

A Hemoperfusion Column Based on Activated Carbon Granules Coated with an Ultrathin Membrane of Cellulose Acetate

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ABSTRACT

A hemoperfusion system has been developed which makes use of activated carbon encapsulated with cellulose acetate. Studies have revealed that there are no stagnant flow regions in the column, there is minimal particle release and the coating is 30 Å thick. The relationships between pore size, pore volume and surface area have been examined. Twenty-five patients in grade IV coma have been treated with the column for treatment of drug overdose or agricultural chemical poisoning; the clinical course of one meprobamate-poisoned patient is described in detail.

activated carbon, cellulose acetate coating, hemoperfusion, poisoning

INTRODUCTION

Its enormous internal surface area ($\sim 1000 \text{ m}^2/\text{gm}$) makes activated carbon (AC) an effective adsorbent for many polar and non-polar molecules from aqueous solutions and blood. In 1964 Yatzidis¹ described the effectiveness of an AC hemoperfusion column for the removal of metabolites and drugs from blood. Ever since, many investigators have applied AC in hemoperfusion systems to adsorb

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toxic substances. Encapsulation of the AC granules with polymeric membranes provides improved blood compatibility and minimizes the release of embolizing microparticles.²⁻⁵

This is a report on a novel hemoperfusion column containing 250 gm of Norit RBX 1 microencapsulated with cellulose acetate. This column has been developed at the Twente University of Technology with the assistance of Organon Teknika (Oss, The Netherlands). The thickness of the coating is approximately 30 Å, which is extremely thin compared to other coated AC hemoperfusion systems used clinically at present (Table). This ultrathin coating affects the rate of removal only very slightly as compared to uncoated AC. The new hemoperfusion column, which will be marketed by Organon Teknika under the name "Hemopur 260", has been applied in the treatment of acute poisoning by drugs and agricultural chemicals. The results in the treatment of a patient poisoned with meprobamate will be described. The patient recovered within a few days without side effects.

DESCRIPTION OF THE COLUMN

Figure 1 shows the column diagrammatically. It contains approximately 250 gm of coated AC granules and is primed with carbon dioxide (CO₂). Prior to clinical use the column is perfused with 2 L of saline. The CO₂ charge provides a wetted carbon surface, allowing optimal participation of the internal surface area in the adsorption process and preventing channeling of the blood flow.

The flow pattern in the column has been studied at a water flow rate of 200 ml/min and temperature of 25°C using a stimulus-response technique.⁶ Stagnant flow regions did not occur within the cylindrical column. The *in vitro* microparticle release has been determined at a water flow rate of 200 ml/min. The particle concentrations in the outflow of the column, collected over a six-hour perfusion period,

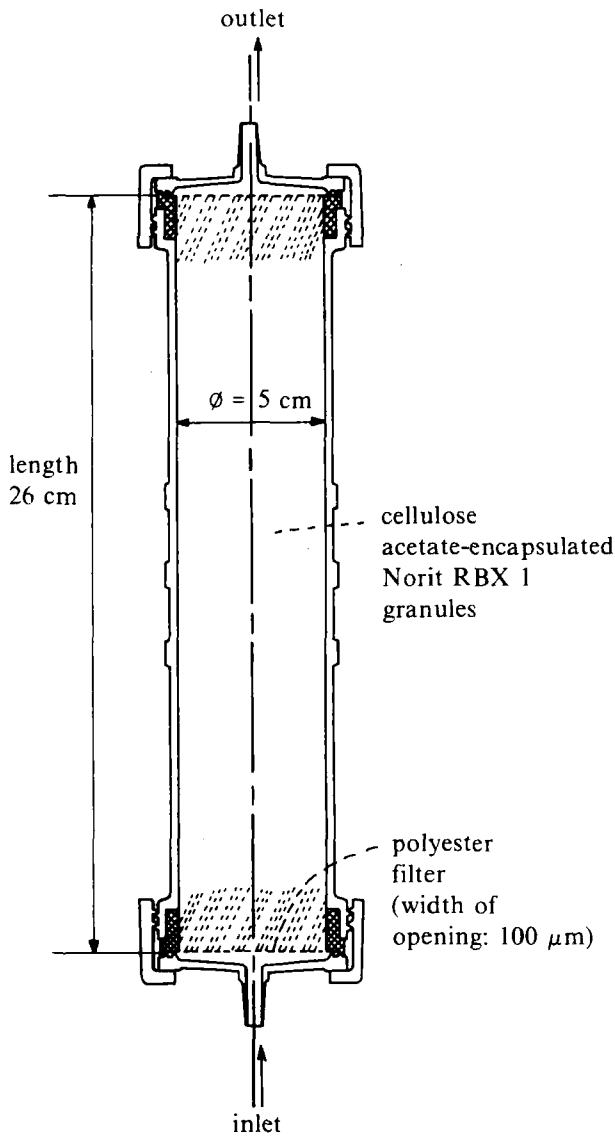


FIG. 1. Diagram of the hemoperfusion column.

