Biokinetics and Dose Estimation of Various Tritiated Compounds and Crops in Rats

各種^{3}H標識化合物及び作物のラットにおける生体内動態と被曝線量評価

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BIOKINETICS AND DOSE ESTIMATION OF VARIOUS TRITIATED COMPOUNDS AND CROPS IN RATS

A thesis
submitted to the Faculty of Medicine, at The University of Tokyo,
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INTRODUCTION

Tritium is a radioactive isotope of hydrogen with a mass of 3. It has a physical half-life of 12.3 years and decays to helium-3 by the emission of a beta-particle with an average energy of 0.0057 MeV and a maximum energy of 0.018 MeV. Amongst the radionuclides that have biological significance, tritium is of particular importance because it is the radioisotope of one of the major constituents of water and organic substances in all biological systems. This is reflected by the widespread use of tritium as a tracer in biology and medicine.

Tritium is considered to be one of the least hazardous radioisotopes. This is partly because its beta-particle has such a low energy. It has a mean range of less than 1 μm in water, and can not give rise to an external radiation hazard. In addition, early research work showed that tritium administered in the form of water is excreted quickly, with a biological half-time of 8-14 days in man, and that no obvious evidence of radiation injury has been found in experimental animals exposed to tritium at even large doses.

Nevertheless, there has been a continuous interest in the biological effects of this nuclide because of its physical and chemical characteristics. This interest has been stimulated by increasing releases into the environment from existing nuclear facilities and by the potentially greater releases from nuclear fusion reactors which are now under development.

Tritium released into the environment is present mainly in the form of tritiated water(Peterson et al. 1969). The nuclide in

this form easily enters plants and animals and is partly incorporated into their organic constituents(Thompson and Ballou 1956, Choi and Aronoff 1966, Hatch and Mazrimas 1972, Kanazawa et al. 1982). Actually, monitoring programs in the neighborhood of nuclear power plants have revealed the entry of tritium into the biosphere even if it is at a low level(Cohen and Kneip 1973, Inoue et al. 1985). Plants and animals labeled with tritium at nuclear weapon testing sites have also been found(Hatch et al. 1970, Martin and Koranda 1972, Koranda and Martin 1973). Accordingly, tritium in the environment exists in not only tritiated water, but also organically-bound forms. Tritium in both forms is taken into human body by ingestion of contaminated water and food. As for other possible sources of human exposure to tritium, there is the use of tritium labeled compounds in research laboratories and in industries where workers may deal with a relatively large amount of tritium. In these cases, a great variety of tritiated compounds are used. Thus, there is a possibility that the general public as well as workers will be exposed to tritium in it's various chemical forms.

For the purpose of limiting exposure to radiation the International Commission on Radiological Protection(ICRP) recommends using the annual limit of intake(ALI) for radionuclides. The ALI for tritium is based on the metabolic data of only one tritiated compound, namely tritiated water(ICRP 1979); therefore, the recommended ALI for tritium is not applicable to other tritiated compounds whose metabolic behavior is different from tritiated water.

In this study, the biological behavior of various tritiated compounds in their organic form, including tritiated food, was investigated in rats and the radiation dose was estimated using the metabolic data obtained. To obtain data useful for setting the ALI for tritium in it's organic form, experiments using tritiated water were concurrently performed and their results were compared with one another.

MATERIALS AND METHODS

Male Wistar strain rats obtained from the animal and plant supply section of our institute(NIRS) were used in this study. Throughout the study the animals were kept in a room with controlled temperature(23±1°C) and air flow, and were fed with a standard chow and water ad libitum. At the start of all the experiments the rats were about 4 months old with an average body weight of 390 g, ranging from 370 g to 410 g.

Tritiated water(^{3}HHO) was purchased from Amercham(England). Various kinds of tritiated organic compounds were purchased from New England Nuclear(USA). They were L-4,5-[^{3}H]leucine(185 GBq/mmol), D-6-[^{3}H]glucose(1110 GBq/mmol), methyl-[^{3}H]thymidine(74 GBq/mmol), L-4,5-[^{3}H]lysine(2760 GBq/mmol), D-6-[^{3}H]glucosamine(375 GBq/mmol) and 6-[^{3}H]uridine(866 GBq/mmol). Before the experiment the tritiated organic compounds were analyzed by paper chromatography. Purity was verified to be more than 95 percent. These tritiated compounds were dissolved in distilled water to an appropriate concentration and administered

to the animals.

The present study was carried out in two series of experiments; one is by single ingestion and the other is by continuous ingestion. In the first series, tritiated water and three kinds of tritiated organic compounds, namely tritiated leucine, tritiated glucose and tritiated thymidine, were administered to different rats using a stomach tube under ether anesthesia. Tritiated water was given to forty rats with an activity of 222 kBq per gram body weight, in a volume of 1 ml. Each of the tritiated organic compound was given to thirty rats with an activity of 7.4 kBq per gram of body weight in a volume of 0.5 ml. At various time points up to 120 days after administration, the animals were sacrificed by decapitation and dissected to obtain various tissue samples. At days 1, 10, 20, 40, 60 and 100 days after the ingestion three rats were used and two rats each at other points. Although a relatively small number of animals were examined at each point, a sufficient number of experimental points was secured.

In the second series of experiments, each of the tritiated compounds including tritiated water, tritiated leucine, tritiated glucose, tritiated thymidine, tritiated lysine, tritiated glucosamine and tritiated uridine was given separately to groups of three or five rats for 22 days. The various compounds were dissolved into their drinking water and adjusted to a concentration of 3.7 kBq/ml. In this series of continuous ingestion experiments, three additional experiments using tritiated crops were carried out. The tritiated crops were obtained by cultivating three kinds of plants(rice, wheat and

soybean) under the presence of tritiated water in a phytotron with controlled temperature and natural light. The edible parts of these plants were harvested and dried naturally for at least one year. Before administration to the animals, the tritiated crops were pulverized and dried in vacuum. The concentration of tritium in the crops was about 100 kBq/g. Tritiated crop was mixed with powdered standard chow to obtain a final concentration of 0.37 kBq/g and administered continuously to rats as food. Each of these tritiated crops was given separately to groups of five rats.

During the experiment by continuous ingestion, the animals were kept in metabolic cages (Metabolica, Sugiyama-gen Iriki Instrument Co.) and the amount of drinking water and food ingested by each animal was measured daily. Daily samples of urine and feces from each animal were also collected during the continuous ingestion. The rats were killed on the 22nd day of continuous ingestion and dissected to obtain various tissue samples.

All samples (tissues, urine and feces) obtained in these experiments were weighed and immediately processed to determine tritium activity in the fresh wet sample(total tritium). Part of the feces and tissue samples was lyophilized for determination of tritium activity in the dry sample(organically-bound tritium ; OBT). Lyophilization was performed up to constant weight and repeated twice with the addition of distilled water to remove both water-form tritium and easily exchangeable OBT. These wet and dry samples were combusted in an oxidizer(Model 306 Tri-Carb Packard Instrument Co.) and their radioactivity was measured

with a liquid scintillation counter(LS-7500 Beckman). Counting efficiencies were determined by the external standard channel ratio method.

Data on radioactivity were expressed in terms of relative concentration, which were calculated as follows:

$$\text{Relative concentration} = \frac{\dfrac{\text{radioactivity in sample}}{\text{weight of sample}}}{\dfrac{\text{radioactivity administered to animal}}{\text{weight of animal at administration}}} \times 100$$

A concept of relative concentration is, therefore, defined as the percentage ratio of the concentration at an arbitrary time to that at the time of administration of tritium. The statistical significance of the differences between the data was analyzed using the Student's t-test.

