CHAPTER I
INTRODUCTION

Recently, Thai herbal substance has evoked considerable interest as food and feed additive and as an alternative to antibacterial agents, antibiotics and synthetic antioxidants etc. Plants and their extracts are compatible with the current thinking on the future of health care, agriculture, and food and consumer opinion that most "thing natural" is better and safer. These herbal substances from the traditional medicine are widely used due to the medicinal plants were extracted that contain several substances with many biological activities including antibacterial, antioxidant, and wound healing (Bettolo, 1980).

In Thailand, they are several types of herbal substances has been used as wound healing during its biological activities such as antifungal, anti-inflammatory and promote cell proliferation towards an intact skin barrier. Thus, traditional medicinal plants have recently attracted much attention.

Gallic acid (GA) and caffeic acid (CA) are a natural phenolic antioxidants which can be extractable, especially green tea, grapes, cherry, coffee bean, and longan seeds. (Rangkadilok, 2007) Gallic acid is reported to showed antioxidant properties and reduced in vitro cell viability of lung cancer cells, and antifungal properties. (Kim, 2008) They are widely used in food, drug, and cosmetic. Moreover, gallic acid is found in longan seed that are the subtropical fruits in Thailand. (Rangkadilok, 2007) Another compound of natural origins that exhibits a strong anti-oxidant activity is caffeic acid (CA) or 3-(3, 4 dihydroxyphenyl)-2-propenoic acid (Olthof, 2001; Feng, 2007; Dastmalchi, 2008). Other biochemical activities of CA are anti-carcinogenic, anti-inflammatory, and anti-mutagenic activities (Feng, 2007; Dastmalchi, 2008; Elegir, 2008).

Mangosteen is a tropical fruit with medicinal properties that is fairly found in Thai, Malaysia, India and Sri Lanka. People in these countries often use *Garcinia mangostana* for traditional medicines for the treatment of skin infections, infected wounds, dysentery, diarrhea, suppuration, leucorrhoea, chronic ulcers and gonorrhea (Chaverri, 2008; Balasjbramanian, 1998; Arunrattiyakorn, 2011; Quan, 2011; Jiang, 2010). The identified compounds of *G. mangostana* pericarp has been exhibited the

complex phenolic compounds, including tannins, flavonoids, xanthones, and other bioactive substances (Naczk, 2011; Zadernowski, 2009; Chaivisuthangkura, 2009; Chin, 2008; Mahabusarakam, 1987). In addition, *G. mangostana* exhibits antitumor and antioxidant abilities (Matsumoto, 2003; Matsumoto, 2004; Matsumoto, 2005; Mahabusarakam, 2000; Jung, 2006; Moongkarndi, 2010) as well as antibacterial properties that combat *Staphylococcus epidermidis and Propionibacterium acnes* (Chomnawang, 2005). Recently, the prenylated xanthones from the hull of *G. mangostana,* in an *in-vitro* test, were found to be active against *Mycobacterium tuberculosis* (Suksamrarn, 2003).

The plant *Eupatorium adenophorum* Spreng (Crofton weed) (Fig. 1.1) is Asteraceae (Compositae) family. The plant *Eupatorium adenophorum* Spreng has been reported to use in folklore medicine such antimicrobial, antiseptic, antipyretic, analgesic, and blood coagulant (Rai and Sharma, 1994; Ansari, *et al.*, 1983). Essential oil (*Eupatorium adenophorum* Spreng.) is known to exhibit antimicrobial, anticancer, antioxidant activities. Moreover, the *E. adenophorum* was extracted with ethanol has been demonstrated to exhibit an antibacterial and antifungal effect with different strains of bacteria and fungi (Bhattarai *et al.*, 2009; Chakravarty, 2010).

Transdermal systems are to deliver the therapeutic agent into cutaneous/subcutaneous levels of skin as a wound healing or as a cosmetic treatment. The wound dressing incorporated of bioactive Thai herbal compound was played important role into wound healing process such as prevent the bacterial infection and accelerate the tissue regeneration (Purna, 2000; Cabodi *et al.*, 2006; Seydim, 2006).

