpenoid from <i>Trigonostemon reidioides</i> and Cisplatin on Antiproliferation of Human Oral Squamous Carcinoma Cells	Sirinya Thungtong
PB045	Protective effect of fenofibrate on cisplatin toxicity in human renal proximal tubular cells	Sunhapas Soodvilai

Activity of Cyprofloxacin from implant with cross link agent genipin in composites to *Staphylococcus aureus* ATCC25923 dan *Escherichia coli* ATCC 25922

Esti Hendradi, Dewi Melani Hariyadi, Muhammad Faris Adrianto

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Abstract- The Research on effectiveness of cyprofloxacin against *Staphylococcus aureus* ATCC25923 and *Escherichia coli* ATCC 25922 bacteria was done. Composite mixture used was Bovine Hydroxyapatite-Chitosan which cross link with genipin as the carrier Ciprofloxacin. The ratio between Ciprofloxacin: BHA: Chitosan = 10:30:60. As Cross linker was genipin 0.7%, the concentration of Ciprofloxacin as active ingredient was 10%. The results showed that the implant can release preparation Cyprofloxacin by sustained released system in vitro and to inhibit bacterial growth *Staphylococcus aureus* ATCC25923 and also *Escherichia coli* ATCC 25922.

Keywords: implant, ciprofloxacin, anti bacteria *Staphylococcus aureus* ATCC25923, anti bacteria *Escherichia coli* ATCC 2592

Introduction

Complications of bone diseases and bone disorders caused by traumatic accidents may result in a gap (defect) on the bone. The healing process of damage or fracture is determined by the level of trauma and soft tissue damage (Strobel et al., 2011). Some cases of damage or injury to the bone cannot undergo natural recovery (Porter et al., 2009). The release of antibiotics on the target network is expected to last continuously for a certain time and achieve a greater concentration than the minimum inhibitory concentration (MIC). Drug delivery systems in a controlled manner (controlled release system) can help increase the bioavailability of antibiotics in target tissues. The system is designed to release the drug at the expected location at a rate that is appropriate for a certain time period (Mourino et al., 2010). In previous research on the optimization of composite test results showed good composite composition was Ciprofloxacin: BHA: Chitosan = 10:30:60. And adding genipin 0.7% as crosslinker had potential effect to retard ciprofloxacin release from Bovine Hydroxyapatite-chitosan-ciprofloxacin implant for 30 days in in vitro (Hendradi et al, 2015). The purpose of this research is to make the preparation of bone implants with Bovine Hydroxyapatite composite Chitosan with Cross-linker genipin with Cyprofloxacin active ingredients can inhibit the bacteria *Staphylococcus aureus* ATCC 25923 (SA-GE) and *Escherichia coli* ATCC 2592 (EC-GE)

Materials and Methods

1) Materials Cyprofloxacin (Shangyu Jingxin Pharmaceutical Co. Ltd) ; Bovine Hydroxyapatite (BHA) from Bank Jaringan RSUD DR Soetomo Surabaya; Chitosan (Biotech Indonesia); Genipin was obtained from Challenge Bioproduct Co., Ltd., Taiwan. Acetic acid glacial p.a (Merck), KBr IR (for Spectroscopy) Na_2HPO_4 p.a (Merck), K_2HPO_4 p.a, KH_2PO_4 p.a, NaCl p.a (Merck-German), Nutrient Agar (Oxoid), and Aquabidest

2) Method 1: Formulation of Bovine Hydroxyapatite-chitosan-ciprofloxacin implant The implant produced by compression method. Cyprofloxacin were dissolved in aquabidest, Bovine Hydroxyapatite added gradually and mixed until homogen with cyprofloxacin. Chitosan powder were added to cyprofloxacin-Bovine Hydroxyapatite blend and mixed until homogen. Aquabidest were added gradually with continuous stirring until form wet granules mass. Wet granules mass were sieved using 1 mm sieve and dried overnight (24 hours) at 40 °C to obtain dried granules. Dried granules were immersed in genipin solution (0.3%, 0.7% concentration) for 24 hours until the colour was change. Granules were washed with aquabidest to remove the residual genipin. At the final stage, granules were washed with phosphate buffer saline (PBS) pH 7.40. Granules were dried in oven at 40 °C for 24 hours. Dried granules were weighed 100 mg, pressed using tablet press machine with 4.0 mm diameter and the compression pressure was 2 tons (Hendradi et al, 2015).

3) Method 2: Test potential dilution method of antibiotic Firstly, the release study of cyprofloxacin from implant was done as sample for test potential. Implant was placed in a vial containing 5 ml of phosphate buffer saline (PBS) pH 7.4. Vial was placed in a shelf and incubated in waterbath at 37 °C $\pm$ 0.5 °C. Sampling was conducted by pipetting 1 ml of elution fluids at predetermined time intervals (1st, 3rd, 5th, 7th) h and replaced with fresh buffer to maintain sink condition. Appropriate dilution was prepared using phosphate buffer saline (PBS) pH 7.4. The release of ciprofloxacin HCL from the implants was assayed in triplicate. Secondly, test antibiotic potential dilution method prints holes (wells)

design 3-3. A total of 10 mL of inoculum of *Staphylococcus aureus* ATCC 25923 or *Escherichia coli* ATCC 25 922 was inserted into the tube containing the seed layer 8 mL media Nutrient Agar that had thawed and then allowed to stand up to a temperature of 45 - 50°C. Homogenized with a vortex, then poured evenly over the surface of the base layer has been solidified in a petri dish, allowed to solidify. Hole was made in order to use the printer for sterile. Each hole was filled with the test solution and standard solution as 50.0µL for each hole. Petri dish and then incubated at 37°C for 24 hours. Diameter of inhibition zone formed at each hole was measured by using a caliper. The resulting inhibition zone diameter compared with the border of the effective inhibition zone, the minimum range of 14-16 mm (Depkes RI, 2014).

Results

The result of potency cyprofloxacin from implant was divided potency the standard (ciprofloxacin) and times 100%. The results can showed in figure1. In this figure showed that potency of cyprofloxacin from implant against *Escherichia coli* ATCC 25922(EC-GE) was higher compared *Staphylococcus aureus* ATCC25923 (SA-GE).

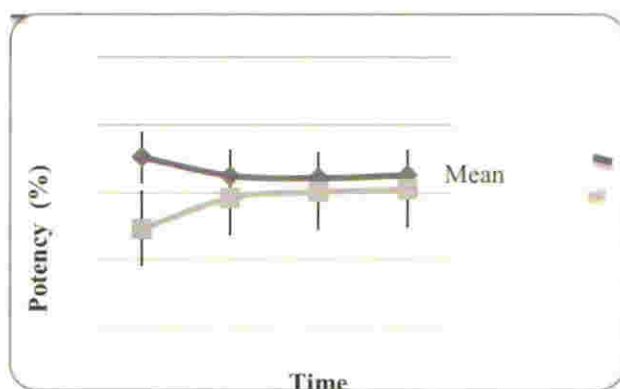


Figure1. Potency cyprofloxacin profil vs time (hour) released from implant BHA-chitosan-ciprofloxacin 0.7% genipin in phosphate buffer saline for 7 hours. Each value represents the mean $\pm$ S.D. of 3 determinations

Conclusion

The results obtained from this study indicated that implants with Bovine Hydroxyapatite composite Chitosan with Cross-linker genipin 0.7% with Cyprofloxacin active ingredients could inhibit the bacteria *Staphylococcus aureus* ATCC 25923 (SA-GE) and *Escherichia coli* ATCC 2592 (EC-GE).

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