RESULTS

1. Biokinetics and dose estimation in rats exposed to tritiated compounds by a single ingestion

Biokinetics of tritiated water

Retention curves of total tritium in various tissues after ingestion of tritiated water are illustrated in Fig. 1. The concentration of total tritium did not vary very much between the different tissues, except for adipose tissue, until about 25 days after the administration of tritiated water when the concentration had fallen to 1-2 % of the initial level. Thereafter the difference in the concentration among the tissues became evident gradually with time. The concentration in the muscle and the brain decreased more slowly than that in the liver and the small intestine. At the end of this experiment, highest concentration was observed in the adipose tissue, followed by the brain and the muscle, and lowest in the liver and the small intestine. The concentration of total tritium in other tissues showed intermediate values.

Fig. 2 shows the variation in the concentration of organically-bound tritium as a function of time. For the first several days, the concentration of organically-bound tritium was relatively low in the adipose tissue, the muscle and the brain, and highest in the liver and the small intestine. However, this situation was reversed after 20 days, and the concentration was relatively high in the adipose tissue, the brain and the muscle, and low in the liver and the small intestine.

Variations in quantity of total tritium and organically-bound tritium in kidney are shown in Fig. 3, which is a typical example. Initially, the amount of organically-bound tritium was 2 to 3 % of total tritium, but the ratio of organically-bound tritium to the total tritium increased gradually with time. After 40 days, the slope of the retention curves for total tritium was parallel with that of organically-bound tritium, indicating that the release of tritium from the tissue during the period was mainly controlled by degradation of organically-bound tritium.

These retention curves for total tritium and organically-bound tritium were approximated by the sum of two exponential components using the least square method. The biological half-lives of tritium in different tissues, which were determined from the slopes of the component lines, are shown in Table 1. The half-life for the short component of the total tritium retention curve was about 3.5 days in all tissues studied. On the other hand, the half-life for the long component of the retention curve varied from tissue to tissue, ranging from 17 to 52 days. These half-lives for the long component were in good agreement with those obtained for the organically-bound tritium in the corresponding tissue. These results indicates that each component of the retention curves for the total tritium probably reflects the excretion or release of tritium from the body water and from the organic constituents of tissues, respectively.

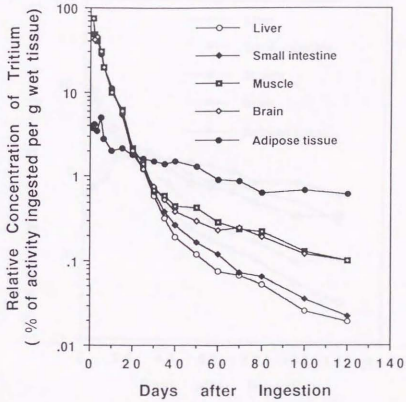

Fig. 1. Variation in the concentration of total tritium in several tissues after administration of tritiated water. Each point represents the average of measurements for two or three animals.

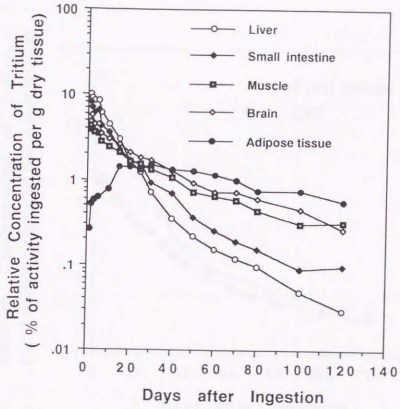

Fig. 2. Variation in the concentration of organically-bound tritium in several tissues after administration of tritiated water. Each point represents the average of measurements for two or three animals.

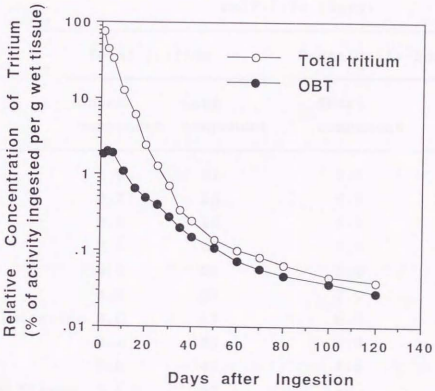

Fig. 3. Variations in the concentrations of total tritium and organically-bound tritium in the kidney after administration of tritiated water. Each point represents the average of measurements for two or three animals.

Table 1. Half-lives of total tritium and organically-bound tritium after ingestion of tritiated water.

Tissue and Urine	Half-life (days)			
	Total tritium		Organically-bound tritium	
	Short component	Long component	Short component	Long component
Liver	3.5	21	6.5	21
Kidney	3.5	23	5.8	23
Testis	3.5	25	6.9	27
Spleen	3.5	35	5.8	35
Lung	3.5	26	5.5	26
Heart	3.5	27	7.0	27
Small intestine	3.5	17	6.3	18
Muscle	3.4	35	6.8	36
Brain	3.6	41	7.5	43
Adipose tissue	3.4	52	—	—

Biokinetics of tritiated organic compounds

Relative concentration is defined as the ratio of the concentration at an arbitrary time to that at the time of administration. The relative concentration of tritium at selected time intervals after the ingestion of tritiated water and tritiated organic compounds are summarized in Table 2 for total tritium and in Table 3 for organically-bound tritium. The results for kidney are graphically shown in Fig.4 for total tritium and in Fig.5 for organically-bound tritium, as typical examples. It is clear from these results that the distribution and the retention of tritium differ according to the chemical compound ingested. Tritiated water was distributed almost uniformly, whereas the distribution of tritium administered in the form of organic compounds was not uniform between the tissues. Its pattern of distribution was different for the organic compounds studied here. These trends were more significant for organically-bound tritium.

The concentrations of organically-bound tritium in the tissues were consistently higher for administered tritiated organic compounds when compared with administered tritiated water. The highest concentrations were found in the case of tritiated leucine and intermediate values were observed in the tissues of rats exposed to tritiated glucose and thymidine. As indicated in Fig.5, the decreasing patterns for organically-bound tritium were somewhat different between the compounds examined. The difference in the decreasing patterns for organically-bound tritium was larger in tissues that a specific tritiated compound was

administered to than in individual tissues that different tritiated compounds were administered. For all the tritiated compounds examined, the decrease in concentrations of organically-bound tritium was relatively fast in the liver, and slow in the brain and adipose tissue.

Table 2. Relative concentration of total tritium in different tissues after ingestion of tritiated water, leucine, glucose and thymidine.

(a)Tritiated water

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	75±5*	11	1.9	0.17	0.08	0.03±0.01
Kidney	76±6	12	2.4	0.24	0.11	0.05±0.02
Testis	79±5	13	1.6	0.24	0.10	0.03±0.01
Spleen	75±4	11	2.3	0.24	0.16	0.06±0.02
Brain	74±6	10	2.0	0.39	0.23	0.12±0.03
Small intestine	75±7	11	1.9	0.27	0.12	0.04±0.01
Adipose tissue	3.7±0.7	2.0	1.8	1.5	0.90	0.68±0.09

a : Relative concentration is expressed as a percentage of the tritium administered per g of body weight and each value is the average(± SD)* of measurements for three rats.