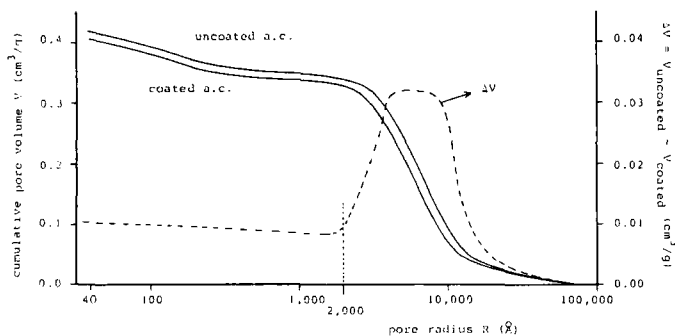


FIG. 2. Volume V of pores with radius $(R) < 75,000\text{ Å}</math> vs. pore radius R for: a. uncoated Norit RBX 1; b. Norit coated with cellulose acetate (0.7% by weight).$

were well below the British⁷ and U.S.⁸ standards for infusion fluids.

THICKNESS OF THE COATING

The thickness of the cellulose acetate (CA) coating has been determined using high pressure porosimetry (porosimeter: Carlo Erba model 70, Italy).⁹ The cumulative pore volume distributions of uncoated Norit RBX 1 have been compared (Fig. 2). From Figure 2 it can be seen that below 2000 Å, the internal surface area of the pores is not coated. The CA membrane bridges these small pores. The surface area of the internally coated pores (radius above 2000 Å) can be calculated from the cumulative pore volume distribution assuming that the AC exhibits cylindrical pores. From the density of the cellulose acetate membrane and the percentage by weight of CA (0.7%) the membrane thickness can be computed.

Columns containing Norit RBX 1 granules coated with 0.32% CA by weight have been used in the treatment of acute poisoning by drugs and agricultural chemicals. The CA membrane thickness is approximately 30 Å.

The Table shows the membrane thickness of the coated AC hemoperfusion system to be small compared to other types used clinically. The membrane thickness is an important parameter with respect to the mass transfer rate of a substance through a membrane. From the membrane thickness point of view the rate of removal of toxic products from the blood to the carbon surface for the CA-encapsulated Norit RBX 1 will be superior to those of other hemoperfusion systems mentioned in the Table.

CLINICAL RESULTS

Thus far, 25 patients in grade IV coma due to an overdose of various drugs and agricultural chemicals have been treated with the described hemoperfusion column. Hydrophobic as well as hydrophilic poisons have been removed effectively. The therapy used to remove the toxins includes: a) stomach wash-out; b) administration of magnesium sulfate and powdered AC via the stomach into the intestines; c) forced diuresis if possible; and d) hemoperfusion. The data of a patient with an overdose of meprobamate will be described, being representative of the authors' experience.

The perfusion circuit is shown in Figure 3. The blood pump produces an antigravity blood flow through the column of 300 ml/min. Figure 4 shows the removal of meprobamate during the hemoperfusion period. The effect of forced diuresis on the meprobamate level will be minimal in this four-hour period.¹⁰ During the four hours of hemoperfusion,

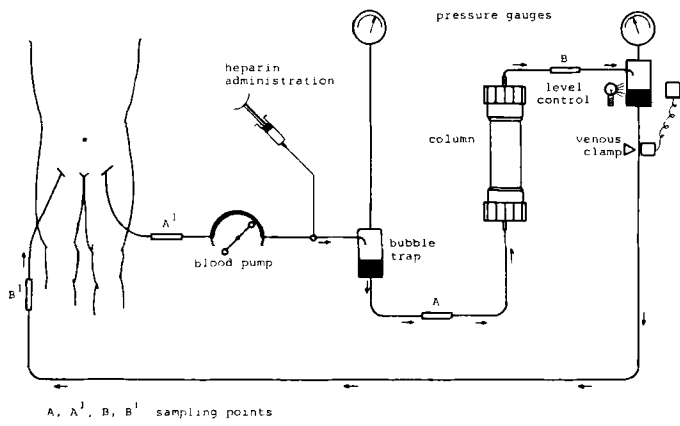


FIG. 3. Hemoperfusion circuit.

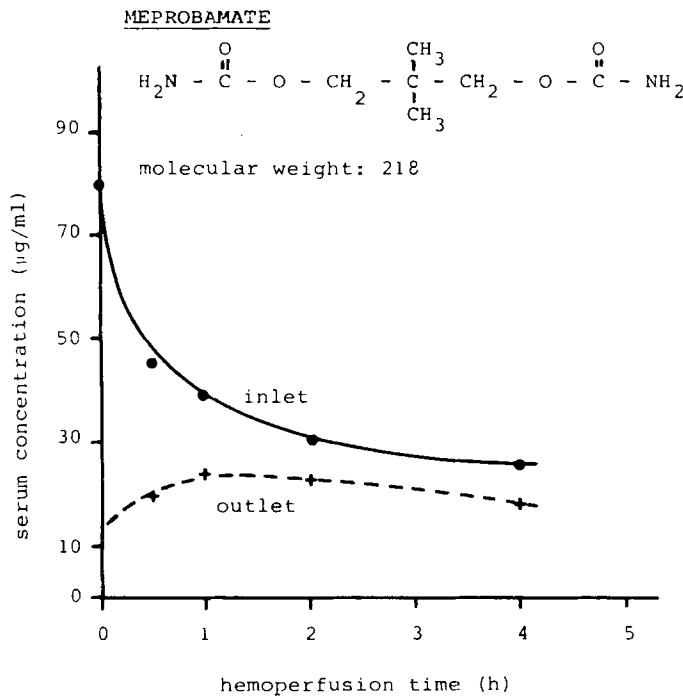


FIG. 4. The removal of meprobamate from a patient by the Organon Teknika Detoxicator at a blood flow rate of 300 ml/min.

