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Preparation of Polyethyleneglycol (PEG) Coatings for Microencapsulation of Charcoal

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ABSTRACT

Polyethyleneglycols (PEGs) with their high solubility in water cannot normally be used as a coating material in aqueous solutions such as blood. A γ-radiation procedure was therefore applied after coating charcoal granules with PEG in a non-aqueous phase, and an 80–90% insoluble polymer matrix on charcoal was obtained. PEGs with different molecular weights from 4000 to 300,000 were used for coating. The performance of this system was determined by using several test solutes, namely creatinine, uric acid, and vitamin B-12. It was observed that the pore size and structure of these membranes can be adjusted by changing the irradiation time and by using PEGs with different molecular weights. Thus, very high mass transfer rates can be achieved.

Index Entries: Hemoperfusion, with PEG-encapsulated charcoal; charcoal, polyethyleneglycol coated for hemoperfusion; polyethyleneglycol-coated charcoal, in hemoperfusion.

INTRODUCTION

It has been suggested that hemoperfusion over a variety of sorbents such as charcoal or resin might be useful in the treatment of patients with

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a severe case of drug poisoning (*1–4*). Having a very wide adsorption spectrum, charcoal is mostly used as an adsorbent for hemoperfusion.

The major problems that are associated with hemoperfusion systems are blood cell deformation, platelet loss, and fine particle generation. Charcoal granules have been coated with different polymeric materials in order to eliminate these side effects.

The selection of the coating material and the coating procedure for charcoal are the most important factors in obtaining suitable systems that have high adsorptive capacity, adsorption rate, and biocompatibility, and do not release fine particles. Various types of polymer coatings and different coating procedures have been proposed and evaluated, many others are being studied by a number of groups (*5–10*).

In this study, polyethyleneglycols (PEGs) with different molecular weights were used as coating materials. A new coating technique was followed. In vitro performance of these PEG-coated charcoal systems was analyzed in detail and reported here.

MATERIALS AND METHODS

Coating Procedure

Extruded charcoal granules (Norit RBX 1) were used as the adsorbent. Prior to the coating procedure, charcoal was washed with tap water and then with distilled water, and dried in an oven at 100°C. Then it was held under a 200 mmHg vacuum to eliminate the remaining fine charcoal particles.

Polyethyleneglycol (PEG) coatings were prepared by following the procedure schematically outlined in Fig. 1. In the first stage (A), a polymer solution was prepared by dissolving different amounts of PEG (depending on desired coating thickness) in 30 mL of chloroform. This solution was then poured into a beaker containing 20 g of previously prepared charcoal granules (B). The suspension was stirred gently with a glass rod at room temperature. The slightly wet coated charcoal was spread out on a tray (C). This was then placed in a well ventilated place for 4–6 h at room temperature.

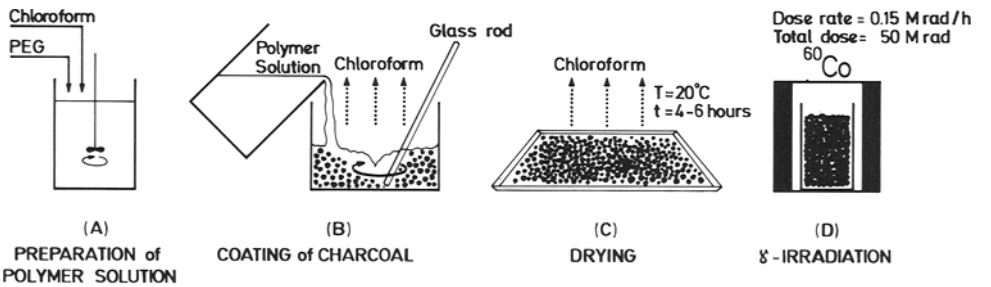

Fig. 1. Preparation of PEG-coated charcoals.

PEGs with their high solubility in water cannot normally be used as membrane systems in aqueous solutions such as blood. To achieve an insoluble polymer matrix structure, the PEG-coated charcoal granules were irradiated by γ-radiation (D). Irradiations were carried out in a cobalt (^{60}Co) source at a dose rate of 0.15 Mrad/h as determined by standard Fricke dosimeter solution. The optimal dosage given to the charcoal samples during the radiation procedure was about 50 Mrad.

PEGs with different molecular weights, 4000, 35,000, 300,000, were used for coating. Three different membrane thicknesses were studied (0.5, 1.0, and 2.0% by weight).