(b)Tritiated leucine

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	133±11*	33	12	3.0	1.3	0.50±0.08
Kidney	148±15	35	12	3.3	1.5	0.72±0.07
Testis	64± 6	25	11	2.3	0.90	0.41±0.05
Spleen	92± 7	26	9.1	3.7	2.5	0.95±0.12
Brain	63± 5	28	11	4.3	2.7	1.6 ±0.3
Small intestine	ND	ND	ND	ND	ND	ND
Adipose tissue	6.8±1.1	5.0	3.7	3.2	2.8	1.9 ±0.4

a : Relative concentration is expressed as a percentage of the tritium administered per g of body weight and each value is the average(± SD)* of measurements for three rats.
ND : not determined

(C)Tritiated glucose

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	77±5*	16	2.9	0.86	0.57	0.14±0.03
Kidney	85±6	12	1.7	0.46	0.34	0.10±0.02
Testis	98±6	12	2.4	0.71	0.26	0.09±0.02
Spleen	87±5	11	1.7	0.80	0.54	0.16±0.05
Brain	77±7	12	3.2	2.3	1.2	0.60±0.12
Small intestine	ND	ND	ND	ND	ND	ND
Adipose tissue	12±3	13	12	7.5	8.4	3.7 ±0.5

a : Relative concentration is expressed as a percentage of the tritium administered per g of body weight and each value is the average(± SD)* of measurements for three rats.
ND : not determined

(d)Tritiated thymidine

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	85±7*	24	5.3	1.3	0.60	0.21±0.06
Kidney	83±6	25	6.0	1.3	0.64	0.26±0.05
Testis	89±7	20	6.4	1.3	0.51	0.16±0.03
Spleen	92±7	25	6.2	2.6	1.2	0.58±0.10
Brain	71±6	13	5.0	1.3	0.66	0.34±0.08
Small intestine	96±8	19	4.5	1.7	0.80	0.38±0.07
Adipose tissue	6.0±1.5	3.5	3.7	2.4	2.0	1.3 ±0.4

a : Relative concentration is expressed as a percentage of the tritium administered per g of body weight and each value is the average(± SD)* of measurements for three rats.

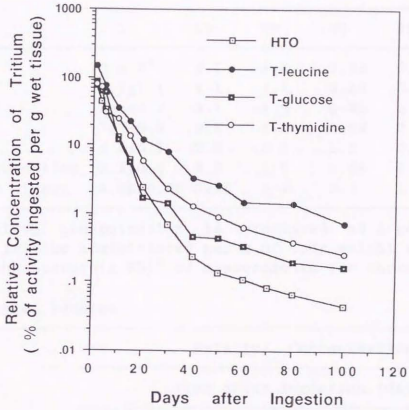

Fig. 4. Retention curves of total tritium in kidney after ingestion of various tritiated compounds. Each point represents the average of measurements for two or three animals.

Table 3. Relative concentration of organically-bound tritium in different tissues after ingestion of tritiated water, leucine, glucose and thymidine.

(a)Tritiated water

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	10 ± 2*	4.5	1.6	0.35	0.13	0.05±0.01
Kidney	6.7±1.1	4.1	1.8	0.56	0.27	0.10±0.02
Testis	5.5±0.7	4.1	1.8	0.80	0.31	0.11±0.02
Spleen	7.3±0.9	3.8	1.6	0.69	0.50	0.20±0.04
Brain	4.8±0.5	3.0	2.1	1.2	0.72	0.44±0.09
Small intestine	8.2±0.4	3.5	1.7	0.68	0.25	0.09±0.02
Adipose tissue	0.26±0.08	0.76	1.4	0.3	1.0	0.73±0.12

a : Relative concentration is expressed as a percentage of the tritium administered per g of body weight and each value is the average(± SD)* of measurements for three rats.

(b)Tritiated leucine

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	297±31*	77	22	6.8	2.6	1.2±0.5
Kidney	381±27	107	31	12	6.7	2.4±0.4
Testis	187±15	100	41	10	4.5	2.1±0.4
Spleen	223±19	65	30	14	9.9	2.8±0.6
Brain	96± 9	72	34	16	8.5	5.1±0.4
Small intestine	ND	ND	ND	ND	ND	ND
Adipose tissue	5.3±1.1	4.5	4.9	3.1	2.8	1.9±0.3

a : Relative concentration is expressed as a percentage of the tritium administered per g of body weight and each value is the average(± SD)* of measurements for three rats.
ND : not determined

(c)Tritiated glucose

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	38±6*	23	13	2.2	1.3	0.45±0.08
Kidney	28±5	8.9	5.9	1.7	1.1	0.70±0.11
Testis	28±3	9.3	6.7	2.4	0.8	0.57±0.07
Spleen	34±4	8.5	3.8	2.0	1.5	0.80±0.09
Brain	39±3	13	10	7.5	4.8	2.4 ±0.3
Small intestine	ND	ND	ND	ND	ND	ND
Adipose tissue	8.6±1.5	14	15	8.2	8.9	5.9 ±0.7

a : Relative concentration is expressed as a percentage of the tritium administered per g of body weight and each value is the average(± SD)* of measurements for three rats.
ND : not determined

(d)Tritiated thymidine

Tissue	Relative Concentration[a]					
	Time after ingestion (days)					
	1	10	20	40	60	100
Liver	29± 4*	8.3	3.3	2.6	1.6	0.55±0.08
Kidney	16± 3	9.0	3.6	3.3	2.3	0.85±0.11
Testis	14± 3	14	6.7	5.3	1.7	0.87±0.09
Spleen	81± 7	17	7.3	6.3	3.1	2.1 ±0.3
Brain	6.4±1.2	7.1	3.6	3.8	1.9	1.2 ±0.3
Small intestine	102±12	9.1	4.9	3.7	2.3	1.2 ±0.4
Adipose tissue	2.5±0.7	3.3	3.6	3.2	2.0	1.7 ±0.4

a : Relative concentration is expressed as a percentage of the tritium administered per g body weight and each value is the average(± SD)* of determinations for three rats.

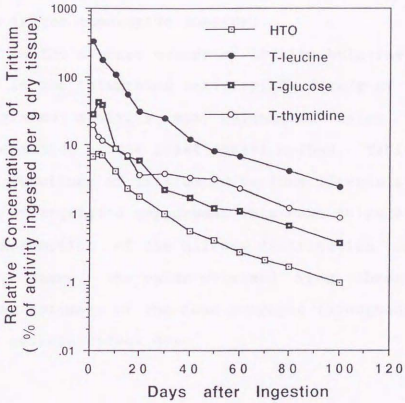

Fig. 5. Retention curves of organically-bound tritium in kidney after ingestion of various tritiated compounds. Each point represents the average of measurements for two or three animals.

Dose estimation

From the metabolic data obtained in the experiments, the cumulative radiation doses were estimated for individual tissues after a single ingestion of tritiated compounds. The cumulative dose was calculated using the following formula;

$D = (51.2/3700)*E*I$

where D is the cumulative dose(Gy)

E is the average energy of tritium beta-ray(0.0057 Mev)

I is the integrated activity(kBq-days/g of tissue weight)

The integrated activity was calculated using the retention function obtained by the least square method. Table 4 shows the retention functions of tritium in various tissues after a single ingestion of tritiated compounds. This dose calculation is based on the assumption of the uniform distribution of tritium in a tissue. Hence, the value obtained from these calculations provides an estimate of the dose averaged throughout the tissue, namely an average tissue dose.

Table 4. Retention function of tritium in various tissues after a single ingestion of tritiated water or tritiated organic compounds.

