CHAPTER I

INTRODUCTION

For centuries silver has been known to have bactericidal properties. As early as 1000 B.C., the antimicrobial properties of silver in rendering water potable were appreciated (Russell, 1994; Richard III, 2002). Silver compounds have been exploited for their medicinal properties for centuries as well (Fu-Ren, 2002). They were popular remedies for tetanus and rheumatism in the 19^{th} century and for colds and gonorrhea before the advent of antibiotics in the early part of the 20^{th} century (Mirsattari, 2004). A detailed historical review about the early usage of silver to treat various conditions has been recently published (Klasen, 2001). Interest in silver salts or silver salt solutions in the treatment of burn patients, however, completely disappeared around the Second World War (Klasen, 2000). It took many years for interest in silver (nitrate) to revive, under the stimulus of a publication by Moyer et al. (Gupta, 1998). At present, silver has reemerged as a viable treatment option for infections encountered in burns, open wounds, and chronic ulcers.

Several products have incorporated silver for use as a topical antibacterial agent, such as silver nitrate, silver sulphadiazine (SSD) (Flammazine™, Smith & Nephew Healthcare Limited, Hull, Canada) (Monafo, 1987), silver sulphadiazine/chlorhexidine (Silverex, Motiff Laboratories Pvt. Ltd. Kare Health specialties, Verna, Goa), SSD with cerium nitrate (Flammacerium, Solvay, Brussels, Belgium), and silver sulphadiazine impregnated lipidocolloid wound dressing Urgotul SSD (Laboratories Urgo, Chenove, France) (Monafo, 1987; Carsin, 2004; Carneiro, 2002). In contrast to these silver agents, newly developed products such as Acticoat™ (Westaim Biomedical Inc., Fort Saskatchewan, Alberta, Canada) and Silverlon (Argentum Medical, L.L.C., Lakemont, Georgia) have a more controlled and prolonged release of nanocrystalline silver to the wound area. This mode of silver delivery allows the dressings to be changed with less frequency, thereby reducing risk of nosocomial infection, cost of care, further tissue damage and patient discomfort (Richard III et al., 2002; Innes et al., 2001; Argentum et al., 2002; Sheridan et al., 1997). Another way is to convert silver ions to silver nanoparicles by using chemical reduction (MacDonald, 1996; Chung, 2004), UV irradiation (Abid, 2002), sonochemical deposition (Pol, 2002) and etc. Nanotechnology has provided a way of producing pure silver nanoparticles. This system also markedly increases the rate of silver ion release (Fan, 1999). Therefore, this mode of silver delivery allows the dressings to be changed with less frequency, thereby reducing risk of infection, cost of care, further tissue damage and patient discomfort (Sheridan, 1997; Innes, 2001). Silver nanoparticle is one of the most effective antimicrobial agents because of the high specific surface or volume fraction so that a large proportion of metal atoms are directly contact with the environment. For commercial products, they are the conventional microfibers that are incorporated or coated with silver complexes or metallic silver. Therefore, the best way is to use electrospinning process to produce nanofibers with high surface area to mass or volume ratio, high density of micro- or nanometer-sized pores of the non-woven mat and vast possibilities for surface functionalization (Yoshimoto, 2003; Wutticharoenmongkol, 2007).

Electrospinning process involves the application of a strong electric filed across a conductive capillary attaching to a polymer liquid-containing reservoir and a collector (Reneker, 1996; Doshi, 1995; Reneker 2008). It has been employed as a new approach for preparing suitable fibrous and porous structures for various biomedical applications such as scaffolding materials for cell/tissue culture (Yoshimoto, 2003; Wutticharoenmongkol, 2006; Suwantong, 2007), wound-dressing materials (Min, 2004; Noh, 2006; Rujitanaroj, 2008), and carriers for topical/transdermal delivery of drugs (Kenawy, 2002; Taepaiboon, 2006; Taepaiboon, 2007; Tungprapa, 2007; Suwantong, 2007). The other applications of electrospun fibers are filters, protective clothing, reinforcement in composite materials and sensors (Jayaraman, 2004). The advantages of using electrospinning are as follows.

- It is capable of producing extremely thin fibers with diameters ranging from microns down to few nanometers (typically hundreds of nanometers in diameter). Such small-size fibers could physically mimic the structural dimension of the extracellular matrix of a great variety of native tissues and organs, which are deposited and characterized by well-organized hierarchical fibrous structures realigning from nanometer to millimeter scale.

- The scaffolds/wound dressing pad was produced with highly porous microstructure with interconnected pores and extremely large surface- area-to-volume ratio, which is conductive to tissue growth.
- It is very versatile and allows the use of a variety of polymers, blends of different polymers, and inorganic materials as well as integration of additives, biomolecules, and living cells for tailoring different application requirements.
- The electrospinning process is a simple, straightforward, and cost-effective method to make various types of scaffolds.

