Studies on the Relationship between the Biodistribution of $^{45}$Ti-AsA in the Rat Kidney and Renal Functions

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Titanium (Ti) is a common element widely spread in the earth's crust, but it is not known whether Ti is an essential element or not. Also its biochemical function is not clearly understood. Pais et al. $^{1)}$ found out that titanium-ascorbate (Ti-AsA) promoted growth in some plants. This implies that Ti has the possibility to play a biological role in plants. We are now investigating the essentiality of Ti in animals. For this purpose, we examined its behavior in the kidney of rats, in order to form a link in the chain of research, using $^{45}$Ti which has a short half life (3.09 hrs), because previously we found that the effects of AsA on the biodistribution of $^{45}$Ti was remarkably characteristic in the kidney. $^{2)}$

$^{45}$Ti was produced by the reaction of $^{45}$Sc(p,n)$^{45}$Ti with 11.5 MeV protons and separated from scandium according to the method of Nelson et al. $^{3)}$, which is an ion-exchange technique (Fig. 1). The special activity and radiochemical purity was verified by HPLC.

$^{45}$Ti-AsA was injected in male Wistar rats through a tail vein. Figure 2 presented the autoradiogram about kidney with varying times (time at 10, 30, 60, 120 minutes after injection). In the normal kidney, uptake of $^{45}$Ti was not found in cortex and medulla, but was found in the pelvis. Uptake in the pelvis was probably due to the fact that the $^{45}$Ti was excreted into the urine. To examine whether $^{45}$Ti excreted into the urine or reabsorped in kidney, blood was collected at ten minute intervals through a cannula from a femoral artery, and urine was collected continuously through a cannula from one of the ureters after injection of $^{45}$Ti-AsA through a femoral vein.

It was found that excretion of $^{45}$Ti into the urine was minimal in normal Wistar rat (Fig. 3), this result suggests that the reabsorption of $^{45}$Ti-AsA is relatively high in normal rat.

We had previously confirmed that the absorption of the mineral was inhibited in renal tubule in stroke-prone spontaneously hypertensive rat (SHRSP) when they were kept on a low protein and a high sodium diet. $^{4)}$ We also performed autoradiography of the kidney 30 minutes after the injection of $^{45}$Ti-AsA in rat with a low protein and a high sodium diet for three months (Fig. 5). The highest uptake of $^{45}$Ti-AsA was found in the medulla, and excretion into the urine was high in SHRSP with a low protein and a high sodium diet compared to that of the SHRSP with a normal diet (Fig. 5). This
result is due to the hinderance of sodium reabsorption in the SHRSP with a low protein and a high sodium diet.

Figure 6 presented the autoradiogram of the kidney of a Wistar rat which had made glomerulonephritis by injecting puromycin aminonucleoside (PAN). The highest uptake was found in the cortex and the amount of excretion of $^{45}$Ti into the urine was same as in the normal one (Fig. 7). These data indicates that the Ti-45 was not filtered and gathered around the cortex because the function of glomeruli was worsed by the PAN injection.

In two renal diseases, concentration of $^{45}$Ti in blood was lower than the normal one, this indicates that $^{45}$Ti concentrates around the damaged side of the kidney.

We suggest that $^{45}$Ti-AsA may be useful as a positron emitting radio-pharmaceutical for diagnosis of renal diseases.

References
Fig. 2. Changes of autoradiographic images in the distribution of injected $^{45}$Ti-AsA in Wistar rats kidney with varying time.

Fig. 3. Urinary excretion and blood clearance in Wistar rat after injection of $^{45}$Ti-AsA.
Fig. 4. Autoradiographic image of kidney 30 minutes after the injection of $^{45}$Ti-AsA in SHRSP.
Right: Normal diet.
Left: Low-protein and high-sodium diet.

Fig. 5. Urinary excretion and blood clearance in SHRSP after injection of $^{45}$Ti-AsA.
Fig. 6. Autoradiographic image of kidney 30 minutes after the injection of $^{45}$Ti-AsA in nephritic rat.

Fig. 7. Urinary excretion and blood clearance in nephritic rat after injection of $^{45}$Ti-AsA.