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Nuclear Medicine Technology Progress Report for Quarter Ending March 31, 1980

F. F. Knapp, Jr.

HEALTH AND SAFETY RESEARCH DIVISION
OAK RIDGE NATIONAL LABORATORY

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NUCLEAR MEDICINE TECHNOLOGY PROGRESS REPORT FOR QUARTER ENDING MARCH 31, 1980

F. F. Knapp, Jr.

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SUMMARY

Of special significance in this progress report is a description of the successful detection of experimentally produced myocardial infarctions in rats and dogs using ^{123m}Te-9-telluraheptadecanoic acid (9-[^{123m}Te]-THDA). The defects in the myocardial images corresponded well with the infarcted areas which were verified by histopathological examination of the excised hearts. Preferential localization of radioactivity in normal myocardial tissue of rats that had experimentally produced infarctions was also demonstrated by tissue distribution studies following injection of 9-[^{123m}Te]-THDA. The effects of chain length on the myocardial uptake of ^{75}Se-labeled long-chain fatty acids has also been studied further. Selenium-75-labeled 13-selenaheneicosonic acid [H_3C-$(CH_2)_7$-^{75}Se-$(CH_2)_{11}$-COOH, 13-[^{75}Se]-SHCA] shows the highest heart uptake in rats of the agents studied ($\sim$1.5% injected dose after 30 min). These results indicate that myocardial imaging may be possible with 13-[^{75}Se]-SHCA and also suggest that potential positron emission tomography of the myocardium with the ^{73}Se-labeled agent should be explored.

In this report, the results of continuing studies with ^{11}C and ^{195m}Pt-labeled agents are described. A variety of ^{11}C-labeled amino acids were prepared and tested as pancreas and tumor localizing agents in a Medical Cooperative Program with the Oak Ridge Associated Universities. The microscale synthesis of ^{195m}Pt-labeled *cis*-dichloro-*trans*-dihydroxy-*bis*-(isopropylamine)platinum(IV) (^{195m}Pt-CHIP) has been developed further and preliminary tissue distribution studies with this important second-generation antitumor drug have been completed in rats. Platinum-195*m*-labeled *cis*-dichlorodiammineplatinum(II) (^{195m}Pt-*cis*-DDP) has been supplied for testing to a number of Medical Cooperative Programs.

Studies of arsenic trioxide (As_2O_3) toxicity for human cells in the diffusion chamber assay system have continued. Further investigation of this arsenic-induced cytotoxicity has demonstrated a linear dose-response relationship and a difference in the permanence of the growth inhibitory effect using different doses.

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SELENIUM-75 AND TELLURIUM-123*m*

F. F. Knapp, Jr. and T. A. Butler

The effects of structural modifications on the uptake of radioactivity in rat hearts after injection of various ^{75}Se-labeled fatty acids were described in the previous quarterly report (ORNL/TM-7223). The compounds investigated included the following ^{75}Se-labeled fatty acids, where the subscript indicates the chain length of the alkanoic acid analogue in which $-CH_2-$ moiety has been replaced by the selenium heteroatom: C_{13}-9-Se, C_{17}-9-Se, C_{25}-13-Se, and C_{25}-9-Se. Two additional members in this series of compounds, 13-selenanonadecanoic (C_{19}-13-Se) and 13-selenaheneicosonic acid (C_{21}-13-Se) have been prepared and tested in rats. The results of these studies are summarized in Tables 1 and 2.

A comparison of the absolute heart uptake (percent injected dose per organ) of the various ^{75}Se-labeled fatty acids is illustrated in Fig. 1. While only marginal heart uptake is exhibited with the C_{19}-13-Se agent, the C_{21}-13-Se fatty acid shows pronounced uptake, indicating that the heart uptake of ^{75}Se-labeled fatty acids in the rat is critically dependent upon chain length. The difference in heart uptake of these two agents was unexpected since they differ in chain length by only two methylene units and the Se-heteroatom is in the same position in both molecules.

Since 13-selenaheneicosonic acid has shown the greatest heart uptake of the agents studied, it will be studied in more detail. Future studies will include attempts to image normal and infarcted hearts of rats and dogs. In addition, large amounts of the unlabeled fatty acid will be prepared for acute toxicity tests in mice. An additional goal will be the preparation and testing of the ^{73}Se-labeled agent for emission computerized tomographic imaging studies.

