

**ELECTROSPUN FIBER MATS AND HYDROGELS CONTAINING  
HERBAL SUBSTANCES FOR BIOMEDICAL APPLICATIONS**

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A Dissertation Submitted in Partial Fulfilment of the Requirements  
for the Degree of Doctor of Philosophy  
The Petroleum and Petrochemical College, Chulalongkorn University  
in Academic Partnership with  
The University of Michigan, The University of Oklahoma,  
and Case Western Reserve University  
2013

I28372931

561053


**Thesis Title:** Electrospun Fiber Mats and Hydrogels Containing Herbal Substances for Biomedical Applications  
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**Program:** Polymer Science  
**Thesis Advisor:** Prof. Pitt Supaphol

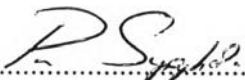
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Accepted by The Petroleum and Petrochemical College, Chulalongkorn University, in partial fulfilment of the requirements for the Degree of Doctor of Philosophy.


  
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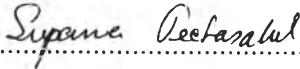
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## ABSTRACT

4982002063: Polymer Science Program

Piyachat Chuysinuan: Electrospun Fiber Mats and Hydrogels

Containing Herbal Substances for Biomedical Applications

Thesis Advisors: Prof. Pitt Supaphol, 159 pp.

Keywords: Electrospinning / Poly L-(lactic acid)/ Polyacrylonitrile (PAN)/

Gallic acid/ Caffeic acid/ *Garcinia Mangostana*/ *Eupatorium*

*adenophorum* / Wound dressing

New biomaterial effective for use as topical/transdermal patches or wound dressings containing herbal substances (gallic acid, caffeic acid, and *Eupatorium adenophorum* essential oil) were developed. In order to improve the antioxidant properties, gallic acid, a natural phenolic antioxidant, was incorporated in PLLA electrospun fiber mats. The release characteristic of gallic acid from these materials were investigated by the total immersion method. Incorporation of gallic acid in the PLLA electrospun fibers improved the antioxidant properties. Caffeic acid (CA) was chemically immobilized onto the individual fiber surface of electrospun PLLA fiber mats to enhance the hydrophilicity and impart the antioxidant activity to the fibrous membrane. Indirect cytotoxicity evaluation, with murine dermal fibroblasts (L929) and human dermal fibroblasts (HDFa) revealed that the neat and the modified PLLA fibrous matrices in the level that were not harmful to the cells. Moreover, the wound dressing application was explored by the studies of gelatin hydrogels containing *E. adenophorum* essential oil emulsion which could be fabricated into casting-films and improved its water resistance properties by crosslinking with glutaraldehyde. It showed the antibacterial activities against Gram positive and Gram negative bacteria. In addition, the mangosteen extract-loaded polyacrylonitrile fiber mats were fabricated for filter application as a surgical mask. This study demonstrated a convenient procedure and the potential to develop antimicrobial and antituberculosis properties of electrospun fibrous membranes containing *Garcinia mangostana* (Mangosteen extract).

## บทคัดย่อ

ปิยฉัตร ช่วยสินวล : วัสดุเส้นใยจากเทคนิคอิเล็กโตรสปินและวัสดุไฮโดรเจลที่มีสารออกฤทธิ์ทางชีวภาพซึ่งสกัดจากสมุนไพรไทยและการประยุกต์ใช้ทางการแพทย์ (Electrospun fiber mats and hydrogels containing herbal substances for biomedical applications) อ. ที่ปรึกษา: ศาสตราจารย์ ดร. พิชญ์ สุภผล 159 หน้า

