Hydrogel coatings for artificial heart implants

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Polyurethanes (PU) are nowadays one of the most widely used types of polymers for biomedical applications. The segmented nature of these materials enables to obtain both flexibility and mechanical strength within the same material. However, there is a need to modify a surface of PU in order to produce highly hemocompatible materials that can be used in fabrication of permanent blood-contacting devices such as vascular implants, valves or hearts. Among many types of modifications, hydrogel coating appears to be very promising. Such modification increases the hydrophilicity of PU which in turn causes an increase in the bio- and hemocompatibility of the material.

The aim of presented study was to create a polyvinylpyrrolidone (PVP) hydrogel coating onto a surface of polyurethane. A possibility of using a free radical polymerization reaction was investigated. The obtained materials were analyzed in terms of durability, swelling ratio and contact angle. The FTIR-ATR analysis confirmed that polyurethane surfaces have been successfully coated with PVP.

Keywords: polyurethane, polyvinylpyrrolidone, hydrogel coating, artificial heart

Introduction

Permanent artificial implants are considered to be the future of the modern medicine. Constant increase in the number of cases of cardiac diseases results in insufficient number of organ donors compared to number of people who need them. This is why it becomes necessary to replace defective hearts with mechanical prostheses. A very important point that has to be considered is the design of a surface that is resistant to clot formation.

This work presents a method of covering polyurethane, a material used in implant production, with polyvinylpyrrolidone — a polymer which forms hydrogels. Such system is expected to increase the biocompatibility of the material and prevent blood from clotting on the surface of the implant.

Biomaterials in cardiosurgery

Blood clotting

The phenomenon of blood coagulation is one of the biggest problems that occur during the blood–biomaterial interaction. It is especially important regarding implants that have a direct contact with blood such as artificial blood vessels, valves or hearts [1].

Blood clotting is a very complex natural process which results in forming of clots that prevent leakages from damaged blood vessels. It begins in the place where the vessel has been damaged and the subendothelial matrix (the inner part of the vessel) has been exposed. The platelets instantly form a plug in the place of damage. Activated platelets initiate a coagulation cascade (Fig. 1) what results in the activation of fibrin. Fibrin fibers form a net which capture red blood cells and form the final clot [2].

The process of clotting described above is caused by damaged blood vessel. However the same process can be caused by other sources of improper vessel surface.

Joseph Lister in 1863 discovered that bovine blood stays liquid when kept in a vein and coagulates quickly when poured to a glass container. His experiment proved that the process of coagulation occurs on a surface of an artificial vessel as well as in a damaged natural vein [4].

Despite their very good biocompatibility, polyurethanes that are used in construction of implants may cause blood coagulation. This can result in serious problems

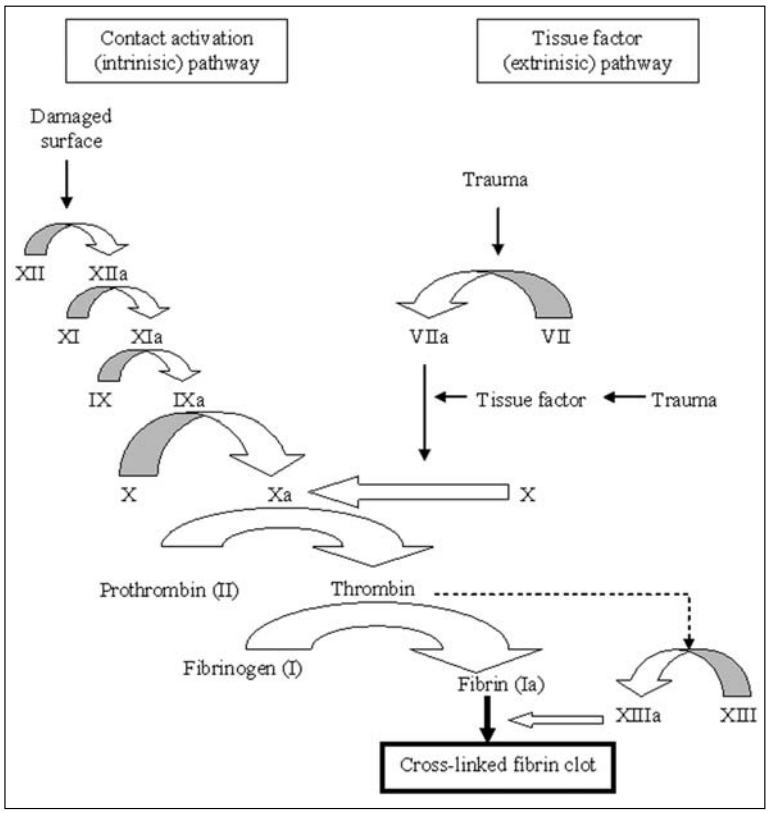

Fig. 1. The scheme of coagulation cascade.

with patients' health such as thrombosis that or even strokes. For that reason, a rigorous examination of materials used to create cardiovascular implants is necessary [5].