In conjunction with Dr. H. William Strauss and his colleagues in the Nuclear Medicine Division at the Massachusetts General Hospital, the tissue distribution and imaging properties of ^{123m}Te-9-tellurahepta-decanoic acid (9-[^{123m}Te]-THDA) in experimentally infarcted rats and dogs have been investigated recently. Since earlier studies in rats had indicated that a unique feature of THDA was the prolonged retention

Table 1. Distribution of radioactivity in tissues of Fischer 344 rats following intravenous administration of ^{75}Se-13-selenanonadecanoic acid [a]

Tissue	Mean percent injected dose/gram (range)			
	Time after injection			
	5 min	30 min	1 h	6 h
Blood	0.36 (0.32-0.46)	0.35 (0.32-0.41)	0.22 (0.21-0.23)	0.22 (0.21-0.24)
Liver	5.42 (5.12-6.15)	4.76 (4.62-4.84)	4.23 (4.04-4.44)	2.21 (2.08-2.41)
Spleen	0.41 (0.33-0.48)	0.32 (0.31-0.33)	0.36 (0.33-0.43)	0.32 (0.30-0.34)
Kidneys	1.58 (1.37-1.94)	1.19 (1.12-1.23)	1.55 (1.39-1.64)	1.58 (1.54-1.61)
Heart	1.09 (0.84-1.32)	0.73 (0.64-0.83)	0.72 (0.69-0.77)	0.41 (0.35-0.48)
Lungs	0.73 (0.66-0.80)	0.87 (0.82-0.92)	0.83 (0.78-0.90)	0.79 (0.68-0.85)

[a]Three rats were used for each time period. Other tissues that were analyzed include the pancreas, large and small intestines, and brain.

Table 2. Distribution of radioactivity in tissues of Fischer 344 rats following intravenous administration of ^{75}Se-13-selenaheneicosonic acid[a]

Tissue	Mean percent injected dose/gram (range)			
	Time after injection			
	5 min	10 min	1 h	4 h
Blood	0.31 (0.28-0.36)	0.47 (0.31-0.64)	0.27 (0.17-0.39)	0.34 (0.30-0.37)
Liver	7.20 (6.73-7.69)	5.72 (5.54-5.90)	4.03 (2.48-5.10)	3.68 (3.42-3.85)
Spleen	0.96 (0.82-1.09)	0.67 (0.53-0.81)	0.56 (0.36-0.68)	0.55 (0.55-0.57)
Kidneys	1.41 (1.36-1.50)	1.31 (1.27-1.34)	1.53 (1.06-1.90)	2.22 (2.16-2.28)
Heart	3.07 (2.22-4.48)	2.90 (2.81-2.98)	1.91 (1.16-2.85)	0.96 (0.71-1.21)
Lungs	1.16 (1.10-1.20)	0.91 (0.75-1.08)	0.87 (0.65-1.13)	1.20 (1.06-1.40)

[a]Three rats were used at each time period. Other tissues that were analyzed include the pancreas, large and small intestines, and brain.

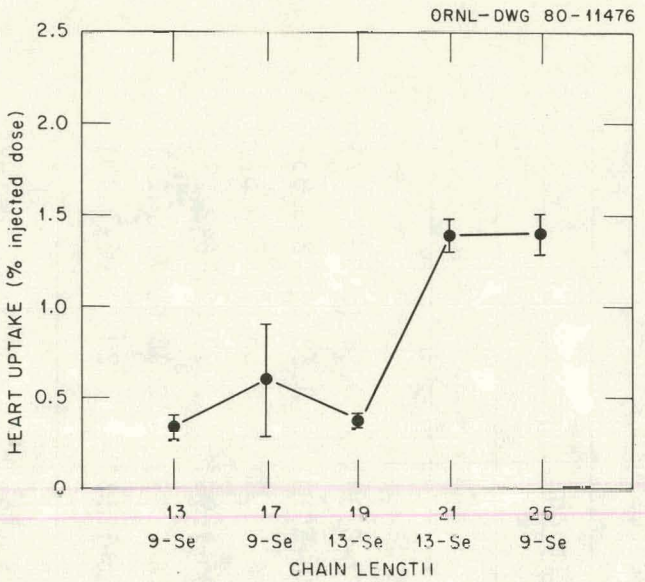

Fig. 1. The absolute heart uptake (percent injected dose) of radioactivity 30 min after intravenous injection of ^{75}Se-labeled fatty acids to female Fischer 344 rats. The mean and range values from three animals are plotted for each compound.