ในปัจจุบันสารสกัดจากสมุนไพรไทยกำลังได้รับความสนใจเป็นอย่างมากเนื่องด้วยคุณสมบัติที่ดีของสารออกฤทธิ์ต่างๆที่มีอยู่ในสารสกัด เช่น สมบัติในการช่วยหายของแผลเร็วขึ้น การศึกษานี้จึงต้องการศึกษากระบวนการขึ้นรูปผลิตภัณฑ์จากพอลิเมอร์ชนิดต่างๆซึ่งมีคุณสมบัติของการออกฤทธิ์ของสารสกัดจากสมุนไพรไทยและการนำไปประยุกต์ใช้ สำหรับการประยุกต์ใช้เป็นวัสดุปิดแผล พอลิแลคติกแอซิดซึ่งมีส่วนประกอบของแกลลิกแอซิดถูกขึ้นรูปด้วยกระบวนการอิเล็กโตรสปินและศึกษาคุณสมบัติในการปลดปล่อยสารออกฤทธิ์พบว่าเส้นใยอิเล็กโตรสปินที่ได้มีคุณสมบัติในการต่อต้านอนุมูลอิสระเมื่อทดสอบด้วย DPPH assay คุณสมบัติพื้นผิวของเส้นใยพอลิแลคติกแอซิดยังได้ถูกปรับปรุงเพื่อให้มีคุณสมบัติในการดูดซับน้ำดีขึ้นและเพิ่มคุณสมบัติในการต่อต้านอนุมูลอิสระโดยการใช้เทคนิค Grafting ด้วยคาเฟอิกแอซิดพบว่าเส้นใยอิเล็กโตรสปินดังกล่าวมีคุณสมบัติที่ดีในการช่วยให้เซลล์ไฟโบรพลาสต์ที่ได้จากผิวหนัง (human dermal fibroblast) ผิวหนังมีความสามารถในการเกาะบนพื้นผิวเส้นใยอิเล็กโตรสปินได้เป็นอย่างดี นอกจากนี้กระบวนการขึ้นรูปเจลลาตินไฮโดรเจลยังได้ถูกศึกษาคุณสมบัติในการใช้เป็นวัสดุปิดแผล จากการศึกษาเจลลาตินไฮโดรเจลซึ่งปรับปรุงคุณสมบัติการป้องกันน้ำด้วยวิธีการ Crosslinking ด้วยกลูตารัลดีไฮด์และมีส่วนผสมของสารสกัดจากสมุนไพรสาบหมาพบว่าวัสดุไฮโดรเจลที่ได้มีคุณสมบัติในการออกฤทธิ์ยับยั้งเชื้อแบคทีเรียชนิดแกรมบวกและแกรมลบชนิดต่างๆได้เป็นอย่างดีซึ่งวัสดุดังกล่าวทั้งหมดสามารถนำไปใช้เป็นวัสดุเพื่อนำไปใช้ทางการแพทย์ที่มีประสิทธิภาพ สำหรับคุณสมบัติในการออกฤทธิ์ยับยั้งเชื้อแบคทีเรียที่ทำให้เกิดโรค เช่น เชื้อวัณโรค โพลีอะครีโรไนไตรด์ซึ่งถูกขึ้นรูปด้วยกระบวนการอิเล็กโตรสปินและมีส่วนผสมของสารสกัดจากเปลือกมังคุดนั้นพบว่ามีคุณสมบัติในการออกฤทธิ์ต่อต้านเชื้อวัณโรคได้ดีโดยวัสดุดังกล่าวสามารถถูกขึ้นรูปในรูปแบบของแผ่นกรองอากาศซึ่งสามารถนำไปประยุกต์ใช้เป็นหน้ากากอนามัยเมื่อจำเป็นต้องสัมผัสกับเชื้อวัณโรคได้ดี

## ACKNOWLEDGEMENTS

Appreciation is expressed to those who have made contributions to this dissertation. First the author gratefully acknowledges her advisors, Prof. Pitt Supaphol from The Petroleum and Petrochemical College, Chulalongkorn University, Assoc. Prof. Sunit Suksamrarn from Srinakharinwirot University and Assoc. Prof. Nuanchawee Wetprasit from Faculty of Biotechnology, Ramhamheng university for giving her invaluable knowledge, meaningful guidance and their encouragement all along the way. She also would like to express her sincere thanks to Assoc. Prof. Supanna Techasakul from the Department of Chemistry, Faculty of Science, Kasetsart University and Chulabhorn Research Institute and Nitirat Chimnoi from Chulabhorn Research Institute for giving her useful advises, encouragement and suggestions.

