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Effect of carbon-disulfide intoxication on the levels of serum copper and ceruloplasmin

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With 1 table

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Carbon disulphide is widely used in many industrial processes as a solvent of fats, sulphur, oils, and most especially, in the xanthathion of cellulose for the preparation of viscose (10, 5). Carbon disulphide in vitro reacts with the amino group of the free amino acids and proteins extracted from the blood plasma or blood corpuscles to form thiocarbamate and thiozolidone (14). *Cohen* et al. (2) presented the hypothesis that chelation of copper ions by dithiocarbamate and thiozolidone, produced during the biotransformation of carbon disulphide in the body, disturbs cellular metabolism and leads to cell injury.

Copper is an essential component of several critical tissue oxidases as aminolevulinic acid dehydrase, dopamine beta oxidase, and monamine oxidase. The chelate thiocarbamate and thiozolidone make copper less available for essential enzyme function (16). Dopamine beta oxidase inhibitor was possible as it was blocked in vivo by diethdithiocarbamate (17).

Different authors also studied the effect of carbon disulphide on serum ceruloplasmin. *Andruszak* (1) reported that in men exposed to carbon disulphide the serum ceruloplasmin level was essentially the same as in controls. Serum copper and ceruloplasmin of rats were not affected by inhalation of 3 mg CS_2/l for 3 weeks, while inhalation of 0.1 mg CS_2/l for 13 weeks depressed blood serum copper and ceroloplasmin. Inhalation of 0.01–0.05 mg CS_2/l for 9 weeks increased excretion of copper in faeces (7).

The aim of the presented work is to study the levels of serum copper and ceruloplasmin changes after intramuscular injection of carbon disulphide in rats for different periods. Such changes might be of help in explaining such derangement due to carbon-disulphide intoxication.

Materials and methods

A. Experimental materials

The animals chosen for this work were the albino rats. The rats were maintained on a stock colony diet consisting of bread, milk, and carrots and were allowed to eat at libidum. The material of this study comprised 80 rats of both sexes weighing 150–200 gm, they were kept under observation for about 15 days before the onset of experiments to exclude any intercurrent infection.

Table 1. Levels of serum copper and ceruloplasmin in controls and carbon-disulphide-intoxicated rats.

Const.		Control	Carbon-disulphide intoxication					Stopp. inj.
			10 inj.	20 inj.	30 inj.	40 inj.	50 inj.	for 20 days
	Mean	97.0	112.0	107.0	86.0	71.0	65.0	79.0
Copper	S.E. ±	4.60	5.78	7.59	7.29	4.36	5.12	7.87
ug %	P	–	0.05	0.15	0.10	0.01	0.01	0.05
	Mean	437	471	451	342	284	258	318
Cerulopl.	S.E. ±	15.84	16.76	22.09	20.61	16.61	17.63	22.86
units	P	–	0.15	0.15	0.01	0.01	0.01	0.05

The rats were divided into six groups each of ten rats, and were daily intramuscularly injected with 0.05 ml of SC_2 in 0.02 ml olive kernel oil/rat over a period of 50 days. Every 10 days, one group was killed by decapitation and blood serum was collected for analysis.

Carbon-disulphide injection was stopped 20 days for group VI after the 50 injections of the experiment to test for the extent of regression of the developed biochemical derangements.

Twenty rats of the same weight were included fed on the same diet, injected with 0.2 ml olive kernel oil alone as controls. A number of these cgntrol rats were sacrificed on the same day on which the different groups gf rats receiving carbon disulphide were decapitated.

B – Methods

1 – Serum copper was determined by atomic absorption spectrophotometer method described by *Sinaha* and *Gabrieli*, (13).

2 – The cerculoplasmin oxidase activity was determined by the method of *Ravin* (11), which is based on the measurement of the rate of oxidation of p-phenylene diamine by ceruloplasmin.

Calculation used in the determination of ceruloplasmin

The conversion factor used by *Ravin* (11) is not applicable to this work, since the conditions are different. To obtain the whole figures, we adopted the method used by *Henry* et al., (8) in which the net optical density is multiplied by 1000, and ceruloplasmin expressed in units.

Results and discussion

The results of the present work indicate that in control rats the mean serum copper and ceruloplasmin were found to be 97.0 ± 4.60 μg% and 437 ± 15.84 units, respectively.

Intramuscular adiminstration of carbon disulphide for the different period caused a slight increase of serum copper and ceruloplasmin levels occurred on groups I and II. Their values were found to be lower in group III, and the decrease was aggravated by prolongation of intoxication.

The observed drop in serum copper and ceruloplasmin may result if restricted mineral uptake due to decreased food consumption as a sequence of loss of appetite. *El-Shobaki* et al. (6) observed the loss of appetite of rats under the effect of carbon-disulphide intoxication, while *Massoud*

et al., (9) found that the workers exposed to carbon disulphide developed general complaints including insomania, loss of weight, abdominal manifestation to gastric pain, palpable liver and spleen, and loss of appetite.

The chelating effect of dithiocarbamate and thiozolidone formed by reaction of carbon disulphide with amino groups of proteins or polypeptides (12) may be a contributing factor. The latter may cause copper ion to be non-available to the organism and may also facilitate its secretion from the kidney. It is worth mentioning that *Djuric* et al. (3) reported an increase in urinary copper content in workers exposed to carbon disulphide. Also, it has been reported that the sodiumazide metabolic test on urine in cases of carbon disulphide intoxication showed an increased metal excretion and metal shift as indicator of carbon-disulphide intoxication (16).

Carbon disulphide was shown to be a monoamine-oxidase inhibitor (17). Although the structure of the active sites of monoamine oxidase has not been entirely elucidated, yet it has been found that some monoamine oxidases contain copperpyridoxal complex. This is very interesting in connection with the finding that carbon disulphide produces copper deficiency.

Copper is incorporated with ceruloplasmin molecule in vivo only at the time of synthesis of the protein by the liver and not later, and the amount of copper incorporated daily into ceruloplasmin in a normal control corresponds closely to the amount of copper absorbed from the diet (15). The manifested histopathological changes in the liver of carbon-disulphide-intoxicated rats may be a contributing factor of abdominal manifestation as hepatomegaly, epigastric pain, loss of weight, and the associated loss of appetite (4). Therefore, the drop of copper levels is associated with decrease of serum-ceruloplasmin level.

Furthermore, by stoppage of dosage at 20 days following intoxication with 50 doses of carbon disulphide, there is a slight elevation in the levels of serum copper and ceruloplasmin, but their levels were still below normal, whereby the animals started to restore their appetite and started to improve. Such improvements in their aspect of copper metabolism may be due to the connection of the affecting factors to metal utilization as dietary supply diminished thiocarbamate and other toxicological action of carbon-disulphide doses.

Summary

Under the effect of carbon-disulphide intoxication on the experimental animals, a significant decrease in serum copper and ceruloplasmin levels was observed. The decrease was aggravated with prolongation of carbon disulphide intoxication due to loss of appetite, formation of chelating compounds with carbon disulphide metabolites and increased loss of copper in urine. However, reinvestigated at 20 days after stoppage of dosage, most of these derangements started to be alleviated.

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