

TIN-FREE BIOELASTOMERIC POLYURETHANES FOR MEDICAL APPLICATIONS

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Introduction

DBTDL (dibutyltin dilaurate) is the most popular and effective catalyst which is used for synthesis of biomedical polymers, including poly(lactic acid)(PLA), polyurethanes, and more [1]. However, it is known from the literature that tin compounds show cytotoxicity and have to be removed from the final products. Therefore, the aim of this work is to find an alternative, non-toxic catalyst suitable for the synthesis of telechelic polyurethane macromonomers to create bioelastomers. Several compounds have already been described as highly active in isocyanate groups reaction [2]. Among them, bismuth- and zinc-based catalysts are of great interest, due to their low toxicity and high catalytic activity [3].

Materials and Methods

Synthesis of telechelic macromonomers was performed based on previous work [4] with modifications. Four different catalysts have been used: dibutyltin dilaurate (DBTDL), bismuth neodecanoate (BiNDE), bismuth tris(2-ethylhexanoate) (BiHex), zinc(II) acetylacetonate (ZnAc). Reactions were performed in two steps. In the first step, 25 ml of ethyl acetate (EtOAc), an appropriate amount of catalyst (2 or 4 mol%) and 6.5 ml (0.052 mmol) of isophorone diisocyanate were added into the flask. Then, 25 g (0.013 mmol) of long-chain diol (Pr, Mn=2000 g/mol) was dissolved in 25 ml of EtOAc and added dropwise into ice-cold mixture. The temperature of the reaction was set to 70°C. Progress of the reaction was controlled by tracking the ratio between FT-IR absorbance at 2262 cm⁻¹ and 1526 cm⁻¹ which correspond to isocyanate groups and N-H bending vibrations in forming urethane, respectively. In the second step, 6 mg (0.03 mmol) of phenothiazine, the same amount of catalyst as in first step and of 2-hydroxyethyl methacrylate (HEMA) were introduced. Reaction was considered as finished when FT-IR absorbance at 2262 cm⁻¹ disappeared. The structure of obtained telechelic macromonomers was characterised with Fourier transform infrared spectroscopy (FTIR, BRUKER ALPHA Platinum apparatus) and nuclear magnetic resonance (NMR, Bruker DPX HD-400 MHz). Obtained liquid macromonomers were photocured with use of photoinitiator 2% w/w, Omnirad 819. 1 mm thick films were produced with use of a steel applicator on glass plate. The composition was irradiated with UV light with maximum intensity at the wavelength λ_{max} of 385 nm in air and argon atmosphere, in a glove box. The intensity of the radiation of the light source (DYMAX Bluewave LED Prime UVA pointer (USA)) was adjusted to 20 mW/cm² with the help of radiometer, AktiPrint (Technigraf GmbH). The exposure time was 150 seconds for 2.25 cm². The cured samples were refluxed for 6 hours by Soxhlet apparatus (Behr Labor-Technik, Germany) to calculate the gel fraction.

The cytotoxicity tests were performed according to ISO10993-5 using L929 cell line. Cell viability was then assessed using light microscopy (Delta Optical IB-100, Mińsk Mazowiecki, Poland) and the resazurin viability assay.

Results and Discussion

Chemical structure of obtained macromonomers has been confirmed by ATR-FTIR, ¹HNMR and ¹³CNMR. Cell viability study showed (FIG. 1) that the use of tin-free catalysts, especially bismuth tris(2-ethylhexanoate) (sample PrBiHex_2) and zinc(II) acetylacetonate (sample PrZnAc_2) resulted in higher cell viability from all tested materials and conditions (catalyst concentration and atmosphere). The differences in cytotoxicity are likely due to the residual amount of DBTDL present in the material. Importantly, we did not observe any effect of atmosphere during photocrosslinking, indicating that the oxygen inhibition is relatively modest.

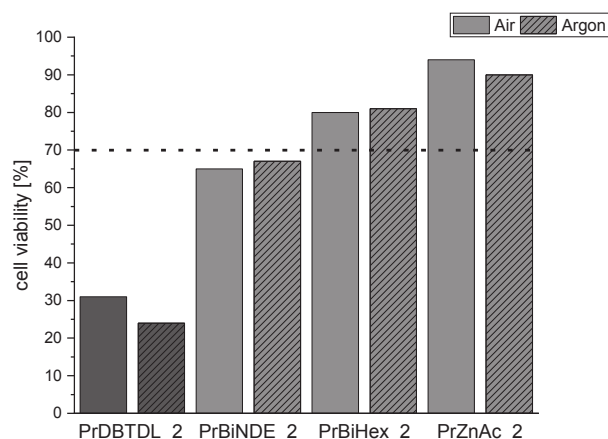


FIG. 1. Cell viability results of materials obtained with 2 mol% of different metallic catalysts.

Conclusions

All catalysts allowed to obtain the same structure of polyurethane macromonomer. Elastomeric networks obtained from macromonomer synthesised with zinc and bismuth catalysts showed lower cytotoxicity as compared to DBTDL. The results indicate high potential of these new materials for medical applications.

Acknowledgments

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