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# SURFACE MODIFICATION WITH HYDROGELS VIA MACROINITIATORS FOR ENHANCED FRICTION PROPERTIES OF BIOMATERIALS

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Key Words: Biomaterials, Hydrogel, Macroinitiator, Friction

## ABSTRACT

A general method of surface modification is described which is based on dip-coating of a substrate with a macroinitiator and subsequent free radical polymerization of functional monomers. Using this method, it is possible to fix poly(acrylic acid) hydrogels on polymer surfaces, e.g. on catheters, which drastically reduces the friction of these materials. Similarly, other biological relevant properties, especially reduced protein or bacteria adsorption can be achieved by choosing appropriate monomers.

The substrate was first homogeneously dip-coated with e.g. the water-insoluble macroinitiator poly(octadecene-co-maleic anhydride), partially reacted to the *tert.*-butyl perester. Homogeneity, thickness, and reactivity of the macroinitiator layer was characterized in detail. After a temper step, surface homo- and copoly-

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merizations of ionic monomers were carried out in water directly from the modified surface. The consistency of the hydrogel coating could be well controlled by the reaction conditions and the monomer composition. The correlation between the experimental parameters, the composition of the surface coating, and the friction properties was established. A relatively thick, slightly crosslinked poly(acrylic acid) hydrogel coating reduces the friction coefficient by 95% compared to that of uncoated surfaces.

## INTRODUCTION

Today, a very broad spectrum of polymeric materials is used in medicine. This covers polymers as carriers for drugs and contrast agents, short and long time body implants as well as all kinds of polymeric gadgets for applications outside the body. The contact of these polymers with body fluids causes several problems and forces the polymer chemists to search for biocompatible materials. One possibility to improve biocompatibility, especially blood compatibility, is the increase of the hydrophilicity of the polymer surface. This can be achieved by surface modification of the polymer e.g. by plasma treatment and subsequent grafting reaction of polyethylene glycol or acrylic acid [1-3]. One the other hand, hydrogels are remarkably successful in different applications in medicine, e.g. as drug delivery system, contact lenses, or coatings, thus surface modification of polymers for medical applications with hydrogels seems to be very promising [4-7]. One important area is the lubrication of biomedical surfaces, especially polymer surfaces [8], since materials with high friction can cause severe damage of tissue and vessels.

We would now like to describe a general method to fix polyacrylic acid hydrogels on different polymer surfaces of irregular shape, e.g. on catheter tubes [9]. This modification reduces drastically the friction of these materials but other biological relevant properties, especially reduced protein adsorption can be achieved similarly by choosing the appropriate monomers.

## EXPERIMENTAL

### Materials

The monomer acrylic acid (purum, Fluka) was purified by vacuum distillation prior to use. Sodium styrene sulfonate (Fluka) and the crosslinkers N,N′-

methylene diacrylamide (MBAA, >98%, MERCK-Schuckardt), pentaerythritol triallylether (PETAE, Polysciences Inc., and ethyleneglycol dimethacrylate (EGDMA, Polysciences, Inc.) were used as received. 1,1-dicyanoethyl)-azo-benzylalcohol was prepared according to the literature [10]. Polyamide-12 foils (Vestamid L2101 F, Hüls) and poly(etherester-*b*-amide) catheter material (PEBAX, Elf Atochem) were used as substrates. Poly(octadecene-co-maleic anhydride) was purchased from Polysciences Inc. ($\overline{Mw}$ = 30,000-50,000 g/mol) and poly(propene-co-maleic anhydride) ($\overline{Mw}$ = 37,000 g/mol) was synthesized by precipitation polymerization in dichloroethane using AIBN as initiator at 70°C [11]. Both polymers were used as received for the modification reaction.