She gratefully acknowledges all faculty members and staffs at The Petroleum and Petrochemical College, Chulalongkorn University for their knowledge and assistance. Moreover she would like to give her special thanks to all members in her research group and all of her friends for their kind assistance continual encouragement and wonderful friendship.

Asst. Prof. Pomthong Malakul, Prof. Pitt Supaphol, Asst. Prof. Hathaikarn Manuspiya, Assoc. Prof. Sunit Suksamrarn and Assoc. Prof. Supanna Techasakul are further acknowledged for being her dissertation committees, making valuable comments and suggestions.

She wishes to express her deep gratitude to her family for their unconditioned love, understanding and very supportive during all these years spent for her Ph.D. study.

Finally, she is grateful for the partial support received from the Petroleum and Petrochemical College; and the Center of Petroleum, Petrochemicals and Advanced Materials (CPPAM), Chulalongkorn University and a doctoral scholarship received from the Development and Promotion of Science and Technology Talents (DPST) Project, the Institute for the Promotion of Teaching Science and Technology. This work would not be carried out successfully without all financial supports.

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## ABBREVIATIONS

<i>A. anitratus</i>	<i>Acinetobacter anitratus</i>
<i>A. baumannii</i>	<i>Acinetobacter baumannii</i>
<i>A. calcoaceticus</i>	<i>Acinetobacter calcoaceticus</i>
<i>A. Iwoffii</i>	<i>Acinetobacter Iwoffii</i>
AA	Antioxidant activity
Abs	Absorbance
AC	Asiaticoside
a-ePLLA	Aminolyzed PLLA fiber mats
Al	Aluminum
ANOVA	One-Way Analysis of Variance
ATCC	American Type Culture Collection
<i>B. cepacia</i>	<i>Burkholderia cepacia</i>
<i>B. cereus</i>	<i>Bacillus cereus</i>
<i>B. subtilis</i>	<i>Bacillus subtilis</i>
<i>C. albican</i>	<i>Candida albican</i>
CA	Caffeic acid
CA	<i>Centella asiatica</i>
CA-g-ePLLA	CA-grafted PLLA fiber mats
CLSI	Clinical and Laboratory Standards Institute
-CONH-	Amide linkage
-COO-	Ester linkage
-COOH	Carboxylic acid
DCM	Dichloromethane
DMAc	Dimethylacetamide
DMEM	Dulbecco's modified Eagle's medium
DMF	Dimethyl formamide
DMSO	Dimethyl sulfoxide
DPPH	1,1-diphenyl-2-picrylhydrazyl
<i>E. adenophorum</i>	<i>Eupatorium adenophorum</i>
<i>E. coli</i>	<i>Escherichia coli</i>

<i>E. faecalis</i>	<i>Enterococcus faecalis</i>
EDC	1-ethyl-3-(3-dimethylaminopropyl)carbodiimide
EI	Electron ionization
ePLLA	Electrospun PLLA fiber mats
e-spinning	Electrospinning
e-spun	Electrospun
FBS	Fetal bovine serum
<i>G. mangostana</i>	<i>Garcinia mangostana</i>
GC-MS	Gas chromatography-mass spectrometry
GSH	Glutathione
GSSG	Oxidized glutathione
GTA	Glutaraldehyde
h	Hour
HDFa	Human dermal fibroblast cell
HFIP	1,1,3,3-hexafluoro-2-propanol
HMD	1,6-hexamethylenediamine
IBU	Ibuprofen
IND	Indomethacin
<i>K. oxytoca</i>	<i>Klebsiella oxytoca</i>
<i>K. pneumonia</i>	<i>Klebsiella pneumonia</i>
<i>L.monocytogenes</i>	<i>Listeria monocytogenes</i>
L929	Murine dermal fibroblasts
MDR-TB	Multidrug-resistant tuberculosis
MH	Mueller-Hinton
MIC	Minimum Inhibitory concentration
MTT	3-(4,5-Dimethyl-2-thiazolyl)-2, 5-diphenyltetrazolium bromide
Na <sub>2</sub> HPO <sub>4</sub> ·7H <sub>2</sub> O	Disodiumhydrogenphosphateheptahydrate
Na <sub>2</sub> S <sub>2</sub> O <sub>5</sub>	Sodium metabisulfite
NaCl	Sodium chloride
NAP	Naproxen
NF	Nanofiltration



