

Control of Rate of Solute Transport in Newly Developed Portable Agar Gel Blood Purification System

Akihiro C. Yamashita, Ryoichi Sakiyama, Hiroyuki Hamada, Kakuji J. Tojo

Department of Biochemical Engineering and Science, Kyushu Institute of Technology at Iizuka, Japan

A blood purification module was developed with edible Agar or Gelrite, in which activated charcoal was dispersed. Tap water (or normal saline) was boiled, and agar (or Gelrite) powder was dissolved in it. The solution was hardened with no additive or activated charcoal in a plastic cylindrical hard shell with a perforated bottom plate to assemble module A (agar only), module AC (agar with various amounts of charcoal), or module GC (Gelrite with various amounts of charcoal), respectively. The hardened gel was thrust with a plastic straw 21 times in the flow direction. Aqueous test solution was prepared for device evaluation. Bromophenol blue (BPB) concentration decreased only by 10% with module A, whereas it gradually decreased according to the amount of activated charcoal dispersed in the agar with module AC; moreover, it reached its lower limit found by direct use of the same amount of intact activated charcoal. Module GC was shown to remove creatinine continuously from bovine whole blood. A portable artificial kidney system may be constructed by combining these modules with a small hemofilter for removing excess water.

(Home Hemodial Int, Vol. 2, 67–70, 1998)

Key words

Diffusion, adsorption, hemofiltration, portable artificial kidney

Introduction

Hemodialysis is a popular blood purification treatment, because it can remove small molecular weight substances that accumulate in many end-stage renal disease patients. One session of hemodialysis treatment, however, requires as much as 150 L of dialysate solution, which precludes a compact system, although small and high-performance hemodialyzers are currently available. Direct hemoperfusion is an alternative therapy for end-stage renal disease patients in which an adsorbent removes solutes of interest without using dialyzing fluid. Yamashita and Sakiyama developed a novel blood purification system with agar gel (edible agar or Gelrite) in which activated charcoal and/or urease was dispersed (1). Agar gel should

play the role of “membrane/dialysate,” and solutes of interest should diffuse from the blood stream into the gel. Activated charcoal and/or urease functions as the secondary device that cleanses the “membrane/dialysate.” Since the system should show relatively low clearances for solutes of interest and since the whole system is small enough for the patients to carry, this system may be suitable for continuous removal of toxic substances. In this study we intended to control the rate of solute removal by changing the amount of activated charcoal or by changing the amount of gel powder that should determine the complexity of the gel structure.

Materials and methods

Assembling modules

The module casing is an acrylic tube (6.4 cm in diameter, 25 cm in length) attached with a perforated bottom plate that has 40 small holes.

EDIBLE AGAR GEL MODULE WITH TAP WATER

After boiling 0.3 L of purified tap water (T), various amounts of commercial edible agar (A) powder (Ina Food Ind. Co., Japan) (2.4×10^{-3} , 2.8×10^{-3} , 3.2×10^{-3} kg) were added. A module with this agar was termed module T-A_x where x represents the amount of agar powder in grams. Likewise, other gel modules with activated charcoal (C) (Nakalai Tesque Co., Japan) were termed module T-A_xC_y. The hardened gel was then thrust straight in a longitudinal direction with a plastic straw 3.0 mm in diameter, 21 times, so that blood (or pseudoblood solution) could flow through (Figure 1).

GELRITE MODULE WITH SALINE SOLUTION

Normal saline (S) was used instead of tap water for preparing experiments with whole blood. Also, Gelrite (G) (Wako Pure Chemical Ind. Co., Japan), a gel designed for plant tissue culture, was used instead of edible agar because Gelrite is known to be superior in antiacidic and antichemical properties to other agar gels. The basic idea, however, is to devise a “solid water” system for a portable artificial kidney by using agar gel, and the nature of agar gel is beyond the scope of this discussion. Modules were assembled with Gelrite and normal saline in the same manner as described above for edible agar and were termed modules S-G_x and S-G_xC_y.

Characteristics of all modules tested in this study are shown in Table I.

