DEGRADATION STUDIES OF POLY(DIOL CITRATES) FOR VASCULAR TISSUE ENGINEERING PURPOSES

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Introduction
Poly(diol citrates) (PDC) have been recognised as potential materials for tissue engineering of blood vessels with diameter <6 mm, due to their biodegradability, cytocompatibility, bioactivity and their capability to be modified in many ways [1,2]. The aim of this study was to evaluate degradation kinetics and mechanism of two types of PDCs obtained via polycondensation and modified or not with panthenol or glutathione.

Materials and Methods
Cross-linked poly(hexamethylene citrate) and poly(octamethylene citrate) (cPHC and cPOC, respectively) were obtained. In brief, citric acid and 1,6-hexanediol/1,8-octanediol in molar ratio 2:3 were melted together at 140°C for 40 min under stirring to synthesise a prepolymer, which was then dissolved in 96% ethanol, precipitated in distilled water, lyophilised (0.37 Ba) and dissolved again in 96% ethanol. Then either panthenol or glutathione (concentrations 0%, 0.4% and 0.8%) were added to the prepolymer and left for post-polymerisation for 10 days at 80°C under vacuum (200 mbar). Round samples (diameter 8 mm) were excised by a hole punch, weighed and incubated in ultra-pure water (UHQ-water – 10 ml/sample, 37°C) for predefined time intervals (up to 3 months) – 3 samples per time interval and material. After incubation, the samples were weighed with analytical balance in a wet state and once again after lyophilisation to evaluate weight loss and water absorption capacity. Shore hardness tests were also conducted to assess decrease in cross-linking density. Moreover, incubation fluid was characterised by pH measurement to further evaluate the degradation progress.

Results and Discussion
Weight loss of the samples was mostly dependent on the type of diol (FIG. 1) – cPHC more hydrophilic alkylene units degraded faster (15-25% weight loss) as compared to cPOC (4-9% weight loss) after 3 months. The influence of the additives used on the weight loss of studied samples was less significant – samples modified with panthenol were degrading slightly slower while the ones modified with glutathione degraded faster than the controls. In all cases notable weight loss became appeared between day 21 and 35 of the experiment. This observation was found in line with decrease in hardness and increase in susceptibility to water absorption. The pH of the degradation fluid was decreasing mostly during the first days of incubation to the values of 3.5 – 4.5 and 4.5 – 5.5 for cPHC and cPOC materials, respectively.

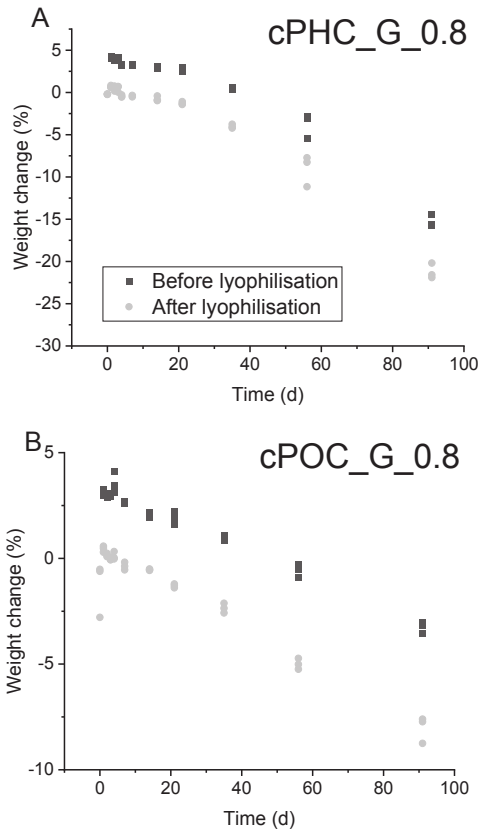

FIG. 1. Weight change for cPHC and cPOC with addition of 0.8% of glutathione. Difference in degradation rate between both polymers is observed.

The results indicate, that the initial increase in samples weight is due to water absorption. It suggests that water molecules enter the structure and expand free spaces between polymer chains. Thus, in the course of hydrolysis of ester bonds the number of cross-links between polymer chains decreases, resulting in lower hardness and higher water absorption. pH changes observed prior to weight loss suggest elution of unreacted monomers. The results show that degradation is gradual and slow. Acidic products of degradation should not inhibit surrounding tissue regeneration, as *in vivo* they will be released to the flowing blood, which has a very good buffering capacity.

Conclusions
We evaluated degradation kinetics of cPHC and cPOC materials, that is rather influenced by the type of diol and post-polymerisation time, as compared to other studies [2], than by the type of a modifier. Slow and gradual degradation creates a good perspective for vascular prostheses, that will not lose their mechanical properties before the native tissue is rebuilt. Obtained materials seem to be promising for vascular tissue engineering purposes.

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