Research outputs:

Preparation and Characterization of an Oral Vaccine Formulation Using Electrosprayed Chitosan Microparticles
Chitosan particles loaded with the antigen ovalbumin (OVA) and the adjuvant Quil-A were produced by electrospray, using mixtures of water/ethanol/acetic acid as a solvent. Three different chitosans designed as HMC+70, HMC+85, and HMC+90 (called as 705010, 855010, and 905010) were tested and its efficacy to be used in oral vaccine delivery applications was investigated. The morphology, size, and zeta potential of the produced particles were investigated, together with the encapsulation efficiency and release of OVA from the three chitosan formulations. Moreover, the mucoadhesion and cytotoxicity of the chitosan microparticles was examined. All the three formulations with OVA and Quil-A were in the micrometer size range and had a positive zeta potential between 46 and 75 mV. Furthermore, all the three formulations displayed encapsulation efficiencies above 80% and the release of OVA over a period of 80 h was observed to be between 38 and 47%. None of the developed formulations exhibited high mucoadhesive properties, either cytotoxicity. The formulation prepared with HMC+70, OVA, and Quil-A had the highest stability within 2 h in buffer solution, as measured by dynamic light scattering. The electrosprayed formulation consisting of HMC+70 with OVA and Quil-A showed to be the most promising as an oral vaccine system.

General information
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Organisations: National Food Institute, Research Group for Nano-Bio Science, Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Technical University of Denmark
Contributors: Moreno, J. A. S., Panou, D., Stephansen, K., Chronakis, I. S., Boisen, A., Mendes, A. C. L., Nielsen, L. H.
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BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.59 SJR 0.752 SNIP 1.101
Web of Science (2017): Impact factor 2.666
Cellular effects and delivery propensity of penetratin is influenced by conjugation to parathyroid hormone fragment 1-34 in synergy with pH

The cell-penetrating peptide (CPP) penetratin, has demonstrated potential as a carrier for transepithelial delivery of cargo peptides, such as the therapeutically relevant part of parathyroid hormone, i.e. PTH(1-34). The purpose of the present study was to elucidate the relevance of modifying the pH for PTH(1-34)-penetratin conjugates and for co-administered penetratin with PTH(1-34) in terms of transepithelial permeation of PTH(1-34) and cellular effects. Transepithelial permeation was assessed using monolayers of the Caco-2 cell culture model, and effects on Caco-2 cellular viability kinetics were evaluated by using the Real-Time-GLO assay as well as by microscopy following Trypan blue staining. Morphological Caco-2 cell changes were studied exploiting the impedance-based xCELLigence system as well as optically using the oCelloscope setup. Finally, the effect of pH on the folding propensity of the PTH(1-34)-penetratin conjugate and its ability to disrupt lipid membranes were assessed by circular dichroism (CD) spectroscopy and the calcein release assay, respectively. The transepithelial PTH(1-34) permeation was not pH-dependent when applying the co-administration approach. However, by applying the conjugation approach, the PTH(1-34) permeation was significantly enhanced by lowering the pH from 7.4 to 5, but also associated with a compromised barrier and a lowering of the cellular viability. The negative effects on the cellular viability following cellular incubation with the PTH(1-34)-penetratin conjugate were moreover confirmed during real-time monitoring of the Caco-2 cell viability as well as by enhanced Trypan blue staining.
uptake. In addition, morphological changes were primarily observed for cells incubated with the PTH(1-34)-penetratin
conjugate at pH 5, which was moreover demonstrated to have an enhanced membrane permeating effect following
lowering of the pH from 7.4 to 5. The latter observation was, however, not a result of better secondary folding propensity at
pH 5 when compared to pH 7.4.
Development of electrosprayed mucoadhesive chitosan microparticles

The efficacy of chitosan (CS) to be used as drug delivery carrier has previously been reported. However, limited work has been pursued to produce stable and mucoadhesive CS electrosprayed particles for oral drug delivery, which is the aim of this study. Various CS types with different molecular weight (MW), degree of deacetylation (DD), and degree of polymerization (DP) were assessed. In addition, the effect of the solvent composition was also investigated. Results showed that stable CS electrosprayed particles can be produced by dissolving 3% w/v of low MW CS in mixtures of aqueous acetic acid and ethanol (50/50% v/v). The stable CS particles displayed diameters of approximately 1 μm as determined by dynamic light scattering. The zeta potential of these particles was found to be approximately 40 mV confirming the mucoadhesion properties of these CS electrosprayed particles and its potential to be used as drug delivery carrier.

General information
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Organisations: National Food Institute, Research Group for Nano-Bio Science, Department of Micro- and Nanotechnology, Nanoprobes, University of Münster
Contributors: Moreno, J. A. S., Mendes, A. C., Stephansen, K., Engwer, C., Goycoolea, F. M., Boisen, A., Nielsen, L. H., Chronakis, I. S.
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Scopus rating (2017): CiteScore 5.58 SJR 1.428 SNIP 1.733
Web of Science (2017): Impact factor 5.158
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.15 SJR 1.419 SNIP 1.75
Web of Science (2016): Impact factor 4.811
Web of Science (2016): Indexed yes
Drug loaded biodegradable polymer microneedles fabricated by hot embossing

This study demonstrates a fast low temperature method for fabrication of drug loaded polymer microneedles (MNs). First, arrays of tapered pillar MNs with a length of 275 ± 3 μm (mean ± SD) and a diameter of 84 ± 1 μm were fabricated in Si with a three-step deep reactive ion etching (DRIE) process. The Si MNs were used as a template for fabrication of polydimethylsiloxane (PDMS) stamps. The stamps were applied for replication of the MNs in spin coated
poly-ε-caprolactone (PCL) films by hot embossing at 60 °C and a pressure of 1.4 MPa for 3 min. The resulting PCL MNs perfectly resembled the Si MNs and had a length of 270 ± 5 μm and a diameter of 84 ± 3 μm. The MNs had sufficient mechanical strength to penetrate the surface of a 10 w/w% gelatine gel without deformation. Finally, PCL MNs containing 20 w/w% of furosemide were fabricated and drug release by diffusion was demonstrated.
Effects of water-absorption and thermal drift on a polymeric photonic crystal slab sensor

A photonic crystal slab (PCS) sensor is a universal refractive index sensor with possibilities and performance very similar to surface plasmon resonance (SPR), which represents the gold standard of biosensing. Cheap PCS sensors can be made vacuum-free entirely out of polymers, but come with additional challenges, besides those relating to temperature-variations, which must be considered in any refractive index based method: The polymeric waveguide core was found to swell by 0.3% as water absorbed into the waveguide core over 1.5 h. This was investigated by monitoring the wavelength of resonant reflection during absorption, by monitoring the release of water using ellipsometry, and by rigorous coupled-wave analysis (RCWA). The approach presented here enables monitoring of water uptake and thermal fluctuations, for drift-free, high-performance operation of a polymeric PCS sensor.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Optofluidics, Technical University of Denmark
Contributors: Sørensen, K. T., Ingvorsen, C. B., Nielsen, L. H., Kristensen, A.
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Web of Science (2017): Impact factor 3.356
Web of Science (2017): Indexed yes
Microfabricated devices for oral drug delivery

Oral administration of drugs is most convenient for patients and therefore the ultimate goal when developing new medication. The physical barriers in the body, low pH of the stomach and degradation by enzymes in the gastrointestinal tract are a few of the obstacles to succeeding with oral drug delivery. Microfabricated devices show promise to overcome some of these hindrances and thereby improve the bioavailability of drugs after oral administration. There is an increasing focus on microfabricated oral drug delivery systems, and so far there have been three main groups of designs: patch-like structures, microcontainers and microwells. Here, we review the newest development in top-down microfabricated devices for oral drug delivery with coverage of the aspects of design, choice of material and fabrication techniques. Furthermore, the drug loading techniques and methods for testing are discussed. In addition, we discuss the future perspectives for microfabricated devices.