Tritiated compound	Tissue	Retention function[a]
Tritiated water	Liver	$C(t)^{b} = 0.819e^{-0.213t} + 0.0079e^{-0.035t}$
	Kidney	$C(t) = 0.805e^{-0.194t} + 0.0044e^{-0.024t}$
	Testis	$C(t) = 0.873e^{-0.203t} + 0.0092e^{-0.034t}$
	Spleen	$C(t) = 0.860e^{-0.218t} + 0.0074e^{-0.025t}$
	Brain	$C(t) = 0.846e^{-0.220t} + 0.0077e^{-0.018t}$
Tritiated leucine	Liver	$C(t) = 1.412e^{-0.148t} + 0.0775e^{-0.027t}$
	Kidney	$C(t) = 1.569e^{-0.153t} + 0.0803e^{-0.024t}$
	Testis	$C(t) = 0.706e^{-0.113t} + 0.0322e^{-0.020t}$
	Spleen	$C(t) = 1.052e^{-0.178t} + 0.0989e^{-0.022t}$
	Brain	$C(t) = 0.656e^{-0.111t} + 0.0720e^{-0.015t}$
Tritiated glucose	Liver	$C(t) = 0.992e^{-0.222t} + 0.0289e^{-0.030t}$
	Kidney	$C(t) = 1.118e^{-0.220t} + 0.0157e^{-0.027t}$
	Testis	$C(t) = 1.262e^{-0.251t} + 0.0280e^{-0.087t}$
	Spleen	$C(t) = 1.334e^{-0.269t} + 0.0241e^{-0.027t}$
	Brain	$C(t) = 0.981e^{-0.248t} + 0.0451e^{-0.022t}$
Tritiated thymidine	Liver	$C(t) = 0.958e^{-0.150t} + 0.0300e^{-0.026t}$
	Kidney	$C(t) = 0.881e^{-0.149t} + 0.0291e^{-0.025t}$
	Testis	$C(t) = 1.044e^{-0.159t} + 0.0489e^{-0.036t}$
	Spleen	$C(t) = 0.909e^{-0.150t} + 0.0592e^{-0.024t}$
	Brain	$C(t) = 0.671e^{-0.146t} + 0.0260e^{-0.021t}$

a : The retention function was obtained assuming that radioactivity ingested is 1 kBq/g of body weight.

b : C(t) represents tritium concentration(kBq/g of tissue weight) at t-th day after ingestion.

Table 5 shows the cumulative doses in mGy received by various tissues following the administration of tritiated water of 222 kBq/g of body weight. The average dose delivered by tritiated water was uniform throughout most of the tissues studied. An exceptionally low dose was observed in adipose tissue. The dose contribution from the organically-bound tritium never exceeded 10 % of total dose in any tissues, with the exception of adipose tissue. However, the contribution was somewhat greater than was expected from the amount of tritium incorporated into the tissue constituents(carbohydrate, protein, fat...) initially.

Table 6 shows the cumulative doses on the 100th day after the administration of tritiated organic compounds and tritiated water. In this Table, the doses(mGy) were calculated assuming that the same amount of radioactivity(37 kBq/g of body weight) was ingested for all the tritiated compounds. This enabled us to compare the doses to each other. The doses due to the administration of tritiated organic compounds differed somewhat between the tissues and were usually higher than those in the case of tritiated water.

Tritiated leucine gave the highest dose which was 1.6 to 3.3 times higher than the dose due to tritiated water. The next highest value was observed in animals exposed to tritiated thymidine. The cumulative doses from tritiated thymidine were 1.4 to 2.0 times higher than those from tritiated water. In the case of tritiated glucose, the doses were not significantly different from those for tritiated water. The extent of difference in the doses ranged only from 1.2 to 1.4. However, as for the adipose tissue, the dose was about 9 times higher than that due to

tritiated water.

The dose contributions from organically-bound tritium to the total dose are given for each tissue in parentheses in Table 6. It was found that the dose contribution from organically-bound tritium after exposure to tritiated organic compounds was larger than after the exposure to tritiated water. In the case of tritiated leucine ingestion, more than 50% of the total dose in all tissues was delivered by organically-bound tritium.

Table 5. Cumulative doses to various tissues of rats on the 100th day after the ingestion of tritiated water.

Tissue	Cumulative doses[a] (mGy)	Dose contribution from organically-bound tritium (%)
Liver	70	9.3
Kidney	74	6.9
Testis	76	4.2
Spleen	70	8.1
Lung	68	6.3
Heart	69	7.2
Small intestine	70	7.1
Muscle	71	8.0
Brain	72	8.5
Adipose tissue	20	64.0

a : Doses from ingestion of 222 kBq/g of body weight

Table 6. Cumulative doses to individual tissues of rats on the 100th day after the ingestion of tritiated water and tritiated organic compounds.

Tissue	Cumulative dose[a] (mGy)			
	Tritiated water	Tritiated leucine	Tritiated glucose	Tritiated thymidine
Liver	12(9.3%)[b]	36(72%)	15(29%)	21(17%)
Kidney	12(6.9%)	39(75%)	15(26%)	20(17%)
Testis	13(4.2%)	21(58%)	17(14%)	24(10%)
Spleen	12(8.1%)	29(79%)	14(24%)	24(28%)
Brain	12(8.5%)	28(64%)	17(36%)	17(15%)
Small intestine	12(7.1%)	—	—	20(26%)
Adipose tissue	3(64%)	10(88%)	26(90%)	8(79%)

a : The dose was calculated assuming that tritium of 37 kBq per g of body weight was ingested.

b : Values in parentheses are percentage contributions from organically-bound tritium.

2. Biokinetics and dose estimation in rats after a continuous ingestion of tritiated compounds and tritiated crops

Biokinetics of tritiated compounds

Fig. 6 shows the variation in the concentration of tritium in urine collected daily during continuous ingestion of various tritiated compounds; the concentration is expressed as percentage of the concentration of tritium in drinking water. The concentration rapidly increased up to about the 10th day after the start of continuous ingestion; thereafter, the concentration increased more slowly and resulted in an almost constant value. The value was different between the tritiated compounds investigated. The highest value was observed in the urine of rats exposed to tritiated water.

Table 7 shows the cumulative amount of tritium excreted in urine and feces during the continuous ingestion of various tritiated compounds for 22 days. The amount of tritium excreted in urine was 41 % of the tritium ingested by the rats when exposed to tritiated water. For the rats exposed to tritiated organic compounds, it ranged from 12 % to 21 %. The amount of tritium excreted in feces was 1.5-2.7 times larger in the rats exposed to tritiated organic compounds than the rats exposed to tritiated water. The largest fecal excretion of tritium was found in the case of tritiated carbohydrate([^{3}H]glucose and [^{3}H]glucosamine). As shown in Table 7, when the rats were exposed to tritiated organic compounds, 41-65 % of the tritium excreted in feces was present in organic form, namely OBT. The

amount of tritium excreted in both the urine and feces of the rats given tritiated water totaled 51% of the administered tritium, while the amount for the rats exposed to tritiated organic compounds ranged between 34 to 44%.

The concentrations of total tritium in wet tissues and OBT in dry tissues of rats at the end of chronic exposure are shown in Tables 8 and 9, respectively. The results were expressed in relative concentration, defined as a percentage of tritium activity ingested per gram of wet or dry tissue during the chronic exposure. It was found that total tritium was almost uniformly distributed between the tissues for all tritiated compounds, but the concentrations of total tritium in the individual tissues were somewhat different between the ingested chemical forms. Higher concentrations were observed in all the tissues of rats exposed to [^{3}H]lysine, [^{3}H]thymidine and [^{3}H]uridine. Lower concentrations were found in the majority of tissues after the exposure to [^{3}H]glucose and [^{3}H]glucosamine. The difference between highest concentration and lowest concentration in particular tissue was within a factor of 3. The concentration of total tritium in the majority of the tissues of the rats exposed to [^{3}H]leucine was not significantly different from that in the rats exposed to tritiated water. The concentrations for individual tissues after the exposure to tritiated water and [^{3}H]leucine were within the range of values that were measured after the exposure to other tritiated compounds.

