博 士 論 文 の 内 容 の 要 旨

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論文題目	Study on biocompatible nanocomposites and nanofibers (生体適合性ナノ複合材料およびナノファイバーに関する研究)

(博士論文の内容の要旨)

Nanomaterials, especially nanofibers, attracted the attention attribute to unique characteristics possessions and application such as electronic, water refinery, and biotechnology. Lately, the low-cost fabrication, capacity to use a wide range of polymers and facile formation by innumerable methods as well as bacterial synthesis and electrospinning furthermore the facility to control the topographical feature caused to use nanofibers for drug delivery system and tissue engineering applications.

The most effective approaches have been employed for loading the silver nanoparticles into the poly (vinyl alcohol) nanofiber and compared. The sequence of the synthesis process significantly affects to resultant nanofiber. The methods designed as; i) solution reduction, which conducted the reduction process of Ag+ before electrospinning, ii) dipping method, which contains an immersion process of electrospun PVA nanofiber into Ag+ solution and then reduced of Ag+, and iii) nanofibers reduction, which performed as electrospun Ag+/PVA nanofibers and then carried out the reduction step. All of the electrospun nanofibers have cross-linked via a chemical reaction between glutaraldehyde and the hydroxyl functional group of PVA to prevent the dissolving in aqueous solution. The nanofiber reduction method showed the best performance to loading silver nanoparticles on nanofibers and avoiding the release of Ag particle from nanofibers. This finding will provide an effective way to fabricating metal/polymer composite nanofiber, and this method will broaden the application of metal/polymeric composite nanofibers. Therefore, the polyacrylonitrile/silver nanofibers by an in-situ method carried out to obtain a washable with a high-dispersed silver nanoparticles film to form the hierarchically prepared antibacterial breath mask and antibacterial air filter. Avoid the influence of bacteria from person to environment and atmosphere to a person was the main subject of these researches. The different amount of Silver nanoparticles was loaded into the polyacrylonitrile nanofiber by using silver nitrate and sodium hydroxide solutions. The basic results showed that AgNPs was homogenously loaded in PAN nanofiber matrixes. Furthermore, the release profile based on two-stage release theory showed that when the negligible amount of AgNPs was loaded into the nanofibers, the release significantly decreased whereas antibacterial activity increased. The tremendous potential antibacterial activity of the lowest amount of AgNPs showed controllable AgNPs release from PAN nanofibers that have a direct relationship with the washability could promote the application of the produced product. Contact lens wear can result in adverse events including bacterially-driven corneal infection and inflammation. These are the result of various kinds of bacteria adhering to contact lenses and either initiating infection of the cornea or producing inflammation of the cornea and conjunctiva. In order to reduce the incidence of these events antimicrobial contact lenses are being developed. In this study, antimicrobial contact lenses containing nanoparticles of silver or copper, or a combination of the two, were produced and evaluated. Silver and copper nanoparticles were produced in polyvinyl alcohol (PVA) polymers by incorporating salts of these metals and then reducing the salts to nanoparticles with sodium hydroxide. The nanoparticle-containing polymers were then evaluated for physical characteristics such as tensile strength, water content, and coloration. PVA containing polymers were evaluated for cytotoxicity to mammalian cells

using a standard assay, and for antimicrobial activity using three different tests that measured their ability to inhibit microbial growth on agar plates, inhibit microbial growth in bacterial suspensions, and to inhibit the viability of adherent bacteria. Nanoparticles of between 50-75nm were produced in PVA polymers. The addition of silver or copper nanoparticles doubled the strength of PVA polymers but halved their elongation before fracture. Silver-containing PVA was cytotoxic but PVA containing copper alone was not cytotoxic. In the agar diffusion assay and inhibition of microbial growth in suspension only silver-containing lenses produced antibacterial activity, but silver and copper nanoparticle-containing lenses reduced bacterial adhesion to lenses. Conclusion: both silver and copper nanoparticle-containing lenses were antibacterial, but this depended on the assay used. PVA containing only copper was not cytotoxic. This indicates the copper nanoparticle-containing lenses might be useful to control bacterial colonization of lenses, and hence the production of bacterially-drive adverse events during lens wear.

On the other hand infections could affect on the wound; therefore application of nanofibers loaded by antibacterial nanoparticles was studied as well. Scientific efforts have been made to research and develop an efficient product to be used beyond conventional antibiotic treatments against bacteria and funguses mainly in the wound dressing. Therefore, in this innovative study, the authors investigated the development of hybrid nanofibers of chitosan/polyvinyl alcohol/nano-hydroxyapatite with the composition of copper nanoparticles for wound dressing potential. Therefore, copper/silver with ratio 1:1, copper nanoparticles and silver nanoparticles were chosen as variable to comparison the biocompatibility and antibacterial properties between copper and silver nanoparticles. The nanoparticle loaded to nanofibers by the in-situ method to prepare the chemical bonding between nanofibers and nanoparticles. All characterization results were appreciable for successful synthesis of nano-hydroxyapatite in the nanofibers matrix and loading metallic nanoparticles with chemical reactions between nanoparticles and nanofibers, due to OH deformation of Cs/PVA/nHA nanofibers and reaction with nano-particles. Although the in-vitro results showed PVA/Cs nanofibers loaded with Cu/Ag nanoparticles, is the most appropriate sample for wound dressings because it has very good inhibition zone against the gram-negative and gram-positive bacteria. This composite also has excellent biocompatibility and no toxicity which is good sign for cell attachment and biocompatibility. Thus, another research investigated to the development of different wound dressings from PVA/PAN core-shell nanofiber loaded by gentamicin and amalgam nanofibers of chitosan/polyvinyl alcohol/Nano hydroxyapatite loaded with the silver, silver/copper and copper nanoparticle. The objective of this research was to the preparation and a comparison of the durable antimicrobial wound dressings for persistent infections. The current study, a novel biocompatible core-shell nanofiber structure was successfully developed to be used as promised dual drug carriers, which could deliver both water-soluble and organic solvent-soluble drugs simultaneously. In this process, for the first time, the simple method employed to prepare core nanofiber from polyvinyl alcohol (PVA) which covered by polyacrylonitrile (PAN) and formed a core-shell nanofiber, which both have the ability to carrying the various drugs.

In separate research, related to the application of nanofibers in ophthalmology, a study aimed to produce composite nanofibers scaffolds with high potential bioactivity to encourage epithelization for artificial cornea application and the possibility of using nanohydroxyapatite as the bioactive material in the artificial cornea. An electrospinning method was employed for the preparation of composite nanofibers from polyvinyl alcohol - hydroxyethyl cellulose - graphite that was cross-linked by glutaraldehyde. The prepared scaffolds were subjected to dipping in calcium and phosphate solutions to load different amounts of nHA on the surface of composite nanofibers.