## Characterization

The following instruments and conditions were applied for characterization of the materials:

$^1$H NMR: Bruker 500 MHz, in $CDCl_3$ solution, TMS standard; FTIR: IFS 66v, Bruker, for determination of layer thickness: Golden Gate-single reflexion diamant ATR unit for FTIR-spectrometers, SPECAC, Si-crystal, 77x12 x 6 mm, angle 45°, 86 nm $SiO_2$, Fa. Korth; AFM: atomic force microscop Nanoscope 3, Digital Instruments, tapping mode; friction: materials universal testing machine Zwick-1456, range of measurement: 10 N, a special equipment has been designed for the measurements on catheters; optical microscope: Leika MZ 12; XPS: ESCA-Lab 220 X-ray photon spectrometer, VG; UV/VIS: Perkin Elmer UV/VIS spectrometer Lambda 2, measured in DMSO solution or in bulk; irradiation unit: LOT ORIEL 200 Watt Hg(Xe) UV Arc Lamp Model 68806; irradiation dose at the sample 50 mW/cm$^2$, Thermal analysis: DSC 7, Perkin Elmer, 10K/min.

## Macroinitiators

*a) Macroinitiator **1** (Perester)*

The macroinitiator **1** was synthesized by reaction of poly(octadecene-co-maleic anhydride) with *tert.*-butylhydroperoxide in the presence of triethylamine (molar ratio 1:0.5:0.5) in acetone (polymer content 50% by weight) [12]. The isolation of the reaction product was performed by precipitation of the diluted reaction mixture in 0.05N HCl. The active oxygen content of one specific sample was 0.5069 mmol/g (estimated iodometrically). From this one, can calculate a conversion of 18.6 mol% of the anhydride functions to peresters.

$^1$H-NMR ($CDCl_3$, (δ in ppm): broad badly resolved signals from 0.5 to 3.0 (CH, $CH_2$), 0.9 ($CH_3$), 1.26 ($CH_3$)

IR ( in $cm^{-1}$, KBr): 3285, 3089, 2918, 2849, 1779, 1727, 1633, 1551, 1464, 721

*b) Macroinitiator **2** (Azo, Based on Poly(propene-co-maleic anhydride))*

Under a nitrogen atmosphere, 1.80 g poly(propene-co-maleic anhydride) (12.8 mmol anhydride) were dissolved in 20 ml dry THF and 10 ml dry pyridine. 683 mg 4-[(1,1-dicyanoethyl)azo]benzylalkohol (3.2 mmol) were added to the solution and the mixture was stirred in the dark at room temperature. After 3 days, the solution was precipitated into 400 ml 2-propanol. The polymeric product was collected and reprecipitated once from a THF solution. The obtained yellow powder was dried in vacuum and stored in the dark at 4°C.

Yield: 2.24 g (polymer contains ca. 20 mol% azo units)

$^1$H-NMR (DMSO-$d_6$, (δ in ppm): 0.9-3.4 (br, m, polymeric backbone: CH, $CH_2$, $CH_3$), 2.23 (3H, s, $CH_3$), 5.0-5.4 (2H, br, $CH_2$), 7.61 (2H, br, $CH_{ar}$), 7.83 (2H, br, $CH_{ar}$), 12.43 (1H, br, COOH)

IR ($\bar{\nu}$ in $cm^{-1}$, KBr ): 3550, 2969, 1857, 1773, 1731, 1459, 1390, 1215, 923

*c) Macroinitiator 3 (Azo, Based on Poly(1-octadecene-co-maleic anhydride))*

Under a nitrogen atmosphere, 1.93 g poly(1-octadecene-co-maleic anhydride) (5,5 mmol anhydride) were dissolved in 15 ml dry THF and 5 ml dry pyridine. 300 mg 4-[(1,1-dicyanoethyl)azo]benzylalkohol (1.4 mmol) were added to the solution and the mixture was stirred in the dark at room temperature. After 3 days, the solution was precipitated at 0°C into a mixture of 200 ml methanol and 200 ml 0.1 n HCl. The polymeric product was collected and reprecipitated once from a THF solution. The obtained yellow powder was dried in vacuum and stored in the dark at 4°C.