Hemocompatibility of a biomaterial mainly depends on the properties of its surface. Therefore, many methods of polymer surface modification were developed.

Surface modifications of polyurethanes

A material that can be used for biomedical application must meet some specific requirements. Biocompatible material cannot cause infections or allergies, cannot affect cells (including blood cells) and must be sterilisable. Polymeric materials for implant construction should not contain low-molecular ingredients such as fillers, plasticizers or monomers [6].

Properties of polyurethanes are only influenced by base components that are used during the process of synthesis. Synthesis of polyurethanes does not require additional substances like plasticizers or stiffeners, which are often toxic to humans. This is why PUs are commonly regarded as biocompatible and have many uses in medicine, e.g. in construction of artificial vascular implants, valves and hearts, production of stitches and dressings, catheters, dialysis membranes etc. [6].

The process of improvement of hemocompatibility of polyurethane materials is usually based on surface modification. It is achieved by coating the PU surfaces with proteins that actively prevent from coagulation e.g. heparin [5], urokinase [7] or thrombomodulin [8]. However, insufficient durability is the main disadvantage of such type of modifications.

Another approach for surface modification is coating PUs with other polymer that exhibits desired chemical properties. This type of modification has an influence on material's contact angle with water.

Hydrogels are three-dimensional polymeric structures that can absorb large amounts of water. Hydrogel coatings make the surface of polyurethane more hydrophilic and give it new, self-cleaning properties. Such surfaces are more resistant to clot formation and more compatible with human tissue [5].

In this work a method of coating PU with hydrogel is presented. Polyvinylpyrrolidone (PVP) was chosen as a polymer material to produce hydrogel layer. PVP is a highly hydrophilic polymer that forms hydrogels in water.

Materials and methods

Polyurethane (PU) in shape of disks (40 mm in diameter and 2 mm thickness) used in the research was a medical polyurethane ChronoThane™ supplied by CardioTech. ChronoThane™ contains aromatic groups in its chemical structure that make it more inert. This material is easily sterilizable and can be formed in high temperatures.

Polyvinylpyrrolidone (PVP) K 90 (average molecular weight 1300 000) was purchased from FLUKA. Its water solutions were used to make hydrogel coatings onto the surface of PU.

Other reagents and solvents: cumene hydroxyperoxide (Sigma Aldrich), ethylene glycol dimethacrylate (Sigma Aldrich), iron (II) chloride (Sigma Aldrich), L-ascorbic acid (Carlo Erba), toluene (Chempur).

Hydrogel coatings were fabricated using dip-coating technique. The modification was performed in two steps (Fig. 2). Samples were immersed in a solution of organic solvent containing cumene hydroxyperoxide (8% v/v) as a source of free radicals and ethylene glycol dimethacrylate as a cross-linking agent in the first step. This part of experiment lasted for 10 minutes. Its purpose was to create a thin layer of cumene hydrohyperoxide and ethylene glycol dimethacrylate onto PU surface. Samples were immersed in water solution containing PVP (15% w/v), iron (II) chloride (1% w/v) and L-ascorbic acid (1% w/v) in the second step. This part of experiment lasted for 40 minutes and was conducted in 55°C. The

process involved a chemical reaction between cumene hydroxyperoxide and iron chloride occurred which resulted in free radicals creation (Fig. 3). The ascorbic acid was added in order to regenerate iron (II) ions that were oxidized during the reaction.

FTIR-ATR analysis was performed to confirm the efficiency of the grafting reaction. Contact angle of fabricated materials was measured using sessile drop optical method. To determine swelling ratio, samples were weighted (W_d), immersed in water solution until swelling equilibrium was reached, removed from water and weighted (W_w). Swelling ratio was calculated according to the formula:

$$S = \frac{(W_w - W_d)}{W_d} \cdot 100\% \qquad (1)$$

where: W_d — the initial weight of sample,
W_w — the weight of swollen sample after time t.

Results and discussion

FTIR spectra analysis was made to confirm that samples were covered with PVP (Fig. 4).

FTIR-ATR spectrum of a modified sample contains a characteristic peak at about 1640 cm^{-1} wavelength. The peak is also visible in a pure PVP spectrum and is absent in an unmodified PU spectrum. It is a proof that PVP is attached to the surface of polyurethane discs.

