

Chemical Modification of Irradiated Bovine Pericardium in Material Heart Valve Substitute

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1. Introduction

Cardiac valves prosthesis can be divided in two groups: mechanical or biological. Biological ones can be easily monitored and do not induce clot formation, but are less durable. To improve the material resistance several chemical and physical reticulation processes have been developed. Nowa days the most consolidated method is reticulation by glutaraldehyde (GA), although GA reticulation can induce calcification in vivo leading to valve failure and necessity of prosthesis changes [Lee Y.S., 1993]. Several efforts have been made to decrease the calcium deposition in valve prosthesis: heparin coating; hyaluronic acid coating; change in reticulation method like Ultra-violet radiation, photochemical cross-link [Moore, M. A., 1994] and utilization of epoxide molecules derived of epichlorohydrin. This work explores new opportunities in biomaterial treatments introducing the utilization of anhydride, aldehydes, epoxides and ionizing radiation.

- **Anhydrides:** react with amines leading to a correspondent acid and an amide.
- **Aldehydes:** react with amines forming Schiff's bases.
- **Ionizing radiation (electron beam):** Broadly utilized in reticulation of rubber, acts by creating radicals which are responsible for cross-linking the material.
- **Epoxides:** react with amines and sulfidric groups.

To evaluate the possible application of the chemically modified pericardium as a material for heart valve substitute in bioprosthesis, the samples were submitted to traction test. This test is one of many required to liberate the application of the treatment for production of heart valve prosthesis.

2. Materials and Methods

2.1 Bovine pericardium

Samples of pericardium were collected at slaughterhouse, cleaned, washed, and stored in glycerol solution. Before use, pericardium was washed with saline solution (NaCl 0.9%).

2.2 Chemical modifications

Glutaraldehyde. Samples of pericardium were treated with glutaraldehyde 0.5% for 10 days in PBS pH: 7.4, with change of reaction medium every 2 days. After the treatment, the samples were stored in formaldehyde solution.

Benzaldehyde. Samples of pericardium were treated with 1.5% of benzaldehyde, 2% and tween 80, 2% in aqueous solution for five days.

Phenethylamine-diepoxide: The synthesis has been based in McKELVEY, 1960 protocol.

2.3 Ionizing radiation

Irradiation was performed in an electron beam accelerator at CTR-IPEN São Paulo, Brazil. Samples were disposed in Petri-dishes and sealed with N₂ atm.

2.4 Mechanical test

The stress-strain tests were with charge cell of 245.1662N and scale sensibility of 0.009806N. Test speed according to norm ASTM D638 for test specimen's type V.

2.5 Data analysis

Computer program made of Matlab 6.5 Software (MathWorks, Inc - USA) was used to obtain stress-strain curve, tensile at rupture and calculate Young's modulus (modulus of elasticity).

3. Results and discussion.

Sample	E	Sd	RT	Sd
GA	181,8	±68,1	24,02	±9,7
Benzaldehyde	14,33	±5,17	20,20	±7,12
Phenethylamine diepoxide	187,48	±34,89	26,73	±4,59
25 KGy dose rate 5,09 KGy/s	91,25	±40,28	15,36	±6,32
25 KGy dose rate 2,42 KGy/s	97,83	±21,96	13,15	±3,11
50 KGy dose rate 2,42 KGy/s	103,05	±49,44	12,60	±6,78
50KGy dose rate 5,09 KGy/s	122,15	±41,40	13,64	±4,18

Table 1 - Young's modulus (E) and rupture tension (RT)

According to data these results were similar to standard treatment (GA). These preliminary tests suggest that one of these treatments can be used as a future material heart valve substitute. Benzaldehyde and phenethylamine diepoxide aromatic rings confer to the molecule non polar characteristics what would help avoiding calcium deposition. A previous test conducted by this group has shown that lyophilization of bovine pericardium before chemical treatments with epoxide compounds inhibited the in vitro calcification process [Aimoli,CG, 2007]. Radiation treated valves are interesting because they do not add to pericardium new antigens or cytotoxic molecules.

4. References

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