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DOSIMETRY OF COPPER RADIONUCLIDES

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Calculations for dosimetry of copper radionuclides based on physiologic considerations are presented.

The radionuclides ^{64}Cu and ^{67}Cu have been used extensively in studies of physiologic and pathologic copper metabolism (*1–6*). Radiocopper has been particularly helpful in defining the abnormalities that lead to copper toxicity in patients with Wilson's disease (*7*) and to copper deficiency in infants with Menkes' syndrome (*8*). As a diagnostic agent, radiocopper can be of considerable help when the diagnosis of Wilson's disease or of its heterozygous carrier state is in doubt (*7*). Radiocopper-labeled ceruloplasmin is also useful in studying the metabolic vicissitudes of the protein and in quantitating losses of serum protein in patients suspected of suffering from protein-losing enteropathy (*9*). Yet, despite a large number of clinical studies, published dosimetry data are incomplete and in some instances conflicting (*10,11*). In this paper we report radiation dosimetry calculations based on the physical properties of copper and on current knowledge of its physiology.

Production and physical properties of radiocopper. Copper-64 is produced through neutron irradiation of ^{63}Cu by (n,γ) reaction or through the ^{64}Zn(n,p) ^{64}Cu reaction. The radionuclide ^{67}Cu can be produced in a fast neutron flux ^{67}Zn(n,p) ^{67}Cu as a carrier-free isotope (*12*). The decay schemes of ^{64}Cu and ^{67}Cu are given in Figs. 1 and 2, respectively (*13*).

Physiologic behavior of radiocopper. In normal subjects about a third of a 2-mg oral dose of radiocupric ion is absorbed principally from the upper gastrointestinal tract (*7,14,15*). Most of this radioactivity appears initially in the blood loosely bound to serum albumin although a variable amount may enter erythrocytes (*16,17*). Within 4 hr, 60–90% of what has entered the circulation is found in the liver (*7*). In turn, 10–20% of this copper is released over several days from the liver into plasma in the form of newly synthesized ceruloplasmin (*18*), 30–40% is excreted in the bile (*19*), and about 50% remains in the liver or is slowly released (*7*). Urinary excretion is essentially zero (*7*). A schematic representation of the routes followed by an oral dose of radiocopper is shown in Fig. 3.

Equilibrium absorbed-dose constants and dosimetry. The values of Δ_i, the absorbed-dose constant for the more prominent particle and photon emissions for ^{64}Cu and ^{67}Cu, arrived at on the basis of

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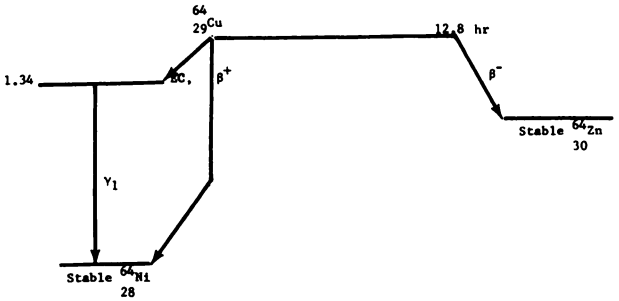

FIG. 1. Decay scheme of ^{64}Cu.

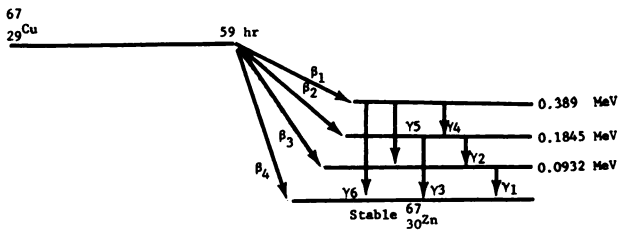

FIG. 2. Decay scheme of ^{67}Cu.

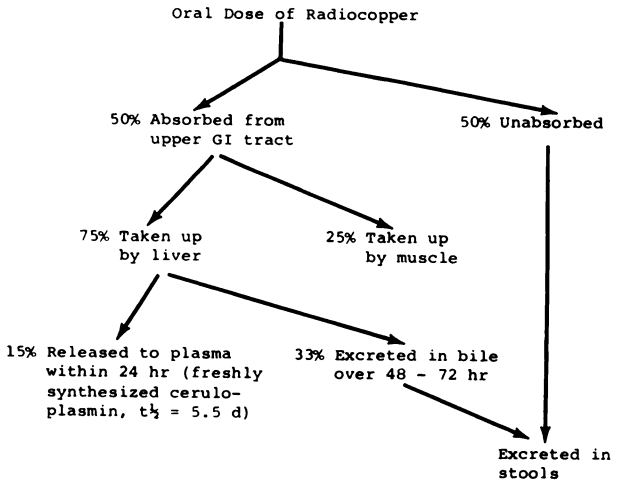

FIG. 3. Metabolic pathway of orally administered radiocopper.

