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Drs V.P. Bond, J.S. Robertson, J. Archambeau

R. G. Fairchild

Neutron capturing compounds

In recent months I have had the chance to talk with Dr. N. A. Frigerio at Argonne, and Dr. Brownell and Dr. Ata-Aka at the Massachusetts General Hospital concerning neutron capturing compounds.

Briefly, Frigerio has been working to improve on the sulfonated uranyl phthalocyanine compound which had tumor-to-blood ratio of 50 and over (ANL 6910), but which suffered from severe photosensitization of the subjects (ANL 6971). He has evidently succeeded in producing small amounts of the red uranyl hematoporphyrzine which would not, presumably, photosensitize subjects (ANL 6971). Work has also been done on proteins, which show a tumor-blood ratio of 10:1 at 12 to 48 hours after injection. The above compounds are described in more detail in Appendix I. Of particular interest is the fact that he has developed a Monte Carlo computer program which can compute neutron energy and tissue dose as a function of position (and of chemical composition) in finite tissue volumes (tissue volumes of therapeutic interest), using monoenergetic neutron beams with energies ranging from thermal to 200 KeV (ANL 6971). A library of dose-energy-spectrum-beam size-penetration charts is being compiled and evidently indicates neutrons in the 5-keV region are most effective for NCT, thus bringing up the possibility of using high-output Van de Graaff accelerators.

In Boston, various boron compounds have been produced with tumor-blood ratios of 5:1 at 24 hours, but with an unspecified concentration. These compounds are described in more detail in Appendix II. It is understood that any information in the appendices may suffer from inaccuracies due to my poor knowledge of the field.

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APPENDIX I

Frigerio

1. Uranium Compounds

To avoid the photosensitization toxicity of uranyl phthalocyanine, we are currently trying to synthesize an analagous compound whose ~~photo~~ absorption characteristics would more closely resemble those of normal tissue compounds; e.g., hemoglobin. Also, it would be pleasant if the compound could be more easily excreted than U_2 PC. Present attempts (partly successful) have yielded the red uranyl hematoporphyrazine.

Further replacement of a corner nitrogen with an enzymatically hydrolyzable bond (e.g., $C = O$) would help excretion. "

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2. Proteins

" We have synthesized borono-azo-bovine serum albumin and the analogous arseno-azo-(bovine)² serum albumins, about 30-40 molecules/molecule protein.

We are currently studying the biological distribution as f(t) of II. It localizes 10:1 tumor/blood in brain tumors over the time period 12-48 hrs after injection. Presumably I will behave similarly. For the first 2 hours or so, however, it is about 98% blood only. After this, blood level drops with a biological T 1/2 of ~ 6 hours while tumor and some organs (liver, kidney) continue to rise for 48 hours or so. Toxicity level is >> 300 mgm/kgm. "

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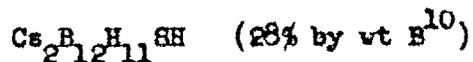
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APPENDIX II

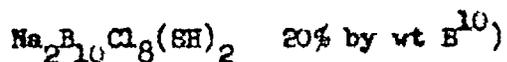
Soloway

The following two compounds have been used in 6-week-old mice, with tumor-blood ratios of ~ 5:1 at 24 hrs. Concentration was low, but not specified.

1. Cesium-1-mercapto perhydrododecaborate



2. Bis-Sodium-bis-sulfhydryde octachlorodecaborate



Also, they are working on a C^{14} Uracil, which evidently has the chance of localizing within the cell.

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