



3 4456 0310655 5

ORNL/TM-11881

# oml

**OAK RIDGE  
NATIONAL  
LABORATORY**

**MARTIN MARIETTA**

## **Nuclear Medicine Program Progress Report for Quarter Ending June 30, 1991**

F. F. Knapp, Jr.  
K. R. Ambrose  
A. P. Callahan  
D. W. McPherson  
S. Mirzadeh  
P. C. Srivastava  
A. Hasan  
C. R. Lambert  
S. J. Lambert  
D. E. Rice

OAK RIDGE NATIONAL LABORATORY  
CENTRAL RESEARCH LIBRARY  
CIRCULATION SECTION  
45004 TEGOM 175  
**LIBRARY LOAN COPY**  
DO NOT TRANSFER TO ANOTHER PERSON  
If you wish someone else to see this  
report, send its name with report and  
the library will arrange a loan  
ORNL/TM-11881

MANAGED BY  
MARTIN MARIETTA ENERGY SYSTEMS, INC.  
FOR THE UNITED STATES  
DEPARTMENT OF ENERGY

This report has been reproduced directly from the best available copy.

Available to DOE and DOE contractors from the Office of Scientific and Technical Information, P.O. Box 62, Oak Ridge, TN 37831; prices available from (615) 576-8401, FTS 626-8401.

Available to the public from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Rd., Springfield, VA 22161.

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

ORNL/TM-11881

Contract No. DE-AC05-84OR21400

Health and Safety Research Division

NUCLEAR MEDICINE PROGRAM PROGRESS REPORT  
FOR QUARTER ENDING JUNE 30, 1991

F. F. Knapp, Jr., Group Leader

K. R. Ambrose  
A. P. Callahan  
D. W. McPherson  
S. Mirzadeh  
P. C. Srivastava

A. Hasan  
C. R. Lambert  
S. J. Lambert  
D. E. Rice

Work sponsored by  
DOE Office of Health and  
Environmental Research

Date Published - September 1991

OAK RIDGE NATIONAL LABORATORY  
Oak Ridge, Tennessee 37831-6285  
managed by  
MARTIN MARIETTA ENERGY SYSTEMS, INC.  
for the  
U.S. DEPARTMENT OF ENERGY



3 4456 0310655 5

## Previous reports in this series:

ORNL/TM-5809	ORNL/TM-9037
ORNL/TM-5936	ORNL/TM-9124
ORNL/TM-6044	ORNL/TM-9343
ORNL/TM-6181	ORNL/TM-9394
ORNL/TM-6371	ORNL/TM-9480
ORNL/TM-6410	ORNL/TM-9609
ORNL/TM-6638	ORNL/TM-9707
ORNL/TM-6639	ORNL/TM-9784
ORNL/TM-6771	ORNL/TM-9937
ORNL/TM-6916	ORNL/TM-10082
ORNL/TM-6958	ORNL/TM-10238
ORNL/TM-7072	ORNL/TM-10294
ORNL/TM-7223	ORNL/TM-10377
ORNL/TM-7411	ORNL/TM-10441
ORNL/TM-7482	ORNL/TM-10618
ORNL/TM-7605	ORNL/TM-10711
ORNL/TM-7685	ORNL/TM-10839
ORNL/TM-7775	ORNL/TM-11014
ORNL/TM-7918	ORNL/TM-11043
ORNL/TM-8123	ORNL/TM-11145
ORNL/TM-8186	ORNL/TM-11224
ORNL/TM-8363	ORNL/TM-11304
ORNL/TM-8428	ORNL/TM-11377
ORNL/TM-8533	ORNL/TM-11427
ORNL/TM-8619	ORNL/TM-11550
ORNL/TM-8746	ORNL/TM-11570
ORNL/TM-8827	ORNL/TM-11721
ORNL/TM-8966	ORNL/TM-11755
	ORNL/TM-11830

## CONTENTS

Summary .....	1
Production of Gallium-66, A Positron-Emitting Nuclide for Potential Radioimmunotherapy .....	2
Preparation and Biodistribution Studies of New Iodine-125-Labeled Quinuclidinyl Esters as Potential Ligands for SPECT Studies of Muscarinic Receptors .....	7
Agents for Medical Cooperatives .....	11
Other Nuclear Medicine Group Activities .....	11
Presentations .....	11
Publications .....	13



## SUMMARY

In this report the excitation functions for production of gallium-66 via  $\alpha$ -induced nuclear reactions on enriched zinc-66 have been measured with  $E_\alpha \leq 27.3$  MeV and  $E_\alpha \leq 43.7$  MeV employing the stack thin-target technique. In addition, the induced activity of gallium-67 in the same sets of targets allowed an evaluation of the excitation functions of the corresponding nuclear reactions. These preliminary studies have demonstrated that sufficient levels of gallium-66 can be produced by  $\alpha$ -induced reactions on enriched zinc targets.

A series of radioiodinated analogues of 1-azabicyclo[2.2.2]oct-3-yl  $\alpha$ -hydroxy- $\alpha,\alpha$ -diphenylacetate (QNB) have been prepared. These new analogues include 1-azabicyclo[2.2.2]oct-3-yl  $\alpha$ -hydroxy- $\alpha$ -(4-iodophenyl)- $\alpha$ -methylacetate (2, I-QNA), 1-azabicyclo[2.2.2]oct-3-yl (3-iodo)-xanthene-9-carboxylate (3, I-QNX), and 1-azabicyclo[2.2.2]oct-3-yl  $\alpha$ -hydroxy- $\alpha$ -(E-1-iodo-1-propen-3-yl)- $\alpha$ -phenylacetate (4, I-QNP), which have also been radiolabeled with iodine-125 with high specific activity. The biodistribution, brain uptake, and receptor specificity of these new analogues are currently being studied.