Correspondence to:

Akihiro C. Yamashita, PhD, Department of Biochemical Engineering and Science, Kyushu Institute of Technology at Iizuka, 680-4 Kawazu, Iizuka, Fukuoka 820 Japan.

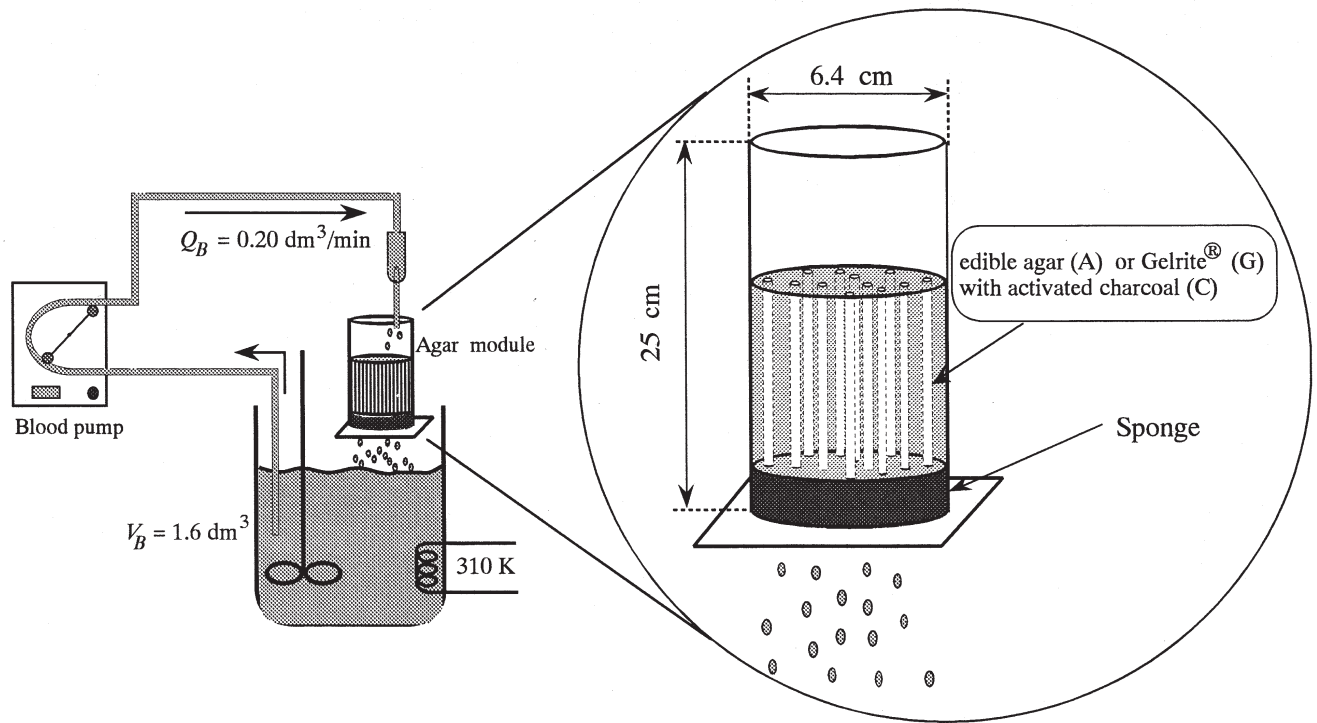


FIGURE 1 Experimental apparatus showing a close view of a newly developed agar module.

TABLE I Modules and solutions used in experiments

Module No.	Name	Water (0.3 L) for the module	Edible agar powder ($\times 10^3$) (kg)	Gelrite ($\times 10^3$) (kg)	Charcoal ($\times 10^3$) (kg)	Solution (1.6 L) solute(s)/solution	Figure No.
1	T-A _{2.4}	tap water	2.4	—	—	BPB/tap water	2,3
2	T-A _{2.4} C ₄	tap water	2.4	—	4.0	BPB/tap water	2,3
3	T-A _{2.4} C ₈	tap water	2.4	—	8.0	BPB/tap water	2,3
4	T-A _{2.4} C ₁₂	tap water	2.4	—	12.0	BPB/tap water	2,3
5	T-A _{2.4} C ₁₆	tap water	2.4	—	16.0	BPB/tap water	2,3
6	T-A _{2.4} C ₈	tap water	2.4	—	8.0	BPB/tap water	4,5
7	T-A _{2.8} C ₈	tap water	2.8	—	8.0	BPB/tap water	4,5
8	T-A _{3.2} C ₈	tap water	3.2	—	8.0	BPB/tap water	4,5
9	S-G _{2.4}	S solution	—	2.4	—	creat/BWB	6
10	S-G _{2.4} C ₈	S solution	—	2.4	8.0	creat/BWB	6

