Urea concentrating ability of artificial renal tubule based on countercurrent multiplier system using electrodialysis, dialysis and filtration

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Abstract— **Countercurrent multiplier systems have been found in various organs of various animal species. In a mammalian kidney, countercurrent multiplier system plays an important role in the process of urine concentration. An artificial renal tubule which can concentrate urea is one of the key elements to develop a wearable artificial kidney for the patients currently undergoing intermittent hemodialysis therapy. The objective of the present study was to develop a biomimetic artificial renal tubule based on the countercurrent multiplier system. We mimicked active transport of NaCl at ascending limbs of the Henle loop by electrodialysis and mimicked passive transport of the solute and water transport via water channel at descending limbs and collecting ducts by dialysis and filtration. The membranes used for electrodialysis, dialysis and filtration were placed parallel to each other to establish countercurrent configuration. We examined urea concentrating ability of the fabricated prototype module of artificial renal tubule based on the countercurrent multiplier system. The fabricated prototype module was capable of concentrating urea approximately 1.3 fold. These results indicate that the countercurrent multiplier system is useful to develop an artificial renal tubule.**

Keywords— **countercurrent multiplier system, wearable artificial kidney, biomimetic, urea concentrating ability, electrodialysis**

I. INTRODUCTION

Countercurrent multiplier systems have been found in various organs of various animal species. For example, in a fish swim bladder, fine countercurrent blood flow in the rete mirabile enhances blood gas partial pressure to tremendous values, up to several 100 atm, encountered in deep sea dwellers [1] and in a mammalian kidney, countercurrent multiplier system plays an important role in the process of urine concentration [2]. According to mathematical and experimental studies [3-5], the urine concentrating ability is attributed to active transport of NaCl from thick ascending limbs of the Henle loop via Na-K-Cl cotransporter as a primary energy source of concentration, which is then multiplied by the countercurrent configuration of renal tubule (Fig. 1).

An artificial renal tubule which can concentrate urea is one of the key elements to develop a wearable artificial kidney for the patients currently undergoing intermittent hemodialysis therapy who need more physiological therapy. Reviewing the results of mathematical calculations [3, 4], we considered that the establishment of a biomimetic artificial renal tubule based on the countercurrent multiplier system is a promising strategy to develop the wearable artificial kidney.

The objective of the present study was to develop a biomimetic artificial renal tubule based on the countercurrent multiplier system. We mimicked active transport of NaCl at ascending limbs of the Henle loop by electrodialysis and mimicked passive transport of the solute and water transport via water channel at descending limbs and collecting ducts by dialysis and filtration. The membranes used for electrodialysis, dialysis and filtration were placed parallel to each other to establish countercurrent configuration. We examined urea concentrating ability of the fabricated prototype module of artificial renal tubule based on the countercurrent multiplier system.

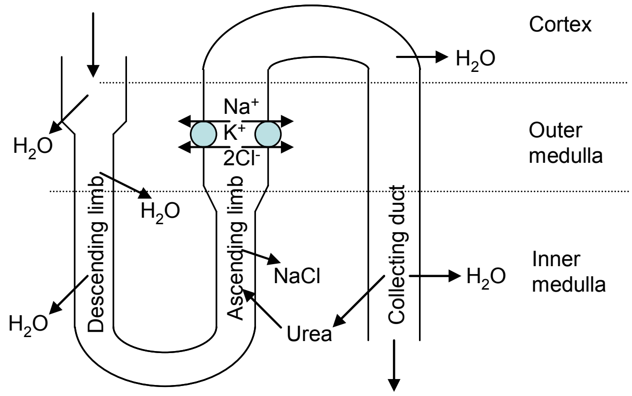

Fig. 1 Urea and ion transport in the renal tubule.

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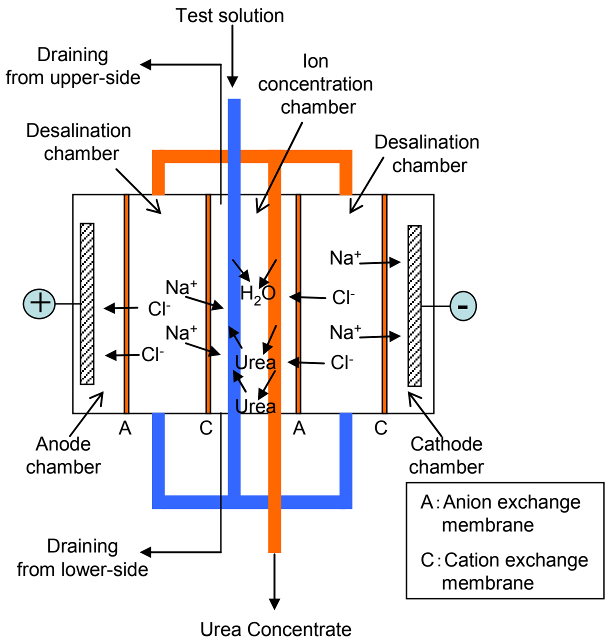

Fig. 2 Diagram of urea and ion transport in the fabricated artificial renal tubule system.