Several shipments of radioactive agents were also made to collaborators during this period. One shipment of iodine-125-labeled 15-(p-iodophenyl)-3-R,S-methylpentadecanoic acid (BMIPP) was made to Brookhaven National Laboratory, (Dr. P. Som, D.V.M.) for continuing studies of the effects of cocaine intoxication on myocardial fatty acid metabolism. In addition, a tungsten-188/rhenium-188 generator was supplied for direct labeling of antibodies with rhenium-188 (University of Washington, Dr. R. L. Vessella). Members of the Nuclear Medicine Group attended several national and international meetings and made 11 presentations during this period.

PRODUCTION OF GALLIUM-66, A POSITRON-EMITTING NUCLIDE FOR  
POTENTIAL RADIOIMMUNOTHERAPY

Radiolabeled monoclonal antibodies for the purpose of radioimmunotherapy are of considerable interest and several  $\beta^-$  and  $\alpha$ -emitting nuclides have been identified for this application (e.g.  $^{67}\text{Cu}$ ,  $^{90}\text{Y}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$  and  $^{212}\text{Pb}/^{212}\text{Bi}$ ). In principle,  $\beta^+$ -emitting radionuclides should also be considered for therapeutic applications, since the radiation dose per decay is comparable to the dose from  $\beta^-$ -emitters and the quantitative imaging ability of positron emission tomography (PET) would enhance dosimetry for  $\beta^+$ -emitters. Furthermore, several  $\beta^+$ -emitters for therapy could be produced in medical cyclotrons. Among possible  $\beta^+$ -emitters, gallium-66 ( $^{66}\text{Ga}$ ) is an excellent candidate because of the convenient 9.45 h half-life, the large  $\beta^+$  branch (51.2%) with high end-point energy (4.15 MeV), and the comparable electron capture (EC) branch (44%) with abundant short-range electrons. These decay characteristics make  $^{66}\text{Ga}$  an attractive candidate for therapeutic applications. The decay and energy properties of gallium radioisotopes of interest for nuclear medicine applications are summarized in Table 1.

Table 1. Gallium Radioisotopes of Interest for Nuclear Medicine Applications

Isotope	$t_{1/2}$	Mode of Decay	$E_{\beta}^{\text{max}}$ , MeV	$E_{\gamma}$ , MeV ( $I_{\gamma}$ , %)
$^{66}\text{Ga}$	9.40 h	$\beta^+$ (56.5%), EC (44%)	0.367 (0.82%) 0.747 (0.97) 0.935 (3.03%) 1.84 (0.54%) 4.15 (51.2%)	833.6 (6.12%) 1039.0 (38.4%) 2190.0 (5.74%) 2752.1 (23.5%)
$^{67}\text{Ga}$	3.26 d	EC (100%)	-	167.0 (77.4%)
$^{68}\text{Ga}$	68.3 m	$\beta^+$ (90%), EC (10%)	$\sim 0.8$ ( $\sim 2$ ) 1.9 (89%)	1077.4 (2.93)

Among several possible routes for production of  $^{66}\text{Ga}$ , we have studied the  $\alpha$ -induced reactions on enriched  $^{64}\text{Zn}$ . The following two reactions represent production routes for  $^{66}\text{Ga}$ .

- I.  $^{64}\text{Zn}[\alpha, 2n]^{66}\text{Ge}(2.3 \text{ h}, \text{EC}) \rightarrow ^{66}\text{Ga}$
- II.  $^{64}\text{Zn}[\alpha, \text{np}]^{66}\text{Ga}$

The excitation functions were measured with  $E_\alpha \leq 27.3$  MeV at the National Institutes of Health (NIH) cyclotron and with  $E_\alpha \leq 43.7$  MeV at the 60" cyclotron at the Brookhaven National Laboratory (BNL). In addition, the induced activity of  $^{67}\text{Ga}$  in the same sets of targets allowed an evaluation of the excitation functions of the corresponding  $[\alpha, n]$  and  $[\alpha, p]$  reactions. Most of these studies were performed in collaboration with Dr. Y. Y. Chu at BNL, and a preliminary report of these results has been published jointly (Proceeding of International Conference on Nuclear Data for Science and Technology, Julich, Germany, May 1991; J. Radiation Effects, *in press*).

For excitation function measurements, thin targets of  $^{66}\text{Zn}$  were prepared by vacuum evaporation of enriched  $^{66}\text{Zn}$  (metal) onto high-purity aluminum (Al) support foils. The Al-supported Zn targets were covered with Al foil and the sealed targets were irradiated for time periods ranging from 10 to 30 min (60" BNL cyclotron). The excitation function of the  $^{64}\text{Zn}[\alpha, 2n]^{66}\text{Ge}$  reaction which was measured in this work and the values reported by Porile *et al.*<sup>1</sup> are shown in Figure 1. Above  $E_\alpha = 20.0$  MeV, the cross-section increases rapidly and reaches a maximum value of 94 mb at  $E_\alpha = 33$  MeV. From the initial threshold value up to 27 MeV (where our two measurements at BNL and NIH overlapped), our measured cross-section values are in good agreement but are almost a factor of 10 higher than the reported values. For the earlier study by others, quantitation of  $^{66}\text{Ga}$  activity was made by the measurement of its annihilation radiation in a NaI detector.<sup>1</sup> At the higher-energy end of the excitation function, our data are generally in agreement with earlier measurements.

The cumulative cross-section values for the production of  $^{66}\text{Ga}$  from the direct  $[\alpha, pn]$  reaction and indirectly from the decay of  $^{66}\text{Ge}$  are also shown in Figure 1. The cumulative cross-section reaches a maximum of 900 mb at  $E_\alpha = 32.5$  MeV with a threshold value of about 19 MeV. At the maximum region of the excitation function, the agreement between our current and earlier measurements is surprisingly good. The subtraction of the excitation function of reaction-I from the cumulative excitation function yields the excitation function for reaction-II. The relative probability of reaction-II to reaction-I,  $\sigma_{(\alpha, pn)}/\sigma_{(\alpha, 2n)}$ , in the maximum region ( $30 \leq E_\alpha \leq 40$ ), remains rather constant at  $6.5 \pm 1.0$ , indicative of substantially lower binding energy of protons in this mass region.

