- 1 -

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TOXICOLOGY OF ACTINIUM EQUILIBRIUM
MIXTURE

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ABSTRACT

The acute toxicity of actinium²²⁷ equilibrium mixture was slightly less than that of americium and plutonium when administered intravenously to 150 g. rats. The thirty day LD/50 of actinium was 0.234 μ c. of α activity per gram body weight. That for americium and plutonium was 0.110 and 0.071 μ c. per gram body weight, respectively. Autoradiographic studies showed that the pattern of deposition of actinium in soft tissues was qualitatively similar to that of plutonium and americium. Detail autoradiographs confirmed the deposition of actinium in the perivascular areas of cortical bone.

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TOXICOLOGY OF ACTINIUM EQUILIBRIUM MIXTURE*

1. INTRODUCTION

A comparative study of the metabolic properties of the actinide elements has been reported by Hamilton.⁽¹⁾ He reported that actinium, americium, and curium behaved metabolically in an almost indistinguishable manner from the lanthanide rare earths. The quality of apparent metabolic identity included the phenomena of high liver uptake and accumulation of material about the small blood vessels of cortical bone. The metabolic studies showed that about 33% of actinium was deposited in the skeleton and about 50% in the liver at one and four days after administration. Under similar conditions americium showed a deposition of about 50% in the liver and 25% in the skeleton. Plutonium, when administered as plutonyl ion, showed about 10% in the liver and about 60% in the skeleton.⁽²⁾ The amounts of the actinide elements available at that time were enough to permit only minimal metabolic studies and no information was obtained on the relative toxicity of the various materials.

The relative acute and chronic toxicity of americium and plutonium was the subject of an earlier report from this laboratory.⁽³⁾ The present report consists of an acute toxicity study of actinium²²⁷ equilibrium mixture for the purpose of comparison with that of americium and plutonium.

* We are indebted to Melvin Bowman and Dwayne Vier for assistance and for supplying the actinium used in this study.

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2. METHOD

Fifteen groups of 20 Sprague-Dawley rats (150 g.) were injected intravenously (caudal vein) with actinium equilibrium mixture. The actinium was in the form of actinium chloride. The injection solution was made up by diluting the sample to the proper strength with 0.5% citric acid solution. The final pH was adjusted to 5.0 with dilute NaOH. The injected doses ranged from 3.95×10^{-1} to 1.8×10^{-2} micro-curies of alpha activity per gram of animal. The animals were housed in wire-bottom cages and given Purina Laboratory Chow and water ad libitum. The cages were checked twice daily for dead animals. The animals that died were examined to determine whether death was caused by factors not associated with the experiment.

3. RESULTS

The per cent mortality was determined as a function of dose at 30, 60, 90, 120, and 150 days after injection. These data are given in Table 1.

A probit analysis of the per cent survival versus dose for the various time intervals is shown in Fig. 1. The LD/50 dose of actinium equilibrium mixture for the various time intervals as determined from the probit analysis is given in Table 2. These data show that the time required for death of 50% of the animals varies inversely as the log of the dose (Fig. 2) in the acute lethal range, i.e., when the time of survival is short compared to the life span of the animal. The 30 day

LD/50 for plutonium and americium obtained in an earlier study⁽³⁾ are also given. These data show that the acute toxicity of actinium equilibrium mixture was less than that of plutonium and americium. The 30 day LD/50 doses of plutonium and americium injected intravenously into rats were 0.071 and 0.110 microcuries per gram body weight, respectively. The 30 day LD/50 for actinium was 0.234 microcuries per gram body weight. It was somewhat surprising to find that actinium equilibrium mixture was less toxic on an acute basis than was plutonium and americium. This may be because of the rapid excretion rate of the radium daughter, Ra²²³ (AcX).

Two animals from one of the higher dose groups were sacrificed two days after injection and some of the organs fixed and sectioned for histologic and autoradiographic studies. Figure 3 shows photomicrographs and autoradiographs of the soft tissues, kidney, liver, and spleen. Figure 4 shows photomicrographs and autoradiographs of bone specimens. A comparison of the photomicrographs with the autoradiographs showed that the deposition of actinium in these tissues closely paralleled that of plutonium and americium. A detailed description of the findings follows:

Kidney—The hematoxylin-eosin stained section showed a completely normal renal parenchyma. The survey radioautograph showed a concentration of radioactivity in the renal cortex. Highest concentration was in the convoluted tubules. The isolated round areas of high density on the autoradiograph do not represent radioactivity in glomeruli but represent areas of particularly high activity in isolated tubules.

Liver—The hematoxylin-eosin stained section showed a normal hepatic parenchyma. The radioautograph showed the highest concentration of radioactivity was in the central and midzonal areas of the triads.

