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COPPER

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Abstract
Many papers have been published regarding copper deficiency. Whatever it may be the copper nutrition field requires a blockbuster, large-scale,broad-scope and copper supplementation study. In this chapter, copper deals with metabolism, Bio availability from foods and supplements and toxicity

Introduction
Copper is responsible for the action of many enzymes such as tyrosinase (melanin synthesis), Cytochrome C oxidase (energy creation), lusyl oxidase (cross-linking collagen), superoxide dismutase (anti-oxidant), dopamine hydroxylase (synthesis of nor adrenaline). Copper circulates on ceruloplasmin which enhance as part of the acute phase response. Regarding clinical aspects, copper shows microcytic anemia, neutropenia and osteoporosis. More zinc consumption can precipitate copper deficiency (via metallothionein synthesis which chelates copper).

Literature Survey

1) Clinical Biochemistry - Lecture Notes) Wiley Black well Publication)
2) Handbook of Minerals as nutritional supplement

Methodology

Copper

Copper plays a role in certain metallo enzymes by cycling between +2 and +1 charges to donate electrons to a substrate. Some of a very few copper enzymes and their functions are given in Table 6.1. Ceruloplasmin plays a double role regarding enzyme function as well as serum copper transport. There are some symptoms of copper deficiency that have been mismatched to lowered activity of a specific copper metalloenzyme. Examples of such symptoms are impairment of

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immune function and an abnormal cholesterol metabolism. In the later case, part of the story might be super oxide 2 , Which removes superoxide o. Super oxide alters the activity of an enzyme participated in cholesterol synthesis.

Role of copper in metabolism

An absorption of copper primarily takes place in upper intestine. The major interference with this process is related to the more consumption of oral zinc. In the part, the mechanism for zinc or antagonism of copper absorption was related to the involvement, particularly in the protein metallothionein. Latest work with METALLOTHIONEIN remove out mice have demonstrated that this is not the major mechanism. After the absorption of copper, its metabolism is linked to the restricting free movement of copper. This shows a beneficial effect because the redox properties of free copper like those of iron lead to occurrence of damage regarding oxidant reactions. According to laboratory animal work, if copper enters the body with the help of diet or injection, it is removed in a fast manner from the blood and enters the liver and kidney, the 2 main copper storage sites. The liver can place copper into metalloenzymes, remove copper via bile stores, this mineral bound to the protein metallothionein, (which also happens in the kidney, and to some extent in other tissues) or secreted back into the blood. The protein ceruloplasmin shows an enzymatic activity as well as transportation of copper to other tissues. Receptors for ceruloplasmin have been observed on tissue samples and cultured cells. These receptors release copper from ceruloplasmin, which is recollection of iron uptake from transferrin, but the copper uptake process exhibits some differences from iron. In spite of these findings on ceruloplasmin receptors, copper transport autonomous of ceruloplasmin can also be demonstrated. Once inside extra- hepatic cells, copper attaches with chaperone proteins with the help of a process that is accumulating substantial research attention.

Assessment of copper regarding nutritional Status.

Heavy copper deficiency can be identified by low values for serum copper or enzyme activity of Cruloplasmin which consists of most of the copper in serum. ceruloplasmin protein values can be influenced by copper status, since copper- poor, ceruloplasmin breaks down in a faster manner than normal. Whatever it may be, during deficiency ceruloplasmin protein values decrease a little less than does ceruloplasmin activity. One problem with identifying more copper deficiency using serum copper or ceruloplasmin values is that Wilson's disease, a genetic disorder of copper toxicity, also leads to the occurrence of low values for serum copper and ceruloplasmin. Generally, in severe copper deficiency anemia and low neutrophil counts often happen. The utility of serum copper or ceruloplasmin values is not ideal because value do not always fall quickly or consistently with marginal copper deficiency. Whatever it may be, values can be influenced by other factors, namely inflammation, menstrual state, oral contraceptive, pregnancy and other physiological stress. A number of other measurements have been identified as alternate for estimating marginal copper deficiency.