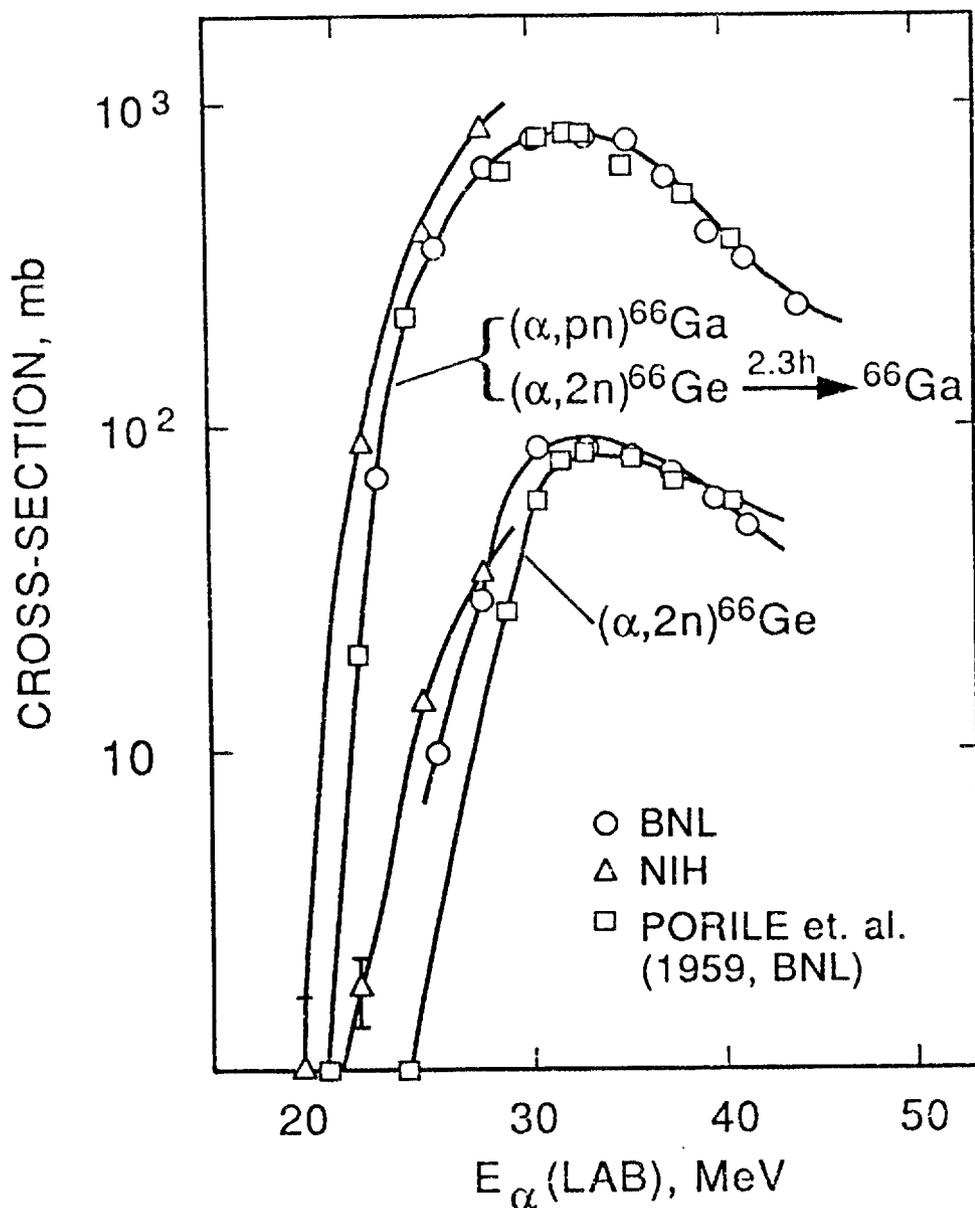


Figure 1. Excitation functions for production of  $^{66}\text{Ga}$  via  $\alpha$ -induced reaction on  $^{64}\text{Zn}$ .

The same set of  $\alpha$ -activated targets yielded excitation functions for production of  $^{67}\text{Ga}$  via the  $(\alpha, p)$  and  $(\alpha, n)$  reactions and the results are shown in Figures 2a and 2b, respectively. In this case, the  $\sigma_{(\alpha, p)}/\sigma_{(\alpha, n)}$  is close to unity at the maximum of the excitation functions which occurs at  $E_\alpha = 20$  MeV, about 13 MeV lower than that of  $(\alpha, 2n)$  or  $(\alpha, pn)$  reactions. The

peak of the excitation function of the  $(\alpha,n)$  reaction is larger than that of the  $(\alpha,2n)$  reaction by almost a factor of 10. However, the situation is reversed in the case of  $(\alpha,p)$  and  $(\alpha,pn)$  reactions, where at the maximum of the excitation functions the ratio of  $\sigma_{(\alpha,pn)}$  to  $\sigma_{(\alpha,p)}$  is  $\sim 2.5$ . The errors of the cross-sections values are estimated at  $\sim 10\%$  at the maximum of the excitation functions and at  $\sim 30\%$  near the threshold. The incident  $\alpha$ -particle energies are most accurate at the highest energy with a relative error of  $\sim 2\%$ . This error increases to  $\sim 10\%$  below 16 MeV due to straggling (fluctuations in average energy loss which results in some distribution in the ranges<sup>2</sup>) process. These preliminary studies have demonstrated that sufficient levels of  $^{66}\text{Ga}$  can be produced by  $\alpha$ -induced reactions, and further reaction studies are in progress.

