Metabolism of Vanadiuim-48 in Mice

III. 18 Metabolism of Vanadium-48 in Mice

Yamamoto F., Ido T., Ishiwata K. and Iwata R.
Cyclotron and Radioisotope Center, Tohoku University

Introduction

Vanadium has been known as an important trace element for living things. It is essential for rats and chicks.[1] However high concentration of vanadium inhibits phosphatase, Na^+, K^+-ATPase and some other enzymes.[2] It is supposed that vanadium is involved in the brain disease such as manic-depressive psychosis.[3]

This study represents the metabolism of ^{48}V in mice.

Materials and Methods

Vanadium-48 was produced by the $^{48}Ti(p,n)^{48}V$ reaction and vanadate(V) was prepared.[4]

The ^{48}V solution (0.3 μg/kg) was injected intravenously into male ddY mice. Tissues were removed and blood was collected at various time intervals after injection, and tissue uptake was measured. The plasma was analyzed by HPLC using gel-filtlation and anion exchange columns.

The ^{48}V solution, with carrier sodium orthovanadate (1.3 and 983 μg/kg), was also injected into mice. At 6 hr after the injection tissue distribution was calculated.

The plasma, liver and brain were homogenized in 0.2 N $HClO_4$, and the acid-insoluble and acid-soluble fractions were separated.

The ^{48}V solution was incubated in the plasma, whole blood or transferrin or albumin in 50 mM Tris-HCl (pH 7.4) for 6 hr at 37°C. In case of the plasma, glutathion (GSH) was added into the incubation mixture, the concentration ratio of GSH to ^{48}V was varied from 0.2 to 100. The protein-binding ^{48}V was analyzed by HPLC.

Results and Discussion

Tissue distribution of ^{48}V is shown in Fig. 1. The ^{48}V uptake in the liver and kidney was high. In the bone the uptake increased for 12 hr after the injection. The brain uptake was the lowest among all tissues. It decreased for 24 hr after the injection.

Figure 2 shows the concentration of V in tissues, calculated from radioactivity uptake after injection of ^{48}V with different carrier amounts. The concentration increased with a loading dose of V, and no saturability was observed.

The plasma obtained after 1, 2 and 6 hr was analyzed by HPLC. An HPLC profile is shown in Fig. 3. Thirty-50% of ^{48}V was found in the 60K protein fraction including transferrin and albumin. The result of anion exchange chromatography shows that most ^{48}V was eluted in transferrin fraction as shown in Fig. 4. Ratio of transferrin-binding fraction increased with time. Free V ion was eluted with 0.5 M NaCl containing buffer.

Parcentages of ^{48}V in the acid insoluble fraction were 26.5, 5.0 and 0.2 % in the liver, brain and plasma, respectively. Consequently it is suggested that in the liver and brain the vanadium bind with certain proteins besides transferrin and that the binding is not separated by the acid treatment.

Table 1 shows the results of in vitro protein binding study. The ratio of protein binding ^{48}V in blood was higher than that in the plasma. By glutathion as a reductant, transferrin-binding ^{48}V was increased. Therefore, it is supposed that vanadyl(IV) is a preferable form for binding with transferrin than vanadate(V), although we did not investigate the ionic form of ^{48}V.

The ratio of protein binding ^{48}V in in vivo study is high. As reductants in blood, glutathion rich in erythrocytes, catecolamine and ascorbate are expected.

References

1) Nielsen F. H. and Sandstead H. H., Am. J. Clin. Nutr. 27 (1947) 515.
2) Nechay B. R., Nanninga L. B., nechay P. S. E. et al., Federation Proc. 45 (1986) 123.
3) Naylor G. J., Smith A. H. W., Bryce-Smith D. and Ward N. I., Physicol. Med. 14 (1984) 767.
4) Ido T., Ishiwata K., Iwata R. et al., First Japan-China Joint Seminar on Radiopharm. Chem. (1987).

Table 1. Binding of ^{48}V with plasma proteins in in vitro study.

	Transferrin(%)	Albumin (%)
in vivo	49.4	3.0
in vitro		
* Plasma (V:GSH=1:0)	7.3	4.1
(V:GSH=5:1)	8.4	5.3
(V:GSH=2:1)	14.2	4.3
(V:GSH=1:1)	26.1	5.2
(V:GSH=1:50)	33.8	6.9
(V:GSH=1:100)	31.4	4.7
Whole blood	12.2	5.4
Transferrin in Tris-HCl,pH7.4	5.0	—
Albumin in Tris-HCl,pH7.4	—	3.8

