TECHNOLOGY FOR BIODEGRADABLE POLYESTERS
PRODUCTION FROM RENEWABLE RESOURCES
„BIOPOL”

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BIOPOL: FINAL POLYESTERS

Polylactides

Poly[(butylene terephthalate)-co-(butylene succinate)-co-(butylene glutarate)-co-(butylene adipate)]

x = 1 (succinate)
2 (glutarate)
3 (adipate)

IBPE
TECHNOLOGY for BIODEGRADABLE POLYESTERS PRODUCTION from RENEWABLE RESOURCES (acronym BIOPOL)

The project is implemented under the Operational Programme Innovative Economy 2007-2013.

- Priority Axis 1. Research and development of modern technologies
- Measure 1.1 Support for scientific research for establishment of a knowledge-based economy,
- Sub-measure 1.1.2 Strategic programmes of scientific research and development works

- Contract number: POIG01.01.02-10-25/09

- Percentage share of funds: European Regional Development Fund 85%, State budget 15% (total budget approx. 10 milion Euro)

The general objective of the project is to carry out strategic research and development of innovative technological solutions for renewable raw material base resulting in the new products palette from biodegradable polymers based on renewable sources, particularly the polymer produced from lactic acid (known under the name "polylactide") and from the biodegradable aliphatic-aromatic polyesters based on the available domestic raw materials.

The specific objectives of the project:

• technologies for polylactide (PLA) production in the model research installation (PLA installation)
• technologies for production of biodegradable aliphatic-aromatic polyester (IBPE) in the model research installation (IBPE installation)
• chemical modification of PLA, IBPE, and PLA-IBPE blends and copolymers
• processing of PLA, IBPE, and PLA-IBPE.
• projects of PLA, IBPE, and PLA-IBPE based industrial goods.

Thus, efforts are made to develop environmentally friendly polymeric high-tonnage products based on new “clean technologies”. It is also possible to use biodegradable polyesters in the biomedical area, for example in controlled drug delivery systems or as bioresorbable implants.
STRUCTURE of the PROJECT CONSORTIUM

- Center of Molecular and Macromolecular Studies
  Polish Academy of Sciences, Łódź
  (Leader of the Consortium)

- Department of Polymer Chemistry
- Department of Polymeric Materials Engineering
- Department of Polymer Physics
- Laboratory of Polymers Structure

- Warsaw University of Technology
  Faculty of Chemistry

- Department of Polymer Chemistry and Technology

- Laboratory of Technological Processes

- Institute of Biopolymers and Chemical Fibers
  Łódź
WORK PACKAGES

WP1: Technology development for polylactide (PLA) production in the model research installation (PLA installation)

WP2: Technology development for biodegradable aliphatic-aromatic polyester (IBPE) production in the model research installation (IBPE installation)

WP3: Studies of chemical modification of PLA, IBPE, and PLA-IBPE blends and copolymers

WP4: Studies of PLA, IBPE, and PLA-IBPE processing

WP5: Literature search

WP6: Management and administration

STAFF

Scientific staff (PhDs): 54
PhD Students: 8
MSci Students: 14
Technical staff: 24
Administration: 34

• Project Manager: Prof. Dr. Stanislaw Slomkowski
• Plenipotentiary to the Project Manager: Prof. Dr. Andrzej Duda
• Scientific Advisor: Prof. Dr. Stanislaw Penczek
POIGs „SUPERCONSORTIUM”

**BIOMASA**
Łódź University of Technology

- Monomers, substrates

**BIOPOL**
Center of Molecular and Macromolecular Studies
Polish Academy of Sciences, Łódź

- Polymers

**BIOGRATEX**
Łódź University of Technology

- Fibers, nonwovens, textiles

**MARGEN**
Center of Polymeric and Carbon Materials
Polish Academy of Sciences, Zabrze

- Packaging materials
SYNTHETIC PATHWAYS to BIODEGRADABLE POLYESTERS

- POLYCONDENSATION

\[
\begin{align*}
\text{nHO} & \text{-R-COH} \quad \text{\textrightarrow} \quad \text{HO} & \text{-R} & \text{-CO} - \text{R}^{(n-1)} & \text{COH} + (n-1) \text{H}_2\text{O} \\
\text{nHOC} & \text{-R'-COH} \quad \text{\textrightarrow} \quad \text{HO} & \text{-} & \text{C} - \text{R'} & \text{-CO} - \text{R''} - \text{O}^{n} & \text{H} + (2n-1) \text{H}_2\text{O}
\end{align*}
\]