Yield: 1.85 g (polymer contains ca. 10 mol% azo units)

$^1$H NMR (DMSO-$d_6$, (δ in ppm): 0.5-4 (br, m, polymeric backbone: CH, $CH_2$, $CH_3$), 2.16 (3H, s, $CH_3$), 5.20 (2H, br, $CH_2$), 7.54 (2H, br, $CH_{ar}$), 7.85 (2H, br, $CH_{ar}$), 12.70 (1H, br, $CO_2H$)

IR ($\bar{\nu}$ in $cm^{-1}$, KBr ): 3550, 2921, 2852, 1854, 1778, 1733, 1707, 1465, 1377, 1171, 925,721

## Polymerization of the Hydrogel

The substrate was coated with the macroinitiator at room temperature by dipping it in an isopropanol solution (different concentrations: 2-10 wt%) of the

macroinitiator with and without crosslinker (MBAA, PETAE, EGDMA, 0-300 mol% based on mol C=C). The coating was dried at room temperature and a subsequent tempering at 120°C for 5-15 minutes. was carried out in the presence of a crosslinker. The surface polymerizations were performed at 90°C under nitrogen in an aqueous solution of the monomer. The monomer content in the solution was 1-15% by weight, the reaction time 1-3 hours. After the reaction, the substrates were removed from the solution, rinsed several times with pure water and air-dried at room temperature. The yield and thus the thickness of the hydrogel layer was determined by weight.

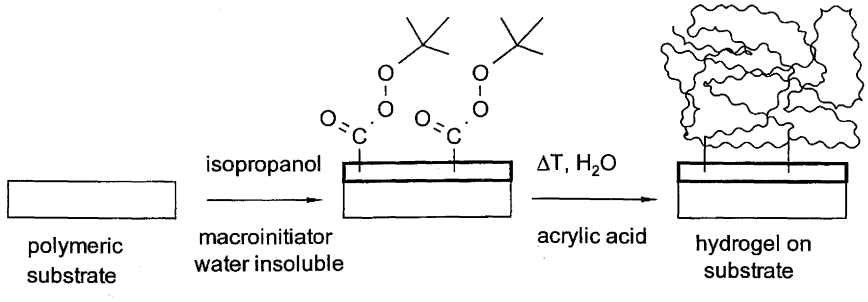
## RESULTS AND DISCUSSION

### Coating Procedure

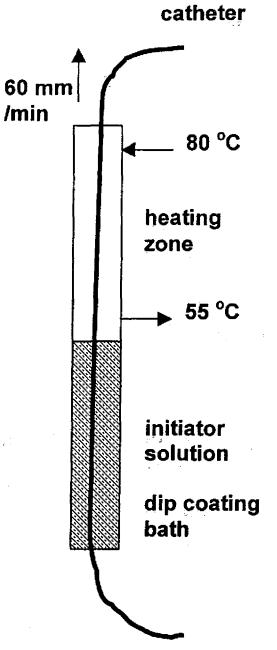
Surface modification by chemical or plasma treatment is often accompanied with a material property change of the bulk material since the modification cannot be fully localized to the surface only. In addition, modification of irregularly shaped materials might be problematic. On the other hand, the synthesis of new bulk materials with the appropriate mechanical properties and a biocompatible surface is difficult and costly.

Therefore, we developed a simple two step principle for surface modification of different substrates with hydrogels. The substrate is first homogeneously dip-coated with an water insoluble macroinitiator. The coating is dried and tempered, and then, surface homo- and copolymerizations of ionic and nonionic monomers are carried out in water (Scheme 1).

Tube-like substrates can be coated with the macroinitiator in a continuous process by moving the tube with a certain speed through the macroinitiator solution and fixing it in a following drying zone (Scheme 2).