NH <sub>2</sub>	Amino groups
NHS	<i>N</i> -hydroxysuccinimide
o/w	Oil in water
<i>P. fluorescens</i>	<i>Pseudomonas fluorescens</i>
<i>P. mirabilis</i>	<i>Proterus mirabilis</i>
<i>P. aeruginasa</i>	<i>Pseudomonas aeruginasa</i>
PAN	Polyacrylonitrile
PBS	Phosphate buffer saline
PDLA	Poly(D,L-lactic acid)
PEVA	Poly(ethylene-co-vinyl acetate)
PLLA	Poly(L-lactic acid)
RS	Reactive species
<i>S. pyogenes</i>	<i>Strephylococcus pyogenes</i>
<i>S. agalactiae</i>	<i>Strephylococcus agalactiae</i>
<i>S. aureus</i>	<i>Staphylococcus aureus</i>
<i>S. boydii</i>	<i>Shigella boydii</i>
<i>S. dysenteriae</i>	<i>Shigella dysenteriae</i>
<i>S. enteritidis</i>	<i>Salmononelia enteritidis</i>
<i>S. epidermidis</i>	<i>Staphylococcus epidermidis</i>
<i>S. flexneri</i>	<i>Shigella flexneri</i>
<i>S. marcescens</i>	<i>Serratia marcescens</i>
<i>S. sonnei</i>	<i>Shigella sonnei</i>
<i>S. typhi</i>	<i>Salmononella typhi</i>
SEM	Scanning electron microscopy
SFM	Serum-free medium
SUL	Sulindac
TCPS	Tissue-culture polystyrene plate
TFA	Trifluoroacetic acid
US-FDA	US Food and Drug Administration
UV-vis	UV-visible spectrophotometer
<i>V. cholerae</i>	<i>Vibrio cholerae</i>
Vit E	vitamin E

WVTR	Water vapor transmission rate
XPS	X-ray photoelectron spectroscopy

## LIST OF SYMBOLS

$A$	Area of bottle mouth
$A_{\text{control}}$	Absorbance values of the testing solution without the presence of the as-loaded or the as-released gallic acid
$A_{\text{sample}}$	Absorbance values of the testing solution with the presence of the as-loaded or the as-released gallic acid
$k$	Rate of the release of gallic acid that incorporates physical characteristics of the matrix/gallic acid system
$M_t$	Cumulative amount of gallic acid released at an arbitrary time $t$
$M_\infty$	Cumulative amount of the substance released at an infinite time
$N$	Exponent characterizing the mechanism with which the release kinetics
$W$	Weight of each specimen after submersion in each respective medium
$W_d$	Weight of dry hydrogels after immersed in phosphate buffer (PBS) solution
$W_g$	Weight of dry hydrogel after extraction
$W_i$	Initial weight of the sample in its dry state
$W_o$	Initial weight of dry hydrogel
$W_s$	Weight of swollen hydrogel
$W_t$	Weight of bottle after placed in oven
$W_w$	Weight of each fiber mat specimen
$\rho_s$	Bulk densities of the fiber mats
$\rho_w$	Density of water