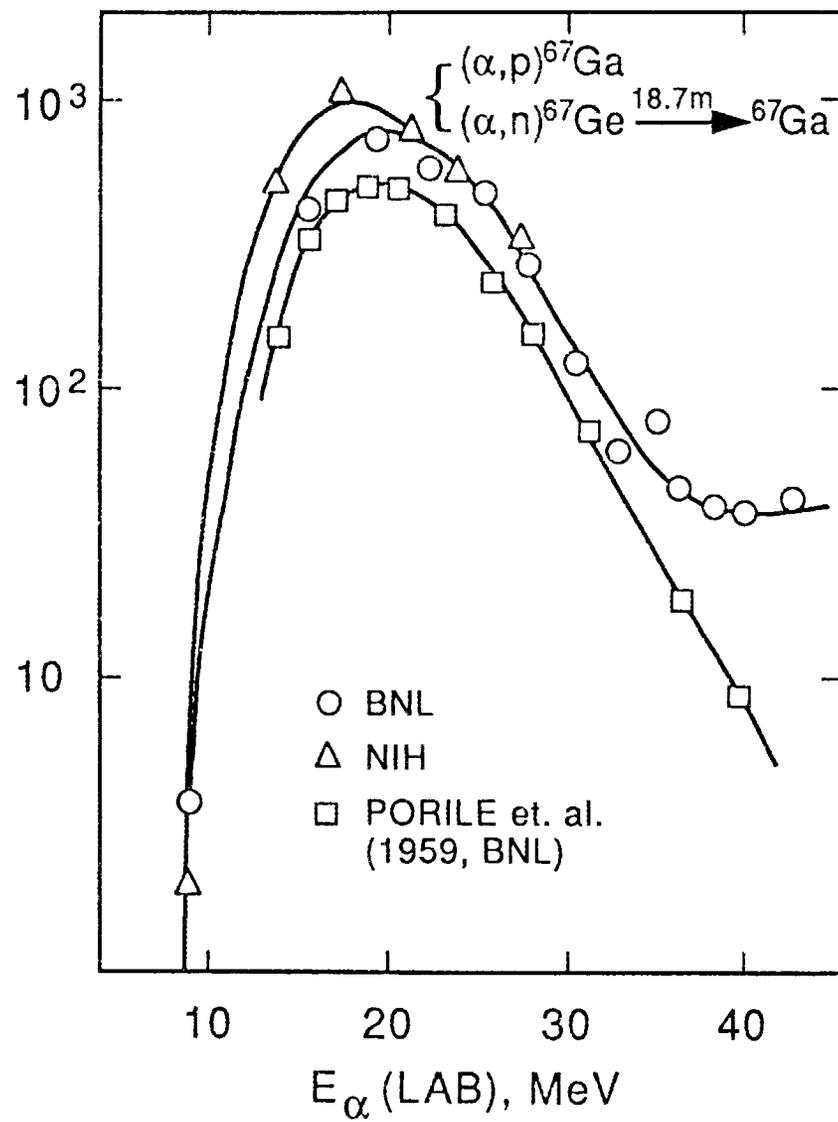
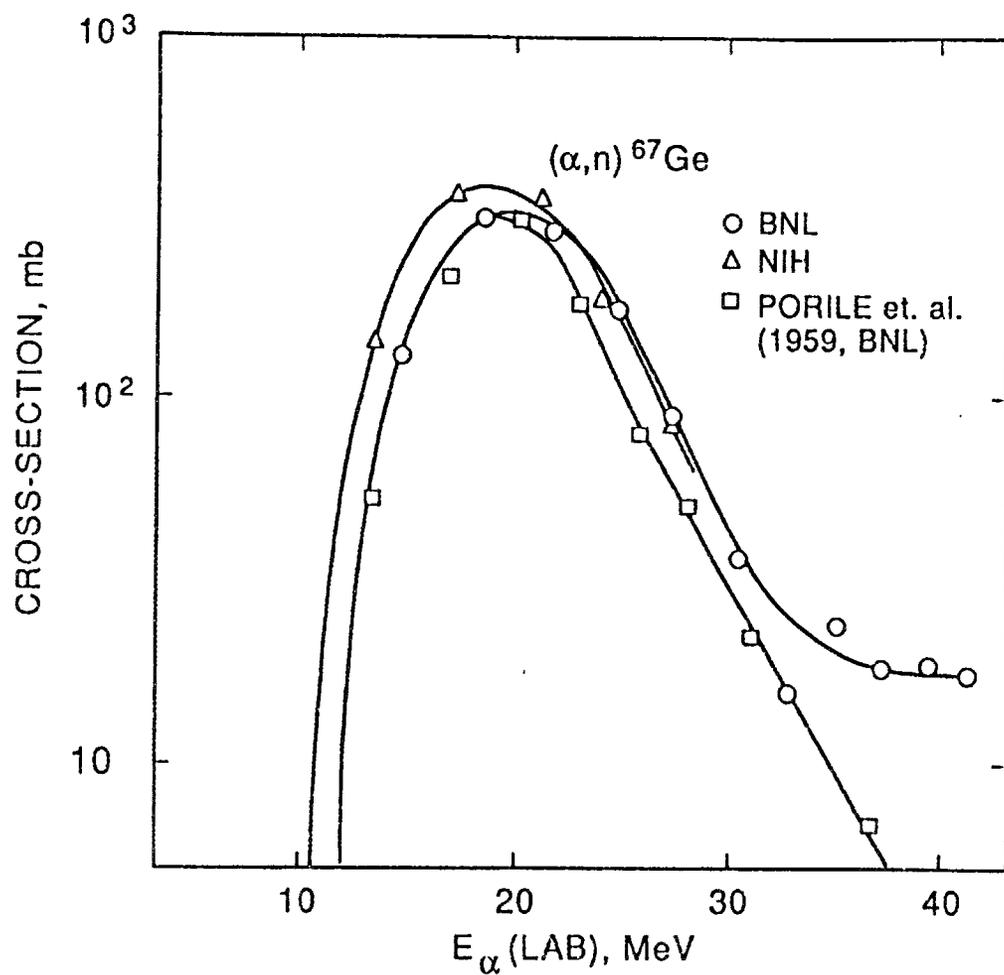
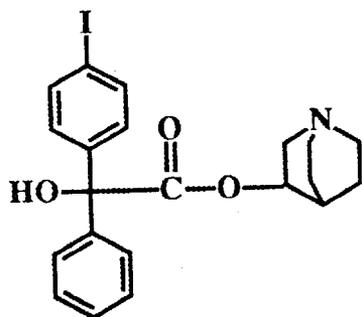


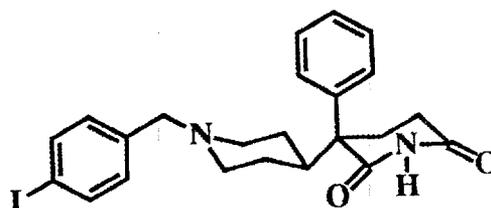
Figure 2a & 2b. Excitation functions for production of  $^{67}\text{Ga}$  via  $\zeta$ -induced reactions on  $^{64}\text{Zn}$ .

