（様式 5）

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学位（博士）論文要旨

(Doctoral thesis abstract)

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論 文 題 目 (Title)	Development of temperature-responsive polysaccharide microparticles for pulmonary drug delivery

論文要旨（2000 字程度）
(Abstract(400 words))
※欧文・和文どちらでもよい。但し、和文の場合は英訳を付すこと。
(in English or in Japanese)

The focus of this doctoral thesis is to develop temperature-responsive microparticles for pulmonary administration. In recent years, much attention has been paid to pulmonary administration, i.e., the administration method by which drugs are delivered to the lungs. The particles used for the pulmonary administration need to satisfy the following three conditions for the delivery of drugs to alveoli: an aerodynamic ability to reach alveoli, a proper control of an aerodynamic diameter of the particles (1-5 μm), and a rapid release of drugs. I have selected the polysaccharide (carrageenan) to form a particle. Some polysaccharides have a property of phase transition (sol-gel transition) from solid (gel) to liquid (sol) at appropriate temperatures. Because carrageenan has a negative charge due to its structure, carrageenan-forming particles are expected to improve the encapsulation efficiency of compounds and control the release properties of positively charged compounds.

In the present thesis, I aim to develop temperature-responsive microparticles that rapidly release drugs in the body by an emulsion technique utilizing the sol-gel transition of carrageenan. By emulsifying an organic solvent in which a surfactant is dissolved and an aqueous carrageenan solution, a w/o (water-in-oil) emulsion is formed. When the resulted w/o emulsion is cooled, the carrageenan performs the sol-gel transition. The resulted solution is then dried to form carrageenan microparticles.

In chapter 1, pulmonary administration and drug carriers (general drug carriers, drug carriers for pulmonary administration, and stimuli-responsive carriers) were introduced. In chapter 2, carrageenan particles having a proper diameter, show their temperature-responsive behavior, and aerodynamic properties in order to achieve a highly efficient delivery of the particles to the lungs were prepared. Both of the factors affecting the preparation of the carrageenan microparticles and their *in vitro* aerosol-dispersion performance were evaluated. In chapter 3, (1) the development of

temperature-responsive carrageenan particles by changing the melting point of the polymeric surfactants (amphiphilic block copolymers that stabilize emulsions) used in particle formation by varying the composition of the block copolymers and using the melting of the surfactants oriented on the particle surface as the driving force for particle dissolution, and (2) the investigation of the release properties of the particles were reported. In chapter 4, cationic nanoparticles were encapsulated into the carrageenan microparticles by electrostatic interaction between the sulfate groups of carrageenan and the cationic nanoparticles to enhance the functionality of carrageenan microparticles. The release properties of multiple inclusions from the carrageenan microparticles were evaluated.