氏名	MA　KE （馬 可）
学位の種類	博士（　工学　　）
学位記番号	甲　第　701　号
学位授与の日付	平成３１年３月２０日
学位授与の要件	信州大学学位規程第５条第１項該当
学位論文題目	Research on development of biomedical nanocomposites in drug delivery system （薬物徐放システムにおけるバイオメディカルナノ複合材料の開発に関する研究　）
論文審査委員	主査　教　授　髙寺　政行 教　授　倪　慶清 准教授　田中　稔久 教　授　玉田　靖 教　授　邱　建輝（秋田県立大学） 教　授　FU SHAOYUN（重慶大学）

論　文　内　容　の　要　旨

Synthesized polymer materials and nature polymer materials are the two classes of conventional materials widely used in different fields such as as filters, wipes, drug delivery systems, biosensors and so on. Over recent decades, the nanocomposites have attracted more attention and versatile exploitations in various applications. In particular, synthesized polymers, such as polycaprolactone (PCL) and nature polymers, such as shellac and silk fibroin (SF), have been reported as efficient candidates for biomedical applications due to their prominent characteristics and performances compared with traditional materials. The nanocomposite applications have been exploited in drug delivery process owing to their large surface areas, high pore volume and stability against thermal and chemical agents. Herein, we introduce a group of smart nanocomposites consisting of controllable drug release rates, and aim to combine good biocompatibility effects and high mechanical effects into one biomedical nanocomposite. The resultant nanocomposites, SF/PU/SF or PCL/shellac/PCL nanofiber composites, are prepared by the one and one layer covering method, and PU/PCL nanofiber composites are fabricated by the blending method. Four kinds of prepared nanocomposites, PU/PCL nanofibrous tubes, PCL multi-layer nanofibrous tubes, SF/PU/SF three layer nanofibrous tubes and PCL/shellac/PCL sandwich structure nanofibers succeed in obtaining good mechanical properties. Especially in the application of skin care system, compared with the untreated PCL/shellac/PCL electrospun nanofiber membranes, the processed nanofiber membranes showed about 8 times tensile strength increase and 38 times Young’s modulus increase.

This dissertation is mainly focus on biomedical nanocomposites which are applied to artificial blood vessels, skin care system and colon/stomach part capsules. For artificial blood vessels, the problem of thrombus has been discussed over decades. Our prepared drug release artificial blood vessels are considered to solve this problem.

A smart method to fabricate nanofiber tubes is proposed and this method is more efficient and easier to control the diameter of nanofibrous tube which compare with traditional steel mandrel method. On the basis of nanofibrous tubes, antithrombotic drug was added into prepared multi-layer PCL nanofibrous tubes. Dual drug release profiles can be obtained and the release rates

can be controlled from 1.5 h to 62.5 days in one prepared tube. These two release profiles correspond to short-term thrombus and long-term thrombus respectively. It proves that the drug release rates of artificial blood vessels show the expected properties. We also try to prepare three layers SF/PU/SF nanofibrous tubes in traditional steel mandrel method. This application combines good biocompatibilities and high mechanical properties. For drug release in skin care system, PCL/shellac/PCL sandwich structure nanofiber membranes are fabricated for the transparence and high mechanical properties. The drug release process is controlled within 8 hours to fit the needs of skin care such as night face mask. For drug release in colon/stomach site system, shellac nanofibers and nanoparticles are studied to find the relationship of physical shapes and chemical properties of nanocomposites with the purpose of controlling the drug release speed. Besides, the strong potential in nano-targeting in drug delivery is revealed by characteristics of nanocomposites.

As a consequence, in this study, we designed release speed, mechanical strength, targeted delivery and even transparency against the needs of applications. This promising merits mainly profit from the characteristics of materials such as high mechanical properties of synthesized polymers (PCL) and good biocompatibility of nature polymers (SF). Besides the single nanofiber membranes, we studied multi-layer structure, sandwich structure and nanocomposites of nanofibers/nanoparticles to obtain applications of controllable release speed, good biocompatibility, mechanical strength and targeted delivery.