Equilibrium Adsorption Studies

Equilibrium adsorption studies were carried out to determine the selectivities and adsorption capacities of both uncoated and PEG-coated charcoal granules. Creatinine, uric acid, and vitamin B-12 were used as test materials. These batch experiments were conducted at 37°C. The 24-h contact time was established as the equilibrium time.

To evaluate the change in adsorption capacities of charcoal granules after coating, the Freundlich isotherms were determined by using the following equation:

$$m_e = Kc_e^{1/n} \quad (1)$$

where m_e is the amount of test solute adsorbed per gram adsorbent, c_e is the equilibrium concentration of test solute in the solution; and K and n are Freundlich constants.

The amount of solute adsorbed per gram charcoal (m_e values) was measured as a function of equilibrium solute concentration (c_e values). The Freundlich constants, n and K, were determined from the slope and intercept of the line that was obtained by plotting log (m_e) vs log (c_e) values.

Adsorption Rates

The determination of performance characteristics of the hemoperfusion columns filled with both uncoated and PEG-coated charcoals were obtained for creatinine, uric acid, and vitamin B-12. In these continuous experiments, the cylindrical columns (length/diameter = 2) containing 20 g of charcoal were tested in a closed recirculation system, as shown in Fig. 2.

Two liters of creatinine aqueous solutions (initial conc. = 100 mg/L), uric acid (initial conc. = 500 mg/L) and vitamin B-12 (initial conc. = 20 mg/L) were used. The solutions were recirculated through the charcoal granules by a peristaltic pump (Watson-Marlow, MHR 200) at a constant flow rate of 200 mL/min. Samples of 0.2 mL were drawn from the reservoir at 15 min intervals to follow the decrease in the concentrations of the

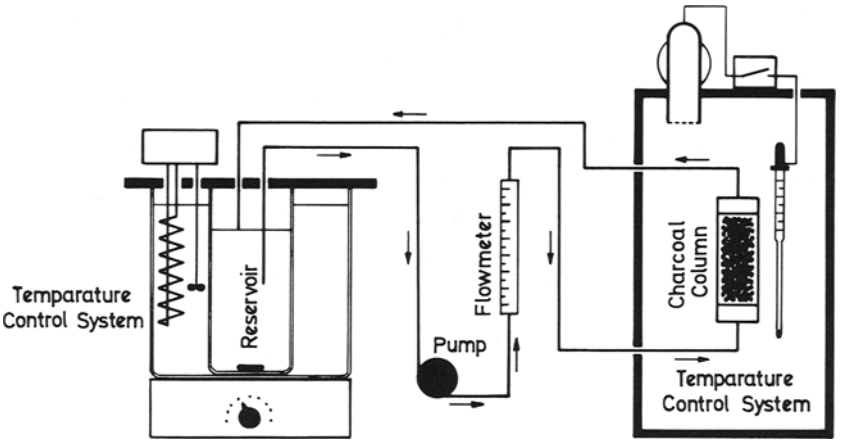

Fig. 2. Schematic drawing of test circuit.

test solutes. The solute concentrations were measured by spectrophotometrical methods. All experiments were performed at 37°C.

Adsorption rates of the solutes were obtained by plotting the solute concentration in the reservoir versus perfusion time. Initial clearance rates (ICR) were also determined to show the column performance. Equation (2) was used to calculate the ICR values.

$$\mathrm{ICR} = -\frac{V}{c}\frac{dc}{dt}\Big|_{t=0} \tag{2}$$

where ICR is the initial clearance rate in mL/min; V is the solution volume in the reservoir, mL; c is the solute concentration, mg/mL; t is time, min.

Blood–Material Interactions

Bovine blood was used to study the biocompatibility of PEG-coated charcoal. The blood was obtained by venipuncture and heparinized (3.5 U/dL heparin). The same test circuit given in Fig. 2 was used for the in vitro blood perfusion experiments. Samples were taken from the reservoir at 15 min intervals for erythrocyte, leukocyte, and platelet counts. Blood cell measurements were performed by following standard procedures.

Fine Particle Generation

During the perfusion studies, the fine carbon particle generation rates of both uncoated and PEG-coated charcoal were investigated by counting the number of carbon particles (1.5–5 μm) by means of a Coulter Counter.

RESULTS AND DISCUSSION

Equilibrium Adsorption Studies

Both uncoated and PEG-coated charcoals were used in the equilibrium adsorption studies. The Freundlich constants were calculated by using the equilibrium adsorption data and Eq. (1). Table 1 gives these constants for uncoated and PEG-coated charcoals together. It can be seen clearly that even the thickest coating evaluated in this study still allows for a substantial adsorptive capacity of charcoal. But an increase in the membrane thickness decreases the adsorptive capacity for all membrane systems. Besides that, lower adsorption capacities are achieved when PEGs with higher molecular weights are used.