II. MATEIALS AND METHODS

A. Prototype of artificial renal tubule

The membranes used for electrodialysis was a strong acidic cation permeable membrane (cation exchange membrane) with mono-cation permselective property (NeoSepta, CIMS, Astom Co., Tokyo, Japan) and a strong basic anion permeable membrane (anion exchange membrane) with mono-anion permselective property (NeoSepta, ACS, Astom Co., Tokyo, Japan). Hollow-fiber hemodialysis membranes made of polyethersulfone (PES-150D, Nipro, Osaka, Japan) were used as a dialysis membrane and filtration membrane of this system.

These membranes were placed parallel to each other to establish countercurrent configuration (Fig. 2). Fabricated electrodialysis module contained one ion-concentration-chamber and two desalination-chambers using two pairs of anion exchange and cation exchange membrane. Desalination-chamber was corresponding to ascending limbs of the renal tubule and ion-concentration-chamber was corresponding to interstitium. Then we assembled 150 hollow-fibers of 30 mm in length and glued and filled at the both end of the fibers by epoxy resin to make dialysis and filtration modules, which were corresponding to descending limbs and collection ducts. Then the modules were inserted to the ion-concentration-chamber of electrodialysis module. Excess water filtered from dialysis membrane modules was drained from either upper-side of the ion-concentration-chamber or from lower-side of the chamber.

B. Urea concentrating ability of prototype module

We prepared a test solution dissolving 30 mg of urea in 100 ml of saline solution and a solution dissolving 30 mg of urea in 100 ml of 0.1N H_2SO_4 solution, which circulate through the cathode and anode chambers. The test solution was forced to flow by peristaltic pump (SJ-1211H, Atto Co., Tokyo, Japan) at a flow rate of 0.8 ml/min. The flow rate at outlet of the test solution was adjusted by changing the openness of the tube at outlet. Concentration of urea and NaCl was measured when the water recovery ratio, meaning the ratio of the filtration rate (flow rate of the drained solution from the ion-concentration-chamber) to the flow rate at outlet of the test solution, was varied ranging from 0 to 150. Urea concentration was determined by a urease-indophenol method and NaCl concentration was measured using a compact sodium ion meter (C-122, Horiba Ltd., Kyoto, Japan)

III. RESULTS

The prototype module was capable of concentrating urea up to 1.3 fold when water was drained from upper-side of the ion-concentration-chamber (Fig. 3). Concentrating ratio of urea increased as the water recovery ratio increased.

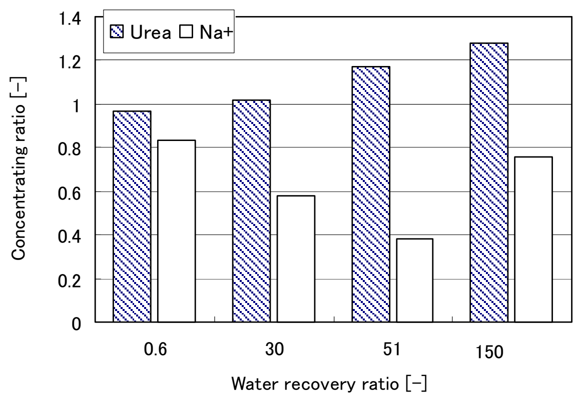

Fig. 3 Concentrating ratio of urea and Na^+ of the prototype module that drains water from upper-side of the ion-concentration-chamber

However, Na^+ concentration ratio decreased to 0.75 at the same time (Fig. 3). On the other hand, the prototype module represented no concentration of urea when water was drained from lower-side of ion-concentration-chamber (data not shown).

IV. Discussion

This artificial renal tubule developed based on countercurrent multiplier system, using electrodialysis with dialysis and filtration, was capable of concentrating urea approximately 1.3 fold when the water recovery ratio was 150. At the same time, Na^+ concentration decreased 0.75 fold. The decrease in Na^+ concentration was considered to be caused by ion transfer to the cathode chamber through cation exchange membrane.

The prototype module represented no concentration of urea, when water was drained from lower-side of ion-concentration-chamber. This result suggests that the concentration of urea was extremely affected by the flow direction in the ion-concentration-chamber. When the water was drained from lower-side of the ion-concentration-chamber, concentration gradient, i.e., increasing concentration towards the bottom cannot be established because of the down flow of low urea concentration solution. In the real renal tubules, excess water transferred from descending limbs and collecting ducts is reabsorbed by the blood and lymphatic vessels near the tubules. Therefore, we could probably enhance the urea concentrating ability of this system by introducing mimic system of the blood and lymphatic vessels in the kidney.

V. Conclusions

We developed an artificial renal tubule based on countercurrent multiplier system using electrodialysis, dialysis and filtration. This artificial renal tubule was capable of concentrating urea approximately 1.3 fold. The flow of interstitial-side of this system is important to concentrate urea. The countercurrent multiplier system is considered to be useful to develop an artificial renal tubule.

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