Table 6.2

Parameters proposed for assessment of moderate copper deficiency.

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- Ceruloplasmin activity to protein ratios.
- Erythrocyte superoxide dismutase activity.
- Plasma or serum diamine oxidase activity.
- Platelet cytochrome C oxidase activity.
- White blood cell copper.

Dopamine hydroxylase	Make norepinephrine
Diamine oxidase	Degradation of poly phenols
Lysyl oxidase	Cross link collagen and elastin in connective tissue
Tyrosinase	Melanin formation
Peptidyl glycine alpha-amidating mono oxygenase	Neuropeptide activation
Others	Copper is likely part of some other enzymes.

Diamine oxidase **a**ctivities should not be utilised, particularly during pregnancy as well as kidney problems, because both conditions greatly Influence serum diamine oxidase activity values. On the other hand, these values are suitable for healthy non- pregnant subjects provided copper supplements.

Effect of Copper on Bioavailability from Foods and Supplements:-

Copper absorption from foods has not been elucidated compare to iron or zinc. Copper absorption from foods is not inhibited by phytate compare to some other minerals. Animal proteins may enhance copper absorption, even though foods like dairy products and beef do not yield more percent of the copper RDA. In the US vegetarian diets often consist of more copper than meat- inclusive diets, but the absorption of copper appears to be lower particularly in meatless diets. An exception to this pattern may be diets that are more in soya products. Soy protein consists of a good amount of copper that seems to be well absorbed, but considerable amount must be eaten to have a vital impact on daily copper intake. In this authors work, subjects with the consumption of 40g of soy protein per day for three to four weeks manifested an enhancement in activities for the copper enzyme diamine oxidase (unpublished effects). Heavy -dose Vitamin C generally decreases copper absorption. This appears to be true in experimental animals provided very high vitamin C doses, but these doses greatly exceed what people typically take, even as so -called mega doses. In human experiments, vitamin C supplements can decrease ceruloplasmin activity. Whatever it may be, in at least some of these cases, this may be quickest effect of vitamin C on ceruloplasmin enzyme activity, rather than decreased copper absorption. The significant known impact on copper absorption from foods is

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zinc supplementation. High- dose zinc supplements can cause severe copper deficiency. High dose iron supplements may pose a problem, even though this has not been given more study like zinc. To complicate matters, some doses of iron, particularly in some circumstances, may enhance good copper status.

Latest Research on Supplementation Use:-

The main existing studies are listed in table 6.3

Table 6.3

Copper supplementation trails

Subject	**Complex**	**Outcome**
Young adult women	Glycinate	2 Cu enzymes up. Oxidant stress markers down
Normal adults	Glycinate	Various Cu enzymes up
Normal adults	Glycinate	Erythrocyte superoxide dismutase up
Rheumatoid arthritis	Glycinate	Erythrocyte superoxide dismutase up
Cystic fibrosis patients	Glycinate	No effect 3 Cu enzymes
Adults (high cholesterol)	Not stated	Reduce serum cholesterol
Males (high cholesterol)	Glycinate	No effect Cholesterol varied effect with analysis on 2 Cu enzymes, lipoprotein oxidation
Young adult men	Sulfate	No depression in total serum cholesterol
Young adult women	Glycinate	Erythrocyte superoxide dismutase up. No effect on sulfate bone markers
Post menopause women	Gluconate	Bone loss down

In experimental animals, a more number of studies reveal high serum cholesterol reading with copper deficiency. That observation is duplicated in a few humans, particularly fed a low -copper diet. Little information is available about how well copper supplementation can influence cholesterol readings in free living people. The practical consequences of copper supplementation for bone health in women is still not settled. A review article yields a nice theoretical basis for coppers importance for bone. Regarding theory, copper status shows its effects on bone structure via Lysyl oxidase, which influences the collagen in bone.Copper is also responsible for antioxidant superoxide dismutase enzymes, which remove superoxide, which can activate bone resorption. One experimental research work explains that copper reduces bone loss in post

