MODIFICATION OF USED POLYURETHANE IN ARTIFICIAL HEART

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RESUMEN. Uno de los principales obstáculos en el uso de los materiales no biológicos para la confección de corazones artificiales (TAH) es su capacidad de inducir trombosis y embolismos. Las investigaciones actuales demuestran que cuando un material sintético se pone en contacto con la sangre fluyente, la mayoría de estos materiales son rápidamente recubiertos con una capa de proteínas, paralelamente con la adhesión de plaquetas, lo que conduce a la formación de trombos. Hasta el momento no se ha encontrado un material que reúna todos los requisitos de biocompatibilidad. Con el objetivo de mejorar las propiedades del PUL, un poliuteruretano usado en la construcción del TAH cubano, se modificó este polímero con silicona. Se evaluaron las propiedades físico-mecánicas y de biocompatibilidad del PUL y de éste modificado. Para evaluar las propiedades *in vivo*, las superficies internas y en contacto con la sangre del TAH cubano, así como sus conexiones con los grandes vasos y aurículas del corazón, fueran hechas con este material y probados en 14 transplantes en terneros. Los experimentos demostraron que el PUL modificado resulta superior a su original.

ABSTRACT. The main obstacles in the use of a nonbiological material in Total Artificial Heart (TAH) implants are surface-induced thrombosis and embolisms. Current research has shown than on exposure of synthetic surfaces to whole flowing blood, most materials are rapidly coated with a layer of proteins in parallel with the adhesion of platelets, leading to thrombus formation. At present there is still no material available that meets all requirements for biocompatibility. Trying to improve the thromboresistance properties of PUL, a polyetherurethane used in the construction of TAH, this polymer was modified with silicone. The physical mechanical as well as i*n vitro* and *in vivo* thromboresistance properties were evaluated on both materials. For *in vivo* studies, the TAH contacting blood surface was covered with this material and quick connectors were made with it and tested in calves. It was demonstrated that the modification made on PUL improves the *in vitro* and *in vivo* thromboresistance properties.

INTRODUCTION

In developing a blood compatible polymer for cardiovascular prosthesis is important to take into account some physical and biological properties like non-toxicity, sterilizability. It is also important for that material to be easy handling, nondegradable, with stable mechanical strength for a prolonged period of time and nonthrombogenic.

Today, no type of material is perfectly good for using in blood contacting surfaces, for that reason many groups are interested in synthesizing new materials or modulating the surface of the material used in cardiovascular devices trying to decrease the thrombogenic events.[1-4]

In this paper, some biological and physical properties of a segmented polyetherurethane (PUL) used in artificial hearts and a modification of this polymer developed by the authors for the construction of the inflow and outflow quick connectors rings of the TAH type CORAMEC-4 are studied.

The substitution of PUL by its modification was due to initial difficulties reported by our surgeons for the connection of the device, probably caused by its not appropriate elasticity for this purpose. For comparing, another polyetherurethane pellethane 2363-80A (PELL) was also tested in some experiments.

MATERIALS AND METHODS

PUL, a segmented polyetherurethane based on polypropylene glycol (average molecular mass 1 200), 4,4-methylenebis (phenylisocianate) and hydrazine hydrate manufactured by Technoplast Chropyne, Czechoslovakia.

Modified PUL (a blend of PUL with Merck 7742 silicone oil), (Mod. PUL). Pellethane 2363-BOA (PELL)-at ypeo f a segmented polyetherurethane based on polybutylene glycol, 4,4-methylenebis (Phenylisocianate) and butylene glycol manufactured by Upjohn Co. U.S.A.

Platelets adhesion studies

Solution of PUL, Mod. PUL and PELL in dimethylformamide were prepared. Films of approximately 0,1 mm were obtained by a dipping and drying process on metal plates. Square samples of (3 x 3) cm were cut out, rinsed with distilled water twice and finally in ethanol. The films were dried in an oven at 60 °C for4h.

Sheep blood platelets were isolated after collection from citrated blood placed in contact with the different polymers and counted under an optical microscope as described elsewhere.[5]

Thirty vision fields were randomly chosen and averaged in identical fashion for all samples. The data were expressed as the number of platelets observed per square centimeter.

Recalcification time evaluation

Tubes of (12 x 75) mm of the different polymers were made and cleaned in a similar way as films. Sheep blood was collected and citrated (1 mL of 3,8 % sodium citrate for 9 mL of blood) and tested for recalcification time according to the Modified Lee-White clotting time test.[6]

Free hemoglobin and eritrocytes count

The tests were performed with polymer films covering the inner surface of 5 mL Petri dishes obtained by slow evaporation at 60 °C of the polymer solution in a vacuum oven.