They are several types of polymers used to prepare wound dressing such as poly (lactic acid), poly (acrylonitrile), chitosan, collagen and alginate (Patel, 2004). Poly (L-lactic acid) (PLLA) is quite attractive as wound dressing because of its biocompatibility, non-irritant and non-toxicity (Sezer *et al.*, 2007). PLLA can be fabricated into fibers for wound dressing area by using electrospinning process and these materials can be used as substrates for delivery of drug, bone cell culture and biosensor (Tsuji, 2005; Gupta, 2007; Badami, 2006; Peesan, 2006; Xu, 2006; Li, 2006). As previously studied, the development of electrospun polymeric fibers as substrate for drug delivery system much attention (Cui, 2006; Taepaiboon, 2007; Sikareepaisan, 2008). Recently, Carriers for transdermal system of electrospun

cellulose acetate fibers incorporated with Thai herbal substances have been developed as wound dressing materials (Suwantong, 2007; Suwantong *et al.*, 2008; Sikareepaisan, 2008). In 2008, Suwantong and coworker prepared the cellulose acetate fiber loading curcumin in 5-20 wt. % based on the weight of CA. The curcumin-loaded elctrospun fibers were success fabricated and showed its free radical scavenging ability. In a subsequent work the cellulose acetate electrospun fibers containing the plant *Centella asiatica* L. in the amount of 40 wt. %. The result showed that The *Centella asiatica* L.-loaded cellulose acetate fiber mats released no toxicity to dermal fibroblasts leading for use as wound dressing materials.

PLLA is hydrophobic polyester composed of non-polar group in its back bone, which results in a scaffold difficult to infiltrate with culture media (Xu, 2006; Li, 2006). There are several methods of immobilizing monomer on a substrate for biomedical applications (Sikareepaisan, 2008; Tsuji, 2005; Gupta, 2007). Immobilization is a way that a desired monomer can be grafted onto the substrate with chemical bond (Yu, 2010; Mattanavee, 2009; Cheng, 2004; Wang, 2003). Surface modification has been recognized as potential methods for enhancing the biocompatibility of the surface. In 2010, Shiu et al., prepared the cellulose acetate immobilized onto chitosan and (3-chloropropyl) trimethoxysilane scaffolds. These materials were exhibited, antioxidant, antibacterial and anti-cancer property (Shiu, 2010).

Gelatin one of natural polymers, is also widely used because gelatin is usually biocompatible, non-irritant and non-toxic properties leading to dermis application easy and safe (Olsen, *et al*, 2003; Young, *et al* 2005; Cataldo, *et al*, 2008; Vlierberghe, *et al* 2008). Gelatin becomes more popular in food and cosmetic industries due to their abilities to absorb large amount of water. At present, gelatin hydrogel can be covalently crosslink of gelatin solution to form matrices able to swelling in aqueous solutions (Young, 2005).

In addition, filtration is a necessary process in various medical applications; such as surgical mask. One of the versatile synthetic polymers is poly(acrylonitrile) (PAN) that have been one of the versatile synthetic polymers that have been used membranes manufacture used for making membranes. Because PAN has many desirable properties including thermal and mechanical properties, solvent resistance,

high tensile strength and posses good insect resistance which are suitable for making membranes. It has been used as a substrate for nanofiltration and reverse osmosis (Nam-Wun, 2001; Wang, 2006). Poly (acrylonitrile) fibers can be fabricated by wet or dry spinning and electrostatic spinning process. (Song 2008; Dong, 2007 *N,N*-dimethylformamide (DMF) is suitable solvent for fabricating an electrospun PAN solution.(Yang, 2003; Lee, 2005; Zhang, 2003).

Electrospinning process (e-spinning), one of fabrication process, are becoming more popular for the fabrication of micro, nano fibers because this method is simplicity, easy, low tooling cost. In this process, the polymer solution in the nozzle container is applied the charge. When increasing the electric field, the polymer jet is ejected to the collector and the electrospun fibers were obtained. In the present, the electrospun fibers are commonly used as wound dressing (Noh, 2006; Zhou, 2008), scaffolds (Sill, 2008), and wound dressing carriers (Cui, 2006; Taepaiboon, 2007; Sikareepaisan, 2008).

Then, the objective of this research work is to study the incorporating and the release characteristics of natural polymeric matrices, namely poly(L-lactic acid) (PLLA), and gelatin that were impregnated/loaded with Thai herbal compounds, which are gallic acid, caffeic acid, and *E. adephorum* essential oil by using electrospinning process and hydrogel formation for wound dressings.. Natural-based polymeric matrices incorporated with Thai herbal substances were characterized by various properties (i.e., morphology, mechanical integrity, swelling and weight loss behavior, the release characteristic as well as antioxidant, antibacterial and antituberculosis properties. In addition, the mangosteen-loaded electrospun PAN fiber mats were successfully fabricated and antibacterial and antituberculosis properties were also investigated for filter application as surgical masks.