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Short Communication

Blood compatibility of tubular polymeric materials studied by biological surface interactions

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Tubular polymeric materials modified by radiation techniques can be used as vascular prosthesis and components of prosthetic devices. The biological interaction between these materials and blood was studied by *in vitro* and *ex vivo* methods. Silicone rubber tubes were copolymerized with acrylamide and N-vinylpyrrolidone by radiation-grafting techniques. The irradiation was performed with γ-rays from a ^{60}Co source at a constant dose rate (0.2 kGy/h) for various time intervals (4-15 h). To evaluate the antithrombogenicity of the grafted tubes, the surface adsorption of ^{125}I-albumin and ^{125}I-fibrinogen was studied. All graft copolymers show a preference for albumin, and the degree of preference appears to correlate with antithrombogenic tendency. In the *ex vivo* experiment with animals, tubes were implanted in the carotid artery of dogs and the blood flow in the graft copolymers was detected with an ultrasonic flow meter. The blood flow rate in the ungrafted implants decreased more rapidly (stopped completely after 15 to 210 min) compared to the flow rate in the grafted ones (decreased slowly from 38 to 35 ml/min and 70 to 60 ml/min). There was a direct relationship between both methods in the study of blood compatibility of the materials. The results suggest that the graft copolymers can be used as biomaterials for long-term use in cardiovascular systems.

Key words: antithrombogenicity, radiation, grafting, silicone rubber, acrylamide, N-vinyl-pyrrolidone.

Biomaterials are a large class of materials which are foreign to the body but that can be used clinically in contact with biological fluids and tissues as

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implants or components of devices. Synthetic polymers make up the broadest and most diverse class of biomaterials because their surfaces may be readily modified physically, chemically or biochemically. These modifications can have significant influence on biologic responses to the biomaterials (1).

Silicone rubber (SiR) is a hydrophobic polymer that has been widely used to manufacture several kinds of medical devices such as diaphragms, pacemakers, catheters, adhesives, and implants (2). Surface graft polymerization of hydrophilic monomers onto hydrophobic polymeric surfaces has been used to improve antithrombogenic properties of commercially available polymers (3,4). The present report describes the study of hemocompatible properties of silicone rubber after its copolymerization with acrylamide (AAm) and N-vinylpyrrolidone (NVP).

Silicone rubber tubes (i.d. 3.0 mm, o.d. 5.0 mm) were cut into 20-40-mm lengths, washed thoroughly with tap water and neutral detergent, and subsequently rinsed with distilled water and acetone in an ultrasonic cleaner for 5 min. The tubes were dried in vacuum at room temperature and weighed before use.

Graft copolymer of SiR-g-AAm and SiR-g-NVP tubing was prepared by simultaneous radiation-induced grafting technique as described by Stannett (5). A weighed sample of SiR tubing was placed in a glass ampoule with a known amount of a hydrophilic monomer (AAm or NVP) in the presence of acetone (AAm) or benzene (NVP). After bubbling nitrogen (N_2) into the solutions, the ampoules were sealed and irradiated with γ-rays from a ^{60}Co source at a given irradiation dose. After irradiation, the tubes were washed with water to extract the homopolymer, dried in vacuum and the extent of grafting of SiR tube was determined gravimetrically.

The biological surface interactions were studied by *in vitro* and *ex vivo* tests. In the first method, albumin and fibrinogen were labelled with ^{125}I by the chloramine T method (6). The experiments were performed under both static and flow conditions. Initially, segments of tubing 40 mm long were filled overnight with phosphate buffer saline (PBS), pH 7.3. PBS was replaced by the ^{125}I-protein solution. After 2 h, the tubes were rinsed with PBS and the radioactivity was measured in a γ-counter. In the flow experiments, the tubes were connected via silastic tubing to an automatic infusion pump (4 ml/min and 12 ml/min ^{125}I-protein solution).

The protein adsorption test demonstrated an increased albumin adsorption and a decreased fibrinogen adsorption with the extent of grafting. For the SiR-g-AAm (grafting degree: 20%) and SiR-g-NVP (grafting degree: 10%) there was a higher adsorption of albumin compared to the fibrinogen adsorption (Table 1). The grafting of hydrophilic monomers such as AAm and NVP resulted in an increased hydrophilicity of the substrates, which influenced the protein adsorp-

Table 1 - *Albumin and fibrinogen adsorption on silicone rubber (SiR) tubes.*

SiR, Ungrafted tubes; SiR-g-AAm, silicone tubes grafted with acrylamide; SiR-g-NVP, silicone tubes grafted with N-vinylpyrrolidone.

Protein solution flow (ml/min)	Adsorbed protein (pg/cm^2)					
	Albumin			Fibrinogen		
	SiR	Sir-g-AAm	SiR-g-NVP	SiR	Sir-g-AAm	Sir-g-NVP
0	20	120	300	80	30	40
4	20	180	300	120	40	50
12	60	250	380	120	50	60

tion on the surfaces (7). The hydrophilic character of the grafted surface showed a higher affinity for albumin. In contrast, there was more fibrinogen adsorption to the ungrafted tubes indicating a thrombogenic behavior of these surfaces (8).

In the *ex vivo* method, the test sample tubes (grafted and ungrafted SiR) were implanted in the carotid artery of the same dog (9). The blood flow through the tubes was monitored by a flow detector. The SiR-g-AAm tube (grafting degree: 20%) and the SiR-g-NVP tube (grafting degree: 10%) were implanted in dog A and B, respectively.

Blood flow in the ungrafted tube in dog A stopped completely after 15 min; whereas for the SiR-g-AAm tube, the blood flow decreased slowly from 70 to 60 ml/min.

In dog B, the blood circulation in the ungrafted tube stopped at 210 min whereas a smaller decrease in the blood flow (from 38 to 35 ml/min) was observed in the SiR-g-NVP tube at 240 min as shown in Figure 1. Al-

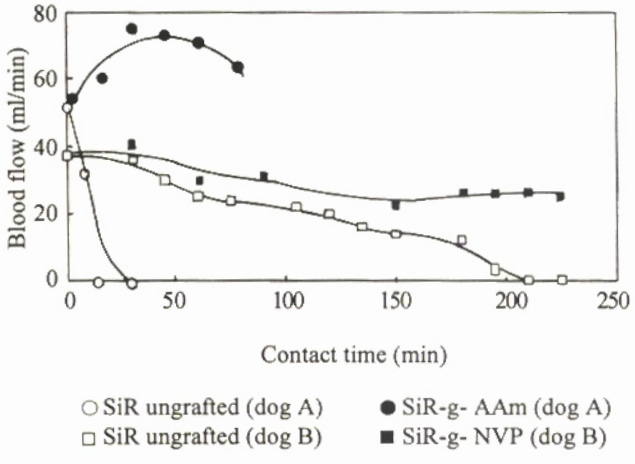

Figure 1 - Comparison of the effect of grafting of N-vinylpyrrolidone (NVP) and acrylamide (AAm) onto silicone tubing (SiR) on blood flow in dogs.

though the carotid artery in each dog was treated identically with respect to implant methodology, the difference in the control, SiR ungrafted in dogs A and B (Figure 1), could be taken as an indication of the influence of surgery on the experiment (damaged tissue surrounding the tubes).

In both animals, the blood flow in the ungrafted tubes decreased more rapidly when compared with the blood flow in the grafted ones indicating the thrombus formation inside the ungrafted tubes. These results show an improved antithrombogenicity of the radiation-grafted silicone rubber (SiR).

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