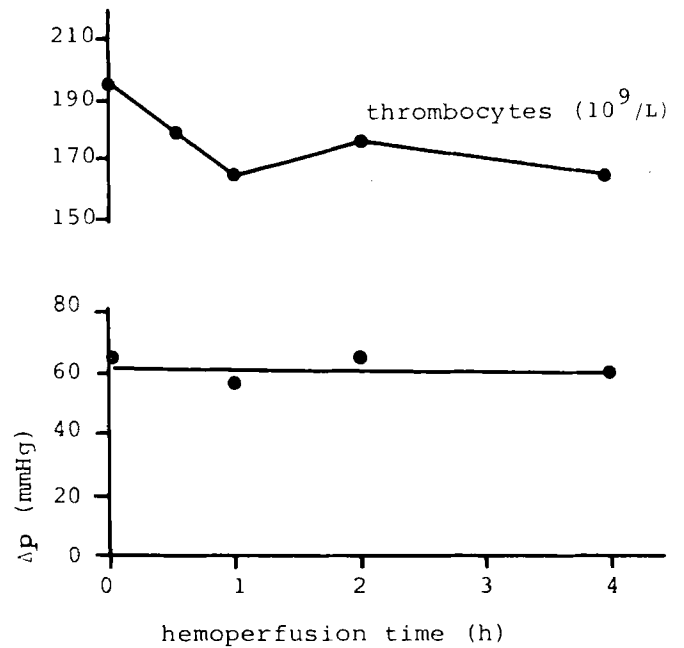
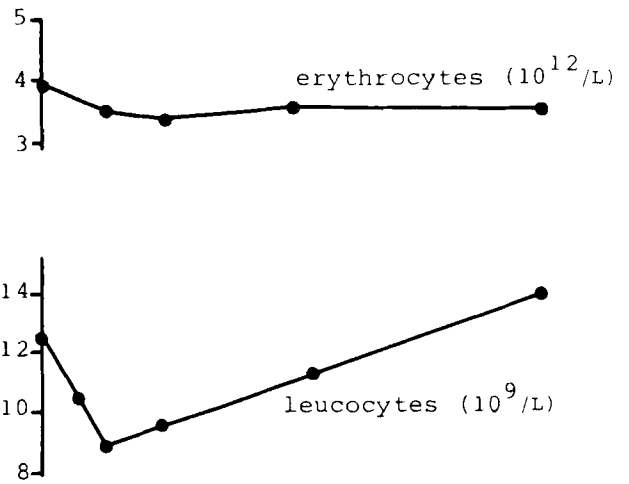


FIG. 5. Blood cell counts and blood flow resistance vs. time during hemoperfusion treatment of the meprobamate-poisoned patient.

the serum level of meprobamate fell from 80 µg/ml to 25 µg/ml with improvement in clinical responses.

Crome *et al*¹¹ reported the treatment of a severe meprobamate poisoning with a coated-AC column of Smith and Nephew (Haemocol, Smith and Nephew, Ltd., London, England). Under similar conditions (blood flow rate of 300 ml/min; four hours of perfusion) the plasma meprobamate

concentration decreased from 97 µg/ml to 62 µg/ml.

The blood cell counts and the blood flow resistance of the column have been plotted as a function of the perfusion time as shown in Figure 5. The platelet level reduction of approximately 16% did not lead to thrombocytopenia. The constancy of the blood flow resistance during hemoperfusion shows the complete absence of flow-inhibiting factors.

TABLE
MEMBRANE THICKNESS FOR VARIOUS COATED-
CHARCOAL HEMOPERFUSION SYSTEMS

System	Activated carbon	Polymeric coating	Membrane thickness (μm)
Chang: ACAC (Canada)	Fisher	albumin-cellulose nitrate	0.05 (= 500 Å)
Gambro: Adsorba 300 C (Sweden)	Norit RBX 1	cellulose	3 - 5
Smith & Nephew: Haemocol (England)	Sutcliffe Speakman	acrylic hydrogel	5
Organon Teknika "Hemopur 260" (The Netherlands)	Norit RBX 1	cellulose acetate	0.0030 (= 30 Å)

CONCLUSIONS

On the basis of the clinical results obtained in the treatment of the 25 poisoned patients the following conclusions can be made: 1) using the Organon Teknika "Hemopur 260" column, patients in grade IV coma due to an overdose of drugs or poisons come rapidly to consciousness, and the recovery period of the patients in the Intensive Care Unit is shortened considerably. 2) During and after the treatment no harmful side effects are noted.

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