Five mililitres of citrated fresh sheep blood were placed at the same time in contact with the films in the Petri dishes andc overed withw atch glassesf or6h.

The dishes, at room temperature, were placed at the same time in a non-constant orbital shaker. The amount of hemoglobin liberated by the lysis of erythrocytes and the number of erythrocytes were determined by the benzidine technique and by microscopy methods [7] respectively.

Mechanical properties

Uniaxel Stress-strain data were taken on a Alwetron TCT-10 (Sweden), at a constant rate of strain of 15 mm/min 25 °C.

In order to know the effect of sterilization on the mechanical properties of the polymer some samples were treated with 15 kGy of radiation.

In vivo testing

Fourteen male calves were used for testing the behavior of PUL (n = 7) and Mod. PUL (n = 7). The inflow and outflow quick connectors of the Cuban TAH were made from this polyurethanes.

The TAH CORAMEC-4, the driving and control unit CORAMEC-100, the pre-operative preparation, anesthesia, surgical method of extracorporeal circulation and post-operative care are described in other papers.[8,9]

At the end of the experiment the TAH was removed and the presence of thrombi in the quick connector was evaluated macroscopically.

Statistical data from different materials were compared using a Krushal-Wallis test with significance assessed at the $p < 0,05$ then, Mann-Witney test was used for determining at what time points pair-wise differences existed.

RESULTS

Platelets adhesion studies

The number of adhered platelets to Mod. Pul was significantly minor than its original PUL and than PELL (Table I)

TABLA I
Platelet adhesion in three polyetherurethanes

Test material	Platelet/c
Mod. PUL	118 ± 45 a
PUL	484 ± 196 b
PELL	210 ± 94 c

Values expressed as $\overline{X} \pm$ ES (from 30 observations of a separated experiments). Different letters mean $p < 0,05$. Equal letters mean $p > 0,05$.

Recalcification time evaluation

All polyetherurethanes showed an enhancement of the recalcification time ($p < 0,05$) in regards to glass tubes. Mod. PUL was the best of all (Table II).

TABLA II
Recalcification time in three polyetherurethanes

Test material	% of plasma recalcification time respect to glass
Mod. PUL	172 ± 41 a
PUL	127 ± 21 b
PELL	123 ± 40b

Values expressed as $\overline{X} \pm$ ES of 7 experiments.

After 6 h of blood contact with films of polyurethanes the number of erythrocytes was higher in Mod. PUL ($p < 0,05$) than in the other two polymers (Table III).

TABLE III
Effect of polymers films on erythrocyte count

Test material	% of erytrocytes respects to Petri dishes
Mod. PUL	137 ± 24 a
PUL	101 ± 9b
PELL	113 ± 23 b

Values expressed as $\overline{X} \pm$ ES of 7 experiments.

All polyurethanes released less hemoglobin than glass. PELL had the best behavior (Table IV).

TABLE IV
Effect of polymer film on the quantity of free hemoglobin

Test materials	% of plasma hemoglobin respect to Petri dishes
Mod. PUL	79 ± 9a
PUL	80 ± 20a
PELL	64 ± 12 b

Values expressed as $\overline{X} \pm$ ES of 7 experiments.

Mechanical properties

Young's and 100 % tensile modulus are listed in Table V. Mod. PUL has lower Young's modulus and 100 % tensile modulus than original PUL.

TABLE V
Mechanical properties

Test material	Young's modulus (MPa)	100 % tensile modulus (MPa)
Mod. PUL	5,9 ± 0,3	5,1 ± 0,2
Irradiated Mod. PUL	5,8 ± 0,4	5,4 ± 0,4
PUL	11,5 ± 0,6	8,5 ± 0,6
Irradiated PUL	11,5 ± 0,7	8,5 ± 0,4

Values expressed as $\overline{X} \pm$ ES of 7 experiments.

Irradiation did not produce significant change on these modulus for both polymers.

In vivo testing

According to the macroscopic appearance, the Mod. PUL and PUL behaves well as their surfaces were without *thrombi.*

DISCUSSION

One of the most important problems in the construction of the different parts of a TAH is the material of which these devices are manufactured. It must have appropriate physical and mechanical properties and good biocompatibility.

Evaluation of the polymers described shows that in regards to hemocompatibility the best behavior could be attributed to Modified PUL, since it was found that the Modification increased plasma recalcification time and the number of erythrocytes and decreases the number of adhered platelets.

On the other hand, no *thrombi* were formed in any of the quick connectors manufactured from Mod. PUL and our surgeons reported that connectors made from this material were easily implanted. This agrees with the results of mechanical properties test that showed that Mod. PUL is more elastic than PUL.

Research is in progress in our group and the housings of our TAH are being manufactured with Mod. PUL.

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