The concentration of OBT in individual tissues differed remarkably according to the chemical forms of ingested tritium.

The concentration after the exposure to tritiated organic compounds was significantly and consistently higher than that after the exposure to tritiated water. Highest OBT concentration was found in the tissues of rats exposed to [^{3}H]lysine, which was 4.1-9.0 times higher than that after the exposure of tritiated water. As can be seen in Table 9, the concentrations of OBT were different from tissue to tissue in the rats which were exposed to each tritiated compound, and the distribution pattern of OBT between tissues was related to the chemical form of the ingested tritium. Some similarities in the distribution pattern were also observed; for example, the concentration of OBT after exposure to all the tritiated compounds investigated was relatively high in the liver and low in the brain.

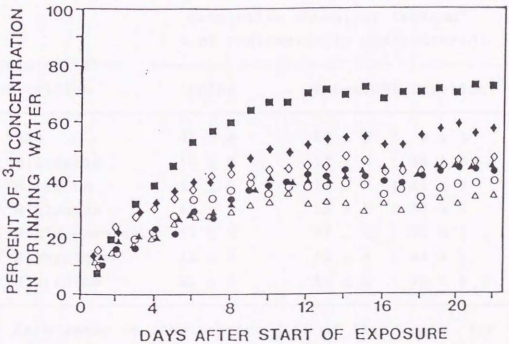

Fig. 6. Tritium concentration in urine of rats, expressed as percentage of tritium in drinking water, during chronic exposure to various tritiated compounds: ^{3}HHO(■), [^{3}H]leucine(○), [^{3}H]lysine(●), [^{3}H]glucose(△), [^{3}H]glucosamine(▲), [^{3}H]thymidine(◇), [^{3}H]uridine(◆).

Table 7. Cumulative amount of tritium excreted in urine and feces of rats during 22 days' chronic exposure to various tritiated compounds.

Chemical form of tritium	Cumulative amount of tritium[a] (% of radioactivity administered)	
	Urine	Feces(OBT fraction)[b]
^{3}HHO	41 ± 4	10 ± 3 (9 %)
[^{3}H]leucine	18 ± 3	17 ± 4 (48 %)
[^{3}H]lysine	19 ± 3	17 ± 3 (41 %)
[^{3}H]glucose	12 ± 2	25 ± 4 (63 %)
[^{3}H]glucosamine	17 ± 4	27 ± 4 (65 %)
[^{3}H]thymidine	19 ± 3	15 ± 3 (44 %)
[^{3}H]uridine	21 ± 3	16 ± 2 (59 %)

a : Each value is the average ± SD of five rats for ^{3}HHO, [^{3}H]leucine, [^{3}H]glucose and [^{3}H]thymidine and three rats for other tritiated compounds.

b : Values in parentheses show the OBT fraction, expressed as a percentage of total tritium activity excreted in feces.

Table 8. Relative concentration of total tritium in wet tissue of rats at the end of chronic exposure to various tritiated compounds for 22 days.

Tissue	Relative concentration (percentage of activity administered per g of wet tissue)[a]						
	^{3}HHO	[^{3}H] Leucine	[^{3}H] Lysine	[^{3}H] Glucose	[^{3}H] Glucosamine	[^{3}H] Thymidine	[^{3}H] Uridine
Liver	14.4±1.3	17.7±1.5	29.7±2.5$	14.0±1.3	10.2±1.3#	23.3±1.8$	29.4±3.1$
Kidney	15.6±1.5	17.4±1.7	28.7±2.0$	13.7±1.1#	9.8±0.9#	24.5±1.2$	26.7±2.8$
Testis	15.4±2.1	14.5±1.5	24.8±3.1$	12.0±1.3#	9.6±0.8#	26.0±2.1$	28.4±4.1$
Spleen	14.5±1.2	14.8±1.1	25.2±2.5$	11.3±1.5#	10.3±0.5#	23.8±2.6$	25.4±2.8$
Lung	13.7±0.9	14.2±1.3	24.7±1.5$	11.6±1.6#	7.9±0.7#	24.8±3.1$	19.8±2.1$
Heart	13.5±1.3	16.8±2.0$	27.0±1.9$	13.0±2.0	8.6±1.2#	23.3±1.5$	22.8±2.3$
Small intestine	13.2±2.2	14.0±2.1	26.0±3.0$	12.1±1.2	11.0±1.6	25.0±1.6$	24.9±2.9$
Muscle	15.7±2.1	15.6±1.6	25.3±2.6$	10.6±0.8#	7.5±0.9#	23.5±1.1$	22.2±1.9$
Brain	15.6±1.7	13.7±1.3	22.5±2.6$	9.9±1.5#	9.9±1.6#	23.7±2.6$	20.4±2.1$

a : Each value is the average±SD of five rats for ^{3}HHO, [^{3}H]leucine, [^{3}H]glucose and [^{3}H]thymidine and three rats for other tritiated compounds.

$: Significantly higher than the values in the corresponding tissues of rats exposed to ^{3}HHO by Student's t-test at $p < 0.05$.

: Significantly lower than the values in the corresponding tissues of rats exposed to ^{3}HHO by Student's t-test at $p < 0.05$.

Table 9. Relative concentration of OBT in dry tissue of rats at the end of chronic exposure to various tritiated compounds for 22 days.

Tissue	Relative concentration (percentage of activity administered per g of dry tissue)[a]						
	^{3}HHO	[^{3}H] Leucine	[^{3}H] Lysine	[^{3}H] Glucose	[^{3}H] Glucosamine	[^{3}H] Thymidine	[^{3}H] Uridine
Liver	5.5±1.0	31.2±3.2	41.5±3.5	15.3±2.5	10.2±2.5	17.5±1.8	29.2±3.8
Kidney	4.8±0.8	25.5±2.8	35.3±3.2	13.2±1.7	9.6±1.2	13.3±1.6	21.4±2.5
Testis	4.5±0.9	26.8±4.1	28.9±2.9	11.5±1.6	7.0±0.5	12.5±1.8	14.3±1.7
Spleen	3.9±0.7	19.5±2.3	30.8±2.5	11.4±1.5	7.5±0.9	8.4±1.4	20.8±2.3
Lung	4.3±1.1	26.3±3.2	30.5±3.4	11.4±1.8	7.3±0.8	8.7±0.6	16.7±1.8
Heart	3.6±0.7	31.1±3.5	32.3±2.6	11.3±1.3	5.5±0.5	9.0±0.5	14.6±1.3
Small intestine	4.4±0.8	17.6±3.2	23.6±2.1$	11.5±2.2	8.9±0.9	19.6±2.5	23.1±3.5
Muscle	3.2±0.8	20.3±2.5	26.5±3.8	7.3±0.6	5.7±0.6	6.8±0.3	7.7±0.9
Brain	3.4±0.5	16.9±1.9	14.3±1.6	8.4±0.9	5.2±0.5	7.3±0.7	7.5±0.8

a: Each value is the average±SD of five rats for ^{3}HHO, [^{3}H]leucine, [^{3}H]glucose and [^{3}H]thymidine and three rats for other tritiated compounds. All values for tritiated organic compounds were significantly higher than those in the corresponding tissues for ^{3}HHO by Student's t-test at $p < 0.01$.

