DOKTORAND:	Maria Teresa Rebelo Calejo
GRAD:	Philosophiae doctor
FAKULTET:	Det matematisk-naturvitenskapelige fakultet
INSTITUTT:	Farmasøytisk institutt
FAGOMRÅDE:	Galenisk farmasi
VEILEDERE:	Sverre Arne Sande, Bo Nyström, Anna-Lena Kjøniksen
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AVHANDLINGENS TITTEL: *Thermoresponsive polymers in controlled drug delivery and gene delivery*

'Smart' materials that respond to temperature changes showed several advantages in drug delivery.
The main purpose of our project was to develop a liquid formulation that could form a solid gel implant when it was injected into the patient. The intended use of the system was for long term treatment of drug addicts, and an additional requirement was therefore a slow release of drug from the gel and into the systemic circulation, which would contribute to achieve a long-standing effect. Ultimately, this kind of system is anticipated to increase patient compliance.
Temperature was chosen as the key trigger for gel-formation. The temperature-responsiveness of the formulation was achieved by combining a cellulose derivative and low toxicity surfactants. The gels that were formed at body temperature were soft, suggesting that they would be comfortable for the patients.
In this project, it was hypothesized that the combination of the solid gel implant with drug-loaded microparticles could help to achieve the envisioned slow drug release. The chosen drug was naltrexone, used in the treatment of opioid addiction. A reduced drug release rate was observed when a hydrophobically modified chitosan, obtained from the shells of shrimp and crab, was used to produce the microparticles. In this case, naltrexone was released for over 50 days into a physiological medium. This suggests that a long-term effect can be attained after only one injection.
During our research we discovered that the temperature-responsive polymers had a potential as carriers for DNA, in gene delivery applications. Gene therapy is a very promising option in the treatment of a number of chronic and life-threatening conditions such as cancer. One approach in gene therapy is to deliver DNA into the nucleus of the cells, where a 'good gene' can replace an 'abnormal', disease-causing gene. In this methodology, the genetic material is incorporated into a carrier, which facilitates the difficult pathway crossing several biological membranes and reaching the nucleus of the cells. In our work, four different temperature-responsive polymers showed to effectively deliver the DNA into the nucleus of cells. The efficiency depended on the structure of the polymer and the used amount. When we looked at the structures formed by the DNA with the polymer carriers, we could relate the effects to the properties of the polymers at different temperatures.
In conclusion, our work opened a new window into the development of 'smart' systems that respond to temperature changes, enhancing the efficacy of the treatment of chronic or severe diseases.