**Scheme 1.**



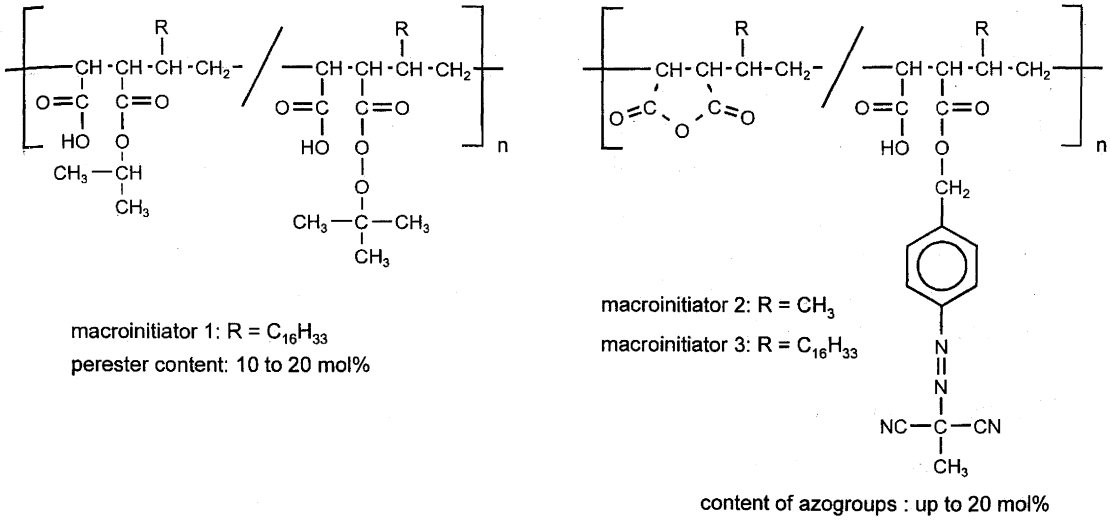

**Scheme 2.**

## Macroinitiators

The use of an appropriate macroinitiator which shows excellent adhesion to the substrate, good film forming properties and high initiator efficiency is essential for the success of this principle. Therefore, the macroinitiator must be optimized for different substrates.

We found that poly(octadecene-co-maleic anhydride), partially reacted to *tert.*-butyl perester (macroinitiator **1**, Scheme 3), is very suitable for the covering of polyamide-12 and poly(etherester-*b*-amide) (PEBAX) substrates which are often used as catheter materials. This macroinitiator has the right ratio of hydrophilic and hydrophobic parts to show good adhesion to the substrate and no water solubility. In addition, acid functional groups can interact with the surface of the substrate. Due to the synthetic procedure of the modification reaction, the macroinitiator contains a mixture of acid, anhydride, perester, and isopropanolester functions. A thin, homogeneous macroinitiator coating could be applied simply by dipping the substrate into an isopropanol solution of the macroinitiator and air-drying the layer.

The perester macroinitiator decomposes thermally with a half life time of approximately 1.15 hours at 100°C in bulk, leading to radicals active for the ini-




**Scheme 3.**



tiation of free radical polymerization. Oxygen radicals, located at the acid functions, and after further decomposition and evolution of $CO_2$, carbon radicals at the polymer backbone are formed. In addition, low molar mass *tert.*-butoxy radicals take part in the initiation process. 10 to 20 mol% of the anhydride functions usually have been modified for the synthesis of the macroinitiator.

An alternative to the perester functions are labile azo units. Derivatives of phenyl-[(1,1-dicyanoethyl)azo have been used already in different macroinitiators [10, 13, 14]. This initiator function can be decomposed not only thermally but also photochemically. The low molar mass azo compound has its $\lambda_{max}$ at 289 nm with an $\varepsilon$ of 14000 L/mol·cm. The half life time of the azo macroinitiators **2** and **3** shown in Scheme 3 are 160 minutes at 80°C and only 35 seconds under UV irradiation (Hg-Xe UV lamp, 50 mW/cm$^2$).

The homogeneity and the thickness of the macroinitiator layer was characterized by ATR-FT-IR spectroscopy and electron microscopy. A film thickness below 0.5 μm was found to be optimal for the subsequent polymerization. In addition, two more steps are necessary to receive a stable hydogel layer afterwards: Low molar mass crosslinkers, e.g., N,N′-methylene diacrylamide, pentaerythritol triallylether, and ethyleneglycol dimethacrylate, were added to the macroinitiator solutions in 20 to 300 mol% based on the C=C content and the initiator functions, respectively. Furthermore, a temper step of 5 to 15 minutes at 120°C had to be added after the substrate was coated with the macroinitiator. As

seen in a model experiment where the macroinitiator was coated on an ATR crystal and the reaction during tempering was followed by FT-IR, a ring closure reaction of the acid functions back to the anhydride takes place under these conditions (Figure 1). The half life time of this ring closure reaction is only 7 minutes. These anhydride functions show a higher reactivity and will cause the formation of chemical bonds between the macroinitiator and the polymeric substrate. A second effect of the tempering is that part of the initiator functions start to decompose, form radicals and those will react with the substrate but also with the added crosslinkers stabilizing the layer.