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Contributors: Nielsen, L. H., Keller, S. S., Boisen, A.
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BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 6.05 SJR 2.158 SNIP 1.586
Web of Science (2017): Impact factor 5.995
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.98 SJR 2.162 SNIP 1.569
Web of Science (2016): Impact factor 6.045
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 5.74 SJR 2.239 SNIP 1.721
Web of Science (2015): Impact factor 5.586
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 5.6 SJR 2.555 SNIP 1.797
Web of Science (2014): Impact factor 6.115
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 5.9 SJR 2.397 SNIP 1.693
Web of Science (2013): Impact factor 5.748
Spray dried cubosomes with ovalbumin and Quil-A as a nanoparticulate dry powder vaccine formulation

Subunit vaccine formulations are often produced as liquid dispersions through complicated processes. It is desirable, however, to have simple, cheap and up-scalable methods to produce nanoparticulate subunit vaccines in powder form. Here, a simple single-step spray drying process for production of powder cubosome precursors with the model antigen ovalbumin (OVA) and the adjuvant Quil-A is presented. The cubosomes were characterized in vitro and evaluated in vivo by subcutaneous and oral administration for their potential as a vaccine formulation. Hydrated cubosomes had average particle size of 257±8nm and zeta potential of −18.0±0.6mV. The powder contained 10.6±0.7% w/w OVA prior to hydration, of which 65±1% was released within the first 20min in 9.5mM PBS at pH 7.3, with the remaining OVA gradually released over the following 24h. Immunization with cubosomes resulted in significantly stronger antigen-specific serum IgG responses (p<0.01), CD8+ T cell expansion (p<0.0001) and target T cell killing compared to controls when given s.c., and was ineffective orally. This study shows that spray drying is a suitable method for producing nanoparticulate vaccine formulations in dry powder form.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Otago, University of Copenhagen, Monash University
Animal models for evaluation of oral delivery of biopharmaceuticals

Biopharmaceuticals are increasingly important for patients and the pharmaceutical industry due to their ability to treat and, in some cases, even cure chronic and potentially life-threatening diseases. Most biopharmaceuticals are administered by injection, but intensive focus on development of systems for oral delivery of biopharmaceuticals may result in new treatment modalities to increase the patient compliance and reduce product cost. In the preclinical development phase, use of experimental animal models is essential for evaluation of new formulation designs. In general, the limited oral bioavailability of biopharmaceuticals, of just a few percent, is expected, and therefore, the animal models and the experimental settings must be chosen with utmost care. More knowledge and focus on this topic is highly needed, despite experience from the numerous studies evaluating animal models for oral drug delivery of small molecule drugs. This review highlights and discusses pros and cons of the most currently used animal models and settings. Additionally, it also looks into the influence of anesthetics and sampling methods for evaluation of drug delivery systems for oral delivery of biopharmaceuticals primarily with examples on insulin.

General information

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Harloff-Helleberg, S., Nielsen, L. H., Nielsen, H. M.
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BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 7.56 SJR 2.463 SNIP 1.85
Web of Science (2016): Impact factor 7.786
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 8.11 SJR 2.738 SNIP 2.074
Web of Science (2015): Impact factor 7.441
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Ciprofloxacin-loaded sodium alginate/poly (lactic-co-glycolic acid) electrospun fibrous mats for wound healing

Wound dressings should ideally be able to maintain high humidity, remove excess wound exudate, permit thermal insulation, provide certain mechanical strength, and in some cases deliver antibiotics to prevent infections. Until now, none of the existing wound dressing products can meet all these requirements. To design a wound dressing with as many of the aforementioned features as possible, in this study, we attempted to prepare ciprofloxacin (CIP), an antibiotic, loaded electrospun hydrophobic poly (lactic-co-glycolic acid) (PLGA) fibrous mats modified with hydrophilic sodium alginate (ALG) microparticles. The results showed that ALG could improve the wettability, water absorption capacity, and enhance the release rate of ciprofloxacin from the PLGA fibrous mats. In addition, the addition of ALG reduced the stiffness of PLGA fibrous mats for better protection of the injured area as indicated by the Young's Modulus. Moreover, the burst release of CIP resulted from the addition of ALG seemed to provide an improved antibacterial effect to the PLGA mats. This study demonstrated the potential of combining hydrophilic and hydrophobic polymers to design the desired wound dressings via the electrospinning process.
Development of a Video-Microscopic Tool To Evaluate the Precipitation Kinetics of Poorly Water Soluble Drugs: A Case Study with Tadalafil and HPMC

Many drug candidates today have a low aqueous solubility and, hence, may show a low oral bioavailability, presenting a major formulation and drug delivery challenge. One way to increase the bioavailability of these drugs is to use a supersaturating drug delivery strategy. The aim of this study was to develop a video-microscopic method, to evaluate the effect of a precipitation inhibitor on supersaturated solutions of the poorly soluble drug tadalafil, using a novel video-microscopic small scale setup. Based on preliminary studies, a degree of supersaturation of 29 was chosen for the supersaturation studies with tadalafil in FaSSIF. Different amounts of hydroxypropyl methyl cellulose (HPMC) were predissolved in FaSSIF to give four different concentrations, and the supersaturated system was then created using a solvent shift method. Precipitation of tadalafil from the supersaturated solutions was monitored by video-microscopy as a function of time. Single-particle analysis was possible using commercially available software; however, to investigate the entire population of precipitating particles (i.e., their number and area covered in the field of view), an image analysis algorithm was developed (multiparticle analysis). The induction time for precipitation of tadalafil in FaSSIF was significantly prolonged by adding 0.01% (w/v) HPMC to FaSSIF, and the maximum inhibition was reached at 0.1% (w/v) HPMC, after which additional HPMC did not further increase the induction time. The single-particle and multiparticle analyses yielded the same ranking of the HPMC concentrations, regarding the inhibitory effect on precipitation. The developed small scale method to assess the effect of precipitation inhibitors can speed up the process of choosing the right precipitation inhibitor and the concentration to be used.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen, Philips Biocell
Contributors: Christfort, J. F., Plum, J., Madsen, C. M., Nielsen, L. H., Sandau, M., Andersen, K., Müllertz, A., Rades, T.
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Scopus rating (2017): CiteScore 4.86 SJR 1.572 SNIP 1.24
Web of Science (2017): Impact factor 4.556
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.84 SJR 1.538 SNIP 1.213
Web of Science (2016): Impact factor 4.44
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
This work explores the potential of polymeric micrometer sized devices (microcontainers) as oral drug delivery systems (DDS). Arrays of detachable microcontainers (D-MCs) were fabricated on a sacrificial layer to improve the handling and facilitate the collection of individual D-MCs. A model drug, ketoprofen, was loaded into the microcontainers using supercritical CO2 impregnation, followed by deposition of an enteric coating to protect the drug from the harsh gastric environment and to provide a fast release in the intestine. In vitro, in vivo and ex vivo studies were performed to assess the viability of the D-MCs as oral DDS. D-MCs improved the relative oral bioavailability by 180% within 4h, and increased the absorption rate by 2.4 times compared to the control. This work represents a significant step forward in the translation of these devices from laboratory to clinic.
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Scopus rating (2017): CiteScore 7.9 SJR 2.684 SNIP 1.802
Web of Science (2017): Impact factor 7.877
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BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 7.56 SJR 2.463 SNIP 1.85
Web of Science (2016): Impact factor 7.786
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 8.11 SJR 2.738 SNIP 2.074
Web of Science (2015): Impact factor 7.441
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 6.86 SJR 2.438 SNIP 2.092
Web of Science (2014): Impact factor 7.705
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 6.31 SJR 2.441 SNIP 2.023
Web of Science (2013): Impact factor 7.261
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 5.84 SJR 2.454 SNIP 2.075
Web of Science (2012): Impact factor 7.633
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 6.33 SJR 2.763 SNIP 2.089
Web of Science (2011): Impact factor 6.499
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.225 SNIP 2.307
Web of Science (2010): Impact factor 7.164
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 2.922 SNIP 2.033
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 2.272 SNIP 1.895
Scopus rating (2007): SJR 2.168 SNIP 1.81
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.788 SNIP 1.779
Scopus rating (2005): SJR 1.57 SNIP 1.826
Scopus rating (2004): SJR 1.485 SNIP 1.775
Microcontainers as an oral delivery system for spray dried cubosomes containing ovalbumin

The purpose of this study was to prepare cubosomes encapsulating the model antigen ovalbumin (OVA) via spray drying, and to characterise such cubosomes with a view for their potential application in oral vaccine delivery. Furthermore the cubosome formulation was loaded into polymeric microcontainers intended as an oral drug delivery system. The cubosomes consisted of commercial glyceryl monooleate, Dimodan®, containing OVA and were surrounded with a dextran shell prepared by spray drying. Cryo-TEM was used to confirm that cubosomes were formed after hydration of the spray dried precursor powder. The precursor powder had a mean particle size of 1.3±0.1μm, whereas the mean diameter of the dispersed cubosomes was 282±7nm (PDI: 0.18) measured by dynamic light scattering. 8.5±0.3% (w/w) of OVA was present in the cubosome powder and OVA was found released slowly over the first 70h, followed by a more rapid release. Total release of 47.9±2.8% of loaded OVA occurred over 96h in a buffer at pH 6.8. When the powder was filled into microcontainers, and the opening covered with the pH sensitive polymer Eudragit S100, the pH sensitive 'lid' was intact at gastric pH, but release of OVA from the cubosomes and microcontainers occurred at pH 6.8, releasing 44.1±5.6% of the OVA in 96h. Small-angle X-ray scattering (SAXS) revealed that the 'dry' particles possessed an internal ordered lipid structure (lamellar and inverse micellar phase) by virtue of a small amount of residual water, and after hydration in buffer at pH 6.8, the particles formed the hexagonal inverse cubic phases, thereby indicating that cubosomes were formed when released from microcontainers.
MICROCONTAINERS FOR INTESTINAL DRUG DELIVERY: in vivo and ex vivo study

**General information**

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Microcontainers for Oral Vaccine Delivery

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Contributors: Nielsen, L. H., von Halling Laier, C., Boisen, A.
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SustainAbstracts2017c.compressed_89.pdf
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Nanomechanical Infrared Spectroscopy with Vibrating Filters for Pharmaceutical Analysis

Standard infrared spectroscopy techniques are well-developed and widely used. However, they typically require milligrams of sample and can involve time-consuming sample preparation. A promising alternative is represented by nanomechanical infrared spectroscopy (NAM-IR) based on the photothermal response of a nanomechanical resonator, which enables the chemical analysis of picograms of analyte directly from a liquid solution in only a few minutes. Herein, we present NAM-IR using perforated membranes (filters). The method was tested with the pharmaceutical compound indomethacin to successfully perform a chemical and morphological analysis on roughly 100 pg of sample. With an absolute estimated sensitivity of 109±15 fg, the presented method is suitable for ultrasensitive vibrational spectroscopy.