Spleen—The hematoxylin-eosin stained section showed a normal splenic parenchyma. The survey radioautograph showed the highest concentration of radioactivity was in the reticuloendothelium of the red pulp with the lowest concentration in the lymphoid follicles.

Bone—Undecalcified bone sections were prepared from vertebra and tibia. Both survey and detail type autoradiographs were prepared and are shown in Fig. 4. Comparison of the photomicrographs of vertebra and tibia (Fig. 4a,c) with the corresponding survey type autoradiographs (Fig. 4b,d) confirmed the observations made by Hamilton⁽¹⁾ that the principal site of deposition of radioactivity was in the epiphyseal line and the endosteal surfaces of trabecular areas. The autoradiograph of the tibia also showed the spots in cortical bone which Hamilton associated with the vascular spaces. The detail autoradiograph of the cortex of the tibia prepared by placing the section on alpha track emulsion is shown in Fig. 4e. This picture further confirmed his observations. Figure 4f is a detail autoradiograph of the epiphyseal union in vertebrae and demonstrated the high degree of localization of the radioactivity in this structure.

4. SUMMARY

The acute toxicity of actinium²²⁷ equilibrium mixture was slightly less than that of americium and plutonium when administered intravenously

to 150 g. rats. The thirty-day LD/50 of actinium was 0.234 $\mu\text{c.}$ of α activity per gram body weight. That for americium and plutonium was 0.110 and 0.071 $\mu\text{c.}$ per gram body weight, respectively. Autoradiographic studies showed that the pattern of deposition of actinium in soft tissues was qualitatively similar to that of plutonium and americium. Detail autoradiographs confirmed the deposition of actinium in the perivascular areas of cortical bone.

5. REFERENCES

- (1) Hamilton, J. G., Rev. Modern Physics, 20, 718 (1948).
- (2) Langham, W. H. et al, J. Biol. Chem., 171, 273 (1947).
- (3) Langham, W. H., Carter, R. E., LA-1309 (1951).

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a. Photomicrograph

b. Autoradiograph x 9

KIDNEY

c. Photomicrograph

d. Autoradiograph x 17

LIVER

e. Photomicrograph

f. Autoradiograph x 9

SPLEEN

Fig. 3.--Survey Autoradiographs Showing Localization of Radioactivity in Rat Tissues Following Intravenous Injection of Actinium Equilibrium Mixture

a. Photomicrograph

VERTEBRA

b. Autoradiograph x 3

c. Photomicrograph

TIBIA

d. Autoradiograph x 3

e. Cortical bone,
Tibia (xl44)

f. Epiphyseal line,
Vertebra (xl20)

DETAILED AUTORADIOGRAPH

Fig. 4.--Survey and Detailed Autoradiographs Showing Localization of Radioactivity in Tibia and Vertebra of the Rat Following Intravenous Injection of Actinium Equilibrium Mixture

Table 1.--Mortality in Adult Rats Following Various Dosages of Actinium Equilibrium Mixture

No. Rats	µc. of α Activity per g.	30 day Survival (%)	60 day Survival (%)	90 day Survival (%)	120 day Survival (%)	150 day Survival (%)
40	(Controls)	100.0	100.0	100.0	100.0	100.0
17	39.5×10^{-2}	0.0	--	--	--	--
18	36.9×10^{-2}	0.0	--	--	--	--
18	34.2×10^{-2}	0.0	--	--	--	--
20	29.6×10^{-2}	15.0	0.0	--	--	--
20	27.1×10^{-2}	0.0	0.0	--	--	--
20	24.3×10^{-2}	25.0	0.0	--	--	--
20	21.6×10^{-2}	80.0	10.0	0.0	--	--
20	18.0×10^{-2}	95.0	40.0	0.0	--	--
20	12.0×10^{-2}	100.0	95.0	20.0	0.0	--
20	9.5×10^{-2}	100.0	90.0	50.0	5.0	5.0
20	6.1×10^{-2}	100.0	95.0	95.0	65.0	35.0
20	4.9×10^{-2}	100.0	100.0	85.0	60.0	55.0
20	3.7×10^{-2}	100.0	95.0	85.0	65.0	55.0
20	2.9×10^{-2}	100.0	100.0	95.0	75.0	60.0
20	1.8×10^{-2}	100.0	95.0	95.0	85.0	60.0

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Table 2.—LD/50 Dose of Actinium Equilibrium Mixture at Various Times after Intravenous Injection (150 g. rats)

Element	Days after Injection	LD/50 Dose, μ c. of α Activity/g. body wt.
Ac ²²⁷	30	0.234
	60	0.158
	90	0.088
	120	0.056
	150	0.042
Pu ²³⁹ *	30	0.071
Am ²⁴¹ *	30	0.110

* From LA-1309 (1951).

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