

PRODUCTS

DRUG DELIVERY

CONTRACT DEVELOPMENT

PHARMACEUTICAL  
INNOVATORS

FACTSHEET

# SynBiosys™

A biodegradable polymeric drug delivery system for peptides and small molecules



**Key attributes of SynBiosys:**

- + Ideal delivery vehicle for small and medium-sized molecules, especially peptide drugs
- + Controllable release profiles
  - Linear to biphasic release
  - 2 weeks to 6 months release
  - Low initial burst release
- + Drug loading of 1 to 30 wt%
- + Based on biocompatible and regulatory approved building blocks
- + Completely bioresorbable with adjustable degradation rates
- + Integrity of the encapsulated drug maintained (absence of pH drop)
- + Elastomeric properties
- + Patent protected

**SynBiosys**

SynBiosys is an innovative biodegradable polymeric drug delivery system for the controlled release of small and medium-sized biologically active compounds. The system is based on a proprietary multiblock copolymer platform technology, which is designed to offer optimal control over drug release kinetics, thereby providing improved therapeutic efficacy and fewer side effects. Physical and degradation characteristics can be easily adjusted, which allows the development of microsphere, film or implant formulations with adjustable sustained release for periods of 2 weeks up to 6 months. SynBiosys offers excellent opportunities to extend patent protection and upgrade current products.

OctoPlus has entered into a collaboration with InnoCore, The Netherlands, to develop and market this novel injectable drug delivery platform. The technology complements OctoPlus' existing drug delivery platforms PolyActive™ and OctoDEX™. With these three platforms, OctoPlus is able to develop tailor-made controlled release formulations for all classes of injectable drug compounds.

**SynBiosys molecular composition**

The SynBiosys polymer platform comprises poly(ether ester) multi-block copolymers composed of various pre-polymeric building blocks of different combinations of DL-lactide, glycolide, ε-caprolactone and polyethylene glycol (Figure 1). By varying the molecular composition, molecular weight (Mw 1200 – 6000) and ratio of the pre-polymer blocks, different characteristics can be induced in the polymers, which enables the creation of a drug delivery system with various physico-chemical properties. Both hydrophobic as well as hydrophilic/swellable polymers and slowly degrading as well as rapidly degrading polymers can be designed. Using the concept of combining pre-made building blocks, SynBiosys is unique in that it provides optimal flexibility and control over the release kinetics of a wide range of drug molecules.

**SynBiosys application forms**

Depending on the desired route of administration and site of application, SynBiosys polymers can be processed into various configurations ranging from injectable microspheres and gels to implantable rods and films.



Adjustable polymer matrix properties are:

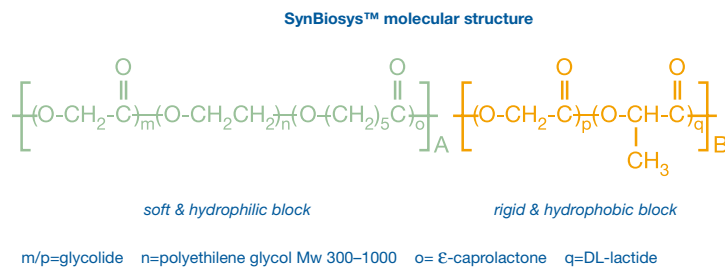
- + Flexibility
- + Hydrophilicity / hydrophobicity
- + Swelling degree
- + Permeability
- + Degradation rate

These variables allow the design of tailor-made drug delivery systems for virtually any drug molecule.

**Encapsulation methods**

- Multi-emulsion evaporation process
- Spray-drying
- (Hot-melt) extrusion
- Polymer/drug/solvent mixing

Figure 1. SynBiosys molecular structure



Together with InnoCore we offer a full range of services to develop delivery systems based on the SynBiosys technology:

- + Feasibility studies
- + Sustained release formulation development
- + Process design, scale-up & validation
- + Synthesis and supply (GMP) of custom made SynBiosys polymer
- + Development & validation of analytical methods
- + Regulatory support
- + cGMP manufacturing and release of material for animal studies and clinical trials
- + Stability studies according to ICH guidelines

Because of the easily adjustable release characteristics and the various configurations into which SynBiosys can be processed, SynBiosys provides an effective delivery system for a wide range of drug molecules and applications.

