BIOCOMPATIBILITY NORMATIVE INVESTIGATION OF NEW CO-POLYMER INTENDED FOR MANUFACTURING OF VENTRICULAR ASSIST DEVICES

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Introduction

Nowadays one of the "gold standard" of end stage heart failure treatment is mechanical circulatory supporting by means of ventricular assist devices (VAD). Pulsating VAD (for adults as well as for children) are made of biocompatible polymers resistant to biodegradation. As a part of the Polish Artificial Heart project [1] the new biocompatible co-polymer intended for Polish pulsatile VADs has been developed.

The goal of presented study was to assess the biocompatibility of developed co-polymer according to regulations mandatory for medical products.

Materials and Methods

The investigated material was poly(aliphatic/aromatic-ester)s (PED) containing hard segments as in poly(ethylene terephthalate) (PET) and soft segments of dimer of linoleic acid (DLA) [2]. The weight percentage content of PET was 65% (hereinafter called PET65) or 70% (called PET70). All tested samples were manufactured of granulate by means of injection moulding and sterilized by radiation (25kGy).

Investigation was carried out according to following sections of PN EN ISO 10993 standard:

s.4: hemolysis: investigation was carried out on human whole blood preserved by means of CPDA-1. Based on plasma free haemoglobin concentration the index of hemolysis (IH) was calculated. Test duration: 8 and 24h.

s.5: cytotoxicity: examinations were carried out on fibroblasts L929 incubated for 24h in Medium 199 supplemented by 10%FCS. Live and necrotic cells were marked by FDA and PI, respectively.

s.6: local effect after implantation: reference biomaterials for PET65 and PET70 were Bionate90A and Bionate55D (DSM Biomedical, USA), respectively. Apiece 5 rabbits were implanted for each biomaterial and for blind test (surgery only, no implant). Observation duration: 4 and 12 weeks. Assessment of AlAT, AspAT, bilirubin, CRP, IL6, C5a, blood morphology and organs histopathological examination after euthanasia was performed.

s.9: biodegradation: biodegradation tests were being carried out for 30, 60 and 180 days in SBF. Following aspects were assessed: matter eluviation to SBF (HPLC), polymer degradation (GPC), chemical and morphological surface degradation (FTIR and SEM, respectively) and glass transition temperature (DSC).

s.10: intradermal reactivity: intradermal injection of PET65 and PET70 extracts in sesame oil and 0.9%NaCl was carried out. As a reference pure solvents were injected. Apiece 3 rabbits per each biomaterial were utilized. Duration of animals' observation: 24, 48 and 72 hours. Assessment of erythema, eschar and oedema according to scoring scale attached in standard was done.

s.10: allergic reaction: examination were carried out in accordance with GPMT test. PET65 and PET70 extracts in acetone solvent as well as pure acetone (as a reference) were used. Apiece 10 and 5 guinea pigs were utilized in tested and reference groups, respectively. The erythema was assessed according to Magnusson-Klingsman scale.

s.11: subacute systemic toxicity: intraperitoneal implantation of PET65 and PET70 (apiece 6 rabbits per one biomaterial and blind test). Observation duration: 28 days. Assessment of AlAT, AspAT, bilirubin, CRP, blood morphology and organs histopathological examination after euthanasia were performed.

s.11: acute systemic toxicity: intravenous injection of PET65 and PET70 extracts in 0.9%NaCl (apiece 3 rabbits per one biomaterial and blind test – pure 0.9%NaCl injection) was done. Observation of animals' behaviour per 7 days was carried out.

Results and Discussion

s.4: hemolysis: in all cases IH<0.5% (upper level=2.0%). Investigated materials are non-haemolytic.

s.5: cytotoxicity: no lysis as well as reduction of cells' growth were pointed out. The level of cytotoxicity of investigated materials is: no toxic.

s.6: local effect after implantation: all biochemical and morphological parameters were in physiological ranges. No statistically significant differences of parameters between tested and control group were pointed out ($p>0.50$). No significant changes in histopathological picture of organs as well as wound were shown.

s.9: biodegradation: no differences in GPC, HPLC and FTIR spectrums as well as SEM pictures acquired before and after degradation were shown. Investigated materials are high resistant for biodegradation.

s.10: intradermal reactivity: the scoring for PET65 and PET70 was 0.66 and 0.64, respectively. Scoring<1 denotes no intradermal reaction of investigated materials.

s.10: allergic reaction: in any case the scoring in Magnusson-Klingsman scale equalled zero. Investigated materials didn't cause allergic reaction.

s.11: subacute systemic toxicity: all biochemical and morphological parameters were in physiological ranges. No statistically significant differences of parameters before and after implantation were pointed out ($p<0.05$). No significant changes in histopathological picture of organs as well as wound were shown.

s.11: acute systemic toxicity: no changes in animals' behaving, weight and site of injection were found.

Conclusions

Normative investigation carried out according to ISO10993 demonstrated, that PET65 and PET70 are non-haemolytic, non-toxic, no allergenic and strongly resistant to biodegradation. High level of biocompatibility makes those materials suitable to application in medical devices. It is recommended to carry out additional investigation concerned the thrombogenicity and industrial processing of designed co-polymer.

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References

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