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Silicon Microtechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Technical University of Denmark, University of Copenhagen, Vienna University of Technology
Contributors: Kurek, M., Camoy, M., Larsen, P. E., Nielsen, L. H., Hansen, O., Rades, T., Schmid, S., Boisen, A.
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BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 11.31 SJR 6.155 SNIP 2.165
Web of Science (2017): Impact factor 12.102
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 10.8 SJR 5.954 SNIP 2.146
Web of Science (2016): Impact factor 11.994
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 11.13 SJR 5.888 SNIP 2.225
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Powder embossing method for selective loading of polymeric microcontainers with drug formulation

The present study introduces powder embossing as a novel method to enhance loading of polymeric microcontainers with drug. With current loading approaches, it is not possible to handle pure powder drug in a scalable, homogenous and reproducible manner. In this work, we demonstrate simultaneous loading of 625 microcontainers with powder formulation. This is achieved in a single step by aligning a shadow mask prepared by micro-milling to an array of microcontainers in
order to limit drug deposition to the container cavities with diameters of 220 μm. A pressure of 8.9 MPa is applied by a bonding press and thereby the desired powder is embossed into the container cavities. Powder in the form of pure drug, lipid-based microparticles, and pure polymer was successfully loaded with minimal residues in between the microcontainers and with 100% loaded cavities demonstrating the versatility of the method. The current work is thus contributing to the loading of powder formulations into microscale drug delivery systems such as microcontainers in a facile and reproducible manner.

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BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 1.87 SJR 0.604 SNIP 0.937
Web of Science (2017): Impact factor 2.02
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Impact factor 1.806
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 1.35 SJR 0.507 SNIP 0.796
Web of Science (2015): Impact factor 1.277
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 1.44 SJR 0.586 SNIP 0.86
Web of Science (2014): Impact factor 1.197
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 1.45 SJR 0.595 SNIP 0.964
Web of Science (2013): Impact factor 1.338
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 1.44 SJR 0.737 SNIP 0.949
Web of Science (2012): Impact factor 1.224
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 1.8 SJR 0.813 SNIP 1.148
Web of Science (2011): Impact factor 1.557
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.934 SNIP 1.093
Web of Science (2010): Impact factor 1.575
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.834 SNIP 1.098
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.027 SNIP 1.06
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.045 SNIP 1.138
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.966 SNIP 1.093
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.952 SNIP 0.989
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1 SNIP 1.1
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.812 SNIP 0.956
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.712 SNIP 0.711
Scopus rating (2001): SJR 0.558 SNIP 0.645
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Web of Science (2000): Indexed yes
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Development of a video-microscopic method to compare the effect of a precipitation inhibitor

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Christfort, J., Plum, J., Madsen, C., Nielsen, L. H., Müllertz, A., Rades, T.
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Event: Poster session presented at 2016 AAPS Annual Meeting and Exposition, Denver, CO, United States.
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Development of a video-microscopic method to compare the effect of precipitation inhibitors

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Christfort, J. F., Plum, J., Madsen, C. M., Nielsen, L. H., Müllertz, A., Rades, T.
Publication date: 2016
Peer-reviewed: No
Event: Abstract from 10th Annual Meeting of the Pharmaceutical Solid State Research Cluster, Copenhagen, Denmark.
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Electrospraying Chitosan Particles for Oral Vaccine Delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, National Food Institute, Research Group for Nano-Bio Science
Publication date: 2016
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Electronic versions:
Abstract_AAPS_2016_electrospray.pdf

Bibliographical note
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Research output: Research - peer-review › Conference abstract for conference – Annual report year: 2016

Electrospraying particles for loading into microcontainers for drug delivery

General information
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Organisations: National Food Institute, Research Group for Nano-Bio Science, Department of Micro- and Nanotechnology, Nanoprobes
Contributors: Sevilla Moreno, J. A., Boutrup Stephansen, K., Nielsen, L. H., Chronakis, I. S., Boisen, A.
Publication date: 2016
Peer-reviewed: Yes
Event: Abstract from 42nd International conference on Micro and Nano Engineering, Vienna, Austria.
Electronic versions:
Electrospraying_particles_for_loading_into_microcontainers_for_drug_delivery.pdf

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Source-ID: 127315846
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Microcontainers - an oral drug delivery system for poorly soluble drugs

In oral delivery, it can sometimes be necessary to employ drug delivery systems to achieve targeted delivery to the intestine. Microcontainers are polymeric, cylindrical devices in the micrometer size range (Figure 1), and are suggested as a promising oral drug delivery system [1],[2]. The purpose of these studies was to fabricate microcontainers in either SU-8 or biodegradable poly-L-lactic acid (PLLA), and fill the microcontainers with poorly soluble drugs. Furthermore, the application of the microcontainers as an oral drug delivery system was investigated in terms of release, in situ intestinal perfusion and oral bioavailability. SU-8 microcontainers were fabricated using lithography resulting in microcontainers with an inner diameter of 220 μm. The PLLA microcontainers were prepared by hot embossing with inner diameter of 240 μm (Figure 1). In terms of drug filling, the SU-8 microcontainers were filled with polyvinylpyrrolidone (PVP) by inkjet printing followed by supercritical CO2 impregnation of ketoprofen into the PVP matrix. As an alternative filling method, the powder of amorphous sodium salt of furosemide, (ASSF) was filled into the SU-8 microcontainers. The PLLA microcontainers were filled with drug formulation by embossing the microcontainers into a polycaprolactone (PCL) and furosemide (4:1 w/w) layer. For the ASSF-filled microcontainers, an enteric-resistant lid of Eudragit L100 was spray coated onto the cavity of the microcontainers. From coated ASSF-filled microcontainers, a fast release in simulated intestinal medium at pH 6.5 was observed. In situ intestinal perfusions were performed in rats of the Eudragit-coated ASSF-filled microcontainers and compared to a furosemide solution. At the end of the study, the small intestine was harvested from the rat and imaged under a light microscope. The absorption rate constant of ASSF was 1.5 fold higher, when ASSF was confined in the microcontainers compared to a furosemide solution. Micrographs of the small intestine after the perfusion showed that the microcontainers were engulfed by the intestinal mucus. For the in vivo studies, the rats were dosed orally with capsules containing ASSF-filled microcontainers coated with Eudragit L100. As control, capsules were filled with the powder of ASSF and the capsules were coated with Eudragit L100. The oral bioavailability study showed that the relative oral bioavailability of ASSF in microcontainers is 220±43% when compared to drug-filled capsules coated with Eudragit
Microcontainers - an oral drug delivery system for poorly soluble drugs

Microcontainers as an oral drug delivery system

Microcontainers as an Oral Drug Delivery System
Polymeric microcontainers improve oral bioavailability of furosemide

Microcontainers with an inner diameter of 223μm are fabricated using the polymer SU-8, and evaluated in vitro, in situ and in vivo for their application as an advanced oral drug delivery system for the poorly water soluble drug furosemide. An amorphous sodium salt of furosemide (ASSF) is filled into the microcontainers followed by applying a lid using Eudragit L100. It is possible to control the drug release in vitro, and in vitro absorption studies show that the microcontainers are not a hindrance for absorption of ASSF. In situ perfusion studies in rats are performed with ASSF-filled microcontainers coated with Eudragit and compared to a furosemide solution. The absorption rate constant of ASSF confined in microcontainers is found to be significantly different from the solution, and by light microscopy, it is observed that the microcontainers are engulfed by the intestinal mucus. An oral bioavailability study in rats is performed with ASSF confined in microcontainers coated with Eudragit and a control group with ASSF in Eudragit-coated capsules. A relative bioavailability of 220% for the ASSF in microcontainers compared to ASSF in capsules is found. These studies indicate that the microcontainers could serve as a promising oral drug delivery system.
Scopus rating (2013): CiteScore 4.17 SJR 1.377 SNIP 1.605
Web of Science (2013): Impact factor 3.785
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 4.1 SJR 1.552 SNIP 1.637
Web of Science (2012): Impact factor 3.458
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 4.01 SJR 1.493 SNIP 1.619
Web of Science (2011): Impact factor 3.35
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.574 SNIP 1.608
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Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.399 SNIP 1.53
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.227 SNIP 1.575
Scopus rating (2007): SJR 1.186 SNIP 1.527
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.995 SNIP 1.398
Scopus rating (2005): SJR 1.043 SNIP 1.589
Scopus rating (2004): SJR 1.045 SNIP 1.464
Scopus rating (2003): SJR 0.981 SNIP 1.355
Scopus rating (2002): SJR 0.793 SNIP 1.265
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.74 SNIP 1.047
Web of Science (2001): Indexed yes
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Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.616 SNIP 0.978
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Research output: Research - peer-review › Journal article – Annual report year: 2016

