รูปแบบรายงานวิจัยฉบับสมบูรณ์ แบบที่ 2 **(สำหรับโครงการเดี่ยวหรือโครงการย่อย)**

รายงานวิจัยฉบับสมบูรณ์

ฤทธิ์ของสารสกัดบริสุทธิ์ rhodomyrtone ต่อเยื่อหุ้มเซลล์ โครงสร้างภายใน และรูปร่างลักษณะของเชื้อ *Staphylococcus aureus* ที่ดื้อยาเมทิซิลลินและแวนโคไมซิน

Effects of rhodomyrtone on membrane integrity, cellular ultrastructure, and morphology of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Staphylococcus aureus*

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ประจำปีงบประมาณ 2555 รหัสโครงการ* SCI550154S

ส่วนที่ 2 เนื้อหา

1. ชื่อโครงการ

(ภาษาไทย): ฤทธิ์ของสารสกัดบริสุทธิ์ rhodomyrtone ต่อเยื่อหุ้มเซลล์ โครงสร้างภายใน และรูปร่างลักษณะของเชื้อ *Staphylococcus aureus* ที่ดื้อยาเมทิซิลลินและแวนโคไมซิน

(ภาษาอังกฤษ): Effects of rhodomyrtone on membrane integrity, cellular ultrastructure, and morphology of methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Staphylococcus aureus*

2. คณะนักวิจัย และหน่วยงานต้นสังกัด (คณะ/ภาควิชา หรือหน่วยงาน)

2.1. ผู้ขอรับทุน: ดร. วิภาวดี เสียงล้ำ
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3. กิตติกรรมประกาศ

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4. บทคัดย่อ

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of serious infections in hospital and community settings,[1] and has also been detected in livestock.[2,3] It continues to evolve resistant to many other commonly-used antibiotic classes such as clindamycin, ciprofloxacin, erythromycin, and gentamycin.[4] A number of new antimicrobial agents including linezolid, quinupristin-dalfopristin, daptomycin, telavancin, new glycopeptides, and ceftobiprole, have been introduced or are in a clinical development for the alternative treatment of the infections due to resistant strains.[5,6] Like all other antibiotics, resistance to these agents is also emerging.[7] Treating resistant bacterial infections has become extremely challenging for the infectious disease physician. Therefore, there is a continuous need to discover and develop novel therapeutic approaches and prophylaxis strategies to combat these emerging multidrug-resistant strains and potentially life-threatening infectious diseases.[8]

Plant extracts from leaves of *Rhodomyrtus tomentosa* (Aiton) Hassk. (Myrtaceae), an evergreen shrub originating from Southeast Asia, exhibits potent antibacterial efficacy against *S. aureus* and *Escherichia coli.*[9] A bioactive compound of the extracts is rhodomyrtone, an acylphloroglucinol[10] which showed remarkable antimicrobial activity against a number of Gram-positive bacteria such as *Enterococcus faecalis*, *S. aureus*, *S. epidermidis*, *Streptococcus* spp., *S. pyogenes*, *Propionibacterium acnes, Bacillus subtilis* including multidrug-resistant organisms.[9-13] Subsequent studies revealed that rhodomyrtone was effective in preventing biofilm formation and also kills the bacterial cells inside the biofilm of *S. aureus*[14] and *P. acnes*. Recently, Srisuwan *et. al.*[15] have reported that rhodomyrtone could act as immunomodulatory regimens which enhance innate immune responses against MRSA infections. Chorachoo *et. al.*[16] proposed the potent antibacterial activity of liposomal encapsulated rhodomyrtone for treatment of acne vulgaris caused by *S. aureus*, *S. epidermidis*, *P. acnes*. A brief report has been published describing the use of rhodomyrtone cream as a tropical agent for *S. aureus* skin infections in rabbits.[17] The previous results showed that rhodomyrtone has gained high interest as a lead candidate for potential novel antibacterial agents. Elucidating fundamental

antibacterial mechanisms of rhodomyrtone is necessary for clinical applications. We have recently undertaken proteome analysis of MRSA upon rhodomyrtone treatment which indicated that the purified compound showed pronounced effects on the expression of several proteins relating with some crucial metabolic and biosynthetic pathways of the bacteria.[11] Meanwhile, comparison of gene expression profiling between MRSA cultures with or without rhodomyrtone provides us with a better understanding of MRSA response to the compound. The most involved genes encode essential proteins in metabolic pathways, amino acid metabolism, membrane function, ATP-binding cassette (ABC) transportation, lipoprotein and nucleotide metabolism, and bacterial cell envelope.[18] However, detailed studies on the mode of action of the compound on bacterial cells has not yet been well-defined.

5. บทสรุปผู้บริหาร (Executive Summary)

5.1 บทนำ

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of serious infections in hospital and community settings,[1] and has also been detected in livestock.[2,3] It continues to evolve resistant to many other commonly-used antibiotic classes such as clindamycin, ciprofloxacin, erythromycin, and gentamycin.[4] A number of new antimicrobial agents including linezolid, quinupristin-dalfopristin, daptomycin, telavancin, new glycopeptides, and ceftobiprole, have been introduced or are in a clinical development for the alternative treatment of the infections due to resistant strains.[5,6] Like all other antibiotics, resistance to these agents is also emerging.[7] Treating resistant bacterial infections has become extremely challenging for the infectious disease physician. Therefore, there is a continuous need to discover and develop novel therapeutic approaches and prophylaxis strategies to combat these emerging multidrug-resistant strains and potentially life-threatening infectious diseases.[8]

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5.2 วัตถุประสงค์

In order to provide a better understanding on the specific and early action of rhodomyrtone, and precise time sequence of the action induced on MRSA cytoplasmic membrane, we investigated the role of membrane permeabilization in the mechanism of