in the myocardium, the retention of radioactivity in the heart of a normal dog was monitored over a five-day period after intravenous administration of 9-[^{123m}Te]-THDA. The results of this study (Fig. 2) indicated that significant levels of radioactivity were also retained in the dog heart over the five-day period. In these anterior gamma camera images of the dog heart, the left ventricular myocardium is observed as a doughnut pattern in the left anterior oblique (LAO)

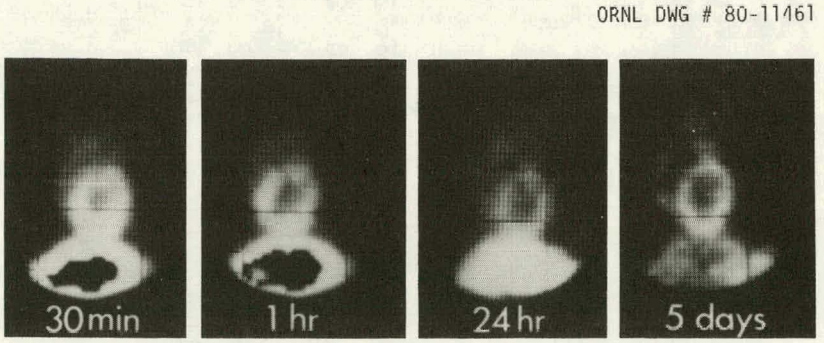

Fig. 2. Anterior gamma camera images of the thoracic region of a dog over a five-day period after intravenous administration of ^{123m}Te-9-telluraheptadecanoic acid.

projection. The right ventricular myocardium also can be observed superior to the left ventricle. The radioactive contents of the myocardium, determined by an analysis of the digital data obtained with a gamma camera, decreased 13% after 24 h and only 36% after 5 days. These data indicate a remarkably long 7.3 day half-time for radioactivity in the dog myocardium after injection of 9-[^{123m}Te]-THDA.

The distribution of radioactivity in normal and infarcted myocardial tissue from rats that had acute myocardial infarctions produced surgically by ligation of the left anterior descending coronary artery (LAD) was determined also (Table 3). Infarcted Sprague-Dawley rats were injected intravenously with 9-[^{123m}Te]-THDA and sacrificed 30 min later by injection of triphenyltetrazolium chloride (TTC). The hearts were removed and the infarcted tissue dissected from the myocardium by the difference in TTC staining. Radioactive analyses

Table 3. Distribution of radioactivity in tissues of infarcted male Sprague-Dawley rats 30 min following administration of ^{123m}Te-9-telluraheptadecanoic acid[a]

Tissue	Number of samples	Mean percent dose/gram	± Standard error
Blood	11	0.180	0.020
Lung	11	1.227	0.104
Infarcted myocardium	9	1.115	0.177
Normal myocardium	11	3.702	0.281
Liver	6	1.609	0.156
Pancreas	6	0.511	0.710
Kidney	6	1.009	0.069
Bone	6	0.134	0.017
Muscle	6	0.178	0.026
Intestines	6	0.216	0.050

[a]Eleven male Sprague-Dawley rats were used for these studies.

indicated that the normal myocardial tissue concentrated radioactivity nearly three-fold greater than the zones of infarction (Table 3).

An additional major goal of these studies was to determine the utility of detecting focal defects in animals with acute experimental myocardial infarcts using 9-[^{123m}Te]-THDA. The myocardial infarctions in Sprague-Dawley rats were produced as described above. A similar procedure was used to produce infarctions in dogs by ligation of the LAD distal to the first septal perforating artery. The 9-[^{123m}Te]-THDA was administered intravenously to the infarcted animals and images of the chest regions with a gamma camera. The infarctions produced in rats (Fig. 3) and dogs (Fig. 4) were visualized clearly after injection of 9-[^{123m}Te]-THDA. The animals were sacrificed by intravenous injection of TTC which stains the normal myocardial tissue. The infarcted tissue was readily differentiated and separated from the normal tissue by the difference in TTC staining at autopsy. In the infarct imaging studies the focal defects in the gamma camera images corresponded exactly with the presence of infarcted tissue determined at autopsy by the TTC staining method.