- RING-OPENING POLYMERIZATION (ROP):
  - Chemical catalysis (metal-based or metal-free)
  - Enzymatic catalysis

\[
\begin{align*}
\text{n R-CO} \quad \text{catalyst / initiator} \quad \text{\textrightarrow} \quad \text{X} & \text{-R-CO}^{n} & \text{Y}
\end{align*}
\]

„Biopolymers”, Vol. 3ab & 4: Polysters I - III
A. Steinbuechel, Y. Doi (eds.), Wiley-VCH, Weinheim 2002

- BIOTECHNOLOGY / GENETICAL ENGINEERING
MAJOR POLY(ALIPHATIC ESTER)S PREPARED by ROP

Lactides (LA), \( R = \text{CH}_3 \)
Glycolide, \( R = \text{H} \)

\( \varepsilon \)-Caprolactone

1,4-Dioxo-2-one (DX)

Trimethylene carbonate (TMC)

\( \beta \)-Lactones (B)

Poly(lactide)s (PLA)
Poly(glycolide)

Poly(1,4-dioxo-2-one) (PDX)

Poly(trimethylene carbonate) (PTMC)

Poly(\( \varepsilon \)-caprolactone)

The best understood systems: controlled \( M_n \) ‘s reaching \( 10^6 \)

ROP of CYCLIC ESTERS – INITIATING/CATALYTIC SYSTEMS

\[
\begin{align*}
\text{M} &= \text{Na, K, Ca, Zn-, Sn(II)-, Al<, Y<, La<, -Sn(IV), -Ti<, -Zr<, etc.}
\end{align*}
\]
Sn(II) CARBOXYLATE/ROH

\[
\text{Sn}[	ext{OCR}']_2 + \text{ROH} \rightleftharpoons \text{ROSnOCR}' + \text{R'COH}
\]

\[
\text{ROSnOCR}' + \text{ROH} \rightleftharpoons \text{ROSnOR} + \text{R'COH}
\]

References:
- Polymer 48, 3952-3960 (2007)
POLYMERIZATION \(L,L\)-LA INITIATED \(\text{Sn(OBu)}_2\)

\[ [\text{LA}]_0 = (1.0 \div 3.0) \text{ mol/L, 80 }^\circ \text{C, THF (o), } [\text{LA}]_0 = 8.1 \text{ mol/L, 120 }^\circ \text{C, bulk (•); 5min - 20h} \]

Molar mass control from \(M_n = 1000\) to \(1000\ 000\)
NEW, METAL-FREE INITIATING SYSTEM

For example:

\[
\text{CF}_3\text{SO}_2 \text{O}^- \text{H}^+ \rightarrow \text{CF}_3\text{SO}_2 \text{O}^- \text{O}^+ \text{O}^- \text{H}
\]

\[
\text{CF}_3\text{SO}_2 \text{O}^- \text{O}^+ \text{O}^- \text{H} \rightarrow \text{CF}_3\text{SO}_2 \text{O}^- \text{O}^+ \text{O}^- \text{H}
\]

Activated monomer mechanism


Novel catalyst: \((\text{CF}_3\text{SO}_2)^2\text{NH}\)

Bis(trifluoromethylsulfonyl)imide – strongly acidic – used as catalyst in organic reactions, very seldom in polymer chemistry

Bulk polymerization of lactide, 120-150°C  \(\rightarrow\)  \(M_n \sim 2 \times 10^4, M_w/M_n \sim 2\)

Also effective for other heterocyclic monomers
CATIONIC COPOLYMERIZATION of L,L-LACTIDIE and β-BUTYROLACTONE INITIATED with TRIFLIC ACID

Poly(BL)-b-Poly(LA)

M. Basko, P. Kubisa & A. Duda 2011
METAL-FREE INITIATING & CATALYTIC SYSTEM „CATALINI”

• „Method of cyclic eter's polymerization, new catalyst and initiator of their polymerization” S. Penczek et al., Patent pending, P. 391993 (2011):

N9-(2'-Hydroxyethyl)adenine 6-(2-Hydroxyethyl)aminopurine 2 (3) (4) Aminopyridine Dipyridamole

4-DHEAP Histamine 1-(2-Hydroxyethyl)imidazole 4-HEAP
L,D- and L,L-LACTIDE POLYMERIZATION