## Hydrogel Formation

Based on the macroinitiator covered substrates, a variety of polymers from monomers suitable for free radical polymerization can be fixed to surfaces. Due to our intention to increase the hydrophilicity of catheter surfaces, we favored water soluble monomers (e.g., acrylic acid, acrylamides, hydroxyethylmethacrylate, sodium-styrene-sulfonate). The consistency of the hydrogel coating, e.g., thickness, crosslinking density, mechanical stability and composition, could be well controlled by the reaction conditions and the monomer composition and concentration in solution. The polymerization was initiated by placing the macroinitiator covered substrate in an aqueous solution of the monomer (1 to 15 wt%) and heating the solution to 90°C for up to 3 hours.

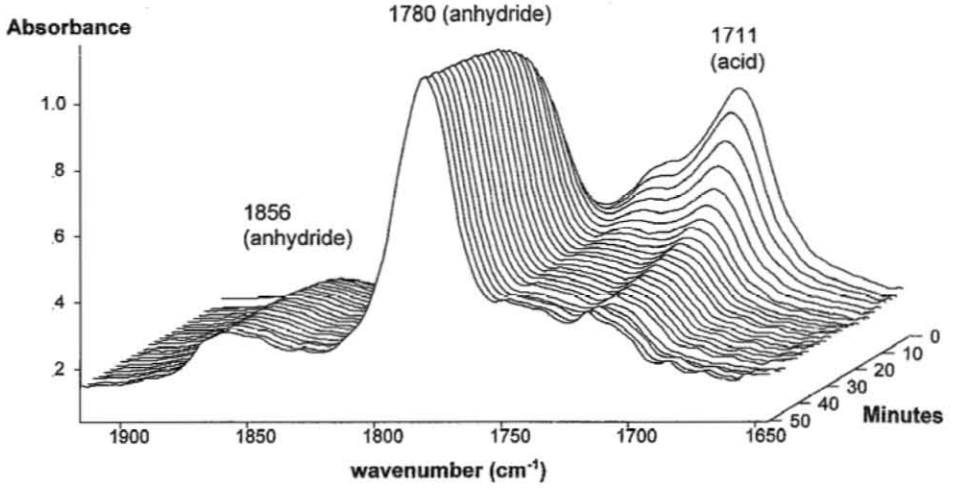



**Figure 1.** ATR-FT-IR spectra of macroinitiator **1**, coated on a Si-crystal; time dependent spectra at 120°C; acid absorption decreases, anhydrid absorptions appear.

It was found that the polymerization from a solid surface is not comparable to solution or bulk polymerization and the influence of the concentration gradient of the radicals, the radical efficiency, and the reduced mobility of the chain ends still have to be studied, e.g., the thickness of the hydrogel layer increases logarythmic with the monomer concentration in the aqueous solution from only 0.17 μm (1 wt%) to 280 μm (15 wt%) after 3 hours polymerization time (Figure 2). There is also an indication of a gradient in the crosslinking density of the hydrogel layer with the highest crosslinking density close to the substrate where the corsslinkers are located.

In the copolymerization of acrylic acid and sodium-styrene-sulfonate it was found that for an acrylic acid content below 70 mol% there was a remarkable deviation of the composition of the polymer layer fixed to the surface (determined by XPS) and the expected composition calculated from the copolymerization parameters. The covering of catheters with a sulfonate containing polymer is of interest in order to reduce bacteria adhesion to the surface.



## Friction Properties

The intention of this study was to cover catheters with a biocompatible hydrogel layer to reduce the friction of the bulk material. The friction of a material can be described by the friction coefficient, which is e.g., in the range of 0.5