Biokinetics of tritiated crops

Fig. 7 shows the variation in the concentration of tritium in the urine and feces of rats during continuous ingestion of three kinds of tritiated crops, together with that for tritiated water. The concentration was expressed as a percentage of the concentration of tritium in the daily ingested drinking water or food. In rats exposed to tritiated water, the tritium concentration in both urine and feces increased gradually until the 10th day of the exposure and thereafter reached an equilibrium. Throughout the period of the exposure, the level of tritium concentration in urine was higher than that in feces. In tritiated rice and tritiated wheat, the concentration of tritium in both urine and feces slowly increased at almost the same rate for both, until the end of continuous ingestion for 22 days. A difference was observed in the rats exposed to the tritiated soybean; the concentration in feces was at a consistently higher level than that in urine, right from the beginning of the exposure.

The cumulative amount of tritium excreted in urine and feces during the continuous ingestion of tritiated water or the tritiated crops is shown in Table 10. As compared with the tritiated water ingestion, the tritiated crop ingestion resulted in lesser urinary excretion and larger fecal excretion of tritium. The amount of tritium excreted in both urine and feces in rats exposed to three kinds of tritiated crops was 44 % of the total ingested activity, which was smaller than that in rats exposed to tritiated water(51%). It was also found that a

greater part of tritium activity in the feces of rats exposed to tritiated crops was in OBT.

Tables 11 and 12 show the relative concentrations of total tritium and OBT in the tissues of rats at the end of continuous ingestion, expressed as a percentage of tritium activity given per gram of wet or dry tissue during the chronic exposure. The concentration of total tritium in the tissues of rats exposed to tritiated crops was about 2 to 3 times higher than that in rats exposed to tritiated water. Significantly high concentration of total tritium was observed in the adipose tissue of rats exposed to tritiated soybean.

When the concentration of OBT was compared, a clear difference was observed between the rats administered tritiated water and the rats administered tritiated crops. Some difference was also observed between the rats administered the three different tritiated crops. The OBT concentrations in the tissues after continuous ingestion of tritiated rice, tritiated wheat and tritiated soybean were, respectively, about 5-8, 6-11 and 10-25 times higher than the OBT concentrations in the tissues of rats exposed to tritiated water.

In the rats exposed to the tritiated crops, the concentrations of OBT were different from tissue to tissue. A difference in the distribution pattern was observed between the tissues of rats administered the three different kinds of tritiated crops. A relatively high concentration was found in the liver, kidney and small intestine, and low concentration in the muscle and brain.

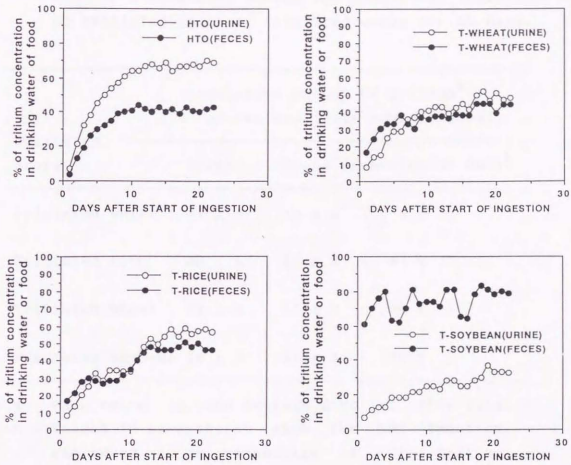

Fig. 7. Variations in the concentrations of tritium in the urine and feces of rats, expressed as a percentage of tritium concentration in drinking water or food, during chronic exposure to tritiated water or tritiated crops.

Table 10. Cumulative amount of tritium excreted in urine and feces from rats during the continuous ingestion of tritiated water or tritiated crops for 22 days.

Tritiated crops	Cumulative amount of tritium[a] (% of radioactivity administered)		
	Urine	Feces	(Fraction of OBT)[b]
Tritiated water	41 ± 4	10 ± 2	(9 %)
Tritiated rice	29 ± 5	15 ± 3	(43 %)
Tritiated wheat	27 ± 4	17 ± 2	(50 %)
Tritiated soybean	16 ± 3	28 ± 4	(90 %)

a : Each value is the average ± SD of five rats.

b : Values in parentheses show the OBT fraction, expressed as a percentage of total tritium activity excreted in feces.

Table 11. Relative concentrations of total tritium in wet tissues from rats after the continuous ingestion of tritiated water or tritiated crops for 22 days.

Rat tissue	Relative concentration of total tritium[a]			
	^{3}H-water	^{3}H-rice	^{3}H-wheat	^{3}H-soybean
Liver	14.4±1.3	35.2±3.5	48.1±3.1	45.5±3.2
Kidney	15.6±1.5	32.5±3.7	41.6±3.2	36.3±4.4
Testes	15.4±2.1	31.3±2.8	38.7±4.3	30.6±3.8
Spleen	14.5±1.2	30.5±2.5	33.2±3.7	34.5±3.2
Lung	13.7±0.9	27.2±2.6	35.1±4.3	31.6±4.4
Heart	13.5±1.3	26.1±2.4	35.8±2.3	33.9±3.7
Small intestine	13.2±2.2	30.5±2.6	33.5±3.8	37.5±3.3
Muscle	15.7±2.1	29.5±3.5	31.3±3.4	27.7±2.9
Brain	15.6±1.7	28.2±2.2	35.2±3.4	26.2±2.5
Adipose tissue	6.8±1.0	35.6±2.1	33.6±4.1	118.1±11

a : The average ± SD determination of the relative concentration of total tritium for five animals is expressed as a percentage of the tritium administered for 22 days, per g of wet tissue.

Table 12. Relative concentrations of OBT in dry tissues from rats after the continuous ingestion of tritiated water or tritiated crops for 22 adys.

Rat tissue	Relative concentration of OBT[a]			
	^{3}H-water	^{3}H-rice	^{3}H-wheat	^{3}H-soybean
Liver	5.5±1.0	34.5±3.3	61.4±6.1	84.2±4.9
Kidney	4.8±0.8	33.1±2.5	40.5±4.3	64.3±3.6
Testes	4.5±0.9	31.0±2.6	27.2±4.3	59.1±4.5
Spleen	3.9±0.7	27.1±2.3	33.3±3.7	58.3±3.8
Lung	4.3±1.1	22.4±2.5	36.4±3.6	65.6±3.4
Heart	3.6±0.7	26.3±2.0	35.8±4.5	60.8±2.9
Small intestine	4.4±0.8	34.6±3.6	37.5±5.2	66.4±3.1
Muscle	3.2±0.8	21.7±2.7	23.3±3.5	35.1±3.7
Brain	3.4±0.5	21.4±3.5	19.4±2.8	32.6±3.6
Adipose tissue	4.2±0.8	33.3±3.7	29.2±3.9	108.7±9.8

a : The average ± SD determination of the relative concentration of OBT for five animals is expressed as a percentage of the tritium administered for 22 days, per g of dry tissue.

Dose estimation

The radiation dose rates from the total tritium and from the OBT at the end of chronic exposure were calculated using the following formula;

$D = (51.2/3700)*E*A$,

where D is the dose rate(Gy/day)

E is the average energy of tritium beta-ray(0.0057 MeV)

A is the tritium concentration(kBq/g)

The contribution of the OBT to the total dose rate was calculated using the values of water content determined for individual tissues of rats in our study(Takeda and Kasida 1979). The dose rates from the total tritium and the OBT contribution on the 22nd day of chronic exposure to tritiated water or various tritiated organic compounds are presented in Table 13. As compared with the dose rate from tritiated water, the dose rates from [^{3}H]lysine, [^{3}H]thymidine and [^{3}H]uridine were a little higher, whereas those from [^{3}H]glucose and [^{3}H]glucosamine were a little lower. The difference between the dose rates from tritiated water and those from tritiated organic compounds was within a factor of 2. It was also shown that OBT contribution to the total dose rate was different from one tritiated compound to another and from tissue to tissue. The OBT contribution in the rats exposed to tritiated water ranged from 4.3 % in the testis to 11.9 % in the liver. The values of OBT contribution in the rats exposed to tritiated organic compounds examined were higher than those for tritiated water. The highest values were found in the case of the exposure to [^{3}H]leucine, which ranged from 27.0 % in testis to 54.4 % in

liver.