the data available from the nuclear tables (*13*), are given in Tables 1 and 2. From the clearance pathways and biologic clearances from the major organs shown in Fig. 3, we calculated the effective half-lives of the activities for each organ and the cumulated activity values. The transit times of the contents through the gastrointestinal tract were estimated as 1, 4, 13, and 24 hr for stomach, small bowel, proximal and distal colon, respectively (*20*), for adults and children. The anatomic data for adults are derived from the MIRD model (*21*). The contents of the stomach, small bowel, and proximal and distal colon were estimated as 250, 400, 200, and 140 gm, respectively. Similar data for the children were obtained from Ref. *22* making the following assumptions regarding the anatomic data: body weight, 25 kg; liver, 710 gm; blood, 1,900 gm; bone marrow, 1,357 gm; stomach, 263 gm (contents, 93 gm); small bowel, 1,175 gm (contents, 270 gm); proximal colon, 290 gm (contents, 150 gm); distal colon, 196 gm (contents, 100 gm); and ovaries 3.4 gm. The muscle mass was assumed to comprise 43% of body weight for both adult and child. The data pertaining to the H/R (height/radius) values, equivalent radii, absorption radii, and absorption fractions are from standard sources (*21,22*). Doses for nonpenetrating radiation delivered by the gut contents to the wall of the small bowel were assumed to be equal to those of its contents whereas the dose delivered to the stomach and large gut walls were assumed to be half that of their respective contents (*20*).

Results and discussion. We have calculated radiation doses for several organs of an adult and of an 8-year-old child following oral and i.v. doses of ^{64}Cu and i.v. doses of ^{67}Cu. Results are given in Table 3. Obviously a larger fraction of the radiation dose affects the gastrointestinal tract following oral rather than intravenous administration of ^{64}Cu. In contrast, the bulk of the exposure following i.v. administration of ^{67}Cu affects the liver.

Vennart and Minski (*10*) reported a much lower dose to the liver based on a 2% uptake by the organ. However, if we use the available data regarding the hepatic uptake of copper and apply an upward correction to these authors' calculations, a dose value of 860 mrad is obtained. This is comparable to the dose we calculate for 500 μCi of ^{64}Cu administered orally. Moreover, our calculated values for ^{64}Cu and ^{67}Cu indicate that the doses to the various organs fall within accepted ranges for specialized nuclear medicine procedures (*23,24*).

TABLE 1. ^{64}Cu EQUILIBRIUM ABSORBED-DOSE CONSTANTS FOR PROMINENT ENERGY COMPONENTS

Radiation (i)	Mean Number/ disintegration n_i	Mean energy (MeV) (E_i)	Δ_i (gm·rad/ (μCi·hr)
β-1	0.38	0.19	0.1538
β-2	0.19	0.276	0.1117
Electron capture	—	—	—
Annihilation radiation	0.38	0.511	0.4136
γ-1	0.005	1.34	0.0143
$K_{\alpha-1}$ x-ray	0.084	0.0075	0.0013
$K_{\alpha-2}$ x-ray	0.04	0.0075	0.0006
K_{β}-x-ray	0.014	0.0083	0.0002

TABLE 2. ^{67}Cu EQUILIBRIUM ABSORBED-DOSE CONSTANTS: VARIOUS PROMINENT ENERGY COMPONENTS

Radiation (i)	Mean number/ distinte-gration (n_i)	Mean energy (MeV) (E_i)	Δ_i (gm·rad/ μCi·hr)
β-1	0.009	0.0512	0.00098
β-2	0.51	0.1106	0.1201
β-3	0.28	0.1355	0.0808
β-4	0.20	0.1616	0.0688
γ-1 and 2	0.23	0.092	0.0451
K int. conv. electron γ-1 and 2	0.18	0.082	0.0314
γ-3	0.40	0.184	0.1568
K int. conv. electron γ-3	0.0075	0.174	0.0028
γ-4	0.0009	0.209	0.004
γ-5	0.0062	0.300	0.004
γ-6	0.0018	0.394	0.0015
$K_{\alpha-1}$ x-ray	0.0463	0.0086	0.0008
$K_{\alpha-2}$ x-ray	0.0232	0.0086	0.0004
K_{β} x-ray	0.0079	0.0096	0.0002

TABLE 3. RADIATION DOSIMETRY OF ^{64}Cu and ^{67}Cu IN A 25-KG CHILD (8 YR) AND A 70-KG ADULT

Isotope and route of administration (Subject)	^{61}Cu/p.o. (Child)	^{67}Cu i.v. (Child)	^{61}Cu/p.o. (Adult)	^{61}Cu i.v. (Adult)	^{67}Cu i.v. (Adult)
Target organ	Radiation dose (mrad/μCi)				
Liver	2.62	22.7	1.05	2.10	8.84
Stomach	0.844	—	0.592	—	—
Small bowel	3.26	0.596	2.2	0.022	0.408
Proximal colon	2.99	1.56	1.99	0.042	1.04
Distal colon	2.95	3.38	2.08	0.044	2.40
Blood	0.292	1.69	0.103	0.16	0.595
Ovaries	0.144	0.102	0.128	0.132	0.0424
Testes	—	—	0.0232	0.0152	0.0063
Red marrow	0.0816	0.368	0.0292	0.0323	0.132
Muscle	0.0744	0.753	0.029	0.058	0.275
Whole body	0.118	0.256	0.046	0.047	0.107

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