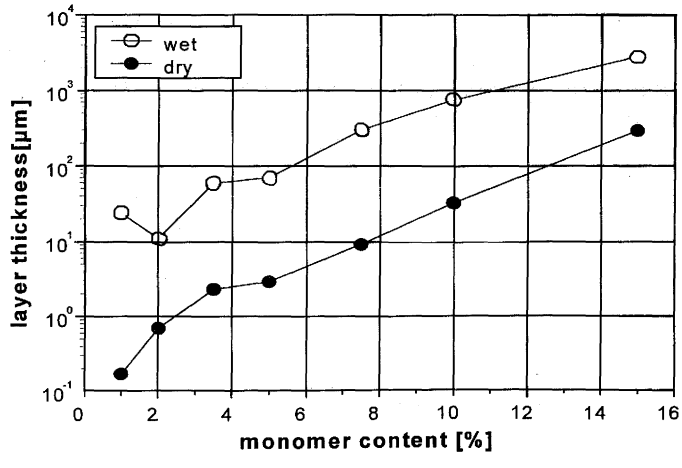



**Figure 2.** Dependence of the poly(acryl acid) hydrogel layer thickness on the acrylic acid concentration (wt%) in the aqueous solution; polymerization conditions: 90°C, 3 hours, 100 mol% ethylenglycol dimethacrylate in the macroinitiator **1** layer, 15 minutes tempering.

to 0.7 for rubber tires versus concrete or 0.014 for ice versus steel. For materials which are going to be used in the body, e.g., catheters, the friction has to be as low as possible in order to prevent damage of the tissue or vessel upon application. Natural materials are usually better than any synthetic substitutes, thus the friction coefficient of cartilage versus cartilage is only 0.002! The friction coefficient for our modified materials towards a base (plate or cylinder) of uncoated material was determined according to Figure 3 by using a Zwick 1456 testing machine.

For this, planar polyamide and poly(etherester-*b*-amide) model surfaces were dip-coated with the macroinitiator shown in Scheme 2 and poly(acrylic acid) hydrogel layers were grafted to the surface. Similarly, the process was transferred to catheter tubes using specialized equipment.

Surprisingly, it was found that the friction coefficients of all materials were strongly dependent on the normal force $F_N$. Therefore, one has to compare the results obtained with identical normal force. Evaluating the materials it was found, that the friction could be drastically reduced by the hydrogel layer. E.g. at $F_N = 1$ N uncoated polyamide-12 exhibits $\mu = 0.37$ and with a poly(acrylic acid) coating the friction coefficient could be reduced to $\mu = 0.03$. Uncoated PEBAX ($\mu = 0.65$) shows a much higher friction than uncoated polyamide-12 and no high normal force $F_N$ can be applied since the material elongates under stress. The friction of PEBAX catheter can be reduced to 0.044 ($F_N = 0.49$) by the hydrogel coating (Figure 4).

The thickness of the hydrogel layer is very important for the reduction of the friction. At least 3 μm poly(acrylic acid) hydrogel (dried layer) have to be grafted on the surface for a significant effect (Figure 5).

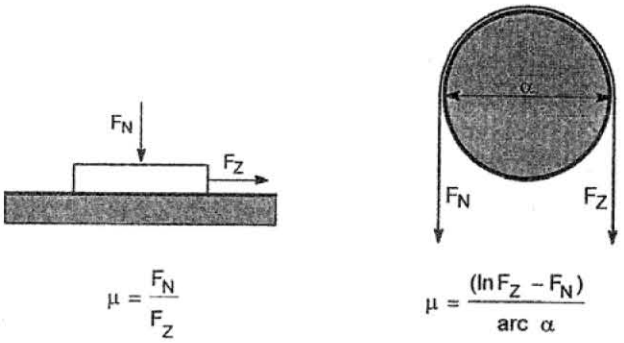



**Figure 3.** Determination of friction coefficients μ for planar objects and tubes; $F_z$ = tensile force, $F_N$ = normal force.

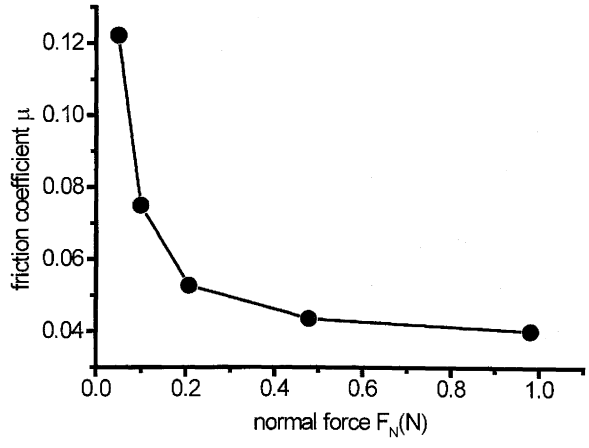



**Figure 4.** Friction coefficient μ of PEBAX-catheter grafted with poly(acrylic acid) (polymerization from 5% aqueous acrylic acid solution at 90°C for 3 hours, 300 mol% pentaerythrithol triallylether in the macroinitiator **1** layer).



