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Electrospun cellulose acetate fiber mats containing curcumin and release characteristic of the herbal substance

Orawan Suwantong [a], Praneet Opanasopit [b], Uracha Ruktanonchai [c], Pitt Supaphol [a,*]

[a] *Technological Center for Electrospun Fibers and the Petroleum and Petrochemical College, Chulalongkorn University, Bangkok, Thailand*
[b] *Nanotechnology for Drug/Gene Delivery Systems Group and The Faculty of Pharmacy, Silpakorn University, Nakhon Pathom, Thailand*
[c] *National Nanotechnology Center, Thailand Science Park, Klong Luang, Phathumthani, Thailand*

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Abstract

Ultra-fine cellulose acetate (CA; $M_w \approx 30{,}000$ Da; degree of acetyl substitution ≈ 2.4) fiber mats containing curcumin from the plant *Curcuma longa* L., widely known for its anti-tumor, antioxidant, and anti-inflammatory properties, were fabricated, for the first time, from the neat CA solution (17% w/v in 2:1 v/v acetone/dimethylacetamide) containing curcumin in various amounts (i.e., 5–20 wt.% based on the weight of CA powder) by electrospinning. Incorporation of curcumin in the neat CA solution did not affect the morphology of the resulting fibers, as both the neat and the curcumin-loaded CA fibers were smooth. The average diameters of the curcumin-loaded CA fibers ranged between ~314 and ~340 nm. The integrity of the as-loaded curcumin in the curcumin-loaded CA fiber mats was intact as indicated by the ^{1}H nuclear magnetic resonance spectrometric results and the ability of the as-loaded curcumin in maintaining its free radical scavenging ability. Investigation of the release characteristic of curcumin from the curcumin-loaded CA fiber mats was carried out by the total immersion and the transdermal diffusion through a pig skin method in the acetate buffer solution containing Tween 80 and methanol or the B/T/M medium at 37 °C. In the total immersion method, almost all of the curcumin loaded in the curcumin-loaded CA fiber mat specimens was released into the medium (~90 to ~95%), while considerably lower values were obtained when the curcumin-loaded CA fiber mats were placed on top of a piece of pig skin. Lastly, the curcumin-loaded CA fiber mats were proven non-toxic to normal human dermal fibroblasts.

Keywords: Topical/transdermal drug delivery; Electrospinning; Cellulose acetate

1. Introduction

In recent years, much interest has been paid on fabricating ultra-fine fibers by a process commonly known as electrospinning (e-spinning). Due to the high surface area to volume or mass ratio of the obtained fibers, the potential for use of these fibrous materials in biomedical applications is in areas such as wound healing [1,2], tissue engineering [3–5], and drug delivery [6–10]. This process involves the application of a strong electrical potential to the end of a capillary containing a polymer liquid (i.e., solution or melt), causing an accumulation of charges on the surface of the liquid. When the voltage reaches a critical value where the Coulombic repulsion of the charges overcomes the surface tension of the polymer droplet at the tip of the capillary, a charged jet is ejected. Acceleration through the electric field causes the charged jet to thin down. Finally, ultra-fine fibers are collected on a grounded electrode, due to the evaporation or the cooling of the charged jet [11]. One of the advantages of the e-spinning process over the conventional film-casting technique is the highly porous nature of the electrospun (e-spun) fiber mats which exhibit much greater surface area that assumingly could allow drug molecules to diffuse out from the matrix much more conveniently [6,12], when these fibrous materials are used as carriers for delivery of drugs.

Cellulose acetate (CA) is the acetate ester of cellulose, the primary structural component of the cell wall of green plants

* Corresponding author. Tel.: +66 2218 4131; fax: +66 2215 4459.
E-mail address: pitt.s@chula.ac.th (P. Supaphol).

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and is one of the most common biopolymers on earth [13]. Cellulose acetate is manufactured by reacting cellulose with acetic anhydride using sulfuric acid as a catalyst. Liu and Hsieh [14] reported the preparation of ultra-fine CA fiber mats as well as regenerated cellulose membranes by e-spinning. They found that the most suitable solvent system for preparing the CA solutions for e-spinning was 2:1 v/v acetone/dimethylacetamide (DMAc), as this mixture allowed the resulting CA solutions (i.e., 12.5–20 wt.%) to be e-spun into fibers with average diameters ranging between ~100 nm and ~1 μm [14]. E-spinning of CA fibers from CA solutions in a new solvent system of acetone/water mixtures with the water content ranging between 10 and 15 wt.% and the deacetylation of the resulting CA fiber mats were investigated by Son et al. [15]. The average diameter of the obtained CA fibers was ~2 μm, with thinner fibers (~0.5 μm) being produced from basic solutions [15].