Table 14 shows the radiation dose rate and OBT contribution to the total dose rate on the 22nd day of the chronic exposure to tritiated crops, as well as from the exposure to tritiated water. The dose rates were generally higher in the rats exposed to tritiated crops than in the rats exposed to tritiated water. As for the doses in the specific tissues, a comparison was made between the exposure due to the administration of tritiated crops and that of tritiated water. When indicated in a ratio of the dose due to the administration of specific tritiated crop to that due to the administration of tritiated water, the range was 1.8 to 2.4 for tritiated rice, 2.0 to 3.3 for tritiated wheat and 1.7 to 3.0 for tritiated soybean, respectively. The ratio in adipose tissue was relatively high because of the relatively low dose rate due to tritiated water.

The data in Table 14 also shows that the OBT contributions to the total dose rates in the tissues of rats exposed to tritiated crops were generally higher than those in rats exposed to tritiated water. The highest OBT contribution was observed in the tissues of rats exposed to tritiated soybean, which ranged from 29 % in the testes to 58 % in the liver. An exceptionally high OBT contribution was found in the adipose tissue of rats exposed to both tritiated water and tritiated crops, because of the low water content in this tissue.

Table 13. Radiation dose rate and OBT contribution to the total dose rates on the 22nd day of chronic exposure to various tritiated compounds.

Tissue	Dose rate (mGy/day)[a] and OBT contribution[b]						
	^{3}HHO	[^{3}H] Leucine	[^{3}H] Lysine	[^{3}H] Glucose	[^{3}H] Glucosamine	[^{3}H] Thymidine	[^{3}H] uridine
Liver	0.43(11.9)	0.52(54.4)	0.87(42.8)	0.41(33.6)	0.30(31.0)	0.68(23.3)	0.86(30.7)
Kidney	0.45 (8.3)	0.51(38.8)	0.84(32.9)	0.40(26.3)	0.29(26.8)	0.72(14.3)	0.78(21.3)
Testis	0.45 (4.3)	0.42(27.0)	0.72(17.0)	0.35(14.2)	0.28(11.1)	0.76(7.2)	0.83(7.4)
Spleen	0.43 (7.0)	0.43(33.3)	0.74(31.0)	0.33(26.5)	0.30(18.9)	0.70(20.1)	0.74(20.5)
Lung	0.41 (7.5)	0.42(43.9)	0.72(29.1)	0.34(23.3)	0.23(22.1)	0.72(8.4)	0.58(19.4)
Heart	0.39 (7.2)	0.49(49.7)	0.79(32.0)	0.38(23.8)	0.25(17.1)	0.68(10.4)	0.67(16.5)
S.intestine	0.39 (9.3)	0.41(34.0)	0.76(24.8)	0.35(26.7)	0.32(22.7)	0.73(22.0)	0.73(25.9)
Muscle	0.46 (5.7)	0.46(36.0)	0.75(28.6)	0.31(18.9)	0.23(23.4)	0.69(8.2)	0.65(9.7)
Brain	0.45 (5.3)	0.40(29.3)	0.66(15.5)	0.29(21.1)	0.26(14.4)	0.69(7.6)	0.60(9.3)

a : The dose rates were calculated assuming tritium exposure to be 37 KBq/g of body weight.

b : The OBT contribution shown in parentheses is expressed as a percentage of total dose rate.

Table 14. Radiation dose rate and OBT contribution to the total dose rate on the 22nd day of chronic exposure to tritiated water or three different kinds of tritiated crops.

Rat tissue	Dose rate(mGy/day)[a] and OBT contribution[b]			
	^{3}H-water	^{3}H-rice	^{3}H-wheat	^{3}H-soybean
Liver	0.43(11.9)	1.02(31)	1.40(39)	1.31(58)
Kidney	0.45(8.3)	0.93(26)	1.20(26)	1.05(48)
Testes	0.45(4.3)	0.90(15)	1.11(11)	0.88(29)
Spleen	0.43(7.0)	0.88(24)	0.96(26)	0.99(45)
Lung	0.41(7.5)	0.79(19)	1.02(25)	0.90(50)
Heart	0.39(7.2)	0.76(27)	1.02(27)	0.96(49)
Small Intestine	0.39(9.3)	0.88(31)	0.97(31)	1.08(49)
Muscle	0.46(5.7)	0.85(19)	0.90(21)	0.79(39)
Brain	0.45(5.3)	0.82(19)	1.02(14)	0.76(31)
Adipose tissue	0.20(52.5)	1.02(78)	0.96(75)	3.45(78)

a: The dose rate was calculated on the assumption that tritium exposure was 37 KBq/g of body weight.

b: The OBT contribution shown in parentheses is expressed as a percentage of the total dose rate.

DISCUSSION

In the present study, the metabolic behavior of tritiated compounds and tritiated crops in rats was investigated and the radiation dose to the rat tissues was estimated so as to evaluate their relative radiotoxicity. The results elucidated that the metabolic behavior was dependent on the chemical form of tritium when it enters the body and consequently different radiation doses were delivered by individual tritiated compounds or crops.

In rats exposed to tritiated water by a single ingestion, the majority of tritium was found to be distributed almost uniformly among the tissues and excreted with a half-life of about 3.5 days in all the tissues. A fraction of the tritium in the body was, however, incorporated into the organic constituents of the tissue and retained there for a relatively long time as an organically-bound tritium(OBT). The retention pattern of OBT was different from tissue to tissue, which seemed to reflect the metabolic activity of individual tissues.

The estimation of cumulative dose in the rat tissues for 100 days after the ingestion of tritiated water revealed that the dose did not differ significantly from tissue to tissue and that the dose contribution from OBT to the total cumulative dose was within 10 % in the majority of the tissues, except for the adipose tissue. These results support the view on tritium metabolism summarized by the ICRP(1979) that was based on previous experimental data(Pinson and Langham, 1957, Snyder et al., 1968, Sanders and Reinig, 1968, Moghissi et al., 1972).

When tritium in the form of organic compounds, such as leucine, glucose and thymidine, was administered to rats, a relatively higher incorporation and a longer retention were observed when compared with the ingestion of tritiated water. Except for the adipose tissue, the cumulative doses delivered by these tritiated organic compounds were generally higher than those from tritiated water, by a factor of 1.6-3.3 for tritiated leucine, 1.2-1.4 for tritiated glucose and 1.4-2.0 for tritiated thymidine.

The radiation hazards should be proportional to the values of the cumulative doses. The ratio of the cumulative dose from tritiated organic compounds to that from tritiated water can, therefore, be used as an index to evaluate relatively the radiotoxicity of tritiated organic compounds as compared with tritiated water. However, it is not easy to evaluate the relative radiotoxicity of each tritiated organic compound because the cumulative dose delivered by each tritiated compound is different from tissue to tissue. To solve this complication, an average of cumulative doses to the various tissues was used as an indicator of the relative radiotoxicity of each tritiated organic compound.