PREPARATION AND BIODISTRIBUTION STUDIES OF NEW IODINE-125-LABELED  
QUINUCLIDINYL ESTERS AS POTENTIAL LIGANDS FOR SPECT  
STUDIES OF MUSCARINIC RECEPTORS

The muscarinic acetylcholine receptor appears to play an important role in various physiological and behavioral responses, including sleep, learning, and memory. In addition, a decrease in the muscarinic receptor density has been observed in post mortem studies of patients with Huntington's chorea and Alzheimer's dementia. These observations have prompted the development of muscarinic receptor-specific radioligands for use in the *in vivo* non-invasive study of muscarinic receptor populations by both positron emission tomography (PET) and single emission computerized tomography (SPECT). Although most of these studies have involved the development of radioligands labeled with carbon-11 and fluorine-18 for use in PET studies, there have been only a few ligands labeled with iodine-123 reported for the *in vivo* study of muscarinic receptor populations by SPECT. These include I-QNB (1) in which the yield of the radioiodinated product is relatively low,<sup>3</sup> thereby making this ligand impractical for routine studies, and more recently,<sup>4</sup> 4-iododexetimide (5). The availability of a muscarinic receptor ligand labeled with iodine-123 is important due to the large number of medical institutions which have access to SPECT facilities thereby allowing this technology to be available to larger patient populations.



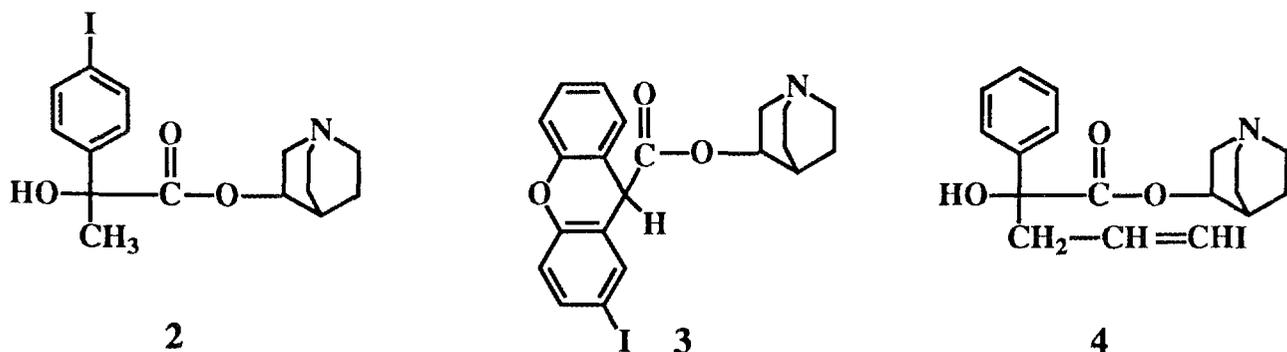
1



5

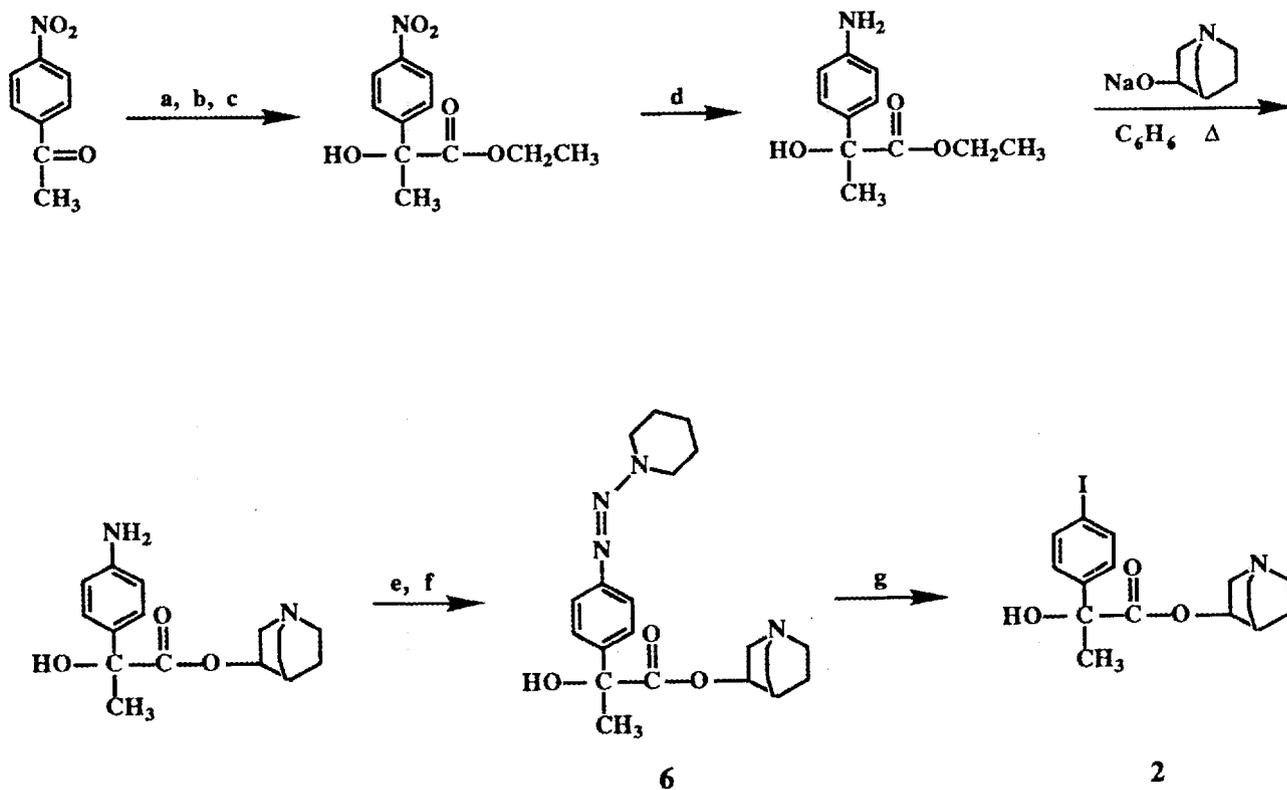
For these reasons we have pursued the preparation of a series of radioiodinated analogues based on QNB (1), a high affinity muscarinic acetylcholine receptor antagonist. The analogues we have prepared are 1-azabicyclo[2.2.2]oct-3-yl  $\alpha$ -hydroxy- $\alpha$ -methyl- $\alpha$ -(4-iodophenyl)acetate (QNA, 2), 1-azabicyclo[2.2.2]oct-3-yl (3-iodo)xanthene-9-carboxylate