Contact angles were measured in order to check if the process of modification has any influence on hydrophilic properties of the materials.

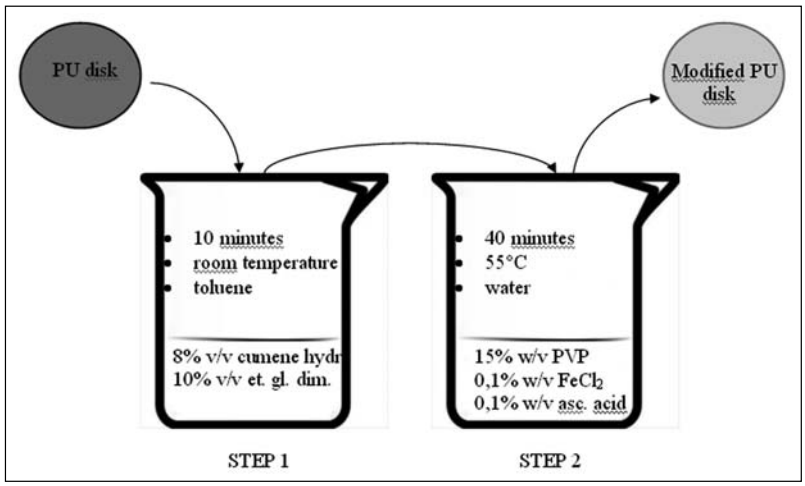

Fig. 2. The scheme of the modification process.

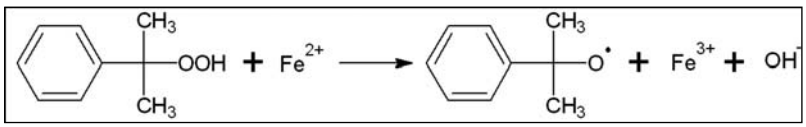

Fig. 3. The free radical reaction performed during the coating process.

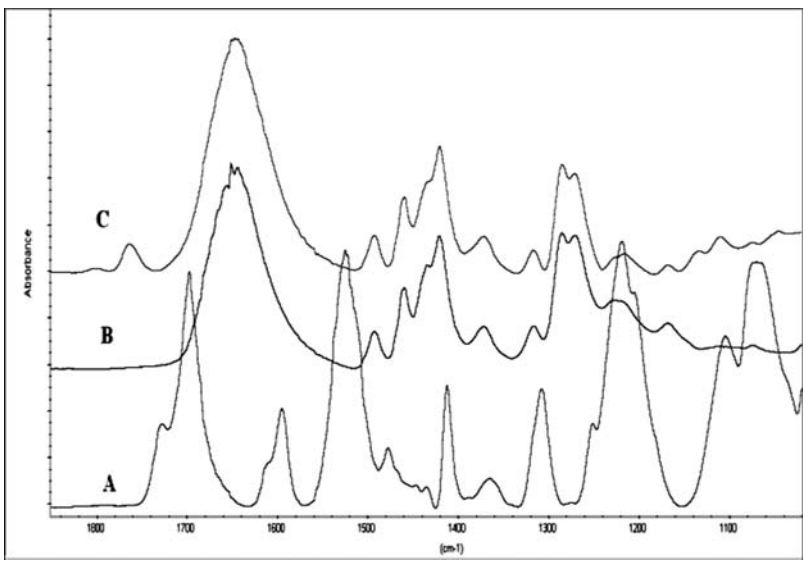

Fig. 4. The comparison of FTIR-ATR spectra of unmodified PU (A), pure PVP (B) and a sample of PU coated with PVP (C).

The contact angles comparison (Fig. 5.) shows that after modification samples became much more hydrophilic than before. The contact angle exhibits different values for unmodified PU (66°) and PU coated with PVP (13°) (Fig. 6).

The radicals created during the process can react with polyurethane, PVP and ethylene glycol dimethacrylate that is present in the solution. Such conditions provide a stable chemical bonding between PU and PVP. However, examined polymers can also bind to each other as a result of different interactions, e.g. hydrogen bonds and physical entanglements between polymer chains. Thus, the experiments were performed with the use of free radicals reaction and without it.

In order estimate the amount of PVP attached to the samples their swelling ratios were compared (Fig. 7).

The comparison above proves that free radicals presence in the solution improves the performance of the process. Samples treated with the solution exhibit much more PVP attached to their surfaces and consequently absorbed more water than samples that were immersed in solution without free radicals.

