COPPER DEFICIENCY - a growing concern

When I travel around the country talking about Nutrigenomics, I am aware that many Clinicians are fearful of prescribing copper to their patients. I gather that this perception has largely arisen on the basis of hair mineral analyses. Just how reliable is this method of determining copper status is not known with certainty. Although I have used Hair Analysis in practice myself, there has always been a lingering doubt that what is in the hair is not reflective of the presence of various trace elements in critical biochemical processes. A reasonably recent (2008) paper, *Evaluation of the use of human hair for biomonitoring the deficiency of essential and exposure to toxic elements* comments on this very issue.

TRACE ELEMENTS AT THE CORE OF ANTIOXIDANT DEFENCES However, hair analyses aside, let’s not lose sight of the fact that copper in conjunction with zinc and manganese is an essential trace element for the Antioxidant enzyme, Superoxide dismutase (SOD). Without optimal function of SOD, it is not possible to optimise cellular function - *NO MATTER WHAT ELSE YOU DO!*

The Superoxide radical sits right up at the top of the redox chain - if it gets out of control because of inadequate antioxidant enzyme activity, the downstream consequences of oxidative stress can be catastrophic.

No other 'antioxidant' supplement can replace the function of SOD and in my personal opinion, the importance of trace elements in redox balance is often forgotten in favour of the latest (largely ineffective) superfruit or ascorbate-style supplement. This is what makes GliSODin such an important 'first line of defence' in the treatment/prevention of any condition.

FROM GliSODin to DefenCell One of the nutrigenomic ingredients in DefenCell is GliSODin, a potent inducer of the 3 Antioxidant enzymes, Superoxide dismutase (SOD), Glutathione peroxidase and Catalase.

Because these enzymes rely on the presence of adequate trace elements for their activity, DefenCell contains appropriate levels of zinc, manganese, copper and selenium. Some Practitioners feel uncertain about prescribing DefenCell because it contains copper; however new evidence shows that copper deficiency is more common than was once thought!\(^1,2,3\) Required only in trace amounts, deficiency can make various enzymes such as SOD non-functional.
COPPER DEFICIENCY AND ISCHAEMIC HEART DISEASE, ALZHEIMER’S AND OSTEOPOROSIS

The status of copper nutriture is a growing concern with reports of increasing incidence of copper deficiency globally. World expert on copper in human health and author of Clinical Nutrition of the Essential Trace Elements and Minerals: A Guide for Health Professionals, Dr Leslie Klevay expresses his concern that copper deficiency is being missed and that diseases such as Ischaemic Heart Disease, Osteoporosis and Alzheimer’s Disease are frequently associated with copper deficiency.

Excerpts from 3 papers on copper deficiency are shown as an Appendix for your interest - one by Klevay from 1994, another by him in 2011 and another 2011 paper by other researchers. The message is difficult to ignore! And why we continue include copper in DefenCell!

DO OUTDATED VIEWS ON COPPER NEED REVISITING?

It seems that out-dated views on copper in human health need to be reconsidered in light of new evidence; it appears too that the popularity of zinc supplementation has further contributed to copper deficiency states since copper and zinc compete for the same uptake carriers. Zinc is now included in so many formulae, so that if a patient is taking several supplements, the combined amount of zinc may exceed reasonable requirements; this can be enough to start the progression towards copper deficiency. A 2005 paper (free online) describes 3 cases of zinc-induced copper deficiency.

THE DefenCell FORMULATION - CORE PRESCRIPTION

DefenCell was carefully formulated to be used as the ‘Essential Daily’ supplement. No other supplement contains clinically-effective levels of nutrigenomic activators of cellular defences (GliSODin and EnduraCell), together with the trace elements necessary to activate these defences. In addition, Vitamin D, chromium, molybdenum, boron, iodine and biotin provide those nutrients so often shown to be deficient.

This makes DefenCell an important CORE Formulation in the same way that we used to think a multivitamin supplement was something everyone should take. DefenCell capsules are smaller than most and with a recommended dose of 2 capsules daily, smaller doses are readily possible for the younger members of the family.

REFERENCES (including Abstracts)


(Page 1 of each paper highlighted and shown below)
Invited review

Is the Western diet adequate in copper?