T = tap water; A = edible agar; G = Gelrite; C = activated charcoal; S = normal saline; BPB = bromophenol blue; creat = creatinine; BWB = bovine whole blood.

Experiments for performance evaluation

AQUEOUS SOLUTION SYSTEM

The aqueous test solution included 9.0×10^{-6} kg of bromophenol blue [BPB, molecular weight (MW) 670] in 1.6 L of purified tap water. The test solution was pumped from the tank to the module at a rate of 0.2 L/min at 310 K to evaluate the solute removal capability of the module. A separate experiment was performed with the same amount of intact activated charcoal as a reference.

BOVINE WHOLE BLOOD SYSTEM

Hematocrit of fresh bovine blood was adjusted to 20% with the normal saline solution that included a high concentration (1.0×10^{-5} kg/1.6 L) of creatinine (MW 113). Sodium citrate with sodium hydroxide was used as an anticoagulant, and modules S-G_{2.4} and S-G_{2.4}C₈ were tested at the blood flow rate of 0.2 L/min at 310 K for 24 hours to remove creatinine.

Solutions (including the whole blood) used in various experiments are also shown in Table I.

Theoretical

Taking the differential mass balance for the test solution in the tank, one should eventually obtain the following well-known equation:

$$\frac{C_B}{C_B(0)} = \exp\left(-\frac{C_L}{V_B} t\right), \quad (1)$$

where C_B is the solute concentration in the test solution (kg/L), V_B is the volume of the test solution (L), and C_L is the solute clearance (L/min). Plotting the natural logarithm of $C_B/C_B(0)$ against t , we obtain a straight line with a slope of $-C_L/V_B$, which enables us to calculate C_L . The clearance was used as a solute transport index.

Results and discussion

Aqueous solution system

Figure 2 shows the normalized BPB concentration [$C_B/C_B(0)$] profile over time with modules T-A_{2.4} (no charcoal dispersed), T-A_{2.4}C_y, and 8.0 g of intact activated charcoal (“charcoal only”) in a semilogarithmic scale. Straight lines with slopes of $-C_L/V_B$ were found, which verifies Eq. (1). BPB is known to have a strong affinity to the activated charcoal, and most of the BPB (9.0×10^{-6} kg = 0.0134 mmol) was rapidly adsorbed by the charcoal. Rapid removal may be important and is used in cases of acute drug intoxication; however, since the purpose of this study is to develop a portable and continuous treatment system for chronic patients, rapid removal is not our goal at this time. With module T-A_{2.4} the concentration decreased by 10% for the first 24 hours and remained constant after the gel should have been saturated with BPB. On the contrary, with four types of modules T-A_{2.4}C_y, rates of solute removal were changed by changing the amount of charcoal dispersed in gel. To analyze the fact quantitatively, clearances were plotted against the amount of activated charcoal dispersed in gel (Figure 3). The relationship between these two parameters was represented by a straight line passing through the origin (intercept close to 0). Thus it is concluded that rates of solute removal can be controlled by changing the amount of adsorbent.

Figure 4 shows the decrease in normalized BPB concentration over time by modules with various amounts of agar powder and 8.0 g of the charcoal (modules T-A_xC₈). From this figure it is obvious that rates of solute removal also varied by changing the amount of agar powder.

Clearances obtained by Eq. (1) were plotted against the amount of agar powder (Figure 5). A negative linear relationship between the clearance and the amount of agar powder implies that rates of solute removal are controlled by the complexity of the gel structure, which determines the diffusion coefficient.