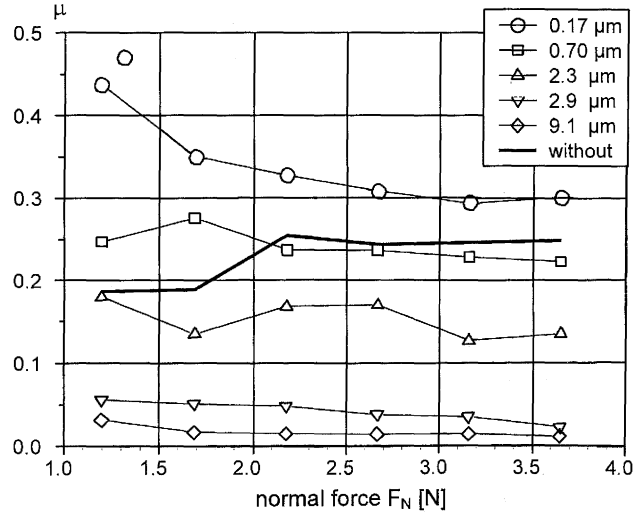



**Figure 5.** Friction coefficients (for polyamides coated with poly(acrylic acid) hydrogel layers of different thickness (dry layer)); polymerization conditions: 90°C, 3 hours, 100 mol% ethylenglycol dimethacrylate in the macroinitiator **1** layer, 15 minutes tempering.

As already mentioned, the mechanical stability of the hydrogel layer has been insufficient when no crosslinking agents were used. This was shown by the fact that the hydrogel coating was partially removed from the substrate after several friction treatments and thus, the friction coefficient increased again. In the presence of sufficient crosslinker and after tempering, no delamination of the coating was observed even when strong mechanical force was applied.

The enormous effect of the coating on the friction is demonstrated in Figure 6 where the large difference of the tensile force which is necessary to overcome the force caused by the friction is given for uncoated and coated PEBAX catheters.

## CONCLUSION

The described method to modify polymeric surfaces is very versatile and can be applied to a variety of substrates and polymeric coatings. Thus, different applications for coatings in biomedical materials but also for materials in technical processes, e.g. membranes and filters are possible. The modification with hydrogels as described here is an highly attractive method for lubricating polymeric substrates which are used for medical devices. But, also first results on the reduction of bacteria adhesion by these hydrophilic layers are very promising.



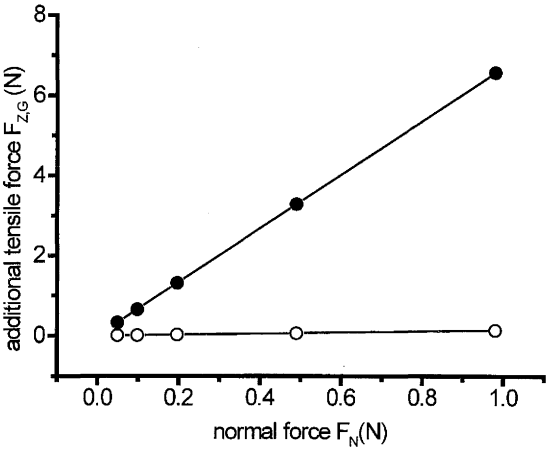



**Figure 6.** Reduction of the tensile force: additional force caused by friction versus applied normal force for ● uncoated catheter (PEBAX) and ○ coated catheter (PEBAX).

The most important role in this concept plays the macroinitiator and its optimization for the substrate. Polyamide and poly(etherester-amides) as substrates can be covered by a hydrogel layer stable towards delamination using macroinitiators based e.g. on poly(octadecene-co-maleic anhydride) with perester or azo initiator groups. It is favorable that the polarity and the solubility of the macroinitiator can be optimized by choosing the appropriate comonomer to maleic anhydride. The design of macroinitiators for different substrates and variation of the grafted polymer layer will be part of our future work.

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