(QNX, 3), and 1-azabicyclo[2.2.2]oct-3-yl  $\alpha$ -hydroxy- $\alpha$ -phenyl- $\alpha$ -(1-iodo-1-propen-3-yl)acetate (QNP, 4). The QNA and QNX analogues are expected to be antagonists for the muscarinic  $M_1$  receptor subtype, while QNP (4), a novel QNB analogue, was designed on the "three point of attachment" model for the interaction of the ligand at the receptor site. The phenyl ring of QNB was modified to a moiety which would allow the rapid incorporation of iodine and would not interfere with the ligand binding at the receptor site.

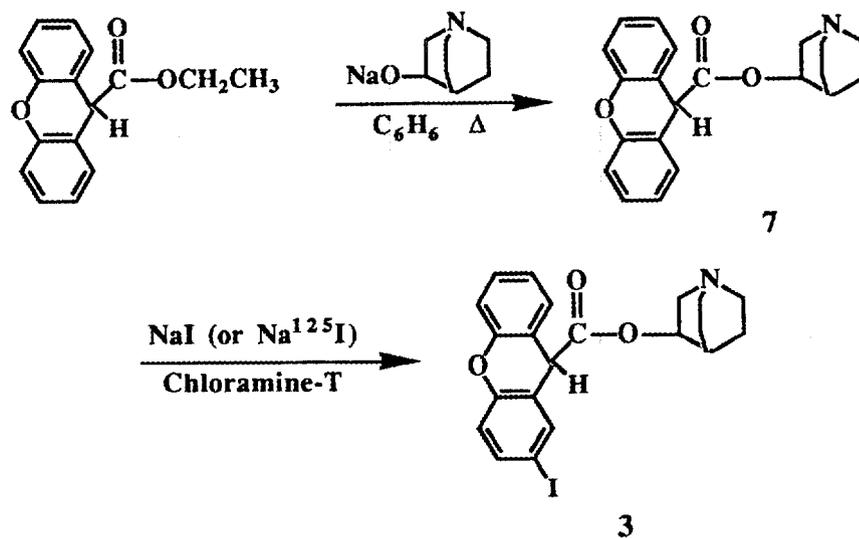


The syntheses of compounds 2, 3, and 4 are illustrated in Schemes I, II, and III, respectively. The preparation of I-QNA (2) involved a multistep reaction sequence for the preparation of the triazine intermediate (6). Treatment of 6 with NaI in trifluoroacetic acid (TFAA) and acetone afforded 2 in a modest yield after purification by column chromatography. Compound 3 was obtained by the direct electrophilic iodination of QNX (7) in the presence of NaI with chloramine-T in THF. Finally, compound 4 was prepared from the  $\alpha$ -propargyl analogue of QNA (8). Treatment of 8 with an excess of tributyltin hydride and AIBN in refluxing toluene afforded 9 as the E isomer after purification by column chromatography. The stereochemistry of the double bond was confirmed as E by 200 MHz nuclear magnetic resonance (NMR) analysis. Treatment of 9 with iodine in chloroform afforded 4 with retention of stereochemistry of the double bond as determined by 200 MHz NMR analysis.

The radiolabeling of these ligands involved similar approaches. For QNA (2), 6 was added to a solution of acetone, TFAA and  $\text{Na}^{125}\text{I}$  and stirred at room temperature for one hour. Purification by  $\text{C}_{18}$  SepPak<sup>®</sup> and preparative TLC (silica,  $\text{CH}_2\text{Cl}_2$ :10% MeOH) afforded 2.



Scheme I. Synthesis of I-QNA (2). (a) TMSCN, (b) HCl, reflux, (c) EtOH, H<sup>+</sup>, (d) H<sub>2</sub>, Pd/C, (e) NaNO<sub>2</sub>, (f) Piperidine, (g) NaI, TFAA (or Na<sup>125</sup>I, TFAA).



Scheme II. Synthesis of I-QNX (3).



2. Friedlander, G., Kennedy, J. W., Macias, E. S., and Miller, J. M. (eds.) Nuclear and Radiochemistry, 3rd Edition, John Wiley & Sons, New York, pp. 208 (1981).
3. Eckelman, W. C., Reba, R. C., Rzesotarski, W. J., Gibson, R. E., Hill, T., Holman, B. L., Budinger, T., Conklin, J. J., Eng, R., and Grissom, M. P. Science 233, 291-293 (1984).
4. Mueller-Gaertner, H. W., Wilson, A. A., Dannals, R. F., Ravert, H. T., Wagner, H. N., Jr., and Frost, J. J. J. Nucl. Med. 32(5), 980 (1991).

