

**ELECTROSPUN CELLULOSE ACETATE FIBER MATS CONTAINING
HERBAL SUBSTANCES FOR DRUG DELIVERY SYSTEM
AND WOUND DRESSING APPLICATIONS**



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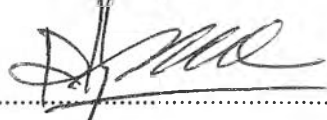
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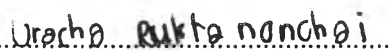
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ABSTRACT

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Containing Herbal Substances for Drug Delivery System and Wound Dressing Applications.

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Ultra-fine cellulose acetate (CA; $M_w \approx 30,000$ Da; degree of acetyl substitution ≈ 2.4) fiber mats containing either curcumin (CM; from the plant *Curcuma longa* L.) or asiaticoside (AC; from the plant *Centella asiatica* L. either in the form of pure substance (PAC) or a crude extract (CACE)), widely known for anti-tumor, antioxidant, anti-inflammatory, and wound healing properties, were successfully prepared by electrospinning. Incorporation of herbal substances in the neat CA solution did not affect the morphology of the resulting fibers, as both the neat and the herb-loaded CA fibers were smooth. The average diameters of these fibers ranged between 301 and 545 nm. Chemical integrity of the herbal substance within the herb-loaded CA fiber mats, mechanical integrity, and swelling and weight loss behavior of neat and herb-loaded CA fiber mats were studied. Moreover, the investigation of the release characteristics of herbal substances from herb-loaded CA fiber mats was carried out by the total immersion and the transdermal diffusion through a pig skin method in buffer solution. The potential for use of these electrospun fiber mats as wound dressings was further assessed *in vitro* with human dermal fibroblast (NHDF) cells in terms of the indirect cytotoxicity, the antioxidant activity, the cell attachment, the cell proliferation, and the collagen quantification. In addition, the morphological observation of cultured cells on these electrospun fiber mats was also investigated by scanning electron microscopy (SEM).

บทคัดย่อ

อรวรรณ สุวรรณทอง : แผ่นเส้นใยอิเล็กทรอนิกส์โตรสปันเซลลูโลสอะซีเตตที่มีสารสกัดสมุนไพรสำหรับการประยุกต์ใช้เป็นวัสดุนำส่งยา และวัสดุปิดแผล (Electrospun Cellulose Acetate Fiber Mats Containing Herbal Substances for Drug Delivery System and Wound Dressing Applications) อ. ที่ปรึกษา : รศ. ดร. พิชญ์ สุภผล และ ดร. อรุษา รักรัยตานนท์ชัย 148 หน้า

เส้นใยเซลลูโลสอะซีเตตที่มีสารสกัดขมิ้น (จากพืชที่มีชื่อทางวิทยาศาสตร์ *Curcuma longa* L.) และสารสกัดเอเชียติโคไซด์ (จากพืชที่มีชื่อทางวิทยาศาสตร์ *Centella asiatica* L.) สามารถเตรียมได้จากกระบวนการปั่นเส้นใยด้วยไฟฟ้าสถิต โดยสารสกัดทั้งสองชนิดที่มีอยู่ในแผ่นเส้นใยเหล่านี้มีคุณสมบัติในด้านต้านการเกิดมะเร็ง, ด้านสารอนุมูลอิสระ, ด้านการอักเสบ และ สมานแผล ดังนั้นจึงเหมาะต่อการนำไปประยุกต์ใช้เป็นวัสดุปิดแผล ซึ่งเส้นใยเซลลูโลสอะซีเตตที่มีสารสกัดสมุนไพรที่ได้จากกระบวนการนี้มีลักษณะเรียบ โดยมีขนาดเส้นผ่านศูนย์กลางเฉลี่ยระหว่าง 301 และ 545 นาโนเมตร นอกจากนี้ในงานวิจัยนี้ได้มีการศึกษาผลกระทบของการใช้ไฟฟ้าในการปั่นเส้นใยที่มีต่อโครงสร้างทางเคมีของสารสกัดสมุนไพร โดยใช้เทคนิคโปรตอนเอ็นเอ็มอาร์สเปกโตรสโกปี รวมทั้งศึกษาสมบัติเชิงกล การบวมน้ำและการสูญเสียน้ำหนักของแผ่นเส้นใยเซลลูโลสอะซีเตตเปล่าและแผ่นเส้นใยเซลลูโลสอะซีเตตที่มีสารสกัดสมุนไพร และยังได้ทำการทดลองเพื่อศึกษาการปลดปล่อยสารสกัดสมุนไพรจากแผ่นเส้นใยเซลลูโลสอะซีเตตที่มีสารสกัดสมุนไพร โดยใช้วิธีการแช่ในสารละลายบัฟเฟอร์ และวิธีการแพร่ผ่านชั้นผิวหนังหมู เนื่องจากความต้องการที่จะประยุกต์ใช้แผ่นเส้นใยอิเล็กทรอนิกส์โตรสปันเหล่านี้สำหรับเป็นวัสดุปิดแผล จึงได้ศึกษาความเข้ากันได้ทางชีวภาพของวัสดุ กับเซลล์ผิวหนัง (NHDF) โดยทดสอบความเป็นพิษ, การต่อต้านอนุมูลอิสระ, การเกาะของเซลล์, การเจริญเติบโตของเซลล์ และการสร้างคอลลาเจน นอกจากนี้ยังได้ศึกษาลักษณะของเซลล์ที่เกาะบนแผ่นเส้นใยอิเล็กทรอนิกส์โตรสปัน โดยใช้กล้องจุลทรรศน์อิเล็กตรอนแบบส่องกราดด้วย

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ABBREVIATIONS

CA	Cellulose acetate
CM	Curcumin
AC	Asiaticoside
PAC	Pure asiaticoside
CACE	<i>Centella asiatica</i> crude extract
DMAc	<i>N,N</i> -dimethylacetamide
M_w	Molecular weight
SEM	Scanning electron microscope
^1H NMR	^1H -Nuclear magnetic resonance
DMSO- d_6	deuterated dimethylsulfoxide
DMSO	Dimethylsulfoxide
B/T/M	Acetate buffer solution containing 0.5% v/v polysorbate 80 and 3% v/v methanol
A/BM	Acetate buffer solution containing 10% v/v methanol
P/B/M	Phosphate buffer solution containing 10% v/v methanol
DPPH	1,1'-diphenyl-2-picrylhydrazyl
%AA	The antioxidant activity
HPLC	High pressure liquid chromatography
NHDF	Normal human dermal fibroblasts
ECM	Extracellular matrix
TCPS	Tissue-culture polystyrene plate
DMEM	Dulbecco's modified Eagle's medium
FBS	Fetal bovine serum
SFM	Serum-free medium
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
h	Hour

LIST OF SYMBOLS

γ	Surface tension
ρ	Density
V_*	Critical Potential
V_c	Critical Voltage
DC	Direct current
M	Weight of sample after submersion in the testing solution
M_i	Initial weight of the sample in its dry state
M_d	Weight of the sample after submersion in the testing solution in its dry state
M_r	Weight of a model drug or vitamins that were released from the sample
M_t	Accumulative amount of drugs released at an arbitrary time t
M_∞	Accumulation amount of drugs released at an infinite time
n	Characteristic exponent
k	Rate parameter ($s^{-0.5}$)
A_{control}	Absorbance value of testing solution without the presence of the as-loaded curcumin
A_{sample}	Absorbance value of testing solution with the presence of the as-loaded curcumin