#### Disease

- Pain management
- Contraception
- Cancer
- Anti-adhesion
- Infection
- CNS (e.g. schizophrenia)

#### Example of delivery systems

- Microspheres
- Rod implant
- Microspheres
- Gel, film
- Microspheres
- Microspheres, gels

#### SynBiosys release characteristics

Drug release from SynBiosys occurs through a combined diffusion/degradation mechanism. As a result, linear release profiles can be achieved for molecules with different physicochemical properties. By varying the building blocks, both the release rate and the release profile (linear, pulsed or delayed) can be adjusted.

#### In vitro release

SynBiosys allows the controlled release of small hydrophilic (e.g. peptides) or hydrophobic (e.g. antibiotics, steroids) compounds. For leuprolide acetate (Figure 2), a peptide drug for the treatment of prostate cancer, a constant and regular release over a period of up to 6 months could be obtained using a (glycolide-ε-caprolactone)-(DL-lactide) SynBiosys polymer. The flexibility of the SynBiosys drug delivery platform is further demonstrated in Figure 3 with the release characteristics of estradiol encapsulated in different SynBiosys polymer matrices.

Figure 2. In vitro release of a peptide drug (Leuprolide, Mw 1300) from SynBiosys™. Drug load: 10% and 20%; SynBiosys™ composition: 50(GA-CL)<sub>2000</sub>-50(LA)<sub>4000</sub>

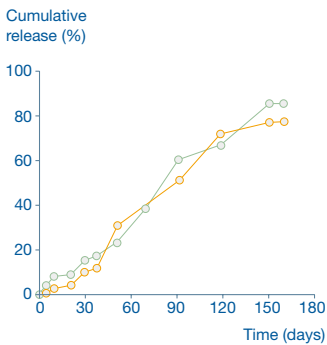
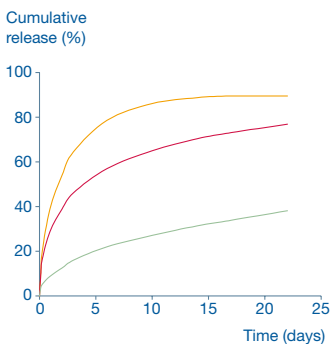


Figure 3. Release profiles of estradiol from 3 different SynBiosys coatings using combinations of 100(DLLA)<sub>4000</sub> and 80(GAPEGCL)<sub>1200</sub> - 20(GALA)<sub>2000</sub> polymers in a matrix-toplayer configuration. The drug load was 37.5% in all cases.



#### Biocompatibility

The biological safety of SynBiosys polymers has been fully proven. A unique aspect of SynBiosys multi-block copolymers is that they are composed of well-known and biologically safe components, which are applied in a new and advanced architecture. The same components are used for many clinical bioresorbable products on the market, such as sutures, orthopaedic fixation devices, nerve guides, nasal dressings, drug eluting stents and pharmaceutical sustained release depots.

#### Biodegradation

Under physiological conditions, SynBiosys polymers degrade via hydrolytic degradation. The resulting non-toxic degradation products are metabolized and/or excreted through the urinary pathway. The degradation rate depends on the chemical composition, molecular weight and ratio of the building blocks of the polymers. Due to their biodegradable nature, SynBiosys polymers disappear completely after delivery of the drug. Consequently, no accumulation of biomaterial occurs, which minimizes the chance of long-term foreign body reactions.

#### Preserved stability of the released compound

During degradation, the pH of the polymer matrix remains (near) neutral since no acidic degradation products accumulate in the polymer matrix. Preservation of a neutral pH is essential to maintain drug integrity especially when biopharmaceutical drugs and biologically derived compounds are concerned.

#### SynBiosys polymer manufacturing

Manufacturing of SynBiosys polymers with tailor-made chemical composition is performed in InnoCore's GMP manufacturing facilities (Groningen, the Netherlands).

#### Partner with OctoPlus for drug delivery with SynBiosys

OctoPlus is actively pursuing new partnerships to develop products based on the SynBiosys delivery system. As a medium sized organisation, OctoPlus is flexible in constructing partnership agreements and we are open to take on some of the risk and cost for the development of promising compounds. Our priority is to build successful long-term drug delivery partnerships. Please feel free to contact us and discuss your ideas.

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