MultiMax with IR control

1 L Stainless steel reactor and PLA strand
CHANGES of IR SPECTRA: LACTIDe POLYMERIZATION
OPTIMIZATION of L,D-LACTIDe POLYMERIZATION
THE SYNTHESIS and CHARACTERIZATION of HYPERBRANCHED POLYGLYCEROL

Glycerol

\[
\begin{align*}
\text{HO-} & \quad \text{OH} \\
\text{OH} & \quad \text{OH} \\
\text{OH} & \quad \text{OH}
\end{align*}
\]

\[ \xrightarrow{+} \]

Glycerol carbonate (GC)

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\]

\[ \xrightarrow{-2 \text{CH}_3\text{OH}} \]

Hyperbranched polyglycerol

DSC analysis

\[
\text{liquid of } T_g \text{ in the range of } -47 \pm -35 \text{ °C}
\]

Fragment of H NMR

Ratio of -\(\text{CH}_2\text{OH}\) to >\(\text{CHOH}\) is 3:2

CH\(_2\) in/out

CH, CH\(_2\) (ether)

Number of hydroxyl groups per molecule: 8 – 25 ...

depends on the ratio of GC to initiator
POLYMERIZATION of LACTIDE or GLYCOLIDE INITIATED with HYPERBRANCHED POLYGLYCEROL

Ring Opening Polymerization

\[ \text{HO} \xrightarrow{\text{R = H or CH}_3} \text{HO} \]

in bulk, 190 °C, cat.: Tin (II) octanoate

GPC chromatogram of 8-arm PLA

- Reaction conditions: Bulk
- Temperature: 190°C
- Time: 180 min
- Weight ratio: LA:PG = 38:1

Mn(HNMR) = 4800
Mn(GPC) = 3100
PDI = 1.6

DSC traces of 13-arm PLA

- Tg\(_1\) = -48.93
- Tg\(_2\) = -48.93

1H NMR spectrum of 8-arm PLA

- PLA end groups
- Polyglycerol core
- CH\(_3\) (PLA)
- CH\(_3\) (PG core)
- CH (PLA)
- LA

Mn (1H NMR) = 11170

Amorphous system

Universal V4.5A TA Instruments
POLYMERIZATION of LACTIDE INITIATED with LINEAR OLIGOESTERODIOLS or OLIGOCARBONATES

Polycondensation

Ring Opening Polymerization

Process Optimization

Time: 3 h
Temp.: 190°C

Mechanical properties

DSC analysis

Mass spectrum

Segment-segment miscibility evaluation

\[ \delta = \left(\Delta E/Vm\right)^{0.5} \]

\[ \chi = (\delta_1 - \delta_2)^2 V_r (R_T)^{-1} \]

Macroinitiator

Polymerization product

PLA-PPBATC-PLA

PPBATC

\[ T_g \]

\[ T_g \]

Heat Flow (W/g)

Temperature (°C)

0
100
200
300

-100
0
100
200
300

-100
0
100
200
300

Obciążenie (N)

Przemieszczenie (mm)

ε = 3%

ε = 8%

ε = 18%

ε = 3%

ε = 8%

ε = 18%

\[ \frac{\delta}{\Delta E/Vm} \]

\[ \chi = (\delta_1 - \delta_2)^2 V_r (R_T)^{-1} \]

PLA

10% PPBATC

Tg

Tg

ε = 3%

ε = 8%

ε = 18%

ε = 3%

ε = 8%

ε = 18%

Universal V4.5A TA Instruments

PLA-PPBATC-PLA

PPBATC

Mechanical properties

DSC analysis

Mass spectrum
PLA CONTAINING MICROSPHERES with SIMVASTATIN on the AORTA WALLS of RAT
Histopathological studies revealed that in the case of rats with induced inflammation treatment with simvastatin containing microspheres resulted in complete elimination of inflammation.

In control group of animals with induced blood vessels inflammation treated with microspheres without simvastatin inflammation and injuries of endothelium were noticed in the case of 60% of animals (after 8 weeks from development of inflammation).

**IN-VIVO TESTS**

SEM microphotographs revealed that microspheres are deposited on walls of blood vessels in spite of the blood flow. Deposition is preferential in places with inflammation.
BONE-FORMING CELLS in POLYESTER SCAFFOLDS

Osteoblasts in poly(L,L-lactide) containing porous scaffold.

Colagen produced by osteoblasts in poly(L,L-lactide) containing porous scaffold.