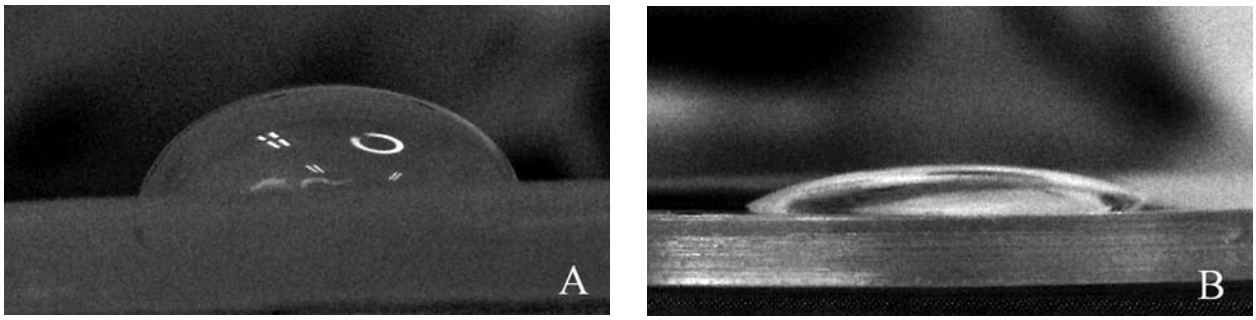

Fig. 5. Drop of water onto unmodified (A) and modified (B) polyurethane surface.

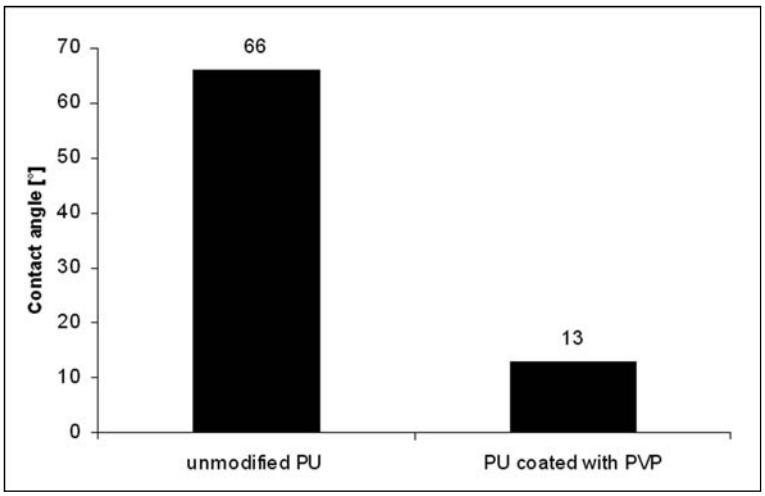

Fig. 6. The values of contact angle: PU and PU coated with PVP.

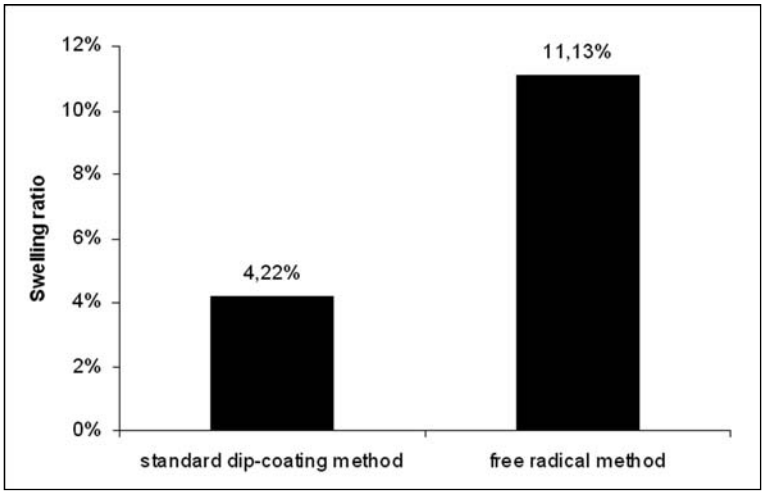

Fig. 7. The swelling ratio of hydrogels obtained by standard dip-coating technique and free radical method.

Conclusions

A simple method of coating polyurethane with hydrogel was presented. Surfaces obtained in the process were hydrophilic and able to absorb water. Presence of polyvinylpyrrolidone onto the surface of samples was confirmed by FTIR-ATR analysis.

There were two methods of creating hydrogel layer applied. The comparison of parameters, e.g. hydrogel layer durability and swelling ratio shows that the free radical reaction significantly influences efficiency of the process.

The obtained surfaces can be examined in terms of platelets adhesion and thanks to their hydrophilic properties are expected to perform much better than unmodified polyurethane. Moreover, it is planned to investigate presented biomaterials as a scaffold for endothelial cell growth during cardiovascular tissue engineering.

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