Leslie M. Klevay

Abstract

Copper has been known to be essential for health for more than three quarters of a century. Myriad experiments with animals reveal that the cardiovascular, musculoskeletal and nervous systems are most sensitive to deficiency. Copper in the Western diet has been decreasing at least since the 1930s; half of the adult population consumes less than the amount recommended in the European Communities and the United Kingdom. At least one fourth of adults consume less than the estimated average requirement published for the United States and Canada. Hundreds of people have been reported in journals about medicine and neurology rather than nutrition to have impaired copper nutrition based on the criteria of low copper concentrations and low activities of enzymes dependent on copper in various fluids and tissues. In contrast, only 46 people have participated in depletion/repletion experiments needed to define requirements. Almost 1000 people have benefited from supplements containing copper in controlled trials. People deficient in copper are being identified increasingly; it is unknown if unusually high requirements or unusually low diets are causal. Alzheimer’s disease, ischemic heart disease and osteoporosis are the most likely human illnesses from low copper intakes.

Introduction

Western diseases are seemingly new, having reached epidemic prevalence only in the 20th century [1–3]. These diseases, diabetes mellitus, essential hypertension, ischemic heart disease, obesity and osteoporosis among them, are associated with affluence and industrialization. No simple, single word totally and exclusively
Invited review

Risks and benefits of copper in light of new insights of copper homeostasis

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ABSTRACT

Copper is an essential micronutrient involved in a variety of biological processes indispensable to sustain life. At the same time, it can be toxic when present in excess, the most noticeable chronic effect being liver damage. Potent, efficient regulatory mechanisms control copper absorption in the digestive tract and copper biliary excretion; absorption ranges between 12 and 60% in humans, depending on Cu intake, presence of other factors in the diet that may promote or inhibit its absorption and on the copper status of the individual. Current evidence suggests that copper deficiency may be more prevalent than previously thought, while copper toxicity is uncommon under customary daily life conditions. Menkes syndrome and Wilson disease are genetic conditions associated with severe copper deficiency and severe copper toxicity, respectively. Effects of milder degrees of copper deficiency and excess copper exposure are not well described, mainly due to lack of sensitive and specific indicators; serum copper concentration and ceruloplasmin are the most frequently used indicators, but they only detect rather intense changes of copper status. Of the many proteins assessed as potential markers of copper status the chaperone of Zn-Cu superoxide dismutase (CCS1) has yielded promising results; data on its performance under different conditions are needed to confirm its use as an indicator of early copper deficiency. Defining copper requirements and upper safe limits of consumption (UL) is a complex process since there are adverse health consequences from both copper deficiency and copper excess (U shape curve). The regulatory framework for risk assessment of essential trace elements introduced by the International Programme on Chemical Safety (IPCS) has proposed a homoeostatic model to determine the Adequate Range of Oral Intake (AROI) of essential trace elements; the nadir of the resulting U shape curve serves to define the AROL. At this range of intake physiological mechanisms allow for normal homeostasis and basically, there are no detectable adverse effects. At present, Recommended Dietary Intakes (DRIs) and Adequate Intakes (AIs) are used to recommend copper intakes at different ages and life situations. Evidence obtained in humans and non-human primates presented here suggest that current copper UL should be re-evaluated.

Developing the scientific basis for a copper UL and evaluating the relevance of copper deficiency globally are future key challenges for copper researchers.

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Abbreviations: Cu, copper; ATP7B, copper transporting beta polypeptide; hCTR1, human copper transport protein 1; DMT1, divalent metal transporter 1; MT, metallothionein; ATP7A, copper transporting alpha polypeptide; GSH, reduced glutathione; CCS1, copper chaperone for Cu/Zn superoxide dismutase; SOD1, superoxide dismutase; ESTAD1, Estimated Safe and Adequate Daily Dietary Intake; NHANES III, Third National Health and Nutrition Examination Survey; EC, European Community; Cp, ceruloplasmin; ICD, Indian Childhood Cirrhosis; ICP, Hepatic Primary Cirrhosis; WHO, World Health Organization; IOM, Institute of Medicine; DRIs, dietary reference intakes; EAR, estimated average requirement; RDA, recommended dietary allowance; AI, adequate intake; UL, tolerable upper intake level; SCF, Scientific Committee for Food; LT, lowest threshold intake; AR, average requirement; PRI, population reference intake; IPCS, International Programme on Chemical Safety; AROI, adequate range of oral intake; RNI, recommended nutrient intake; ATSDR, Agency for Toxic Substances and Diseases Registry; MRI, oral minimum risk level; NOAEL, no observed adverse effect level; LOAEL, lowest observed adverse effect level.