The prolonged retention of radioactivity in rat and dog heart tissue following administration of 9-[^{123m}Te]-THDA suggests that this agent is metabolically "trapped" in the myocardium. This observation could be of considerable importance in the development of improved myocardial imaging

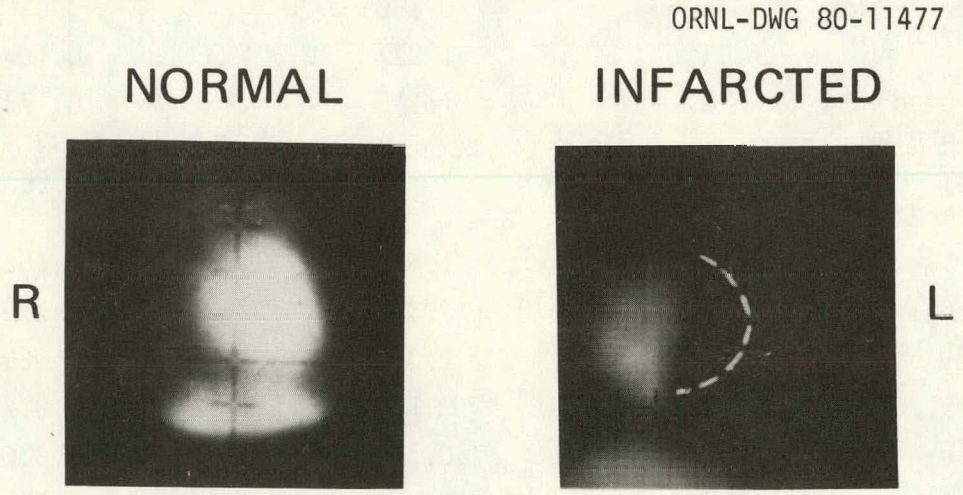

Fig. 3. Anterior gamma camera images of normal and infarcted rat hearts after intravenous administration of ^{123m}Te-9-telluraheptadecanoic acid.

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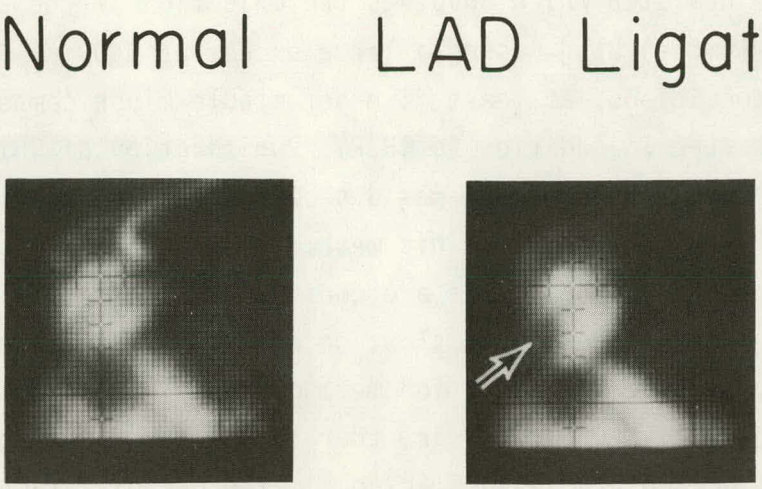

Fig. 4. Lateral gamma camera images of normal and infarcted dog hearts after intravenous administration of ^{123m}Te-9-telluraheptadecanoic acid. The arrow indicates the focal defect which represents the infarction produced by LAD ligation.

agents. If the alkyl moiety of THDA is retained in a similar manner to that observed for 9-[^{123m}Te]-THDA, incorporation of other radionuclides into this region may be a unique and effective way of retaining radioactivity in the myocardium for improved imaging studies. Studies are now in progress to determine the tissue distribution of 10-[^{14}C]-9-THDA.

PLATINUM-195*m*

J. D. Hoeschele and T. A. Butler

Studies of the synthesis of ^{195m}Pt-labeled *cis*-dichloro-*trans*-dihydroxy-*bis*-(isopropylamine)platinum(IV) (^{195m}Pt-CHIP), an important potential second-generation Pt(IV) antitumor drug, are continuing. As reported earlier (ORNL/TM-7223), ^{195m}Pt-CHIP is being investigated in conjunction with a Medical Cooperative Program recently established with the Richard Dimbleby Department of Cancer Research at the St. Thomas's Hospital School of Medicine in London, England. Improvements in the microscale synthesis and purification of ^{195m}Pt-CHIP, preliminary tissue distribution studies in the rat, and future experimental work with this agent are described below.