This phenomenon might be explained by the highly crosslinked structure of the resultant polymer coat when PEGs with higher molecular weights are used. This structure results in a decrease in the total mass transfer area available for adsorption. Thus, lower adsorption capacities are obtained.

Adsorption Rates

The results of the continuous column studies are given in Figs. 3–6. These experiments were carried out to determine the adsorption rates of the test solutes, namely creatinine (MW 113), uric acid (MW 168), and vitamin B-12 (MW 1355). Both uncoated and coated charcoals were used.

TABLE 1
Freundlich Constants for Uncoated and PEG-Coated Charcoals

Coating material	Coating thickness (% BY WEIGTH INCREASE)	Creatinine		Uric acid		Vitamin B-12	
		K	n	K	n	K	n
Uncoated	0	43.3±1.7	2.63±0.10	54.5±2.1	2.50±0.04	8.7±0.8	2.91±0.08
PEG 4000	0.5	40.3±2.1	2.69±0.08	48.6±2.3	2.64±0.06	8.6±0.4	3.02±0.06
	1.0	39.3±1.3	2.72±0.08	47.9±2.0	2.66±0.05	8.5±0.5	3.05±0.05
	2.0	38.5±1.5	2.75±0.07	46.0±1.9	2.70±0.05	8.4±0.5	3.09±0.04
PEG 35000	0.5	39.0±1.5	2.75±0.06	48.0±2.1	2.68±0.05	8.5±0.4	3.09±0.06
	1.0	38.0±1.3	2.79±0.05	45.6±2.0	2.73±0.08	8.4±0.7	3.12±0.04
	2.0	36.5±1.7	2.85±0.05	43.2±1.6	2.80±0.03	8.2±0.3	3.19±0.04
PEG 300 000	0.5	37.8±1.6	2.78±0.04	46.8±2.0	2.70±0.07	8.3±0.7	3.11±0.03
	1.0	35.1±1.0	2.86±0.08	43.1±2.2	2.76±0.06	8.1±0.5	3.18±0.06
	2.0	33.2±1.8	2.94±0.10	40.5±1.8	2.85±0.07	7.7±0.6	3.28±0.05

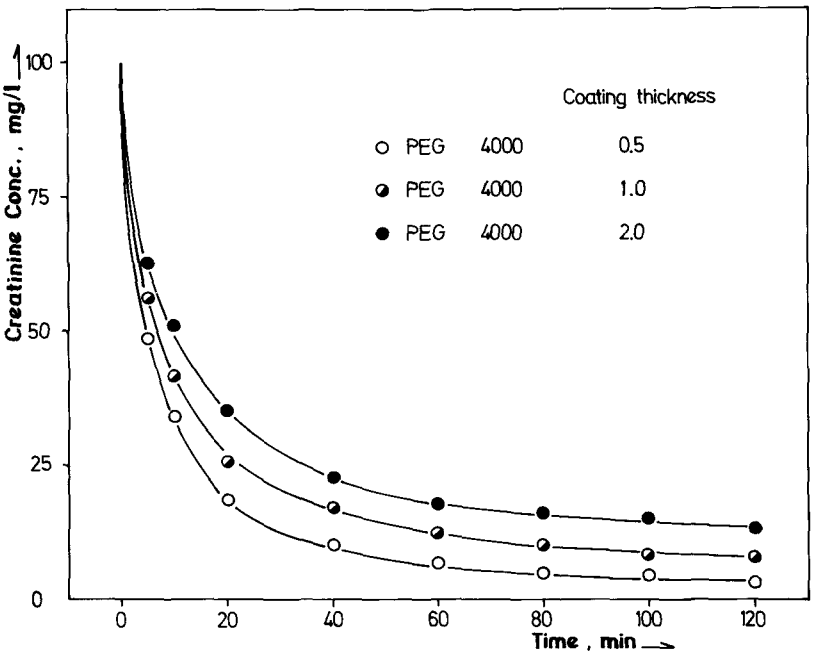

Fig. 3. Creatinine adsorption on uncoated and PEG-coated charcoals. (Coating thickness = 0.5 wt%).

Coats were obtained by using PEGs with three different molecular weights. Three different coating thicknesses were studied.

Figures 3, 4, and 5 give the adsorption rates data of the test solutes where the thickness of the coats was 0.5 wt%. As seen in the figures, the adsorption rates decrease when the PEGs with higher molecular weights are used for coating. Results are similar for all test solutes evaluated in this group of experiments. As is expected, the lowest adsorption rates were obtained for vitamin B-12, which has the largest molecular weight among the test materials.