Spray Drying of Cubosomes for Oral Vaccine Delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark, University of Copenhagen
Publication date: 2016
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Event: Poster session presented at 2016 AAPS Annual Meeting and Exposition, Denver, CO, United States.
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A triple co-culture cell model of Caco-2 cells, dendritic cells and macrophages (Figure 1) has previously been developed for studying intestinal permeability in a state of inflammation [1],[2]. The aim of this study was to investigate the applicability of this cell model for testing the immunostimulatory ability of particulate vaccine formulations designed for oral delivery. Levels of cytokine production in response to vaccine administration were measured following particulate vaccine administration, as an indication of dendritic cell and macrophage activation. Precursors of cubosomes containing the model antigen ovalbumin was spray dried to obtain a particulate vaccine model system for testing in the cell model. The precursors were shown to form cubosomes when dispersed in aqueous medium, and was therefore used as the vaccine formulation for testing on the co-cultures. After 11 days, the TEER values of the co-cultures were found to be 860-1340 Ω·cm²; the formulations were incubated with the co-cultures at this time point. From confocal microscopy images, it was observed that the THP-1 cells (macrophages) migrated into the overlying Caco-2 cell monolayer when the co-cultures were incubated with particle formulations. This was not the case when incubating with ovalbumin solution or blank. The ELISA screening assay showed production of a wide range of cytokines following culture incubation with cubosomes (with and without ovalbumin) and LPS solutions, indicative of a stimulatory effect; this was not observed with ovalbumin and blank solution. An example of the results is shown in Figure 2 for IL-17A. An established co-culture of Caco-2, THP-1 and MUTZ-3 cells showed promise as an in vitro model for testing of oral vaccine formulations. Mobility of co-culture immune cells as well as cytokine production observed following treatment with spray dried cubosomes as a particulate vaccine formulation will be further investigated.
Triple co-culture cell model as an in vitro model for oral particulate vaccine systems

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Helmholtz Institute for Pharmaceutical Research Saarland, Saarland University, University of Copenhagen, Monash University
Contributors: Nielsen, L. H., De Rossi, C., Lehr, C., Rades, T., Boyd, B., Boisen, A., Gordon, S.
Publication date: 2016
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Microcontainers - an oral drug delivery system for poorly soluble drugs

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Valencia, University of Copenhagen
Contributors: Nielsen, L. H., Petersen, R. S., Marizza, P., Keller, S. S., Melero, A., Rades, T., Müllertz, A., Boisen, A.
Number of pages: 2
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Event: Abstract from 2015 AAPS Annual Meeting and Exposition, Orlando, FL, United States.
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Research output: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Microcontainers as an oral drug delivery system

General information
State: Published
Organisations: Biomaterial Microsystems, Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, University of Copenhagen
Contributors: Petersen, R. S., Nielsen, L. H., Marizza, P., Keller, S. S., Rades, T., Müllertz, A., Boisen, A.
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Research output: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

Microcontainers improve oral bioavailability of furosemide

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Biomaterial Microsystems, University of Valencia, University of Copenhagen

Microcontainers improve oral bioavailability of furosemide

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Biomaterial Microsystems, University of Valencia, University of Copenhagen
Microcontainers improve oral bioavailability of furosemide

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Valencia, University of Copenhagen
Contributors: Nielsen, L. H., Melero, A., Keller, S. S., Rades, T., Müllertz, A., Boisen, A.
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Event: Poster session presented at 1st European Conference on Pharmaceutics, Reims, France.
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Research output: Research - peer-review › Poster – Annual report year: 2015

pH-triggered drug release from biodegradable microwells for oral drug delivery

Microwells fabricated from poly-L-lactic acid (PLLA) were evaluated for their application as an oral drug delivery system using the amorphous sodium salt of furosemide (ASSF) as a model drug. Hot embossing of PLLA resulted in fabrication of microwells with an inner diameter of 240 μm and a height of 100 μm. The microwells were filled with ASSF using a modified screen printing technique, followed by coating of the micowell cavities with a gastroresistant lid of Eudragit® L100. The release behavior of ASSF from the coated microwells was investigated using a μ-Diss profiler and a UV imaging system, and under conditions simulating the changing environment of the gastrointestinal tract. Biorelevant gastric medium (pH 1.6) was employed, after which a change to biorelevant intestinal release medium (pH 6.5) was carried out. Both μ-Diss profiler and UV imaging release experiments showed that sealing of microwell cavities with an Eudragit® layer prevented drug release in biorelevant gastric medium. An immediate release of the ASSF from coated microwells was observed in the intestinal medium. This pH-triggered release behavior demonstrates the future potential of PLLA microwells as a site-specific oral drug delivery system.

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Saarland University, University of Copenhagen
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Publication information
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.07 SJR 0.538 SNIP 0.639
Web of Science (2017): Impact factor 2.077
Polymeric microcontainers improve oral bioavailability of a poorly soluble drug

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Valencia, University of Copenhagen
Contributors: Nielsen, L. H., Melero, A., Keller, S. S., Rades, T., Müllertz, A., Boisen, A.
Number of pages: 2
Publication date: 2015
Peer-reviewed: Yes
Electronic versions:
Polymeric_microcontainers_improve_oral_bioavailability_of_a_poorly_soluble_drug.pdf

Bibliographical note
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Spray drying of cubosomes for oral vaccine delivery

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Helmholtz Institute for Pharmaceutical Research Saarland, University of Copenhagen, Monash University
Contributors: Nielsen, L. H., Gordon, S., Rades, T., Boyd, B.
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Publication date: 2015
Peer-reviewed: Yes
Event: Abstract from 2015 AAPS Annual Meeting and Exposition, Orlando, FL, United States.
Electronic versions:
Abstract_AAPS_2015_cubosomes.pdf

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
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Stabilisation of amorphous furosemide increases the oral drug bioavailability in rats
A glass solution of the amorphous sodium salt of furosemide (ASSF) and polyvinylpyrrolidone (PVP) (80: 20 w/w%) was prepared by spray drying. It was investigated if PVP was able to stabilise ASSF during storage and dissolution and whether this influenced the in vivo performance of the glass solution after oral dosing to rats. The glass solution had a glass transition temperature of 121.3 ± 0.5 degrees C, which was significantly higher than that of the pure drug (101.2 degrees C). ASSF in the glass solution was stable for at least 168 days when stored at 20 degrees C and 0% relative humidity. The glass solution exhibited fast dissolution in simulated intestinal medium, pH 6.5; the intrinsic dissolution rate was found to be 10.1 ± 0.6 mg/cm(2)/min, which was significantly faster than the pure ASSF. When investigating the stability during dissolution in simulated intestinal medium at pH 6.5, the ASSF in the glass solution showed signs of crystallinity after 1 min of dissolution, but crystallised to a lesser extent than pure ASSF. The stabilising effect of PVP on ASSF, led to improved relative oral bioavailability in rats of 263%, when compared to the pure ASSF. (C) 2015 Elsevier B.V. All rights reserved.

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Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, University of Copenhagen
Contributors: Nielsen, L. H., Rades, T., Müllertz, A.
Number of pages: 7
Pages: 334-340
Publication date: 2015
Peer-reviewed: Yes
Drug Formulations for Microcontainers

The purpose of this PhD thesis was to investigate the potential of microcontainers as an oral drug delivery system with mucoadhesive properties for poorly water soluble drugs.