The microscale synthesis of CHIP (0.2 mmole scale) is well defined except for the final step which involves the oxidation of the precursor, *cis*-[Pt(isopropylamine)$_2$Cl$_2$], using a large excess of H_2O_2 at 85°. Under these reaction conditions, at least five detectable minor components are produced in this step in addition to CHIP. Purification of CHIP can be achieved by recrystallation of the residue obtained upon evaporation of the reaction mixture to dryness. This method is impractical for our purposes, however, since the yields are consistently low (<25%) and variable and the rate of crystallization is slow, necessitating an overnight recrystallization. Other purification methods, such as ion-exchange column chromatographic techniques, are therefore being investigated. Results of purification studies utilizing a mixed bed of cation and anion exchange resins indicate that only one of the six components is completely removed. Two other components are reduced in quantity by passing an aqueous solution of the crude reaction mixture through the mixed bed resins. The remaining impurities that are observed are likely to be neutral rather than ionic species since the latter would be strongly adsorbed by the resins. Approximately 10-15% of the radioactivity is retained by the resin per pass. The presence of these multiple impurities indicates that this is not a satisfactory system for purification of CHIP.

A new adsorption column chromatographic system for the purification of CHIP which employs the conditions used in the thin-layer chromatographic separation of these impurities will be examined. This system includes alumina or silica gel as the column material and acetone:ethyl acetate:0.1 *N* HCl as the elution solvent. Purity certification will be assisted by high pressure liquid chromatographic analyses. It is anticipated that the development of the microscale synthesis of CHIP will be completed during the next quarter.

Preliminary tissue distribution studies with ^{195m}Pt-labeled CHIP were performed using Fischer 344 female rats. In one study, the distribution of radioactivity was determined 24 h after both intraperitoneal and intravenous administration of ^{195m}Pt-CHIP (Table 4). A more detailed tissue distribution study was also performed at a variety of time periods from 0.25 h to 13 days after intraperitoneal injection of ^{195m}Pt-CHIP (Tables 4 and 5). The ^{195m}Pt-CHIP used for these studies was administered at a dose of 7.5 mg/kg body weight and contained three minor impurities.

Table 4. Distribution of radioactivity in tissues of Fischer 344 female rats 24 h after administration of ^{195m}Pt-*cis*-Dichloro-*trans*-Dihydroxy-*bis*-(isopropylamine)-platinum(IV), CHIP at a dose of 7.5 mg/kg[a]

Tissue	Mean percent injected dose/gram ± S.D.	
	Intraperitoneal injection	Intravenous injection
Blood	0.187 ± 0.024	0.164 ± 0.006
Liver	0.801 ± 0.091	0.591 ± 0.047
Spleen	0.297 ± 0.064	0.202 ± 0.008
Pancreas	0.308 ± 0.021	0.267 ± 0.009
Stomach	0.230 ± 0.180	0.0908 ± 0.0782
Small intestine	0.166 ± 0.032	0.102 ± 0.014
Colon	0.967 ± 0.264	0.669 ± 0.165
Adrenals	0.185 ± 0.025	0.113 ± 0.002
Kidneys	1.79 ± 0.19	1.62 ± 0.10
Genitals	0.140 ± 0.045	0.103 ± 0.031
Heart	0.109 ± 0.014	0.0985 ± 0.0021
Lungs	0.154 ± 0.016	0.136 ± 0.005
Brain	0.0068 ± 0.0010	0.0070 ± 0.0008
Skin	0.0570 ± 0.0068	0.0508 ± 0.0028

[a]Four 151-175 g rats were used in each study.

Several qualitative comparisons can be made between these data and similar data obtained after intravenous administration of ^{195m}Pt-*cis*-DDP (ORNL/TM-7223), which is the platinum antitumor agent that has been studied most extensively. The levels of radioactivity in the liver, blood, and colon (Table 4), are nearly twice the values detected after similar administration of ^{195m}Pt-*cis*-DDP. The levels of radioactivity in the reproductive organs and brain after injection of ^{195m}Pt-CHIP, however, are substantially lower than that observed after administration of ^{195m}Pt-*cis*-DDP. The levels of radioactivity detected in all other tissues are comparable for the two ^{195m}Pt-labeled agents. It is interesting to note that the levels of radioactivity in the kidneys are comparable for the

Table 5. Distribution of radioactivity in tissues of Fischer 344 female rats following intraperitoneal administration of ^{195m}Pt-*cis*-Dichloro-*trans*-Dihydroxy-*bis*-platinum(IV), CHIP, at a dose of 7.5 mg/kg[a]