Poly(L,L-lactide) containing porous scaffold.
TECHNOLOGY for BIODEGRADABLE AROMATIC-ALIPHATIC POLYESTERS PRODUCTION

1. SUBSTRATES:

\[ \text{CH}_3\text{OOC-C}_6\text{H}_4\text{-COOCH}_3 + 2 \text{HO(CH}_2\text{)}_4\text{OH} \rightarrow 140-230 ^\circ C \]

\[ \text{HO(CH}_2\text{)}_4\text{OOC-C}_6\text{H}_4\text{-COO(CH}_2\text{)}_4\text{OH} + 2 \text{CH}_3\text{OH} \]

\[ \text{CH}_3\text{OOC-(CH}_2\text{)}_n\text{-COOCH}_3 + 2 \text{HO(CH}_2\text{)}_4\text{OH} \rightarrow \]

\[ \text{HO(CH}_2\text{)}_4\text{OOC-(CH}_2\text{)}_y\text{-COO(CH}_2\text{)}_4\text{OH} + 2 \text{CH}_3\text{OH} \]

2. ESTER EXCHANGE:

\[ \text{nHO(CH}_2\text{)}_4\text{OOC-C}_6\text{H}_4\text{-COO(CH}_2\text{)}_4\text{OH} + \text{nHO(CH}_2\text{)}_4\text{OOC-(CH}_2\text{)}_y\text{-COO(CH}_2\text{)}_4\text{OH} \rightarrow \text{230-250} ^\circ C \]

\[ \text{HO(CH}_2\text{)}_4\text{O[OC-C}_6\text{H}_4\text{-COO(CH}_2\text{)}_4\text{OOC-(CH}_2\text{)}_y\text{-COO(CH}_2\text{)}_4\text{O}]n\text{H} + \text{nHO(CH}_2\text{)}_4\text{OH} \]
**SELECTED IBPE PARAMETERS**  
**ALIPHATIC/AROMATIC 55/45**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting temperature</td>
<td>118 °C</td>
</tr>
<tr>
<td>Enthalpy of melting</td>
<td>20 J/g</td>
</tr>
<tr>
<td>Glass transition temp.</td>
<td>-25 °C</td>
</tr>
<tr>
<td>Onset temp. (mass 1% /20 °C/min.)</td>
<td>330 °C</td>
</tr>
<tr>
<td>$M_n$</td>
<td>25 000 g/mol</td>
</tr>
<tr>
<td>$M_w$</td>
<td>93 000 g/mol</td>
</tr>
<tr>
<td>Flow index</td>
<td>20 g/10 min</td>
</tr>
</tbody>
</table>
IBWCh

REACTOR 30 L

GRANULATED IBPE

IBPE STRAND

IBPE NONWOVEN

REACTOR 0.9 L
PLA as a PLASTIC MATERIAL

1. catalyst deactivation  
2. thermal stabilization  
3. processing aids  
4. hydrolysis prevention, water absorbers  
5. antioxidants  
6. Degassing  
7. control of dispersity of molecular weight  
8. control of monomer content  
9. defining of required characteristic of PLA as a plastic material

**Chemical Compounds:****

- **Ultranox 626**
- **Irganox MD1024**
- **Irganox 1076**
- **Stabaxol P**
- \( \text{(C}_{14}\text{H}_{16}\text{N}_{2}\text{O}_{2})_x \)
PHYSICAL MODIFICATION of PLA

1. crystallization
2. plasticization
3. plasticization + crystallization
4. modification by incorporation of soft inclusions
5. composites with biodegradable micro and nanofibers
6. composites with particulate mineral nanofillers
7. all-PLA composites

PLA with 25 wt.% of rubbery inclusions
CRYSTALLIZATION of ALIPHATIC-AROMATIC COPOLYESTERS

Heat Flow (W/g)

-0.3
-0.2
-0.1
0.0
0.1
0.2
0.3
0.4

Temperature (°C)

-50
0
50
100
150
200
250

Heat Flow (W/g)

crystallization

T_g

melting

Temperature (°C)
CRystallization of Biodegradable IBPE Copolyesters

• IBPE is a nearly random copolymer
• Aromatic part of IBPE crystallizes in form of PBT crystals
• Although the mean aromatic length is around 2 there are sequences as long as 5-6 aromatic monomers
• IBPE crystallizes in the form of spherulites filling entire volume
• Size of spherulites is in the range of 5-10 μm
• Self-nucleation of crystallization is very strong
• Self-nuclei melt and dissolve around 175°C
• Crystal thickness is at the level of 1 nm and below
• Crystals are fiber-like
• There are efficient nucleating agents accelerating crystallization; the best appear to be green phthalocyanine and talc