Załącznik nr 3 do wniosku o wyznaczenie recenzentów i komisji egzaminacyjnych w przewodzie doktorskim mgr inż. Michała Grzymajło - streszczenie rozprawy doktorskiej w języku angielskim

Doctoral dissertation of mgr inż. Michał Grzymajło is entitled "**Composite materials made of poly (glycerol adipate) and bioglass with potential application in bone tissue engineering**".

The dissertation deals with the synthesis of the biodegradable polymer - poly(glycerol adipate) (PGA), as well as the preparation of a composite material based on PGA and its formation into a porous scaffold with potential application in bone tissue engineering.

In the first part of the work, the conditions for the synthesis of poly(glycerol adipate) prepolymer (pPGA) were optimized. The optimization was based on the choice of time (8, 24, 48 and 72h) and synthesis temperature (40, 50, 60 and 70°C). The prepolymer was made from glycerol and divinyl adipate in THF in the presence of the *Candida Antarctica* enzyme catalyst (Lipase type B). From the ^{1}HNMR, FTiR and GPC analysis, the PhD student determined the optimal synthesis conditions (24h, 40°C). Under these conditions, the polymer had highly linear structure and satisfactory molecular weights.

Then, the purification of the prepolymer from solvent residues and low molecular weight polycondensation reaction products was made. A number of systems were tested including: THF - diethyl ether, THF - diisopropyl ether, THF - water, where the polymer was dissolved in THF and added dropwise to the other solvent mentioned in the system. The purification methods were complemented by pPGA dialysis through the membrane (MWCO 1kDa). In the following work, pPGA purified by dialysis was used, as it was shown that this method was the most effective in removing the solvent and low molecular weight fractions of the prepolymer.
In the further part of the work, a number of composites of poly (glycerol adipate) prepolymer and bioglass were produced. In this section it has been shown that it is possible to obtain a highly filled prepolymer system with 70 wt.% bioglass content.
In the next stage of the research, attempts to optimize the thermal cross-linking of pPGA were made. The cross-linking conditions were changed in the range of 100-200°C, and the reaction time in the range of 0.5-24h. The experiments allowed for the determination of cross-linking parameters - 180°C during 12 hours, and under these conditions, porous PGA / bioglass composites with a bioglass content of 50-80 wt.% were successfully produced. The materials were obtained by the technique of thermally induced phase separation supported by salt (NaCl) leaching (TIPS-SL) with a grain size range of 150-315 µm and 315-400 µm. The composites were thermally crosslinked prior to the salt leaching step. Porous materials with a density of 0.36-1.28 g/cm^3 and a porosity of 45-80% were obtained. However, the obtained material showed cytotoxicity.
Then, chemical cross-linking of pPGA with the use of lysine methyl ester diisocyanate was conducted. The tests were carried out in the ratio of isocyanate groups: 25%, 50% and 100% with respect to the content of hydroxyl groups in the polymer. The biological tests showed no cytotoxicity for the last of the above-mentioned samples. After obtaining positive biological results, the formation of porous composites PGA/bioglass and PGA/bioglass modified with L-lysine and filler contents of 10 and 20 wt.% was started, also using TIPS-SL technique. The materials were chemically crosslinked. The obtained composites showed porosity of 85-91%, a density of 0.12-0.16 g/cm^3 and a water absorption of 700-930%. Additionally, the scaffolds were examined mechanically, showing their good flexibility - after compressing the samples 10 times (90% strain), the samples showed a return to their original shape. There was also no decohesion between the polymer and bioglass, which indicates good compatibility of both materials.
Preparation of PGA/bioglass specimens (chemically cross-linked with lysine methyl ester diisocyanate) for in vivo tests (studies of implants on rabbits) was the final step of the work.