	Mean percent injected dose/gram ± S.D.		
	Hours after injection		
Tissue	0.25	1.0	6.0
Blood	0.830 ± 0.016	0.325 ± 0.015	0.224 ± 0.013
Liver	1.91 ± 0.41	1.71 ± 0.19	0.922 ± 0.038
Spleen	0.474 ± 0.042	0.295 ± 0.034	0.236 ± 0.004
Pancreas	1.17 ± 0.17	0.524 ± 0.015	0.374 ± 0.024
Stomach	0.299 ± 0.050	0.199 ± 0.152	0.0953 ± 0.0176
Small intestine	0.784 ± 0.352	1.31 ± 0.28	0.299 ± 0.189
Colon	0.225 ± 0.049	0.0898 ± 0.0249	1.83 ± 0.15
Adrenals	0.999 ± 0.098	0.3765 ± 0.0674	0.169 ± 0.011
Kidneys	3.44 ± 0.54	2.31 ± 0.091	1.90 ± 0.10
Genitals	0.992 ± 0.234	0.275 ± 0.025	0.194 ± 0.013
Heart	0.334 ± 0.015	0.165 ± 0.007	0.123 ± 0.005
Lungs	0.709 ± 0.149	0.258 ± 0.012	0.184 ± 0.003
Brain	0.0225 ± 0.0037	0.0108 ± 0.0005	0.0075 ± 0.0006
Skin	0.307 ± 0.035	0.131 ± 0.048	0.0588 ± 0.0032

[a]Four 151-175 g rats were used for each time interval.

same dose of either agent, although *cis*-DDP exhibits much greater nephrotoxicity than CHIP. After 24 h, the order of tissue retention of radioactivity was found to be very similar for the two routes of administration (Table 4). The decreasing order of tissue retention (percent dose per gram) after intraperitoneal injection is as follows:

kidneys > colon > liver > pancreas > spleen > stomach > blood > adrenals > small intestine > lungs > reproductive organs > heart > skin > brain.

With the exception of the blood and lungs, the order is the same in animals that received the ^{195m}Pt-CHIP by the intravenous route. Intraperitoneal injection of ^{195m}Pt-CHIP led to a consistently higher absolute tissue retention of radioactivity than observed after intravenous administration. Although the results of intraperitoneal injection of ^{195m}Pt-CHIP over a 13-day period have not been analyzed in detail, these data demonstrate a relatively rapid loss of radioactivity from all tissues examined (Tables 5 and 6).

BIOHAZARDS FROM ENERGY TECHNOLOGIES — ARSENIC TOXICITY

K. R. Ambrose

Arsenic, a pollutant of coal conversion processes, has been investigated to determine toxic effects on human target cells in vivo. In previous reports (ORNL/TM-7072 and 7223) we described studies in which arsenic trioxide (As_2O_3) in aqueous solution caused an inhibition in the growth of human embryonic lung cells (Flow 2000) in diffusion chambers. The chambers containing the human target cells were implanted surgically in the peritoneal cavities of rats or hamsters which were then injected with either the As_2O_3 solution or water. With a comparison of the cell numbers in control chambers and arsenic-exposed chambers, a measurement of the toxicity or growth inhibition was obtained.

Similar diffusion chamber studies were performed this quarter to determine (1) the 24 h dose-response of Flow 2000 cells with acute exposure of hamsters to arsenic trioxide, and (2) the persistence of growth inhibition in the Flow 2000 cells after acute As_2O_3 exposure. As with the previous studies, six to nine chambers comprised each test or control group at each assay period, and the differences in cell population means

Table 6. Distribution of radioactivity in tissues of Fischer 344 female rats following intraperitoneal administration of ^{195m}Pt-*cis*-Dichloro-*trans*-Dihydroxy-*bis*-platinum(IV), CHIP, at a dose of 7.5 mg/kg[a]

	Mean percent injected dose/gram ± S.D.		
	Days after injection		
Tissue	3	8	13
Blood	0.139 ± 0.006	0.0970 ± 0.0016	0.110 ± 0.007
Liver	0.475 ± 0.029	0.262 ± 0.007	0.367 ± 0.015
Spleen	0.300 ± 0.009	0.379 ± 0.034	0.613 ± 0.023
Pancreas	0.234 ± 0.011	0.120 ± 0.014	0.169 ± 0.057
Stomach	0.0500 ± 0.0139	0.0178 ± 0.0076	0.0240 ± 0.0283
Small intestine	0.0535 ± 0.0084	0.0243 ± 0.0087	0.0275 ± 0.0049
Colon	0.104 ± 0.018	0.0623 ± 0.0246	0.0325 ± 0.0035
Adrenals	0.190 ± 0.023	0.104 ± 0.0181	0.180 ± 0.055
Kidneys	1.56 ± 0.07	1.234 ± 0.0335	1.43 ± 0.1195
Genitals	0.118 ± 0.034	0.0695 ± 0.0170	0.125 ± 0.021
Heart	0.0780 ± 0.0022	0.0508 ± 0.0025	0.0532 ± 0.0021
Lungs	0.101 ± 0.007	0.0613 ± 0.0043	0.0655 ± 0.0078
Brain	0.0053 ± 0.0005	0.0033 ± 0.0005	0.0040 ± 0.0000
Skin	0.0438 ± 0.0033	0.0295 ± 0.0047	0.0330 ± 0.0028

