Effects of Ionizing Radiation on the In Vivo Metabolism
of Monocarbon Fragment Precursors to CO$_2$

T. M. NGO and H. S. WINCHELL

Donner Laboratory, University of California, Berkeley, California, U.S.A.

Introduction

In the previous study, we have demonstrated that in vivo oxidation of the No. 2 carbon atom of the imidazole ring of histidine to CO$_2$ was inhibited following ionizing radiation [1]. This result postulated that ionizing radiation might interfere with monocarbon fragment transport by an in vivo inactivation of tetrahydrofolic acid or the enzymatic processes responsible for its production. The present study is a further evaluation of this finding. The rate of $^{14}$CO$_2$ excretion in the breath of rats given $^{14}$C-labeled formate, glycine, serine, and methionine was studied in rats prior to, and subsequent to, exposure of various doses of X-irradiation.

Material and Methods

Inbred male Buffalo rats (Simonsen Laboratory, Gilroy, California) weighing 230 to 250 g were used in all experiments. These animals had free access to food and water during the period of study.

In the first series of studies, 7 male rats were divided into 2 groups of 3 sham irradiated rats and 4 irradiated rats. The irradiated rats were subdivided further into 2 pairs of rats exposed to 400 to 600 R of X-rays. The source of X-rays for these experiments was an X-rays machine operated at 150 kVp and 15 mA and with an inherent filtration of 1 mm of aluminum and 1 mm of copper. Tube-target-distance was 10 inches. The dose rates, measured in air, were 15 to 27 r/min. Animals were studied at 20 minutes and then at 2, 5, 9, 16, and 21 days after sham irradiation or irradiation procedures. Each rat received 14 μCi of L-methionine-CH$_3$-$^{14}$C intravenously (specific activity: 14.77 mCi/mM, New England Nuclear Corp., 575 Albany Street, Boston, Massachusetts 02118, U.S.A.), after a light anesthesia with diethyl ether.

In the second series of studies, 16 rats were divided into 2 groups of 7 sham irradiated rats and 9 irradiated rats studied in groups receiving 400 and 600 R of X-rays. Irradiation procedure was similar to that has been described previously. Sham irradiated rats and irradiated rats were studied at 20 minutes and then at 3, 5, 7, 12, and 20 days after sham irradiation or irradiation procedure. In each study, the rat received 2.5 μCi of L-glycine-$^{14}$C intravenously (specific activity: 5.0 mCi/mM, Nuclear Chicago, 333 H. Howard Ave., Des Plaines, Illinois 60018, U.S.A.).
In the third series of studies, 8 rats were divided into 2 groups of 4 sham irradiated rats and 4 rats given 400 and 600 R of X-rays. Sham irradiated and irradiated rats were studied in pairs after sham irradiation or irradiation and then studies were repeated at 3, 5, 9, 14, and 21 days later. In each study, the rat, after anesthetization with diethyl ether, received 2.5 μCi of L-serine-3-14C intravenously (specific activity: 8.5 mCi/mM, Nuclear Chicago).

In the fourth series of studies, 12 rats were divided into sham irradiated and irradiated groups. The first experiments were studied at 20 minutes and repeat studies were then performed at 2, 5, 9, 14, and 20 days after irradiation. In each study, the rat received 2.5 μCi of 14C-formate intravenously (specific activity: 4.62 mCi/mM, New England Nuclear Corp.).

In each study, immediately after the intravenous administration of the 14C-labeled material, 14CO₂ excretion was measured continuously by a breath analyzer (Fig. 1). The procedure for such measurement has been described previously [2-6].

![Diagram of the 14CO₂ breath analyzer](image)

**Fig. 1.** Diagrammatic representation of the 14CO₂ breath analyzer. The expired air is serially passed through a water absorber, an ionization chamber, an infrared CO₂ analyzer, a paramagnetic O₂ analyzer, and a flowmeter

**Results**

Fig. 2 presents representative curves showing the rate and appearance of 14CO₂ in the breath of 3 control rats (upper curve) and 2 rats 2 days after exposure to 600 R (lower curve) subsequent to the intravenous administration of L-methionine-CH₃-14C. The ordinate represents 14CO₂ excretion rate expressed as μCi per minute and the abscissa as time in minutes following intravenous injection of the 14C-labeled methionine. In the normal curve, each point represents the mean of the rate of 14CO₂ excretion of 3 control rats of the given time. The vertical bars through each point represent 1 standard error for the mean of this group. It is clear that there is a qualitative difference between the two 14CO₂ breath curves.

Fig. 3 presents composite data of the serial change in $T_{max}$, the time at which maximum rate of 14CO₂ excretion occurred in control and irradiated rats subsequent