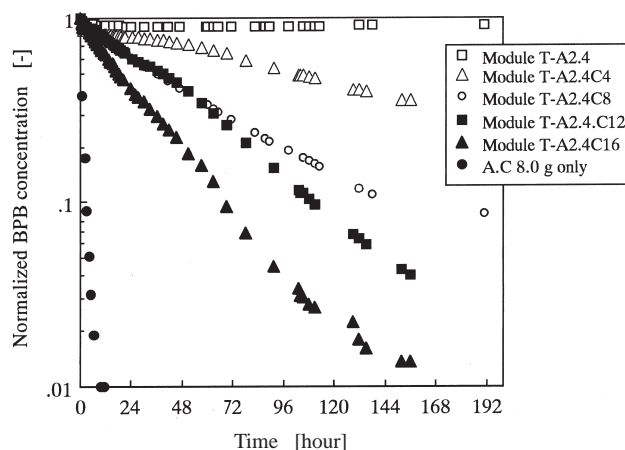


FIGURE 2 Time course of normalized bromophenol blue (BPB) concentration decreases with module T-A_{2.4}C_y (semilogarithmic scale).

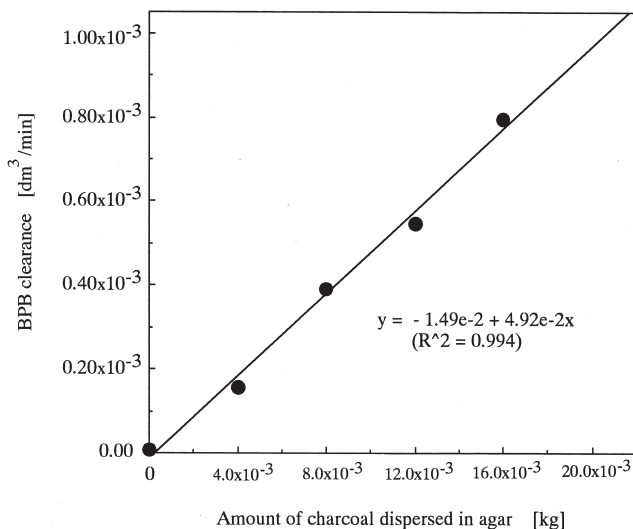


FIGURE 3 Relationship between BPB clearance and the amount of activated charcoal dispersed in module T-A_{2.4}C_y.

Whole blood system

A steady decrease of creatinine concentration is seen with module S-G_{2.4}C₈, whereas two controls show different patterns. A rapid 20% initial concentration decrease is seen for module S-G_{2.4} and approximately 80% decrease within 12 hours with charcoal only; both modules show relatively constant concentration thereafter (Figure 6). It was demonstrated that the rate of creatinine removal with module S-G_{2.4}C₈ was controlled at a certain level with $C_L = 9.2 \times 10^{-4}$ L/min, which counted 9.3 L/week. Therefore, a clinical system should be approximately 5.4 times larger to satisfy the minimum weekly creatinine clearance of 50 L/week

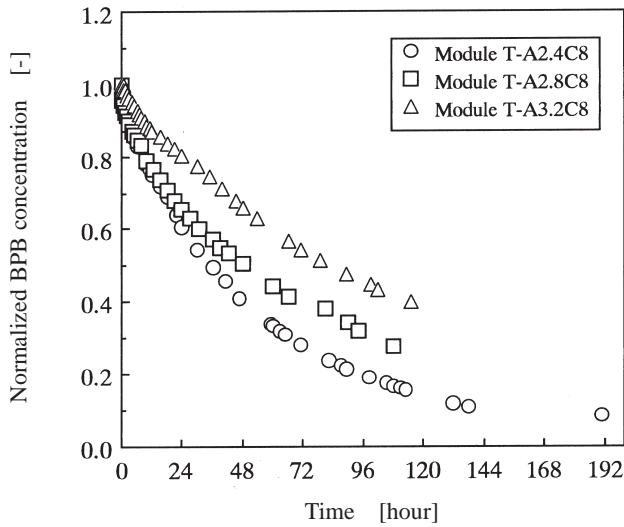


FIGURE 4 Time course of normalized BPB concentration with module T-A_xC₈.