E-spun CA fiber mats have been explored as affinity membranes [16] antimicrobial membranes [17], three-dimensional (3D) structures resembling the urinary bladder matrix (UBM) [18], and drug-delivery membranes [9,10]. The affinity CA fibrous membranes were prepared from a CA solution in 3:1:1 v/v/v acetone/dimethylformamide (DMF)/trifluoroethylene (TFE) by e-spinning [16]. The membranes were subsequently heat-treated and later treated in a NaOH solution to obtain regenerated cellulose (RC) membranes, in which Cibacron Blue F3GA, a sulfonated triazine dye, was coupled on their surface [16]. The antimicrobial CA fibrous membranes were prepared from a CA solution in 80:20 w/w acetone/water containing $AgNO_3$ by e-spinning [17]. Ag^+ ions were photoreduced into Ag nanoparticles by irradiating the e-spun fibers with UV light [17]. The 3D structures resembling the UBM were fabricated from CA solutions in acetone by e-spinning under various solution and processing conditions [18]. Lastly, e-spun CA fiber mats were used as carriers for transdermal or topical delivery of model vitamins, i.e., *all-trans* retinoic acid or vitamin A acid (Retin-A) and α-tocopherol or vitamin E (Vit-E) [9], and four different types of model drugs, i.e., naproxen (NAP), indomethacin (IND), ibuprofen (IBU), and sulindac (SUL) [10]. CA solutions in 2:1 v/v acetone/DMAc were used as the base spinning solutions into which Retin-A and Vit-E in the amount of 0.5 and 5 wt.% (based on the weight of CA), respectively [9], and NAP, IND, IBU, and SUL in the amount of 20 wt.% (based on the weight of CA) were added [10].

Curcumin (see chemical structure in Fig. 1) is a naturally-occurring compound found in the plant *Curcuma longa* L. Its major constituents are curcuminoids, which are polyphenols normally existing in at least two tautomeric forms, keto and enol. The enol form is more energetically stable, both in the solid phase and in solution [19]. Curcumin is widely known for its anti-tumor, antioxidant, and anti-inflammatory properties [20–23]. It can enhance cutaneous wound healing in rats and guinea pigs. Sidhu et al. [24] have evaluated the efficacy of curcumin treatment by oral and topical applications on impaired wound healing in diabetic rats and genetically-diabetic mice using a full-thickness cutaneous punch wound model. Wounds of the animals treated with curcumin showed early re-epithelialization, improved neovascularization, increased migratory activity of various cells including dermal myofibroblasts, fibroblasts, and macrophages into the wound bed, and a higher collagen content [24]. Gopinath et al. [25] have incorporated curcumin into a collagen matrix. They found that the presence of curcumin helped to increase wound reduction, enhance cell proliferation, and provide efficient free radical scavenging activity [25].

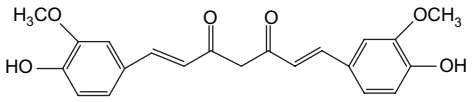

Fig. 1. Chemical structure of curcumin (keto form).

In the present contribution, curcumin was loaded into a CA solution which was later fabricated into ultra-fine fibers by e-spinning. The curcumin-loaded e-spun CA fiber mats were assessed for their potential use as carriers for topical or transdermal delivery of curcumin. Various properties (i.e., morphological, mechanical, swelling and weight loss, and cytotoxicity properties) of both the neat and the curcumin-loaded e-spun CA fiber mats as well as the release characteristic of curcumin from the curcumin-loaded e-spun CA fiber mats were investigated. Comparisons were made against the corresponding solvent-cast films. Both the chemical integrity and the antioxidant activity of the as-loaded curcumin in the curcumin-loaded e-spun CA fiber mats were also investigated.

2. Experimental details

2.1. Materials

Cellulose acetate (CA; white powder; $M_w \approx 30{,}000$ Da; acetyl content = 39.7 wt.%; degree of acetyl substitution ≈ 2.4) was purchased from Sigma–Aldrich (Switzerland). Curcumin (≥95.0% purity) was purchased from Fluka (Switzerland). Acetone (Carlo Erba, Italy), *N*,*N*-dimethylacetamide [DMAc, Labscan (Asia), Thailand], sodium acetate (Ajax Chemicals, Australia), and glacial acetic acid (Carlo Erba, Italy) were of analytical reagent grade and used without further purification.

2.2. Preparation of neat and curcumin-loaded CA fiber mats and films

A weighed amount of CA powder was dissolved in 2:1 v/v acetone/dimethylacetamide (DMAc) to prepare the base CA solution at a fixed concentration of 17% w/v. Curcumin-loaded CA solutions were prepared by dissolving curcumin powder in the amounts of 5, 10, 15, and 20 wt.% based on the weight of CA powder in the base CA solution. Prior to e-spinning, the as-prepared solutions were characterized for their viscosity and conductivity using a Brookfield DV-III programmable viscometer and a SUNTEX conductivity meter, respectively. All experiments were carried out at 25 °C. These mixtures were then e-spun under a fixed electric field of 17.5 kV/15 cm. The feeding rate of the solutions was controlled at