* pO2=173.7~184.0 mmHg pCO2=6.9~9.3 mmHg

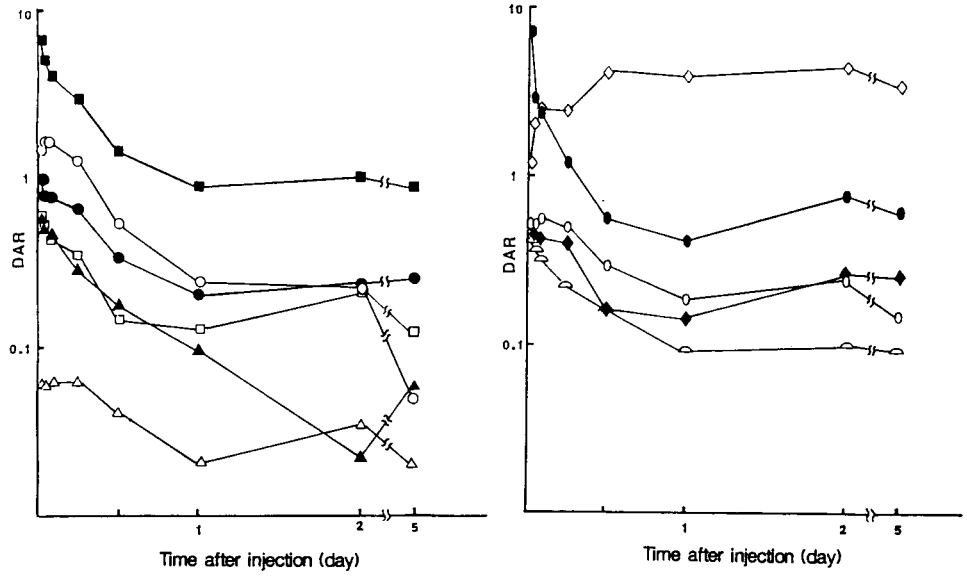

Fig. 1. Tissue distribution of ^{48}V in male ddY mice (n = 4-5). ■ - ■ kidney; ● - ● lung; □ - □ pancreas; ▲ - ▲ small intestine; ○ - ○ blood; △ - △ brain; ◇ - ◇ bone; ⬮ - ⬮ liver; ◆ - ◆ spleen; 0 - 0 heart; ⌓ - ⌓ muscle.

$$DAR = \frac{\text{(tissue radioactivity) x (body weight)}}{\text{(total injected radioactivity) x (Tissue weight)}}$$

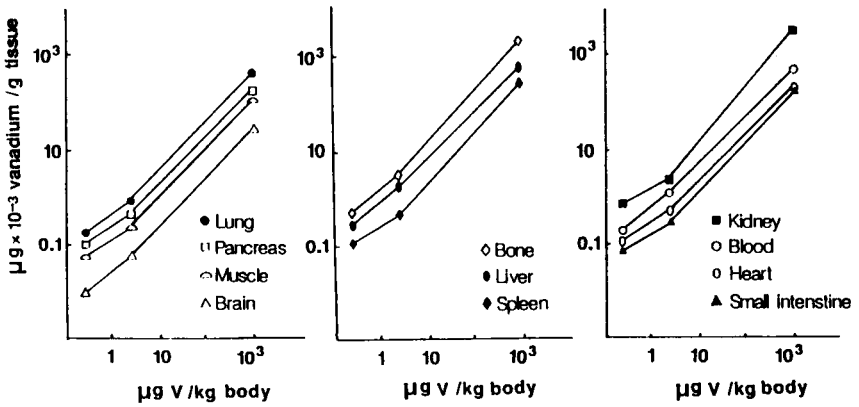

Fig. 2. Concentration of V in mice tissues after i. v. injection of ^{48}V with diferent loading doses.

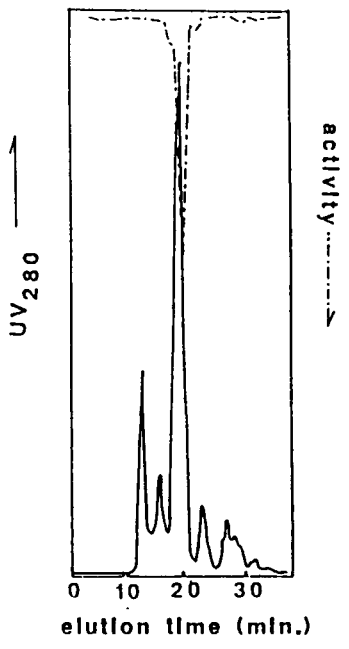

Fig. 3. HPLC analysis of the plasma incubated with ^{48}V.
Column: TSK-GEL G3000SW
Eluent: 0.15 M NaCl, 20 mM AcONa (pH 7.8)
Flow rate: 1 mL/min.

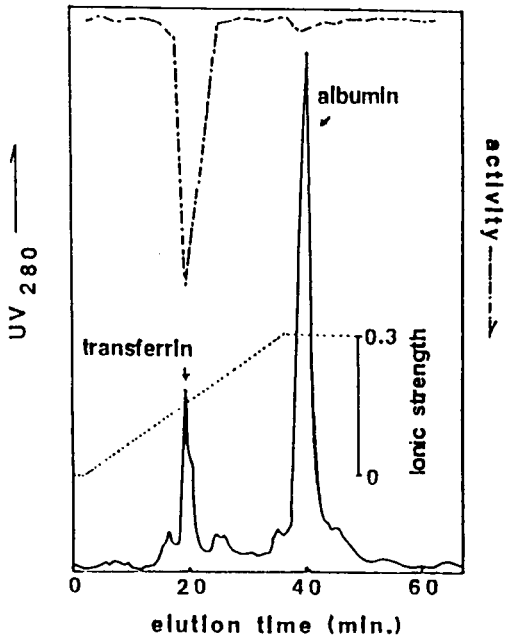

Fig. 4. HPLC analysis of the plasma incubated with ^{48}V.
Column: TSK-GEL DEAE-5PW
Eluent: 0.02 M Tris-HCl (pH 8.0), 0 - 0.3 M AcONa
Flow rate : 0.5 mL/min.