Table 15 shows the cumulative dose averaged for all the examined tissues except for the adipose tissue and the ratio of the dose from each tritiated organic compound to that from tritiated water. It indicates that tritiated leucine, tritiated glucose and tritiated thymidine would be more hazardous than tritiated water by a factor of 2.6, 1.3 and 1.8, respectively.

Table 15. Average cumulative dose and the ratio of the dose from tritiated organic compounds to that from tritiated water.

Tritiated compounds	Average cumulative dose to the tissues except adipose tissue (mGy)	Ratio of average dose from organic tritium to that from tritiated water
Tritiated water	12	1
Tritiated leucine	31	2.6
Tritiated glucose	16	1.3
Tritiated thymidine	21	1.8

From the experiments of chronic exposure to various tritiated compounds(tritiated water, leucine, lysine, glucose, glucosamine, uridine and thymidine), the dose rates at the end of chronic exposure for 22 days were estimated. The result showed that the dose rates from tritiated organic compounds such as lysine, thymidine and uridine were relatively high, while the dose rates from two tritiated monosaccharides(glucose and glucosamine) were lower than those from tritiated water.

The estimation of dose rate delivered by chronic exposure to three kinds of tritiated crops was also performed. The result showed that the dose rates from tritiated crops were consistently higher than those from any tritiated compounds in a single

chemical form. As can be seen in Table 16, the average value of dose rates from tritiated crops were 2.0-2.5 times higher than that from tritiated water, although the ratio of the average dose rate from tritiated organic compounds to that from tritiated water was within a factor of 2.

Table 16. Average dose rate and the ratio of the dose rate from tritiated organic compounds to that from tritiated water.

Tritiated compounds	Average dose rate to the tissues except adipose tissue(mGy/day)	Ratio of average dose from tritiated crop to that from tritiated water
Tritiated water	0.43	1
Tritiated leucine	0.45	1.1
Tritiated lysine	0.76	1.8
Tritiated glucose	0.35	0.8
Tritiated glucosamine	0.27	0.6
Tritiated thymidine	0.71	1.7
Tritiated uridine	0.72	1.7
Tritiated rice	0.87	2.0
Tritiated wheat	1.07	2.5
Tritiated soybean	0.97	2.3

The ratio of average dose rate shown in Table 16 could be used as an index to evaluate the relative radiotoxicity of tritiated organic compounds or tritiated crops as compared with tritiated

water, if the dose rates were estimated under an equilibrium condition of chronic exposure in which tritium concentrations had became constant. However, there was no evidence in the present study that such an equilibrium condition was attained during the 22 days of chronic exposure.

Therefore, we carried out the supplementary experiments on rats for chronic exposure to tritiated water or tritiated wheat for about 100 days(H.Lu and H.Takeda 1992). The purpose of these experiments was to examine the time necessary to attain an equilibrium condition. It was found that the equilibrium for tritium was attained in about 3 weeks in the case of tritiated water, and in about 10 weeks in the case of tritiated wheat. It was also found that the tritium concentrations in various tissues after 10 weeks of continuous ingestion of tritiated wheat were higher by a factor of 1.5-2.0 than those at the end of the 3rd week. Therefore, the ratio of dose rate from tritiated wheat to that from tritiated water, when the equilibrium condition is completely attained, can be obtained by multipling the ratio(2.5) at the 3rd week of the continuous ingestion by the difference in attainment at the end of 10 weeks. Thus, it can be concluded that tritiated wheat may be more hazardous by a factor of 5 at maximum than tritiated water.

The result derived from these dose estimations in the present study will contribute to set an Annual Limit of Intake(ALI) for organic tritium, for which the ICRP has not made any recommendation. In addition to the organic tritium examined in this study, a large number of compounds and foods containing tritium in the organic form are, however, present in our

environment. Balonov et al. (1984) have previously reviewed numerous dosimetric and radiobiological data of the various kinds of tritiated compounds and proposed that the ALIs for organic tritium be divided into two classes according to their chemical and biological properties; namely soluble tritiated organic compounds and tritiated nucleic acid precursors. In his proposal, the ALIs for soluble tritiated organic compounds and for tritiated nucleic acid precursors were evaluated to be 2.5 and 5 times respectively smaller than that for tritiated water according to the difference in the radiation dose or radiation effect.

The ICRP also notes in Publication 30 that the ALI for ingestion of tritiated thymidine, that would be effectively incorporated into chromosomes in DNA-synthesizing cells and result in a selective irradiation to the cell nucleus, might be 10 times smaller than that for tritiated water. This value was derived from the dose estimation for stem cell nucleus in bone marrow which would be most responsible for radiation hazards according to the studies by Feinendegen and Cronkite(1977,1978). Whereas, Lambert(1973) concluded from the dose calculation for cell nucleus in his own experiments(Lambert and Clifton, 1968, Lambert, 1969) and from literature reviewed, that tritiated thymidine is no more than five times more toxic than tritiated water.

In another of our own studies(Takeda and Iwakura, 1987), we also estimated the cumulative doses to the cell nucleus of various tissues in experiments for single exposure to tritiated thymidine and tritiated water. The results indicated that the

dose to the nucleus when tritiated thymidine was administered, was greater by a factor of 2.2-4.0 than when the same amount of tritiated water was administered. This suggests that the radiotoxicity of tritiated thymidine would be not larger than five times that of tritiated water.

On the basis of these data in the present study and taking into consideration the necessity for simplicity of use in regards to radiation protection, we would like to propose a new ALI for all organic tritium, including the tritiated precursors of nucleic acid and tritiated foods. The proposed value of ALI will be smaller by a factor of 5 than that recommended for tritiated water by the ICRP.

SUMMARY

The metabolic behavior of tritium was investigated in rats singly or continuously exposed to various tritiated compounds or some tritiated crops. The radiation doses to the tissues were then estimated from the metabolic data. In the cases of the exposure by single ingestion, the cumulative doses from tritiated organic compounds were higher than those from tritiated water, by a factor of 1.2-1.4 for tritiated glucose, 1.4-2.0 for tritiated thymidine and 1.6-3.3 for tritiated leucine. The estimation of average dose rate on the 22nd day of a continuous ingestion showed that the doses from tritiated crops such as ^{3}H-rice, ^{3}H-wheat and ^{3}H-soybean were 2.0-2.5 times greater than those from tritiated water. These results indicate that organic tritium is generally more hazardous than tritiated water, suggesting that the annual limit of intake(ALI) for organic tritium should be smaller than the present ALI recommended by the ICRP.

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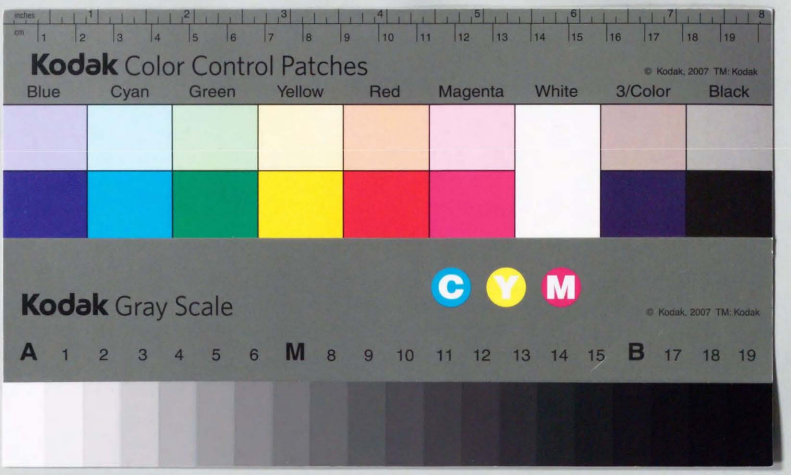
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