Microcontainers are small polymeric devices consisting of a flat base with a walled reservoir. In the studies described in this thesis the microcontainers were either fabricated from SU-8, or from the biopolymer, poly-L-lactic acid (PLLA). The microcontainers were to be filled with a poorly soluble drug/formulation. In early work, the solubility and dissolution rate of furosemide, a poorly soluble drug intended for use with the microcontainers, was improved by employing the strategy of converting the drug into an amorphous salt form. Amorphous furosemide sodium salt was prepared by spray drying and characterised in vitro and in vivo. The amorphous salt was found to exhibit a high physical stability at ambient storage conditions, as well as a significantly greater biorelevant apparent solubility and dissolution rate compared to both amorphous and crystalline acid of furosemide. However, the amorphous salt demonstrated instability during biorelevant dissolution, and converted immediately at the point of drug wetting to a trihydrate form of furosemide. Following oral dosing of amorphous salt, and amorphous and crystalline acid forms of furosemide to rats, the amorphous salt was found to exhibit a faster Tmax compared to the two other forms. In an attempt to improve the stability of amorphous furosemide during storage and dissolution, solid dispersions containing hydroxypropyl methylcellulose (HPMC) were prepared by spray drying. It was found that 20 w/w% HPMC was sufficient for stabilising amorphous furosemide during storage, but from a dissolution point of view, 80 w/w% HPMC was required for stabilising the amorphous furosemide form during biorelevant dissolution. Following characterisation and optimisation, furosemide drug powder was filled into the microcontainers by direct filling. The furosemide-filled microcontainers were spray coated with a protective lid of the pH-sensitive polymer, Eudragit L100 (dissolution at pH > 6), and the release of furosemide from sealed microcontainers was investigated in biorelevant gastric (pH 1.6-2) and intestinal (pH 6.5) media. Either no furosemide or very small amounts of drug were released in the gastric media, whereas an immediate release was observed in the intestinal media. For evaluation of the microcontainers as a mucoadhesive system for attachment to the mucus in the small intestine, the microcontainers were spray coated with a lid of chitosan. A thickness of the chitosan layer of 5.4 µm was found to show mucoadhesive properties, by using the tensile force model; however, the chitosan layer did result in hindrance of the release of furosemide from the microcontainers. The permeability of furosemide loaded in microcontainers through a Caco-2 cell layer was evaluated, but as the integrity of the cell layer was not maintained during the cell studies, such permeability investigations are currently inconclusive. The microcontainers were furthermore investigated for their ability to stabilise amorphous drugs by spatial confinement, with the aim being for the microcontainers to restrict the progression of crystal growth to distances corresponding to the diameter of the microcontainers. For these studies, the amorphous form of a second poorly soluble drug, indomethacin, was prepared in the microcontainers. It was found that the degree of
crystallisation of amorphous indomethacin was decreased by confinement of the drug into 174 µm and 223 µm diameter microcontainers compared to amorphous bulk indomethacin. Moreover, it was discovered that the stability of amorphous indomethacin could be improved further by slow cooling of the indomethacin melt, without influencing the dissolution behaviour of amorphous indomethacin.

In conclusion, the microcontainers were found to show promise for utilisation as an oral drug delivery system with mucoadhesive properties for poorly water soluble drugs. Further characterisation and optimisation of the microcontainer system is however still required in order to improve their efficacy and efficiency in drug delivery.

General information
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Organisations: University of Copenhagen
Contributors: Nielsen, L. H.
Publication date: 2014

In vitro characterization of microcontainers as an oral drug delivery system.
We here present in vitro studies showing the promise of microcontainers (fabricated in either SU-8 or Poly(lactic acid) (PLLA)) as an oral drug delivery system for the poorly watersoluble drug, furosemide.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Nielsen, L. H., Keller, S. S., Petersen, R. S., Jacobsen, J., Boisen, A., Müllertz, A.
Publication date: 2014
Peer-reviewed: Yes
Event: Abstract from 41th Annual Meeting andamp; Exposition of the Controlled Release Society, Chicago, United States.
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Conference poster contribution: 41st Annual Meeting & Exposition of the Controlled Release Society, Chicago, USA, July 2014
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Source-ID: 97048489
Research output: Research - peer-review » Conference abstract for conference – Annual report year: 2014

Microcontainers, an innovative oral drug delivery system for poorly soluble drugs

General information
State: Published
Organisations: Nanoprobes, Department of Micro- and Nanotechnology, University of Copenhagen, Saarland University
Contributors: Nielsen, L. H., Nagstrup, J., Keller, S. S., Gordon, S., Østergaard, J., Rades, T., Boisen, A., Müllertz, A.
Number of pages: 2
Microcontainers as an oral drug delivery system.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Nielsen, L. H., Keller, S. S., Jacobsen, J., Rades, T., Boisen, A., Müllertz, A.
Publication date: 2014
Peer-reviewed: Yes
Event: Abstract from Globalization of Pharmaceutics Education Network biennial meeting, Helsinki, Finland.
Electronic versions:
Nielsen_Abstract.pdf
Research output: Research - peer-review › Conference abstract for conference – Annual report year: 2014

Microcontainers as oral drug delivery systems for small molecules and proteins

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Rønholt, S., Nielsen, L. H., Davidsen, A. B., Keller, S. S., Müllertz, A., Boisen, A., Nielsen, H. M.
Publication date: 2014
Peer-reviewed: Yes
Event: Poster session presented at 2014 AAPS Annual Meeting and Exposition, San Diego, CA, United States.
Electronic versions:
AAPS_abstract_microcontainers_20140528_1.pdf
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Source-ID: 101975268
Research output: Research - peer-review › Poster – Annual report year: 2014

Microcontainers for Unidirectional Release in the Upper Intestine

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Marizza, P., Keller, S. S., Nielsen, L. H., Petersen, R. S., Nagstrup, J., Müllertz, A., Boisen, A.
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Microfabricated containers for oral drug delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Keller, S. S., Nielsen, L. H., Müllertz, A., Boisen, A.
Number of pages: 1
Publication date: 2014

Refining stability and dissolution rate of amorphous drug formulations

Introduction: Poor aqueous solubility of active pharmaceutical ingredients (APIs) is one of the main challenges in the development of new small molecular drugs. Additionally, the proportion of poorly soluble drugs among new chemical entities is increasing. The transfer of a crystalline drug to its amorphous counterpart is often seen as a potential solution to increase the solubility. However, amorphous systems are physically unstable. Therefore, pharmaceutical formulations scientists need to find ways to stabilise amorphous forms. Areas covered: The use of polymer-based solid dispersions is the most established technique for the stabilisation of amorphous forms, and this review will initially focus on new developments in this field. Additionally, newly discovered formulation approaches will be investigated, including approaches based on the physical restriction of crystallisation and crystal growth and on the interaction of APIs with small molecular compounds rather than polymers. Finally, in situ formation of an amorphous form might be an option to avoid storage problems altogether. Expert opinion: The diversity of poorly soluble APIs formulated in an amorphous drug delivery system will require different approaches for their stabilisation. Thus, increased focus on emerging techniques can be expected and a rational approach to decide the correct formulation is needed.

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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 4.92 SJR 1.432 SNIP 1.394
Web of Science (2017): Impact factor 5.553
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
A slow cooling rate of indomethacin melt spatially confined in microcontainers increases the physical stability of the amorphous drug without influencing its biorelevant dissolution behaviour

Amorphous indomethacin was prepared by melting the γ-form of indomethacin, spatially confined within microcontainers (inner diameter of 223 μm), followed by cooling of the melt at a rate of 14, 23 or 36 K/min. The physical stability of the amorphous indomethacin within microcontainers was investigated using Raman microscopy. Furthermore, the dissolution behaviour of confined amorphous indomethacin was evaluated in biorelevant intestinal media at pH 6.5. After 30 days of storage, 10.3±1.2 % of the amorphous indomethacin cooled at 14 K/min and confined within microcontainers was found to be crystalline. When the melt of indomethacin was cooled at 23 or 36 K/min, 20.7±1.5 and 31.0±2.6% of the indomethacin were found to be crystalline after storage for 30 days. Scanning electron microscopy showed a smooth surface of amorphous indomethacin...
within the microcontainers when cooling the melt at 14 K/min, whereas cracks and an uneven surface were observed when cooling at rates of 23 and 36 K/min. The uneven surface is hypothesised to be the main reason for the lower physical stability, as the cracks could act as nucleation sites for crystal growth. The rate of cooling was not seen to have any effect on the dissolution of amorphous indomethacin from the microcontainers.

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Contributors: Nielsen, L. H., Keller, S. S., Boisen, A., Müllertz, A., Rades, T.
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Web of Science (2017): Impact factor 3.395
Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 2.76 SJR 0.976 SNIP 0.71
Web of Science (2016): Impact factor 3.094
Scopus rating (2015): CiteScore 1.95 SJR 0.701 SNIP 0.509
Web of Science (2015): Impact factor 1.887
Scopus rating (2014): CiteScore 1.67 SJR 0.64 SNIP 0.515
Scopus rating (2013): CiteScore 1.52 SJR 0.596 SNIP 0.422
ISI indexed (2013): ISI indexed no
Scopus rating (2012): CiteScore 2.24 SJR 0.755 SNIP 0.676
ISI indexed (2012): ISI indexed no
ISI indexed (2011): ISI indexed no
Original language: English
Keywords: Amorphous indomethacin, Amorphous form preparation, Physical stability, Biorelevant dissolution, Raman microscopy
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Biodegradable microcontainers as an oral drug delivery system for poorly soluble drugs

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Saarland University, University of Copenhagen
Contributors: Nielsen, L. H., Nagstrup, J., Keller, S. S., Gordon, S., Østergaard, J., Rades, T., Müllertz, A.
Publication date: 2013

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Source: dtu
Source-ID: u::10888
Research output: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Biodegradable microcontainers as an oral drug delivery system for poorly soluble drugs.

