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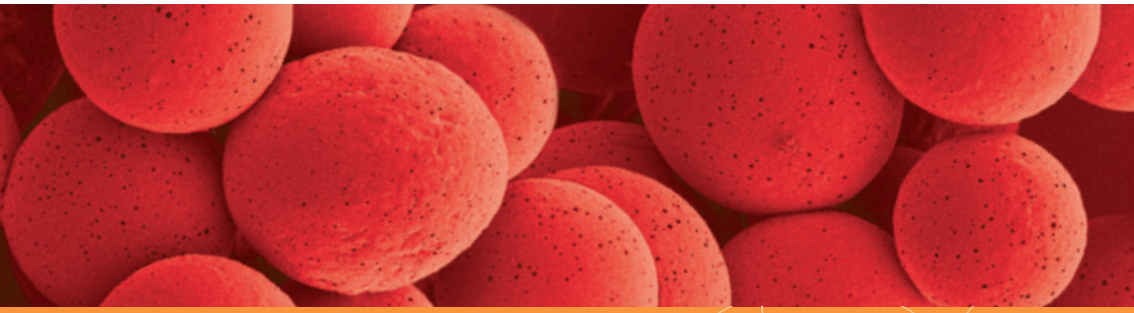
pharmaceuticals



SynBiosys®

Biodegradable polymer platform for delivery of biological therapeutics

SynBiosys® is an advanced biodegradable polymeric drug delivery platform designed to offer optimal control over the release kinetics and bioactivity of biological therapeutics.

SynBiosys® is designed to offer optimal control over the release kinetics and bioactivity of therapeutic agents, thereby improving pharmacotherapeutic efficacy and reducing side effects.

SynBiosys®

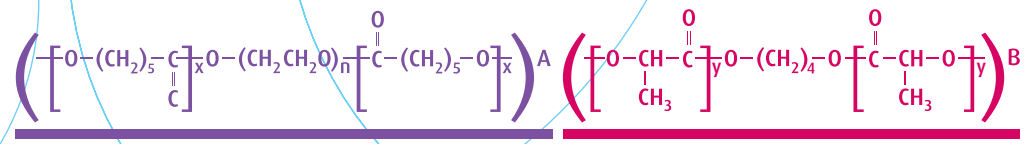
The SynBiosys® drug delivery platform is based on proprietary bio-degradable multi-block polymers that are designed for precisely controlled delivery of biological therapeutics. Peptides, as well as large protein molecules such as growth factors, cytokines and therapeutic antibodies can be formulated into parenteral depot formulations and released structurally intact and with preserved activity from several days up to 6 months. SynBiosys® polymers can be processed as microparticles, solid injectable implants, or implant coatings.

InnoCore has successfully established partnerships with biotech and pharma companies throughout the world to develop SynBiosys®-based long-acting injectable drug delivery products and drug eluting medical devices. The SynBiosys® drug delivery platform is well protected through several patent families.

SynBiosys® molecular composition

The SynBiosys® polymer platform comprises poly(ether ester) multi-block copolymers composed of various building blocks of different combinations of DL-lactide, glycolide,- caprolactone and polyethylene glycol (Figure 1). Critical polymer attributes like hydrophilicity, swelling degree and degradation rate can be optimized by varying the molecular composition. This results in a unique and versatile platform with unsurpassed ability to control the release kinetics of a wide range of therapeutics.

Fig. 1 - SynBiosys molecular structure



Soft and hydrophilic block

Rigid and hydrophilic block

Key attributes of SynBiosys

- Sustained release
  - Peptides, proteins, antibodies
  - Low burst release
  - Up to 6 months
- Protein integrity and bioactivity preserved
- Excellent safety and biocompatibility
- Clinically validated polymer platform
- Marketed products (coronary stents)
- Strong patent protection

Therapeutic areas

- Post surgical pain
- Prostate cancer
- Diabetes
- CNS (e.g. Schizophrenia, Parkinson)
- Macular degeneration
- Cardiac diseases
- Osteoarthritis
- Anticonception

SynBiosys® micro-particles offer superior injectability and precisely controlled release of therapeutic agents for systemic and site-specific drug delivery.

Safety and clinical data

SynBiosys® polymers are solely composed of well-known and regulatory accepted monomers that are arranged in an advanced molecular architecture. Under physiological conditions, SynBiosys® degrades into biologically safe degradation products that are metabolized and/or excreted through the urinary pathway. After completion of drug delivery, the polymers disappear completely, avoiding biomaterial accumulation. Next to extensive toxicity and biocompatibility (ISO-10993) testing, SynBiosys® microparticles, implants and coatings have been extensively tested in multiple animal studies (rats, rabbits, pigs, primates) and used as a drug eluting coating in coronary stents in thousands of patients. Following CE approval in 2013 the SynBiosys-based Combo sirolimus-eluting dual therapy stent is marketed by OrbusNeich.

Microparticle manufacturing and scale-up

SynBiosys® microparticles are manufactured via a membrane emulsification-based solvent extraction/evaporation process which provides absolute control over the microparticle formation process resulting in uniformly-sized microparticles. Loss of expensive product due to fractionation is avoided. The process provides excellent reproducibility and linear scalability throughout the complete product development pathway and is suitable for aseptic cGMP manufacturing for phase I/II clinical studies.