#### AGENTS FOR MEDICAL COOPERATIVE PROGRAMS

One shipment of the iodine-125-labeled 15-(p-iodophenyl)-3-R,S-methylpentadecanoic acid (BMIPP) methyl-branched fatty acid analogue was made to the Brookhaven National Laboratory (Dr. P. Som, D.V.M.) for a continuing collaborative study to evaluate the harmful effects of cocaine on myocardial fatty acid metabolism by SPECT. A tungsten-188/rhenium-188 generator was supplied to the University of Washington (Dr. R. L. Vessella) through a collaborative program to assess a new "direct" labeling method for attachment of rhenium-188 to antibodies specific for prostatic and ovarian carcinomas.

#### OTHER NUCLEAR MEDICINE GROUP ACTIVITIES

##### **Presentations**

F. F. Knapp, Jr., presented an invited lecture entitled "The Development of Radionuclide Generator Systems for Nuclear Medicine Applications" at the "Fourth European Symposium on Radiopharmacy and Radiopharmaceuticals" which was held in Baden (Zurich), Switzerland, on May 1-4, 1991. Proceedings of the symposium will be published by Kluwer Publishers, The Netherlands. During this trip, he also visited the Clinic for Nuclear Medicine at the University of Bonn, Germany, to discuss and coordinate continuing collaborative studies on the preclinical and clinical evaluation of radiopharmaceuticals developed at ORNL.

Saed Mirzadeh presented two papers at the "International Conference on Nuclear Data for Science and Technology" in Julich, Germany, on May 13-17. The papers were entitled:

"Production of Gallium-66, A Positron Emitting Nuclide for Radioimmunotherapy," by S. Mirzadeh and Y. Y. Chu.

"Production of Tungsten-188 and Osmium-194 in a Nuclear Reactor for New Clinical Generators," by S. Mirzadeh, F. F. Knapp, Jr., and A. P. Callahan.

Members of the Nuclear Medicine Program co-authored a presentation at the recent "International Symposium on Radiopharmacology" held in Boston, Massachusetts, describing collaborative studies with Immunomedics, Inc., on antibody radiolabeling with rhenium-188 from the ORNL tungsten-188/rhenium-188 radionuclide generator system.

Griffiths, G. L., Knapp, F. F., Jr., Callahan, A. P., Ostella, F., Hansen, H. J., and Goldenberg, D. M. "The Generation of Rhenium-188-Labeled Antibodies by Direct Labeling Methods."

Members of the Nuclear Medicine Group also presented and co-authored several papers at the recent 38th Annual Meeting of the Society of Nuclear Medicine held in Cincinnati, Ohio, on June 11-15, 1991:

Griffiths, G. L., Knapp, F. F., Jr., Callahan, A. P., Tang, Z., Jones, A. L., Ostella, F., Hansen, H. J., and Goldenberg, D. M. "The Use of Carrier-Free Re-188 from an In-House W-188/Re-188 Generator for Preparation of Re-188-Labeled Monoclonal Antibodies."

Hasan, A., Allred, J. F., Buchsbaum, D. J., and Srivastava, P. C. "[I-125]Iodovinylazomycin Acyclonucleosides Retain Tumor Uptake and Show Low *In Vivo* Deiodination as Compared to [I-125]Iodoazomycin Acyclonucleoside."

Lisic, E., Mirzadeh, S., Callahan, A. P., and Knapp, F. F., Jr. "A New Tandem Generator/Ion Exchange System Providing Carrier-Free Rhenium-188-Perrhenic Acid for Antibody Labeling."

McPherson, D. W., Callahan, A. P., Lambert, C. R., and Knapp, F. F., Jr. "Preparation and Biodistribution of a Series of Iodine-125-Labeled Quinuclidinyl Esters as Potential Ligands for SPECT Studies of Muscarinic Receptors."

McPherson, D. W., Callahan, A. P., Ambrose, K. R., and Knapp, F. F., Jr. "Stability of Copper(II)-Bis-(N<sup>4</sup>-Substituted)Thiosemicarbazone (TSC) Protein Complexes."

Mirzadeh, S., Callahan, A. P., and Knapp, F. F., Jr. "Iridium-194 – A New Candidate for Radioimmunotherapy (RAIT) from an Osmium-194/Iridium-194 Generator System."

Srivastava, P. C., Hasan, A., Kilbourn, M. R., and Buchsbaum, D. J. "[F-18]Fluoroazoycin Acyclonucleoside. A New 2-Nitro-imidazole Nucleoside Analogue for PET Imaging of Hypoxic Tumors."

#### **Publications**

Srivastava, P. C., Buchsbaum, D. J., and Hasan, A. "Design, Synthesis and Tumor Specificity of Azomycin Ribo- and Acyclonucleosides," *Nucleosides & Nucleotides*, 10(1-3), 235-238 (1991).

Roselli, M., Schlom, J., Gansow, O. A., Brechbiel, M. W., Mirzadeh, S., Pippin, C. G., Milenic, D. E., and Colcher, D. "Comparative Biodistribution Studies of DTPA-Derivative Bifunctional Chelates for Radiometal Labeled Monoclonal Antibodies," *Int. J. Rad. App. Inst., Part B, Nucl. Med. Biology*, 18, 389-394 (1991).



## INTERNAL DISTRIBUTION

- |                                |                                 |
|--------------------------------|---------------------------------|
| 1. K. R. Ambrose               | 23. D. W. McPherson             |
| 2. J. F. Allred                | 24. J. C. Miller                |
| 3. J. T. Bell                  | 25. S. Mirzadeh                 |
| 4. T. A. Butler (Consultant)   | 26. B. Patton                   |
| 5. A. P. Callahan              | 27. G. Prosser                  |
| 6. E. D. Collins               | 28. D. Pruett                   |
| 7. K. F. Eckerman              | 29. D. W. Ramey                 |
| 8. R. K. Genung                | 30. D. E. Rice                  |
| 9. M. M. Goodman (Consultant)  | 31. D. E. Reichle               |
| 10. G. D. Griffin              | 32. P. S. Rohwer                |
| 11. A. Hasan                   | 33. P. C. Srivastava            |
| 12. J. R. Hightower            | 34-35. Central Research Library |
| 13. G. W. Kabalka (Consultant) | 36. Document Record Section     |
| 14. S. V. Kaye                 | 37-38. Laboratory Records Dept. |
| 15-19. F. F. Knapp, Jr.        | 39. Lab. Records, ORNL RC       |
| 20. C. R. Lambert              | 40. ORNL Patent Section         |
| 21. S. J. Lambert              |                                 |
| 22. E. C. Lisic (Consultant)   |                                 |