Figure 6 shows the effects of membrane thickness on the adsorption rates of creatinine on the PEG (MW 4000) coated charcoal. As can be seen in this example when the coating thickness is increased the adsorption rates decrease significantly.

As was previously noted, these data suggest that a greater cross-linking and formation of more a tight polymer structure is obtained when PEGs with higher molecular weights are used, or when the coating thickness is increased. As a result of the tight structure, higher resistance to the diffusion of solutes through the membrane results in lower adsorption rates.

Blood–Material Interactions

In this group of experiments for determining the biocompatibility of the PEG-coated charcoals, in vitro blood perfusion tests were carried out

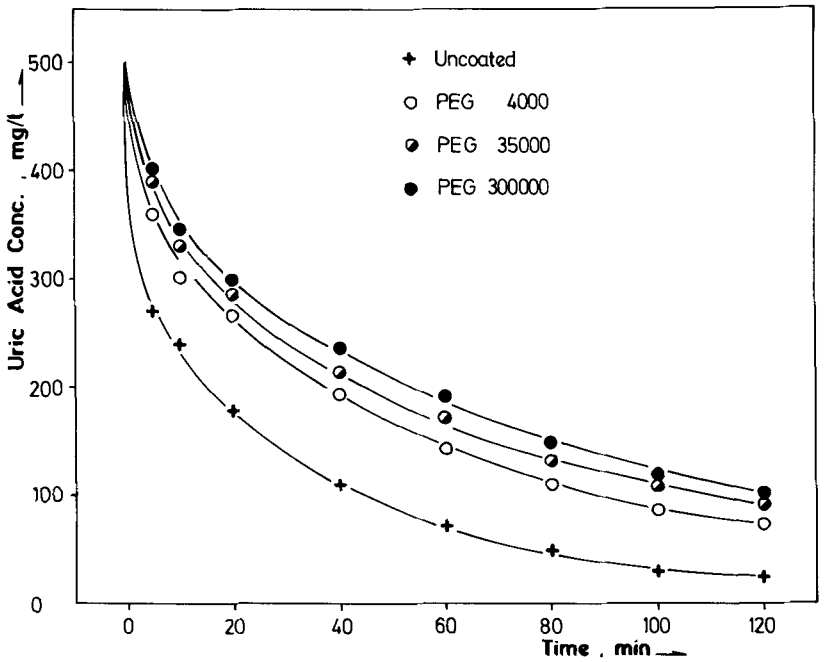

Fig. 4. Uric acid adsorption on uncoated and PEG-coated charcoals. (Coating thickness = 0.5 wt%).

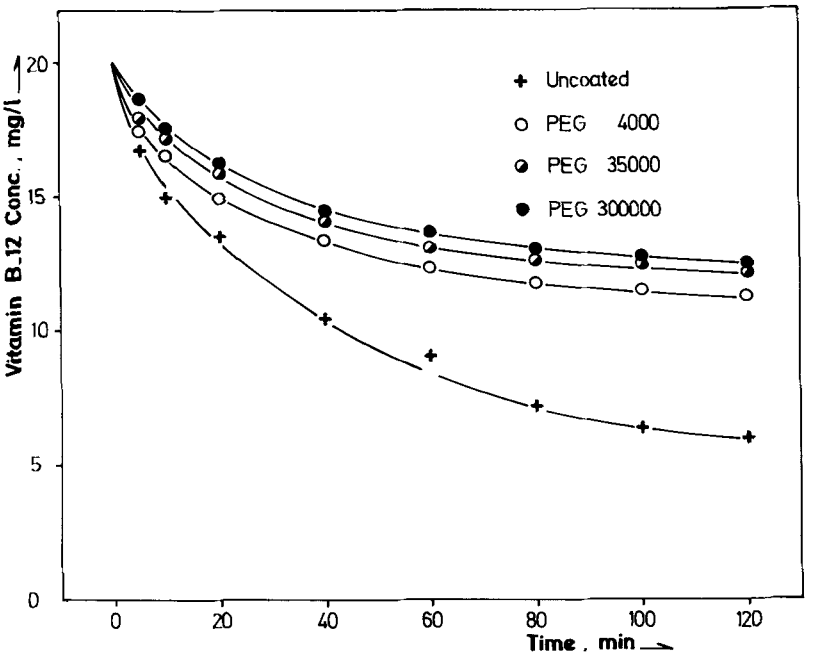

Fig. 5. Vitamin B-12 adsorption on uncoated and PEG-coated charcoals. (Coating thickness = 0.5 wt%).