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Copper: an antioxidant nutrient for cardiovascular health

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Dietary copper often is low in the Western diet; low intakes may affect all stages of atherosclerosis adversely. Impaired oxidative defense in copper deficiency contributes to hypercholesterolemia, hypertension, and impaired prostaglandin metabolism. Free copper ion does not exist in vivo; some in vitro experiments are conducted with millions-fold excesses.

Current Opinion in Lipidology 1994, 5:22–28

Introduction

Approximately one-third of the elements in the periodic table have been related to the atherosclerotic process [1–3,4**]. One-third of these elements, in turn, produce relevant biological effects by enhancing or inhibiting copper [4**]. Copper will be emphasized here for the sake of both brevity and unity because of its importance to many (perhaps all) of the temporal stages of atherosclerosis (vide infra). Three major consequences of copper deficiency — hypercholesterolemia, hypertension, and thrombosis — are the result of impaired defense against oxidative damage.

Copper and lipid metabolism were linked 20 years ago when excessive zinc ingestion induced mild copper deficiency and hypercholesterolemia in rats [5,6,7**]. Hypercholesterolemia from copper deficiency without excess zinc [8] has been confirmed in many laboratories and several species and is generally accepted [9,10]. Since then, nearly 70 anatomical, chemical, and physiological similarities between animals deficient in copper and people with ischemic heart disease have been collected [11,12**]—from hundreds of experiments published since 1928, when copper was shown to be an essential nutrient [13]. The first adverse effects of copper deficiency on the cardiovascular system were found little more than 10 years later [14,15]. Recently, men and women have been found to respond to diets low in copper, with potentially harmful changes in lipids [16,17], glucose tolerance [18], blood pressure [19], and electrocardiograms [16,20].

The Western diet so closely associated with heart disease risk seems to be low in copper [11,21**]. Data from 10 dietary surveys were evaluated [11] and pooled [21**]. One-third of the chemically analysed diets contained less than 1 mg of copper/day and 61% contain less than 1.5 mg/day, which is the lower limit of the estimated safe and adequate intake in the USA [22].

The ready accessibility to diets low in copper, the numerous similarities between animals deficient in copper and people with ischemic heart disease, and the finding that people and animals respond similarly to diets low in copper have contributed to the copper deficiency theory of ischemic heart disease. This theory is consonant with much epidemiology and some iatrogenic maneuvers and experiments of nature [11,12**,23,24,25**].

Atherosclerosis begins very early in life [26,27]; its pathogenesis [28,29] involves an early accumulative stage when monocyte-derived macrophages acquire lipid to form foam cells. Foam-cell formation (lipid-laden macrophages) leads to development of the fatty streak, the earliest lesion of atherosclerosis and the progenitor of the mature occlusive lesion. These early inflammatory and later proliferative stages are part of a continuum of pathological change. The accumulation of lipid by macrophages involves oxidative damage to LDL by peroxidation of lipid components and modification of apolipoprotein B such that its interaction with the classical LDL receptor is impaired. Macrophages, however, express a scavenger receptor (the modified LDL receptor), which results in unregulated accumulation of modified LDL lipid components [30].

Copper as an antioxidant

The antioxidant role of copper resides in its catalytic function in copper-dependent superoxide dismutase [31]. Both cytosolic and extracellular copper-dependent superoxide dismutase activities have been characterized [32,33]. Enzyme activity can be decreased by diets low in copper [23,34].

Saari and Johnson [35,36] were the first to notice that antioxidants could decrease or prevent some of the

Abbreviation

HMGCoA—3-hydroxy-3-methylglutaryl coenzyme A.