[a]Four 151-175 g rats were used for each time period.

of test and control groups were analyzed for statistical significance using the Wilcoxon nonparametric statistical test.

In the dose-response study, hamsters bearing diffusion chambers containing Flow 2000 cells were injected intraperitoneally with As_2O_3 solution at dosage levels of 2.5, 5.0, 7.5 and 10.0 mg/kg or with water equal in volume to the 10 mg/kg dosage level. Twenty-four hours after the injections, the chambers were removed and the cells harvested and counted microscopically in a hemocytometer. The mean cell counts from all the arsenic-exposed groups were significantly lower than the mean of the control cell population at the 95-99.9% confidence level. In Fig. 5 the average cell count in each treatment group is plotted logarithmically against the dosage level of As_2O_3 employed. A linear dose-response relationship exists at these selected doses. The percentage of growth inhibition induced by 5.0 mg/kg of As_2O_3 was 56%; this number is in close agreement with 52% growth inhibition observed in two previous studies (ORNL/TM-7223).

In the time study of arsenic-induced toxicity, two doses of As_2O_3 (5 and 10 mg/kg) were chosen for single injections into hamsters that had received intraperitoneal chambers 24 h previously. At 24, 48, and

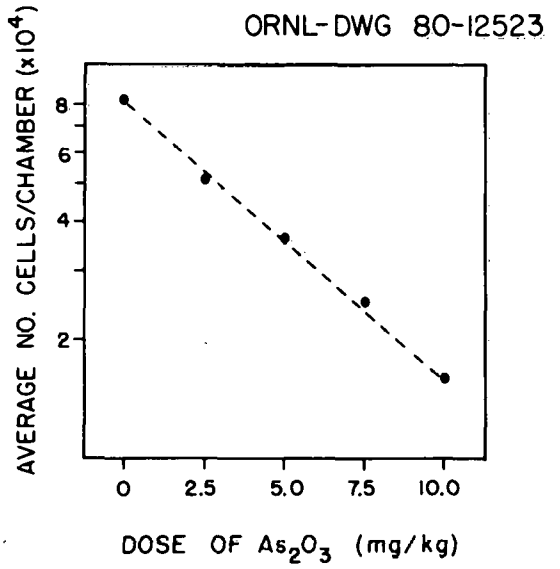

Fig. 5. The effect of As_2O_3 treatment on the proliferation of Flow 2000 cells within diffusion chambers implanted in the peritoneal cavities of hamsters.

72 h post injection, cell population numbers in test and control groups were determined using the Royco tissue cell counter (Royco Instruments, Menlo Park, Calif.). As in the previous study the "high" dose of 10 mg/kg of As_2O_3 caused no observable health effects in the injected hamsters. The target cells within the chamber, however, were inhibited in their growth by both dosage levels. The "low" dose of As_2O_3 (5 mg/kg) induced only a temporary 24-h inhibition; after 24 h the doubling time in this population resembled that observed in chambers from control animals. In the chambers of animals receiving 10 mg/kg of As_2O_3 the growth inhibitory effect was more prolonged in that these arsenic treated cells never achieved the control doubling time within the 3 days of assay. It is not possible to say whether this prolonged effect was due to an extended inhibition of cell division (cytostasis) or to death of the target cells (cytotoxicity) over the 72-h assay period. In this study the percentages of growth inhibition observed at 24 h in the 5 and 10 mg/kg As_2O_3 dosage groups were lower than those described in our previous studies, however, the change in counting techniques may be the cause of this discrepancy. With the establishment of the toxicity (growth inhibition) of arsenic for human target cells in animals receiving acute exposure to arsenic trioxide, the effect of chronic exposure (1-2 weeks) will be investigated next.