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menopausal women, but the results are hard to interpret. For young adult women, 2 studies each provide negative results for copper supplementation effects on blood and urine markers for bone metabolism. In one experimental work, copper does not show any effect on 2 urinary markers of collagen degradation. Deoxy pyridinoline (DPD), a crosslink in collagen and type one collagen helical peptide. Whatever it may be, if a ratio of DPD to type one collagen helical peptide is examined, copper enhances this ratio. The deficiency of copper in cystic fibrosis is disappointing. These people are prone to a heavy marginal copper deficiency than is typical. One cause for the negative results may be that cellular copper uptake processes are damaged in these subjects. Possibly, a novel copper complex could be designed to treat this situation.

Toxicity:-

Based on the latest knowledge, copper supplementation at doses typically utilized by the public appear to be a safe unless they create GI track upsets. The present upper level for copper is 10 milligram, which is well beyond what is observed in any typical copper supplement. In a 12 week experimental work, a 10 milligram daily dose of copper produces no clear physical or clinical chemistry symptoms. In hypercholesterolemic post menopausal women, 12 weeks of supplementation of 3 milligram copper per day reduces lymphocyte proliferation when the cells are expelled from the body (the type of copper complex used is not matched). Nausea or any other GI tract disturbances can be an early symptom in so many people, particularly with copper poisoning. In fact, this author has observed from his own experience that some people get nauseated even from a 2 or 3 milligram copper dose if consumed on an empty stomach. Thus there is some built in protection against oral copper supplementation toxicity. Even so, this is not necessarily a final proof safeguard, since the study of 10 milligram copper per day as gluconate reports no more GI complications than Placebo. Most medical reports on copper toxicity are linked to environmental and occupational exposures or genetic condition Wilson's disease, rather than dietary copper intake or high dose supplementation. There has been some supposition that moderately high copper consumption can advance breast cancer as well as cardiovascular disorder. One argument for the later arises from an epidemiological linking of high serum copper with cardiovascular disorder, especially in Finland. Whatever it may be, these high serum copper values likely just denote physiological stress. Serum levels of Ceruloplasmin, which consists of nearly all serum copper, tend to hike with most any stress. This author has demonstrated that in rats, stress causes high serum copper or ceruloplasmin levels even with marginal copper deficiency. Another cause that copper sometimes enhance cardiovascular disorder is that copper ions and the copper protein ceruloplasmin can oxidise lipoproteins in vitro. Oxidised lipoproteins are responsible to enhance atherosclerosis, whatever it might be catalytic ally active , low molecular weight copper ion is normally absent from serum. Moreover, this authors explains that enhancement of ceruloplasmin levels in rats does not enhance lipoprotein vulnerability to oxidation. In addition to ceruloplasmin promotion of LDL oxidation, in vitro needs a loosely bound copper. This author and others explain that such loose copper is not treated as part of native ceruloplasmin and can be easily eliminated by serum albumin. This elimination should occur readily in the blood during real- life situations. It should be observed that in humans, a fairly more dose of (6 milligrams per day) does not enhance lipoprotein oxidation. Plus, in an experimental work, copper supplementation at reduced levels originally decreases lipoprotein

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oxidation in some people. The breast cancer issue is close to the cardiovascular issue in that there is an epidemiological linking of high serum copper with high risk of breast cancer. In this authors opinion, the most common copper supplement doses (one to 3 milligram per day) do not pose any known problems.

Conclusion

There are causes to trust that marginal copper deficiency is a problem in many people and that correction, as well as that by supplementation, can exhibit many health benefits. whatever it may be, this concept is still missing excessively many pieces of research puzzle to make important conclusions. Copper toxicity of supplements needs more research, even though at present no major disorders have been plainly identified for typical doses.

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