In this work, it focused on two applications. The first was the electrospun fiber mats in filter application as surgical mask and the second was the electrospun fiber mats for wound dressing material. Poly(acrylonitrile) and glatin were chosen to produce the filter and wound dressing material, respectively. Filtration is a necessary process in various medical and engineering applications. Filtration efficiency or capture efficiency of filter media has been shown to be inversely proportional to the diameters of the fibers in filters. Because of the very high surface area-to-volume ratio and the resulting high surface cohesion of nanofibers, tiny particles on the order of less than 0.5 mm are easily trapped in the nanofiber mats. Moreover, nanofibers containing silver nanoparticles can not only capture the tiny particles but also kill bacteria or virus. For wound dressing material, wound dressing with electrospun fiber mats can meet the requirement such as higher gas permeation and protection of wound from infection and dehydration (Rho, 2006). The best biomaterials for wound dressing should be biocompatible and promote the growth of dermis and epidermis layers (Chen, 2008). The use of topical antimicrobial agents has been fundamental in that regard and has helped to improve the survival of patients with major burns and to minimize the incidence of burn wound sepsis, a leading cause of mortality and morbidity in these patients (Fraser, 2004).

Poly(acrylonitrile) (PAN) is a vinyl polymer. It is made from the monomer acrylonitrile by free radical vinyl polymerization. Homopolymers of poly(acrylonitrile) have been used as fibers in hot gas filtration systems, outdoor awnings, sails for yachts, and even fiber reinforced concrete. Mainly, copolymers containing poly(acrylonitrile) are used as fibers to make knitted clothing, like socks and sweaters, as well as outdoor products like tents and similar items. Poly(acrylonitrile) is one of the versatile polymers that are widely used for making membranes due to its good solvent resistance property. It has been used as a substrate for nanofiltration (NF) (Nam-Wun, 2001; Wang, 2006) and reverse osmosis (RO) (US Patent 4283359). Poly(acrylonitrile) in form of micro- and nanofibers can be fabricated by wet or dry spinning and electrostatic spinning techniques, respectively (Song, 2008; Dong, 2007). Suitable solvents for preparing an electrospinnable poly(acrylonitrile) solution is *N,N-dimethylformamide* (DMF) (Yang, 2003; Lee, 2005; Zhang, 2003).

Gelatin is widely used in food, cosmetic, pharmaceutical and medical applications (Young, 2005). Depending on its usage, gelatin can be fabricated in many forms, e.g., films (Jongjareonrak, 2006), micro- or nanoparticles (Huss, 2007; Vandervoort, 2004), and dense or porous hydrogels (Tabata, 1994; Liu, 2006; Liu, 2007). Gelatin in the form of micro- and nanofibers can also be fabricated by gel and electrostatic spinning techniques, respectively (Fukae, 2005; Huang, 2004; Zhang, 2005; Ki, 2005). Because of the inherent properties of gelatin and the unique characteristics of the e-spun fibers, e-spun gelatin fibers are ideal materials to be used as scaffolds for cell and tissue culture (Zhang, 2005; Li, 2005; Li, 2006), carriers for topical/transdermal delivery of drugs, and wound dressings. Suitable solvents for preparing an electrospinnable gelatin solution are 2,2,2-trifluoroethanol (TFE) (Huang, 2004; Zhang, 2005), formic acid (Ki, 2005), 1,1,1,3,3,3-hexafluoro-2-propanol (HFP) (Li, 2005; Li, 2006), and acetic acid (Choktaweesap, 2007; Songchotikunpan, 2008).

In the present contribution, mats of poly(acrylonitrile) and gelatin fibers containing nanoAg^0 were prepared by e-spinning and these e-spun fiber mats were proposed to be used as surgical mask and wound dressing pads, respectively. The nanoAg^0-containing poly(acrylonitrile) and gelatin fiber mats were characterized for various properties (i.e., morphological, mechanical, swelling, and weight loss), the release characteristic of the as-loaded silver as well as their anti-bacterial activity against some common bacteria found on air pollution and burn wounds. Moreover, *in vitro* and *in vivo* biological evaluation of neat and nanoAg^0-containing e-spun gelatin fiber mats with intended uses as wound dressing materials were investigated by studying the cytotoxicity and cell spreading of human dermal fibroblast (NHDF) or monocytes/macrophage on materials. Morphologies of the fibroblast cells and monocytes/macrophage attached on these fibers were observed by scanning electron microscope (SEM) and confocal microscopy, respectively.