PURPOSE: To fabricate microcontainers in biodegradable polylactic acid (PLLA) polymer films using hot embossing, and investigate the application of fabricated microcontainers as an oral drug delivery system for a poorly soluble drug.

METHODS: For fabrication of the PLLA microcontainers, a film of PLLA was produced by spin coating. The film was heated above the polymer glass transition temperature (Tg), and a stamp was forced into the film. Following cooling of the film the stamp was removed, exposing the formed microcontainers. Microcontainers were filled with amorphous
furosemide sodium salt (produced by spray drying) using a simplified version of a screen printing technique. An enteric-resistant lid of Eudragit L-100 was subsequently spray coated onto the cavity of the microcontainers. Release of amorphous furosemide salt from the coated microcontainers was investigated using a μ-Diss profiler. Release experiments were carried out in biorelevant gastric medium (pH 1.6) for 2 h, followed by 3 h in a biorelevant intestinal medium (pH 6.5). Moreover, biorelevant flow through dissolution was also carried out in conjunction with UV imaging to visualize the release of amorphous furosemide salt from the coated microcontainers.

RESULTS: Fabricated PLLA microcontainers had an inner diameter of 220 μm and a height of 100 μm. The screen printing technique was shown to be an optimized set-up to fill the microcontainers with drug. From the release experiments it was observed that the Eudragit layer prevented drug release in biorelevant gastric medium, while an immediate release of the amorphous furosemide salt was seen in the biorelevant intestinal medium. The same trend was observed in the UV imaging experiments – negligible drug release was observed in gastric medium, whereas following re-equilibration of the dissolution cell with the intestinal medium, a release of furosemide was observed after 1 min with an increased release after 5 min of dissolution.

CONCLUSIONS: Biodegradable microcontainers were successfully fabricated and loaded with drug. Coating with Eudragit L-100 proved to be useful for protecting drug release from microcontainers in gastric medium, and facilitated an immediate release in the intestinal medium. The fabricated microcontainers therefore show considerable future potential as oral drug delivery systems.

Biorelevant characterisation of amorphous furosemide salt indicates conversion to a furosemide hydrate during dissolution

Biorelevant dissolution behaviour of the amorphous sodium salt and amorphous acid forms of furosemide was evaluated, together with investigations of the solid state changes during in vitro dissolution in medium simulating the conditions in the small intestine. UV imaging of the two amorphous forms, as well as of crystalline furosemide salt and acid showed a higher rate of dissolution of the salt forms in comparison with the two acid forms. The measured dissolution rates of the four furosemide forms from the UV imaging system and from eluted effluent samples were consistent with dissolution rates obtained from micro dissolution experiments. Partial least squares-discriminant analysis of Raman spectra of the amorphous acid form during flow through dissolution showed that the amorphous acid exhibited a fast conversion to the crystalline acid. Flow through dissolution coupled with Raman spectroscopy showed a conversion of the amorphous furosemide salt to a more stable polymorph. It was found by thermogravimetric analysis and hot stage microscopy that the salt forms of furosemide converted to a trihydrate during dissolution. It can be concluded that during biorelevant dissolution, the amorphous and crystalline furosemide salt converted to a trihydrate, whereas the amorphous acid exhibited fast conversion to the crystalline acid.
Biorelevant Characterisation of Amorphous Furosemide Salt Indicates Conversion to a Furosemide Hydrate During Dissolution

General information
State: Published
Organisations: University of Copenhagen, Saarland University
Number of pages: 2
Publication date: 2013
Peer-reviewed: Yes
Event: Abstract from 7th Annual PSSRC Symposium, Lille, France.

Bibliographical note
Oral presentation.

Characterisation during storage and dissolution of solid dispersions containing furosemide and hydroxypropyl methylcellulose

General information
State: Published
Organisations: University of Copenhagen
Contributors: Nielsen, L. H., Rades, T., Müllertz, A.
Number of pages: 7
Pages: 409-415
Publication date: 2013
Peer-reviewed: Yes

Publication information
Journal: Journal of Drug Delivery Science and Technology
Volume: 23
Issue number: 4
ISSN (Print): 1773-2247
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 1.9 SJR 0.517 SNIP 0.587
Web of Science (2017): Impact factor 2.297
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.25 SJR 0.387 SNIP 0.514
Web of Science (2016): Impact factor 1.194
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 0.72 SJR 0.25 SNIP 0.235
Web of Science (2015): Impact factor 0.62
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 0.68 SJR 0.251 SNIP 0.389
Web of Science (2014): Impact factor 0.476
BFI (2013): BFI-level 1
Preparation of an amorphous sodium furosemide salt improves solubility and dissolution rate and leads to a faster Tmax after oral dosing to rats

General information
State: Published
Organisations: United States Food and Drug Administration, University of Copenhagen, H. Lundbeck A/S
Contributors: Nielsen, L. H., Gordon, S., Holm, R., Selen, A., Rades, T., Müllertz, A.
Pages: 942-951
Publication date: 2013
Peer-reviewed: Yes

Publication information
Journal: European Journal of Pharmaceutics and Biopharmaceutics
Volume: 85
Issue number: 3
ISSN (Print): 0939-6411
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 4.67 SJR 1.342 SNIP 1.378
Web of Science (2017): Impact factor 4.491
Spray coating of microcontainers with eudragit using ferromagnetic shadow masks for controlled oral release of poorly water soluble drugs.
PURPOSE: To form a lid of Eudragit S-100 or L-100 on the cavity of drug-filled microcontainers (micro scale oral drug delivery devices) by utilizing ferromagnetic masks. Furthermore, investigations of drug release in biorelevant gastric and intestinal media were evaluated for testing the ability of controlling the drug release of poorly soluble drugs from the microcontainers.

METHODS: Cylindrical microcontainers (inner diameter of 240 μm) were fabricated in SU-8, using photolithography on silicon substrate. The microcontainers were filled with either cinnarizine (weak base) or amorphous furosemide salt (weak acid). The cavity of the drug-filled microcontainers were spray coated with a 2 wt% solution of either Eudragit S-100 (soluble below pH 5) or Eudragit L-100 (soluble above pH 6) in isopropanol. The spray coating process was performed using ferromagnetic shadow masks (380 μm) allowing for magnetic clamping to the substrate and therefore precise deposition of the polymer on the microcontainers to form a lid. The release of cinnarizine and amorphous furosemide salt from the coated microcontainers was performed in fasted biorelevant gastric (pH 1.6) and intestinal media (pH 6.5), respectively.

RESULTS: By use of the ferromagnetic shadow masks it was possible to deposit the Eudragit precisely and therefore possible to form a lid of the cavity of the microcontainers. The thickness of the Eudragit layer on the cavity of the microcontainers was approximately 8-10 μm for both types of Eudragit. It was possible to control the drug release of cinnarizine by using Eudragit L-100 in the gastric medium and also possible to control the release of amorphous furosemide salt by the Eudragit E-100 coating in the intestinal medium.

CONCLUSIONS: The ferromagnetic shadow masks made it possible to deposit a lid of Eudragit on the cavity of the microcontainers and this is important in terms of utilizing the microcontainers as an oral drug delivery system as the drug release can be controlled.

Addition of hydroxypropyl methylcellulose to furosemide increases physical stability of the amorphous form of furosemide

General information
State: Published
Organisations: University of Copenhagen
Contributors: Nielsen, L. H., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012

Peer-reviewed: Yes

Amorphous furosemide salt exhibits higher dissolution rate and stability compared to amorphous furosemide acid

General information
State: Published
Organisations: University of Copenhagen
Contributors: Nielsen, L. H., Gordon, S., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012
Amorphous furosemide salt exhibits higher dissolution rate and stability compared to amorphous furosemide acid

General information
State: Published
Organisations: University of Copenhagen
Contributors: Nielsen, L. H., Gordon, S., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012
Peer-reviewed: Yes
Event: Abstract from Globalization of Pharmaceutics Education Network biennial meeting (GPEN), Melbourne, Australia.

Amorphous furosemide salt exhibits higher solubility and dissolution rate compared to amorphous furosemide acid

General information
State: Published
Organisations: University of Copenhagen
Contributors: Nielsen, L. H., Gordon, S., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012
Peer-reviewed: Yes
Event: Abstract from Nordic Chapter Meeting, Reykjavik, Iceland.

