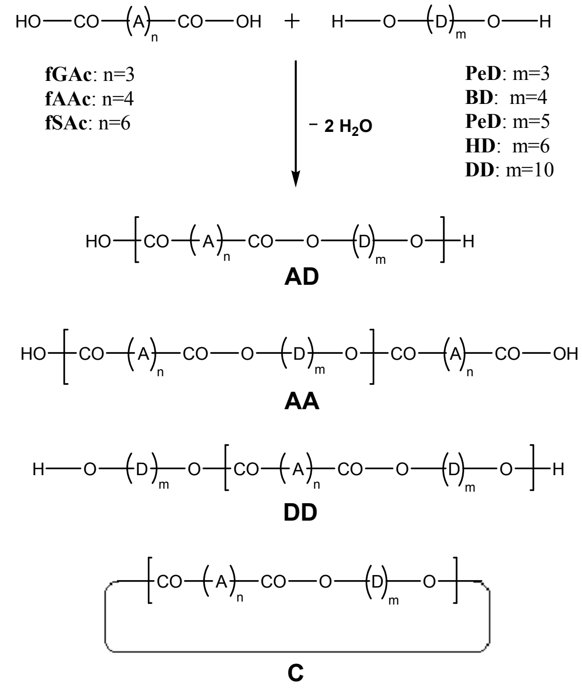
# Hipenzo (220461) – Final Report

## Final Publishable Summary Report

A growing awareness of the need for greener, more sustainable technologies has focused attention on the use of atom efficient catalytic methodologies for the manufacture of fine chemicals and pharmaceuticals. The use of alternative reaction solvents such as supercritical fluids or fluorous biphasic systems that are readily recycled, such as fluorous solvents and $scCO_2$ has therefore become the focus of significant research that could circumvent the problems associated with many of the traditional volatile organic solvents. Thus novel and effective methods, enzyme recovery and recycling are receiving increasing attention. New approaches tackling these issues were objectives of this project. Enzyme solubilisation in fluorous solvents and $scCO_2$ by Hydrophobic Ion Pairing with perfluorinated surfactants was investigated. Various commercially available lipases capable of catalysing esterification and transesterification reactions were screened to select a lipase that could be efficiently ion paired with fluorinated surfactants. The complexation efficiencies of 60-70 % were achieved with several lipases giving 9-15 mg/ml [enzyme] in fluorous solvent. Two hydrophobically ion paired lipases *Candida cylindracea* and *Pseudomonas cepacia* demonstrated reasonable catalytic activity and good enantioselectivity towards the kinetic resolution of *rac*-1- phenylethanol in a perfluoromethylcyclohexane/hexane biphasic system. When HIP-lipases were employed for the ring-opening polymerisation of various lactones in fluorous biphasic system lipases *Rhizopus arrhizus* and *Pseudomonas fluorescens* were active and yielded polyesters. Further HIP-lipases were tested for the polycondensation polymerisation of polyesters. The ability to solubilise lipases in fluorinated solvents provided an opportunity to perform homogenous polymerisation of highly fluorinated monomers. Several hydroxyl-terminated fluorinated diols and fluorinated acids were examined in order to generate fluorinated polyesters with unique physical and chemical properties. The major challenge of these experiments was monomer and product solubility. The higher the degree of fluorination, the lower is solubility of the polymer which makes analysis of the products a challenging task. Therefore instead partially fluorinated polyesters from nonfluorinated aliphatic diols and fluorinated aliphatic acids were synthesised by bulk/melt polymerisation. These polymerisation reactions proved to be self-catalyzed even at relatively low reaction temperatures. One of the monomers, the fluorinated acid, acted as a catalyst as it is a strong acid ($pK_a$ 0.6) therefore a biological catalyst was not required. Polyesters with different lengths of fluorinated and nonfluorinated segments were synthesised by varying the chain length of aliphatic diols and fluorinated acids. Reaction kinetics at different reaction temperatures was analysed. Results showed semifluorinated polyester formed with reasonable molecular weights already after 8 hours of reaction at 90 $^{o}$C in melt. Products were characterised by the means of GPC, MALDI, NMR, GC, DSC and TGA techniques. Polymer molecular weight, polydispersity, monomer conversion, glass transition temperature and degradation temperature were calculated. Polymers with unique low glass transition temperature and high thermostability were produced. Furthermore, mass spectrometry analysis has shown the major detectable reaction product to be cyclic (Fig. 1). These findings do not agree with the fundamental theory of step-growth polymerisations presented in textbooks mostly based on the work of Carothers [Chem. Rev. 8, 1931, p.353]. His theory assumes that linear monomers react with each other yielding linear oligomers and finally linear polymers.

Fig.1



Cyclization was considered to be a negligible side reaction and was not taken into account. However, at that time, detection of cyclic polymers was difficult and only the development of MALDI ToF mass spectrometry during the past two decades has provided a new powerful tool for qualitative analyses of cyclic polymers that reveals these polymers to us. Usually only small amounts of cyclic oligomers are formed during bulk condensation polymerizations, but cyclic oligoesters can be prepared as major products by using classical high dilution technique. Our findings show that cyclic oligomers and polymers can be the major products in melt polycondensation also. More and more cyclic oligomers and polymers are produced during our reactions until conversion reaches 100 %, and the cyclization limits the chain growth.

Research activities on the synthesis and characterisation of the cyclic polymers are expanding rapidly. The increasing interest is related with the importance of large cyclic structures, such as circular DNA, cyclic peptides and cyclic oligosaccharides and polysaccharides in biological chemistry and molecular biology.

No cyclic fluoropolymers have been reported previously. Fluorinated materials are known for their distinctive properties relative to their non-fluorinated analogs. Because of unique thermal, water repellency, chemical proof, lubricant, electric insulation properties of these materials they can be applied for manufacturing of variety of unsticky, self-cleaning, antifouling, biocompatible coatings and thin films. A characteristic property of cyclic polymers, the hydrodynamic volume, is different from that of linear polymers which leads to different solution properties, including higher GPC elution volume, lower intrinsic viscosity and lower translational friction coefficient. The cyclic polymers have also higher density and melt viscosity (greater at low molecular weights, but smaller at high molecular weights), higher refractive index and higher glass transition temperature. In melts, ring polymers assume more compact conformations compared to linear chains. Cyclic polymers may be used as a feedstock for ring opening polymerisation or as additives to linear polymers for fine-tuning of the rheological properties.

The Project provided excellent training on variety of different subjects such as communicating research, teaching, leadership, supervision of junior researchers, research management, knowledge transfer and commercialization and, all of which are vital skills for an independent researcher in the 21st Century. Furthermore, the fellowship facilitated expansion of general scientific knowledge and practical experience in the areas of green technologies in supercritical fluids, fluorous multiphase catalysis, polymer synthesis and characterisation, biocatalysis and protein characterisation, and development of new environmentally sustainable processing of organic materials.