

# EFFECT OF MICRODOSES OF COPPER ON TISSUE RESPIRATION OF THE RABBIT LIVER

E. S. Belozеров and L. A. Konovalova

UDC 612.26:612.35.015.31:546.56

Administration of microdoses of copper to healthy rabbits and rabbits with experimental toxic hepatitis caused by  $\text{CCl}_4$  stimulates the cyanide-sensitive link in tissue respiration of the liver.

\* \* \*

Trace elements play an important role in the mechanism of tissue respiration: iron and copper occur in the composition of cytochrome oxidase, responsible for the cyanide-sensitive link of tissue respiration, while manganese and magnesium are activators of enzymes in the tricarboxylic acid cycle of Krebs [2-4].

Changes in tissue respiration of the rat liver in chronic hepatitis have been described in the literature, notably a lowering of its general level [1].

The effect of microdoses of copper on the state of tissue respiration in acute experimental toxic hepatitis produced by subcutaneous injection of  $\text{CCl}_4$  was studied in the present investigation.

## EXPERIMENTAL METHOD

$\text{CCl}_4$  was injected on alternate days in a dose of 0.5 ml of a 40% solution in peach oil, each rabbit receiving 3 injections. Control rabbits received physiological saline on the same days.

Copper was given orally on the 7th day of the experiment in a dose of 100  $\mu\text{g}$  of the metal sulfate per 100 g body weight. The rabbits were sacrificed next day by decapitation.

Tissue respiration was determined in a Warburg apparatus at 37°. Ringer-Locke solution was used as the medium. The determination was carried out for 1 h. Respiration was expressed in  $\mu\text{l O}_2/\text{h/g}$  dry tissue.

Both qualitative and quantitative aspects of intracellular respiration were investigated in the Warburg apparatus. To study the quality of tissue respiration (ratio between cyanide-resistant and cyanide-sensitive links) a 0.0001 M solution of potassium cyanide was used as inhibitor.

Four series of experiments were carried out in the spring on chinchilla rabbits weighing 1.8-2.5 kg; intact rabbits (10), rabbits receiving microdoses of copper (10), rabbits with acute experimental hepatitis (10), and rabbits with experimental hepatitis and receiving copper (10).

## EXPERIMENTAL RESULTS

The results of the investigations of respiration as a whole and of the relationship between cyanide-resistant and cyanide-sensitive links are shown in Table 1.

The total level of tissue respiration of the liver from intact rabbits and rabbits with acute hepatitis was increased (Table 1), although the increase is not statistically significant. The relationship between cyanide-resistant and cyanide-sensitive links for these groups of animals varied. Under normal conditions, 85.9% of tissue respiration was effected by enzymes of the cyanide-resistant link, while under the influence of copper the relative importance of the cyanide-sensitive link of respiration increased.

---

Department of Infectious Diseases and Department of General Biology, Tyumen' Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR S. E. Severin.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 68, No. 11, pp. 43-44, November, 1969. Original article submitted July 8, 1968.

©1970 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.

TABLE 1. Tissue Respiration of Rabbit Liver

Rabbits	Total respiration (in $\mu\text{g}/\text{mg}/\text{h}$ )	Cyanide-resistant link (in %)	Cyanide-sensitive link (in %)
Intact	$1.57 \pm 0.15$	85.9	14.1
Receiving copper	$1.90 \pm 0.11$	69.4	30.6
With hepatosis	$1.80 \pm 0.12$	84.2	15.8
With hepatosis and receiving copper	$1.81 \pm 0.10$	64.1	35.9

The increase in  $\text{O}_2$  absorption in the liver of rabbits with hepatosis also was not significant. However, under the influence of copper, an increase in activity of the cyanide-sensitive link was observed.

The changes observed in the character of tissue respiration and, in particular, activation of the cyanide-sensitive link under the influence of biotic microdoses of copper both in intact animals and in animals with acute experimental toxic hepatosis, evidently was the result of the general physiological action of this trace element. Whatever the case, this phenomenon had nothing to do with the toxic action of the metal, for in response to its toxic action the cyanide-resistant link, concerned with adaptive reactions of the tissue, plays an increased role.

It can be concluded from the results of this investigation that tissue respiration in the liver of intact rabbits is effected principally by enzymes of the cyanide-resistant link. Administration of microdoses of copper to rabbits leads to qualitative changes in tissue respiration through an increase in importance of the cyanide-sensitive link. Copper acts in a similar manner on tissue respiration in the liver of animals with hepatosis.

#### LITERATURE CITED

1. N. Kh. Abdullaev, Pat. Fiziol., No. 3, 36 (1966).
2. A. I. Venchikov, Biotics [in Russian], Moscow (1962).
3. J. Horejsi, Fundamentals of Clinical Biochemistry in Internal Medicine [in Russian], Prague (1967).
4. E. E. Kriss and K. B. Yatsimirskii, Uspekhi Khimii, 35, No. 2, 349 (1966).