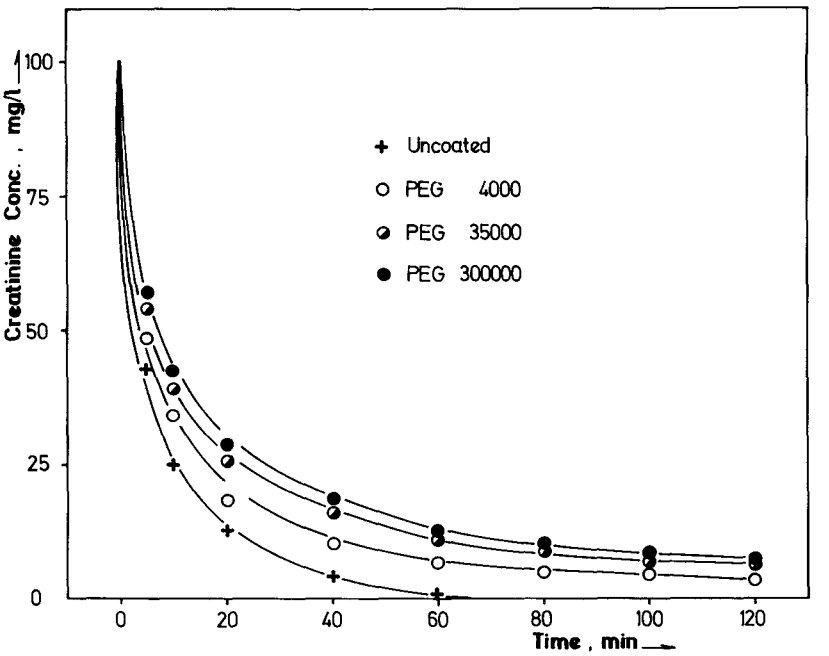

Fig. 6. Effects of coating thickness on the adsorption rate of creatinine (coating material = PEG 4000).

in a closed recirculation system. Samples for erythrocytes, leukocytes, and thrombocytes were taken from the blood reservoir and were analyzed by standard techniques.

Platelets were counted in a Coulter Counter, and the results were expressed as a percentage of the initial platelet count (mean ± SD, n = 10), as shown in Table 2. The platelet levels after 120 min were almost the same in all the different PEG-coated charcoals, and considerably higher than those observed with uncoated charcoal.

Hemoperfusion through the columns filled with PEG-coated charcoals showed no significant effect on erythrocytes and leucocytes.

Fine Particle Generation

In-vitro microparticle release rates for PEG-coated charcoals were evaluated in the same perfusion circuit that was used for adsorption rate studies. The number of charcoal particles released from the PEG-coated charcoal was measured in the samples taken from the reservoir by means of a Coulter Counter. No appreciable fine particles were observed in the samples.

CONCLUSION

Finally, something should be said about the possible use of PEG-coated charcoal for hemoperfusion. Since polyethyleneglycols are

TABLE 2
Platelet Counts for Uncoated and PEG-Coated Charcoals

Coating material	Coating thickness (% BY WEIGTH INCREASE)	Platelet count* ± SD				
		Time , min				
		0	30	60	90	120
Uncoated		100.0	72.0±6.0	52.0±2.1	30.1±1.5	20.5±1.6
PEG 4000	0.5	100.0	94.2±5.2	91.6±2.6	90.3±3.9	88.2±4.6
	1.0	100.0	94.0±4.8	93.2±5.0	91.2±6.2	89.1±5.3
	2.0	100.0	96.6±6.9	92.5±7.2	92.0±4.3	89.7±4.0
PEG 35000	0.5	100.0	95.8±7.3	90.8±4.3	91.1±6.2	87.7±1.9
	1.0	100.0	96.3±8.8	94.6±4.8	92.5±4.0	88.8±2.8
	2.0	100.0	95.4±8.5	92.9±4.6	90.6±6.8	88.9±1.8
PEG 300 000	0.5	100.0	94.5±6.9	94.0±5.2	91.4±4.5	88.0±3.3
	1.0	100.0	97.5±9.1	93.7±6.8	92.5±5.9	90.1±2.8
	2.0	100.0	97.6±7.3	93.8±7.1	90.8±3.2	89.8±1.5

* Count values normalized to 100 at zero minutes.

nontoxic and biocompatible materials, they may be suitable for the coating of charcoal. There is no significant change in adsorption capacity and adsorption rates of charcoal after coating with low molecular weights of PEGs.

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