Therapeutic compounds

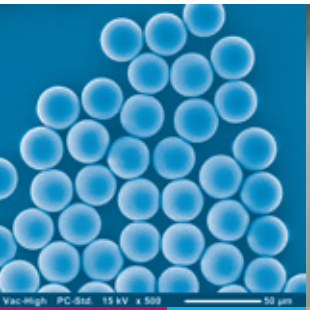
- Peptides
- Proteins
- Growth factors
- Antibodies and antibody fragments

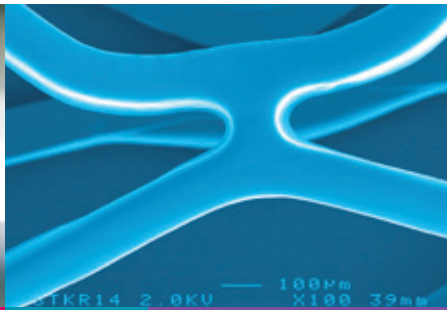
Configuration

- Microspheres
- Gels
- Implants
- Films
- Coatings

Key attributes of SynBiosys Microparticles

- Absolute control over particle size
- Superior injectability
- Small needles: 23-30 Gauge
- API dose up to 100 mg/mL
- Well-scalable manufacturing process
- High drug loadings of 15-20%





Superior Injectability

The total control of particle size is a crucial parameter for designing microparticles for drug delivery. A narrow particle size distribution allows the use of smaller needle diameters (23-27 Gauge) resulting in less painful injections and improved patient compliance, the administration of more concentrated microsphere suspensions (higher API dose) and prevents activation of the immune system by undersized particles.

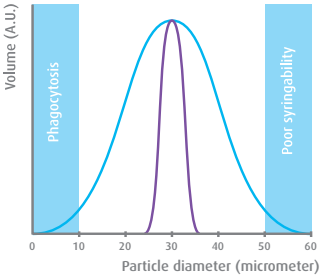


Fig 2 - Particle size distribution of SynBiosys Microspheres as compared to standard microspheres

Drug release characteristics

Drug release from SynBiosys® occurs through a combined diffusion/degradation mechanism. In combination with a proper selection of suitable SynBiosys® grades, this allows the development of depot formulations with customized release profiles over extended periods of time.

Preserved activity of biologicals

SynBiosys® microparticles are unique in that the structural integrity and bioactivity of encapsulated and released biologicals are preserved. This feature is attributed to the hydrophilic and water-swellable character of the poly(ethylene glycol)-based multi-block copolymers. As a consequence, a hydrogel-like matrix is formed in which acidic degradation products do not accumulate and an in situ pH drop is prevented.

Fig. 3 - In vitro release of leuprolide (1209 Da)

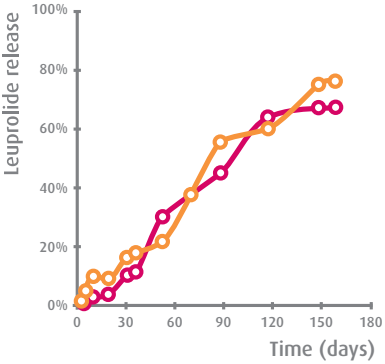


Fig 4 -In vitro release of hepatocyte growth factor (~69 kDa)

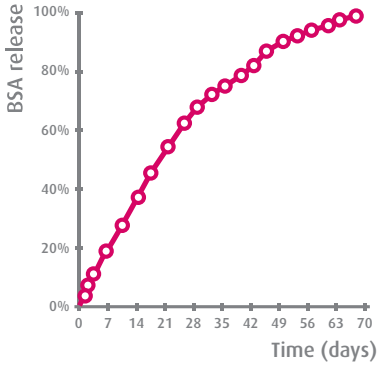
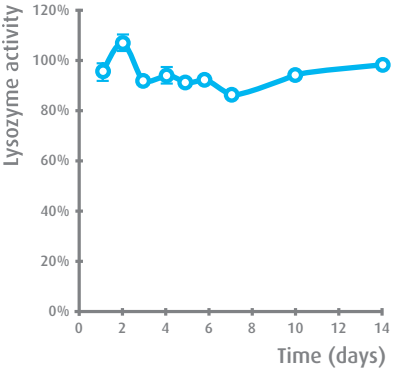


Fig. 5 - Bioactivity of released lysozyme



Development and cGMP manufacturing services

InnoCore has extensive experience in development, scale-up and cGMP manufacturing of long acting injectable sustained release microparticle formulations for a broad spectrum of drugs using its proprietary SynBiosys® polymers. Besides out-licensing of our proprietary technologies, we offer fully integrated pharmaceutical development of SynBiosys® based sustained release formulations to third parties.

Partnering with InnoCore

InnoCore offers its proprietary drug delivery technologies and depot formulations currently under development for licensing to third parties. Since our inception in 2004, we have successfully established partnerships with biotech and pharma companies throughoutthe world. InnoCore is interested in new partnerships to co-develop parenteral drug delivery products based on its proprietary technologies. Our target-driven and cost-efficient organization is committed to delivering products and services that offer added value to our partners and improve the quality of life of patients. Flexibility, compliance with the highest international quality standards and a true belief in the value of collaborative partnerships are the key elements of the InnoCore approach.

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InnoCore Pharmaceuticals is a biopharmaceutical drug delivery company specialized in the development and manufacturing of long acting injectable drug delivery products for the treatment of chronic and site-specific diseases.

InnoCore Pharmaceuticals is based in Groningen. The city of Groningen is located in the northern part of The Netherlands.

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