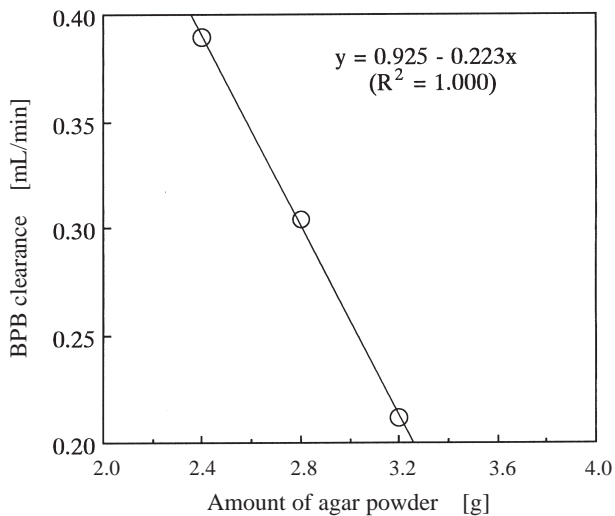


FIGURE 5 Relationship between BPB clearance with module T-A_xC₈ and the amount of agar powder.

required in continuous ambulatory peritoneal dialysis patients (2).

As the authors have already reported, urea or other poorly adsorbable substances may be decomposed by some enzyme dispersed in the gel (1) when the coating technique previously used by Chang and Malouf (3,4) is not used. For his experimental version of the device we used agar gels and a charcoal adsorbent. It is shown that continuous removal of uremic substances with relatively low and controllable

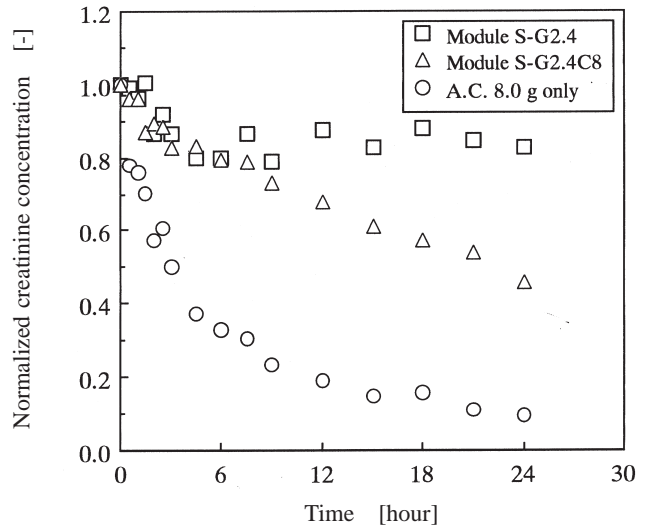


FIGURE 6 Time course of normalized creatinine concentration decreases with module S-G_{2.4}C₈ in the bovine whole blood experiment (hematocrit = 20%).

clearances may be feasible with the device described. These results indicate that it is possible to construct a portable blood purification device by combining this system with a small ultrafilter that removes excess amount of water.

Conclusions

A novel blood purification system with agar and activated charcoal showed the following features:

1. Rates of solute removal can be controlled by changing amounts of activated charcoal dispersed in gel.
2. Rates of solute removal can be controlled by changing amounts of gel powder that determines the complexity of the gel structure.
3. Creatinine in whole blood (hematocrit = 20%) was continuously removed with the device.

References

- 1 Yamashita A, Sakiyama R. Development of a novel portable artificial kidney with agar gel. *Jpn J Artif Organs* 1997; 26:429–32.
- 2 Churchill DN, Taylor DW, Keshaviah PR. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: Association with clinical outcomes. *J Am Soc Nephrol* 1996; 7:198–207.
- 3 Chang TMS. Semipermeable microcapsules. *Science* 1964; 146:524–9.
- 4 Chang TMS, Malouf C. Artificial cells microencapsulated multienzyme system for converting urea and ammonia to amino acid using α-ketoglutarate and glucose as substrate. *Trans Am Soc Artif Intern Organs* 1978; 24:18–23.