## EXTERNAL DISTRIBUTION

41. S. J. Adelstein, M.D., Shields Warren Radiation Lab., Boston, MA 02115.
42. H. L. Atkins, M.D., Radiology Dept., State Univ. of New York, Stony Brook, NY 11794
43. H. J. Biersack, M.D., Director, Klinik fuer Nuklear Medizin, Der Universitat Bonn, Sigmund Freud Strasse 25, 5300 Bonn 1, West Germany
44. C. Brihaye, Centre de Recherches du Cyclotron, Universite de Liege, Belgium
45. A. B. Brill, M.D., Ph.D., Commonwealth of Massachusetts, Univ. of Massachusetts Medical Center, 55 Lake Avenue North, Worcester, MA 01605
46. T. F. Budinger, M.D., Donner Lab., LBL, Berkeley, CA 94720
47. D. W. Cole, Jr., U.S. DOE, MS-ER-73, GTN, Washington, D.C. 20585
48. J. G. Davis, M.D., Medical and Health Sciences Division, ORAU, Oak Ridge, TN 37831
49. S. J. DeNardo, M.D., Univ. California, Davis Medical Center, Sacramento, CA 95817
50. R. F. Dannals, Division of Nuclear Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21205
51. R. Dudczak, M.D., Dept. Nuclear Medicine, I. Medizinische Universitatsklinik, A-1090 Wien, Lazarettgasse 14, Vienna, Austria
52. D. R. Elmaleh, Physics Research Dept., Massachusetts General Hospital, Boston, MA 02114
53. L. Feinendegen, Institut fur Medizin, Postfach 1913, D-5170, Julich 1, Germany

54. A. Fritzberg, NeoRx Corporation, 410 West Harrison, Seattle, WA 98119
55. D. M. Goldenberg, M.D., Center of Molecular Medicine and Immunology, 1 Bruce Street, Newark, NJ 07103
56. M. Guillaume, Chef de Travaux, Centre de Recherches du Cyclotron, Universite de Liege, Belgium
57. D. R. Hamilton, Director, Division of Technical Development, OTA/CDRH/FDA, 1901 Chapman Avenue, Rockville, MD 20857
58. J. Hiltunen, Technical Research Centre of Finland, Reactor Laboratory, Otakaari 3 A, SF-02150 Espoo, Finland
59. K. Hubner, M.D., Department of Radiology, UT Memorial Hospital, Knoxville, TN 37920
60. A. Jones, Dept. of Radiology, Harvard Medical School, Boston, MA 02115
61. G. Kirsch, Department of Chemistry, Universite de Metz, Metz, France
62. J. Kropp, M.D., Klinik fuer Nuklear Medizin, Der Universitat Bonn, Sigmund Freud Strasse 25, 5300 Bonn 1, West Germany
63. D. E. Kuhl, M.D., Division of Nuclear Medicine, University of Michigan Hospitals, University Hospital BIG 412/0028, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-0028.
64. S. Larson, M.D., Sloan-Kettering Inst. for Cancer Research, New York, NY 10021
65. D. J. Maddalena, FRACI, Department of Pharmacology, Sydney University, NSW 2006, Sydney, Australia
66. J. N. Maddox, DOE-OHER, MS-ER-73, GTN, Washington, DC 20585
67. Office of Assistant Manager for Energy Research and Development DOE-ORO, Oak Ridge, TN 37831
68. R. Patterson, M.D., Nuclear Cardiology, Crawford Long Hospital, 550 Peachtree Street, NE, Atlanta, GA 30365-2225
69. C. L. Partain, M.D., Professor and Vice Chairman, Dept. Radiology and Radiological Sciences, Vanderbilt University Medical Center, Nashville, TN 37232
70. R. C. Reba, M.D., George Washington Univ. Med. Center, Washington, DC 20037
71. S. N. Reske, M.D., Department of Nuclear Medicine, Municipal Hospital, Wuppertol D-5600, Germany
72. M. Robbins, Mallinckrodt, Inc., 675 McDonnell Blvd., P.O. Box 5840, St. Louis, MO 63134
73. M. P. Sandler, M.D., Chief, Nuclear Medicine Section, Vanderbilt University Medical Center, Nashville, TN 37232
74. R. E. Schenter, Westington Hanford Co., Richland, WA 99352
75. F. Snyder, ORAU, Oak Ridge, TN 37831
76. A. Solomon, M.D., UT MRCH, 1924 Alcoa Highway, Knoxville, TN 37920-6999
77. P. Som, DVM, Medical Department, BNL, Upton, NY 11973
78. S. C. Srivastava, Bldg. 801, Medical Dept., BNL, Upton, NY 11973
79. H. W. Strauss, M.D., Nuclear Medicine Div., Massachusetts General Hospital, Boston, MA 02114
- 80-90. Office of Scientific and Technical Information, DOE, Oak Ridge, TN 37831
91. F. Visser, M.D., Cardiology Dept., Free University Hospital, De Boelelaan 117, Amsterdam, The Netherlands
92. H. N. Wagner, Jr., M.D., Div. of Nuclear Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21205
93. A. P. Wolf, BNL, Upton, NY 11973

94. R. Wolfangel, Mallinckrodt, Inc., 675 McDonnell Blvd., P.O. Box 5840, St. Louis, MO 63134
95. D. V. Woo, Centocor, 244 Great Valley Parkway, Malvern, PA 19355
96. R. W. Wood, Jr., DOE-OHER, Washington, DC 20585
97. S. Wynchank, Research Institute for Medical Biophysics (RIMB), Republic of South Africa