CHAPTER VII
CONCLUSIONS AND RECOMMENDATIONS

7.1 Conclusions

In this research work, 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)) were successfully prepared by electrospinning process and were developed for transdermal drug delivery system or wound dressing applications. Herbal substances (i.e., curcumin or asiaticoside) were added to the neat cellulose acetate solution in various amounts (i.e., 5-20 or 40 wt.% based on the weight of CA powder). Both the neat and the herb-loaded CA solution were electrospun into ultra-fine fiber under a fixed electric field of 17.5 kV/15 cm. The obtained fibers were smooth, without the presence of any kind of aggregation on their surface. The average diameter of the neat CA fibers was ~301 nm, while those of the herb-loaded ones were in the range of ~314 to ~545 nm. Chemical integrity of the as-loaded herbal substances in the herb-loaded CA fiber mats was intact after the electrospinning process. The swelling and the weight loss of both the neat and the herb-loaded CA fiber mats in the buffer solution were greater than those of the corresponding solvent-cast CA films. This could be a result of the highly porous nature of electrospun fiber mats that provides much greater surface area per unit volume or mass of the materials than the dense structure of the corresponding as-cast films.

The release characteristics of CM from CM-loaded electrospun fiber mats and the corresponding as-cast films were tested in acetate buffer solution containing Tween 80 and methanol (i.e., the B/T/M medium) at 37 °C. In the total immersion method, the maximum amounts of the CM released from CM-loaded fiber mat specimens into B/T/M medium were ~90 to ~95%, while only small amounts of CM released from the CM-loaded film counterparts were ~3 to ~9%. On the other hand, The release characteristics of AC from both the PAC- and the CACE-loaded e-spun CA fiber mats and the corresponding as-cast films were tested in acetate or

phosphate buffer solution containing methanol (hereafter, A/B/M or P/B/M medium) at either the skin or the physiological temperature of 32 or 37 °C, respectively. In the total immersion method, the maximum amounts of the AC released from the PAC- and the CACE-loaded e-spun CA fiber mats into the A/B/M medium were ~98 and ~77% (based on the weight of the specimens), while those of the AC released into the P/B/M medium were ~99 and ~92%, respectively. Considerably lower amounts of herbal substances were released into the releasing medium, when the herb-loaded e-spun CA fiber mats were placed on top of a piece of pig skin.

The potential for use of the herb-loaded electrospun CA fiber mats and corresponding as-cast CA films as topical/transdermal patches or wound dressings was assessed by investigation of the cytotoxicity of these materials. The results showed that these materials posed no threat towards normal human dermal fibroblast (NHDF) cells. Moreover, these electrospun fiber mats were further investigated *in vitro* in terms of the antioxidant activity, the cell attachment, the cell proliferation, and the quantification of synthesized collagen. The results were compared with the corresponding solvent –cast films. Considerably the antioxidant activity of herbal substances, the CM was a better antioxidant than either CACE or PAC. The observed superiority in the antioxidant activity of CM in comparison with that of CACE and PAC was obviously not a result of the content, but should be a result of its chemistry. The neat CA fiber mats provided the better support for both the attachment and the proliferation of the fibroblasts. Similar results were obtained for all of the herb-loaded CA fiber mats. However, while the cells that had been cultured on the 2 wt.% CACE- and the 40 wt.% PAC-loaded CA fiber mats appeared in their phenotypic spindle-like shape, those that had been cultured on all of the CM-loaded CA fiber mats were round. Among these various herb-loaded CA fiber mat substrates, the 40 wt.% PAC-loaded ones exhibited the greatest ability to support the attachment and the proliferation of the fibroblasts, followed by the 2 wt.% CACE-loaded ones. The large numbers of the cells that had been proliferated on these substrates on day 7 agreed particularly well with the great amounts of collagen synthesized by these cells. Despite its ability to mediate the collagen production in the cultured fibroblasts, asiaticoside was inferior to CM in terms of the antioxidant activity.

7.2 Recommendations

In this research work, only a single syringe was used in the electrospinning process, resulting in limited scale of production of electrospun fibers. In order to use this contribution in the industry, mass production of electrospun fibers is needed. Therefore, a multi-syringes electrospinning set-up should be used to achieve a large quantity of fibers within a shorter spinning time.

In case of the release study, it should be recommended that the modification of these electrospun fiber mats needed to be further studied. In order to develop this contribution, the herbal substances and the polymer matrix have to be appropriately chosen and/or modified to achieve the suitable release characteristic for specific applications.

In addition, the potential for use of herb-loaded CA fiber mats as wound dressing or skin regeneration applications should be further investigated *in vivo* or in an animal study.