Dissolution characteristics of amorphous furosemide salt

General information
State: Published
Organisations: University of Copenhagen
Contributors: Nielsen, L. H., Gordon, S., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012
Peer-reviewed: Yes
Event: Abstract from Dissolution Group Meeting, Copenhagen, Denmark.

Dissolution Rate of Spray Dried Amorphous Salts of Furosemide and HPMC in Biorelevant Dissolution Media Obtained by μ-diss Profiler
Higher apparent solubility and faster dissolution rate of amorphous furosemide salt leads to faster Tmax after oral dosing in rats compared to amorphous and crystalline furosemide acid.

Improved in vitro properties of furosemide through utilisation of the amorphous sodium salt.

Investigations by Raman Microscopy if Spatial Confinement of Amorphous Indomethacin Can Lead to Increased Stability.
Physical stability and dissolution of spatially confined amorphous indomethacin: The effect of different heating and cooling rates

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Nielsen, L. H., Keller, S. S., Boisen, A., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012
Peer-reviewed: Yes
Event: Abstract from Annual Meeting and Exposition of the American Association of Pharmaceutical Scientists (AAPS), Chicago, United States.

Preparation of amorphous furosemide salt formulations by spray drying

General information
State: Published
Organisations: University of Copenhagen
Contributors: Nielsen, L. H., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012
Peer-reviewed: Yes
Event: Abstract from Nordic Chapter Meeting, Reykjavik, Iceland.

Spatial confinement can lead to increased stability of amorphous indomethacin
The aim of this study was to investigate whether the physical stability of amorphous indomethacin can be improved by separating the drug material into small units by the use of microcontainers. Crystallisation from the spatially confined amorphous indomethacin in the microcontainers was determined and compared with the crystallisation kinetics of amorphous bulk indomethacin. Amorphous indomethacin in both a bulk form and contained within microcontainers was prepared by melting of bulk or container-incorporated γ-indomethacin, respectively, followed by quench-cooling. Microcontainers of three different sizes (diameters of 73μm, 174μm and 223μm) were used for the confinement of amorphous indomethacin, in order to elucidate whether the size of the microcontainer had an influence on the stability of the amorphous form. Following preparation, all samples were stored at 30°C and 23% RH. A sample of 100 microcontainers of each size was selected and measured on a Raman microscope over a period of 30days to ascertain whether the indomethacin in each container was amorphous or crystalline. Over time, a crystallisation number was obtained for the amorphous indomethacin in the microcontainers. The crystallisation numbers from the microcontainers were compared with the crystallisation kinetics of the amorphous bulk indomethacin, as determined by FT-Raman spectroscopy. Comparison of the numeric crystallisation in the microcontainers with the crystallisation kinetics of the amorphous bulk indomethacin showed that spatial confinement of indomethacin led to a significantly lower extent of crystallisation of the amorphous form. In the 174μm microcontainers, 29.0±2.6% of the amorphous indomethacin crystallised to the stable γ-form over a period of 30days, whilst 38.3±1.5% of the amorphous indomethacin crystallised in the 223μm microcontainers. Both these values were significantly different from that observed in the amorphous bulk indomethacin, where 51.0% crystallised to the γ-form after 30days. Comparing the 174 and 223μm microcontainers also revealed a significantly greater stabilising effect of the 174μm microcontainers (p-value of 0.0061). Surprisingly, for microcontainers with an inner diameter of 73μm, no stability improvement was found when compared to amorphous bulk indomethacin. It was observed that the amorphous indomethacin within these containers converted to the α-form of indomethacin (a metastable polymorph) which was unexpected at the storage conditions at 30°C and 23% RH.
Stability of amorphous drug formulations in microcontainers

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen, University of Otago
Number of pages: 1
Publication date: 2012
Peer-reviewed: Yes
Event: Abstract from Day of Research, Copenhagen, Denmark.

Bibliographical note
Oral presentation.
Source: PublicationPreSubmission
Source-ID: 97539232
Research output: Research - peer-review › Conference abstract for conference – Annual report year: 2012

Various heating and cooling conditions influence the release of amorphous indomethacin from microcontainers

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Contributors: Nielsen, L. H., Keller, S. S., Boisen, A., Rades, T., Müllertz, A.
Number of pages: 1
Publication date: 2012
Peer-reviewed: Yes
Event: Abstract from Drug Delivery Australia, Melbourne, Australia.

Bibliographical note
Poster presentation.
Source: PublicationPreSubmission
Source-ID: 97539299
Research output: Research - peer-review › Conference abstract for conference – Annual report year: 2012

Spatial confinement of amorphous indomethacin increases stability

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen, University of Otago
Contributors: Nielsen, L. H., Rades, T., Gordon, K. C., Müllertz, A.
Publication date: 2011
Peer-reviewed: Yes
Event: Poster session presented at Annual meeting of the American Association of Pharmaceutical Scientists (AAPS), Washington, United States.
Source: PublicationPreSubmission
Source-ID: 97539226
Research output: Research - peer-review › Poster – Annual report year: 2011
Spatial confinement of amorphous indomethacin increases stability

Stability, liposome interaction, and in vivo pharmacology of ghrelin in liposomal suspensions

Ghrelin is an appetite-stimulating peptide hormone. It is a pharmacologically interesting peptide because of its involvement in e.g. appetite and metabolism, but it has a very short half-life in the body. Ghrelin carries a Ser-3-octanoyl group, and it has previously been suggested that acylated peptides can bind to or be incorporated into liposomes. Therefore, neutral dipalmitoylphosphatidylcholine (DPPC) liposomes and phosphatidylcholine:cholesterol (PC:Chol) (70:30) liposomes as well as negatively charged dipalmitoylphosphatidylcholine:dipalmitoylphosphatidylcholine:dipalmitoylphosphatidylserine (DPPC:DPPS) liposomes (70:30) were prepared, and ghrelin was added. The chemical and physical stability of ghrelin was examined. Affinity capillary electrophoresis (ACE) revealed an interaction between ghrelin and the negatively charged (DPPC:DPPS) liposomes, whereas only very small affinities were discerned in the other liposomal formulations of ghrelin. Differential scanning calorimetry showed no changes in phase transitions (T-m). In vivo pharmacokinetics following subcutaneous administration of ghrelin in buffer and in the liposomal formulations was examined in rats. The PC:Chol formulation had a longer-lasting effect as compared to the ghrelin buffer solution and the other two liposomal formulations. The prolonged effect of the PC:Chol formulation is suggested not to be caused by association between ghrelin and the liposome. (C) 2009 Elsevier B.V. All rights reserved.
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 4.13 SJR 1.347 SNIP 1.551
Web of Science (2014): Impact factor 3.65
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 4.17 SJR 1.377 SNIP 1.605
Web of Science (2013): Impact factor 3.785
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 4.1 SJR 1.552 SNIP 1.637
Web of Science (2012): Impact factor 3.458
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 4.01 SJR 1.493 SNIP 1.619
Web of Science (2011): Impact factor 3.35
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.574 SNIP 1.608
Web of Science (2010): Impact factor 3.607
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.399 SNIP 1.53
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.227 SNIP 1.575
Scopus rating (2007): SJR 1.186 SNIP 1.527
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.995 SNIP 1.398
Scopus rating (2005): SJR 1.043 SNIP 1.589
Scopus rating (2004): SJR 1.045 SNIP 1.464
Scopus rating (2003): SJR 0.981 SNIP 1.355
Scopus rating (2002): SJR 0.793 SNIP 1.265
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.74 SNIP 1.047
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.703 SNIP 1.05
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.616 SNIP 0.978

Original language: English

Keywords: Animals, Calorimetry, Differential Scanning, Cholesterol, Drug Stability, Electrophoresis, Capillary, Ghrelin, Liposomes, Male, Particle Size, Phospholipids, Rats, Rats, Sprague-Dawley, Static Electricity, Transition Temperature, 97C5T2UQ7J Cholesterol, buffer, cholesterol, dipalmitoylphosphatidylcholine, dipalmitoylphosphatidylserine, ghrelin, glycerophospholipid, liposome, phosphatidylcholine, thioflavine, unclassified drug, animal experiment, appetite, article, capillary electrophoresis, chemical interaction, controlled study, differential scanning calorimetry, drug absorption, drug blood level, drug formulation, drug stability, high performance liquid chromatography, in vivo study, light scattering, male, nonhuman, phase transition, priority journal, rat, suspension, turbidity, zeta potential, Delivery, In vivo, Liposome, Liposome interaction, Prolonged effect, PHARMACOLOGY, CAPILLARY-ELECTROPHORESIS, GROWTH-HORMONE, SUBCUTANEOUS INJECTION, UNILAMELLAR VESICLES, INTRAVENOUS GHRELIN, APPETITE REGULATION, BINDING CONSTANTS, RAT GHRELIN, FOOD-INTAKE, INSULIN, cholesterol 57-88-5, dipalmitoylphosphatidylcholine 2644-64-6, dipalmitoylphosphatidylserine 3036-82-6, ghrelin 304853-26-7 hormone-drug pharmacokinetics, subcutaneous administration, 10060, Biochemistry studies - General, 10066, Biochemistry studies - Lipids, 10067, Biochemistry studies - Sterols and steroids, 12512, Pathology - Therapy, 22002, Pharmacology - General, 22016, Pharmacology - Endocrine system, Pharmacology, affinity capillary electrophoresis electrophoretic techniques, laboratory techniques, differential scanning calorimetry laboratory techniques, spectrum analysis techniques, Biochemistry and Molecular Biophysics, Methods and Techniques, Pharmaceuticals
Projects:

**3D printing of micro-container for oral delivery of probiotics**
Chang, T., PhD Student
Boisen, A., Main Supervisor, Department of Micro- and Nanotechnology
Hwu, E. T., Supervisor, Department of Micro- and Nanotechnology
Nielsen, L. H., Supervisor, Department of Micro- and Nanotechnology
Samfinansieret - Andet
01/09/2018 → 31/08/2021
Award relations: 3D printing of micro-container for oral delivery of probiotics
Project: PhD

**Evaluating microcontainers for oral delivery of probiotics**
Christfort, J. F., PhD Student
Boisen, A., Main Supervisor, Department of Micro- and Nanotechnology
Nielsen, L. H., Supervisor, Department of Micro- and Nanotechnology
Zor, K., Supervisor, Department of Micro- and Nanotechnology
Samfinansieret - Andet
01/09/2018 → 31/08/2021
Award relations: Evaluating microcontainers for oral delivery of probiotics
Project: PhD

**Microcontainers for Oral Delivery of Probiotics**
Kamguyan, K., PhD Student, Department of Micro- and Nanotechnology
Boisen, A., Main Supervisor, Department of Micro- and Nanotechnology
Nielsen, L. H., Supervisor, Department of Micro- and Nanotechnology
Zor, K., Supervisor, Department of Micro- and Nanotechnology
Fonde
15/06/2018 → 14/06/2021
Award relations: Microcontainers for Oral Delivery of Probiotics
Project: PhD

**Microcontainers for oral drup delivery**
Hansen, S. E., PhD Student, Department of Micro- and Nanotechnology
Boisen, A., Main Supervisor, Department of Micro- and Nanotechnology
Nielsen, L. H., Supervisor, Department of Micro- and Nanotechnology
Samfinansieret - Andet
01/02/2018 → 31/01/2021
Award relations: Microcontainers for oral drup delivery
Project: PhD

**Drug transport in in vitro intestine models**
Jepsen, M. L., PhD Student, Department of Micro- and Nanotechnology
Dufva, M., Main Supervisor, Department of Micro- and Nanotechnology
Boisen, A., Supervisor, Department of Micro- and Nanotechnology
Nielsen, L. H., Supervisor, Department of Micro- and Nanotechnology
Grundforskningsfonden
15/12/2016 → 14/12/2019
Award relations: Drug transport in in vitro intestine models
Project: PhD

**Loading of microcontainers for oral drug delivery**
Mazzoni, C., PhD Student, Department of Micro- and Nanotechnology
Boisen, A., Main Supervisor, Department of Micro- and Nanotechnology
Microcontainers for oral vaccine delivery
von Halling Laier, C., PhD Student, Department of Micro- and Nanotechnology
Boisen, A., Main Supervisor, Department of Micro- and Nanotechnology
Nielsen, L. H., Supervisor, Department of Micro- and Nanotechnology
Rades, T., Supervisor
Larsen, N. B., Examiner, Department of Micro- and Nanotechnology
Christensen, D., Examiner
Lavelle, E., Examiner
Samfinansieret - Andet
01/09/2015 → 31/08/2018
Award relations: Microcontainers for oral vaccine delivery
Project: PhD

I propose the utilisation of biopolymer microcontainers as an oral vaccine delivery system. These microcontainers (MCs) will be filled with a particulate vaccine formulation and sealed with a mucoadhesive layer followed by a pH-sensitive lid. The MCs will provide: 1) protection of the vaccine against enzymatic degradation, 2) adherence to the desired site of action and 3) provision of a unidirectional drug release. In the design of such a system, it is intended that the vaccine will be released only upon reaching the intestine, in close proximity to the epithelial cell barrier, allowing for effective uptake of the antigen and the initiation of an immune response. The project will be based at DTU Nanotech with collaborations to KU Pharma, Denmark, Helmholtz Institute for Pharmaceutical Research Saarland, Saarbrücken, Germany and University of Otago, Dunedin, New Zealand.

Nielsen, L. H., Project Participant, Department of Micro- and Nanotechnology, Nanoprobes
External Project ID: DFF – 4004-00120B
01/07/2014 → 30/06/2017
Keywords: Oral vaccine delivery, Microcontainers, Triple Co-culture cell model, Targeted drug delivery
Documents:
Microcontainers for oral vaccine delivery
Project: Research

Activities:

3D printed system for testing intestinal drug transport
Period: 21 Mar 2018
Morten Leth Jepsen (Other)
Line Hagner Nielsen (Other)
Kristoffer Almdal (Other)
Anja Boisen (Other)
Martin Dufva (Other)
Department of Micro- and Nanotechnology
Fluidic Array Systems and Technology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Applied Mathematics and Computer Science

Related event
11th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
21/03/2018 → …
Granada, Spain
Activity: Talks and presentations › Conference presentations
Loading of poorly soluble drugs by supercritical CO2 impregnation into microcontainers for oral drug delivery
Period: 19 Mar 2018 → 22 Mar 2018
Chiara Mazzoni (Other)
Anastasia Antalaki (Other)
Rasmus Due Jacobsen (Other)
Jacob Mortensen (Other)
Fabio Tentor (Other)
Roman Sylvesters (Other)
Oleksii Ilichevskyi (Other)
Stephan Sylvest Keller (Other)
Line Hagner Nielsen (Other)
Anja Boisen (Other)
Department of Micro- and Nanotechnology
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Nanoprobes
Department of Applied Mathematics and Computer Science

Related event
11th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
21/03/2018 → …
Granada, Spain
Activity: Talks and presentations › Conference presentations

3D printed system for based on hydrogels for drug transport
Period: 29 Jan 2018
Morten Leth Jepsen (Other)
Line Hagner Nielsen (Other)
Kristoffer Almdal (Other)
Anja Boisen (Other)
Martin Dufva (Other)
Department of Micro- and Nanotechnology
Fluidic Array Systems and Technology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Applied Mathematics and Computer Science

Description
3D printed system for based on hydrogels for drug transport

Related external organisation
University of Southern Denmark
Niels Bohrs Allé 1, Niels Bohrs Allé 1, Niels Bohrs Allé 1, Niels Bohrs Allé 1, Niels Bohrs Allé 1, 5230, Odense, Denmark
Activity: Talks and presentations › Conference presentations

Loading of poorly soluble drugs by supercritical CO2 impregnation into microcontainers for oral drug delivery
Period: 29 Jan 2018 → 31 Jan 2018
Chiara Mazzoni (Speaker)
Anastasia Antalaki (Other)
Rasmus Due Jacobsen (Other)
Jacob Mortensen (Other)
Related event

Northern Pharma Network Meeting
29/01/2018 → 31/01/2018
Odense, Denmark
Activity: Talks and presentations › Conference presentations

Microcontainers for oral vaccine delivery
Period: 29 Jan 2018 → 31 Jan 2018
Line Hagner Nielsen (Guest lecturer)
Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
Oral presentation
Documents:
Odense meeting_Microcontainers for oral vaccine delivery

Related event

Northern Pharma Network Meeting
29/01/2018 → 31/01/2018
Odense, Denmark
Activity: Talks and presentations › Conference presentations

Microcontainers for oral vaccine delivery
Period: 18 Sep 2017 → 22 Sep 2017
Line Hagner Nielsen (Guest lecturer)
Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
Oral presentation
Documents:
MNE2017 Microcontainers for oral vaccine delivery

Related event

43rd International conference on Micro and Nano Engineering
18/09/2017 → 22/09/2017
Electrospraying Chitosan Particles for Oral Vaccine Delivery
Period: 16 Jul 2017 → 19 Jul 2017
Line Hagner Nielsen (Guest lecturer)
Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
Poster presentation
Documents:
Abstract CRS 2017_electrospray

Related event
44th Annual Meeting & Exposition of the Controlled Release Society
16/07/2017 → 19/07/2017
Boston, United States
Activity: Talks and presentations › Conference presentations

Microcontainers as an Oral Drug Delivery System
Period: 16 Jul 2017 → 19 Jul 2017
Line Hagner Nielsen (Guest lecturer)
Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
Poster presentation
Documents:
Abstract CRS 2017_microcontainers

Related event
44th Annual Meeting & Exposition of the Controlled Release Society
16/07/2017 → 19/07/2017
Boston, United States
Activity: Talks and presentations › Conference presentations