RADIONUCLIDES FOR MEDICAL COOPERATIVE PROGRAMS

F. F. Knapp, Jr., J. D. Hoeschele and T. A. Butler

Carbon-11

During the period from January 1 through March 30, 1980, a variety of ^{11}C-labeled amino acids were produced for tumor localization and pancreas imaging studies in patients at the Oak Ridge Associated Universities (ORAU). Three batches of ^{11}C-DL-tryptophan and two batches of ^{11}C-DL-valine were prepared from $^{11}CO_2$ produced in the 86-inch cyclotron and used for pancreatic tomographic visualizations studies in patients at the ORAU Medical and Health Sciences Division. In addition, five batches of ^{11}C-1-aminocyclobutanecarboxylic acid (^{11}C-ACBC) and three batches of ^{11}C-1-aminocyclopentanecarboxylic acid (^{11}C-ACPC) were synthesized for tumor localization studies.

Platinum-195*m*

Platinum-195*m*-labeled *cis*-dichlorodiammineplatinum(II), *cis*-DDP, was provided to a number of Medical Cooperative Programs including the School of Pharmacy at the University of the Southern California (Dr. W. Wolf) for continuing radiopharmacokinetic studies in animal model systems. This agent was also supplied to the University of California at Los Angeles Medical School (Dr. E. Petrilli) for tissue distribution studies in dogs following intraperitoneal injection. These studies are being conducted in anticipation of potential clinical trials employing this route of administration for the chemotherapeutic treatment of ovarian cancer. In addition, ^{195m}Pt-*cis*-DDP was supplied to the Biology Division at the Oak Ridge National Laboratory (Dr. R. Rahn) for studies directed at elucidating the nature of the Pt-DNA lesion formed in vitro by the *cis*-DDP-DNA interaction.

Selenium-75 and Tellurium-123*m*

Radiolabeled tellurium fatty acids were supplied to collaborators in the Medical Cooperative Program to continue investigations in the pre-clinical studies of potential unique myocardial-imaging agents. The Nuclear Medicine Division of Massachusetts General Hospital (Dr. H. William Strauss) was supplied ^{123m}Te-methyl-9-telluraheptadecanoate and Oak Ridge Associated Universities (Dr. R. Hayes) was supplied ^{123m}Te-9-telluraheptadecanoic acid in a solution of bovine serum albumin.

OTHER NUCLEAR MEDICINE TECHNOLOGY GROUP ACTIVITIES

Seven shipments of ^{43}K were distributed on a cost recovery basis through the Isotopes Sales Office. Four shipments were made to the University of Mississippi Medical Center and three shipments to the National Institute for Environmental Health Sciences.

Visitors for this period included David C. House, M.D., and three collaborators from the Department of Medicine at Queen's University in Kingston, Ontario, Canada, with whom discussions were held as a result of their interest in hot-cell chemistry and the preparation of ^{11}C-labeled amino acids. In addition, a group of high school students visited on March 7 as part of the 1980 Junior Science and Humanities Symposium.

PAPERS AND PUBLICATIONS

Papers

F. F. Knapp, Jr., "Selenium and Tellurium as Carbon Substitutes," International Symposium on Radiopharmaceuticals: Structure-Activity Relationships, Hartford, Connecticut, March 21-23, 1980.

Publications

D. W. A. Bourne, J. W. Triplett, T. L. Hayden, P. A. DeSimone, and J. D. Hoeschele, "Pharmacokinetics of *cis*-Dichlorodiammineplatinum(II) in Rats Using an External Loop-Eigenfunction Expansion Technique," *J. Pharm. Sci.* 68, 1571, 1979.

F. F. Knapp, Jr., "The Synthesis of ^{123m}Te-Labeled 17β-Hydroxy-2-Tellura-A-Nor-5α-Androstane," *J. Label. Cmpds. Radiopharm. XVII,* 81, 1980.

F. F. Knapp, Jr., K. R. Ambrose, and A. P. Callahan, "Tellurium-123*m*-Labeled-23-(Isopropyl Telluro)-24-Nor-5α-Cholan-3β-ol: A New Potential Adrenal Imaging Agent," *J. Nucl. Med.* 21, 251, 1980.

F. F. Knapp, Jr., K. R. Ambrose, and A. P. Callahan, "The Effect of Structural Modifications on the Adrenal Uptake of Steroids Labeled in the Sidechain with Tellurium-123*m*," *J. Nucl. Med.* 21, 251, 1980.

Reports

F. F. Knapp, Jr., *Nuclear Medicine Technology Progress Report for Quarter Ending December 31, 1979,* ORNL/TM-7223.

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