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AN AUTHORITATIVE REFERENCE SOURCE

Handbook of Copper Pharmacology and Toxicology, 1st Edition, *Edited by* Edward J. Massaro. Hard Bound, 7" x 10".
Humana Press Inc., 999 Riverview Drive, Suite 208, Totowa, New Jersey 07512; Publication Date 8 July, 2002. xvi + 608 pages, ISBN 0-89603-943-9 (acid-free Paper). Price $175.00

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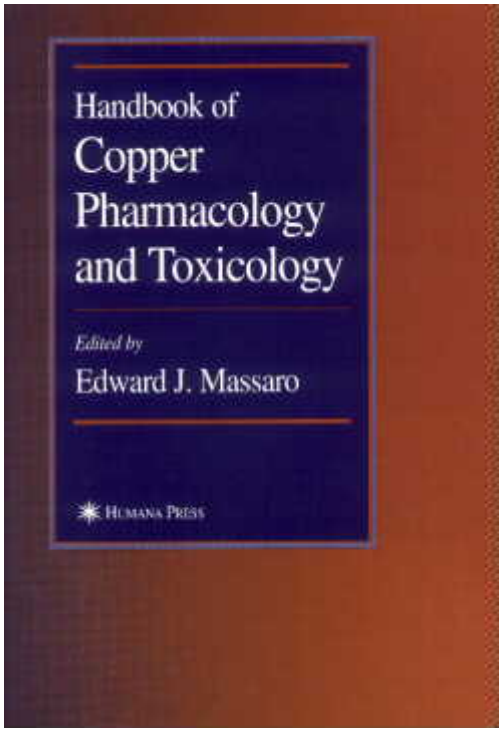

Copper is an essential trace element, and is in fact a normal constituent of the human body. It is present in serum in two forms - one which is bound to albumin (7% of total serum copper), and one which is bound to the copper enzyme caeruloplasmin (93%). Urine normally contains only traces of copper (5 to 25 mg/day).

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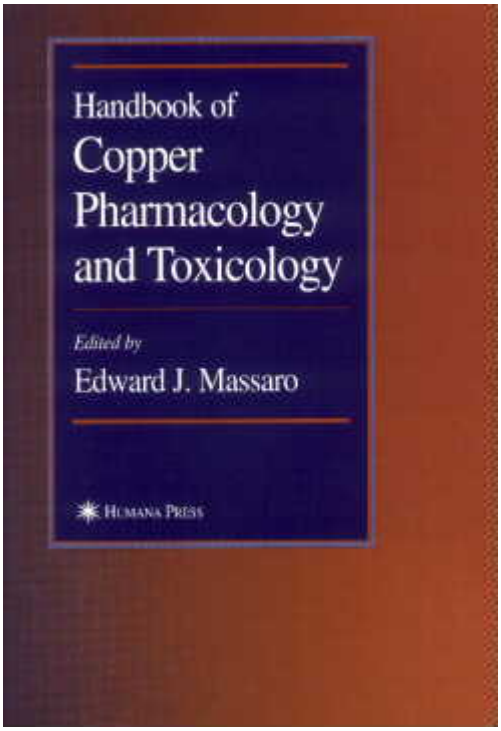
About 0.1 to 1.3 ng of copper is excreted through the bile daily and lost in the faeces. Total body copper content is 150 mg. Copper can be absorbed through gastrointestinal mucosa, and from intact skin.

Publisher's blurb



Although copper is an essential trace element necessary for the survival of organisms ranging from bacteria to mammals, it is also highly toxic and must be absorbed by the body in precisely orchestrated biological processes. In *Handbook of Copper Pharmacology and Toxicology*, Edward I. Massaro and a panel of leading biomedical researchers and clinical practitioners review, in-depth, the status of our current knowledge concerning the biochemistry of copper in general, and its role in health and disease in particular. Drawing on the wealth of new information emerging from the molecular biology revolution, these experts survey the most important research areas of copper pharmacology and toxicology, including copper proteins and transport, copper toxicity and therapeutics, and copper metabolism and homeostasis. They also discuss the molecular pathogenesis of copper in a variety of metabolic diseases - Menkes and Wilson's diseases and occipital horn syndrome - as well as the role of copper in Parkinson's disease, prion disease, familial amyotrophic lateral sclerosis (ALS), and Alzheimer's disease. The elucidation of the precise mechanisms of copper trafficking, metabolism, and homeostasis will be of considerable importance in understanding the pathophysiology and treatment of such diseases.

Comprehensive and timely, the Handbook of Copper Pharmacology and Toxicology authoritatively provides researchers with all the up-to-date information needed to work productively in copper biology today.

Features

- Up-to-date, in-depth review of the wealth of new research findings on copper biology
- Discussion of the molecular pathogenesis of diseases of copper metabolism
- New insights into the role of copper in ALS, Parkinson's, and Alzheimer's disease
- Review of the mechanisms of copper trafficking, metabolism, and homeostasis

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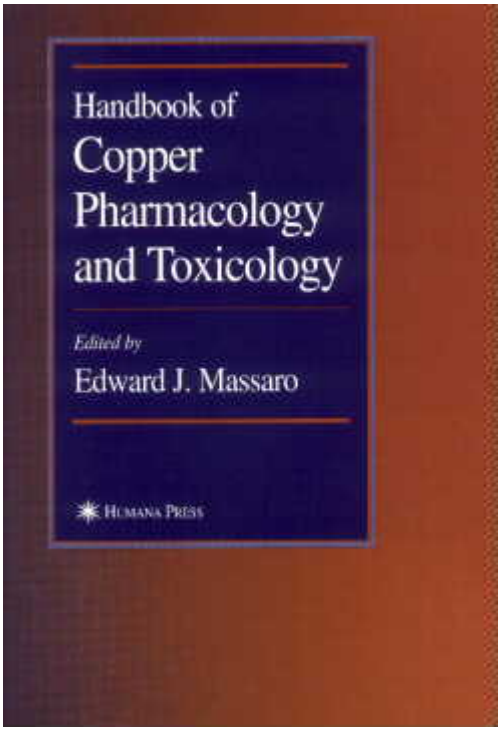
Because copper ions can adopt distinct redox states, they play an important role in cell physiology as cofactors in the redox chemistry of enzymes involved in a wide array of biological activities, for example, mitochondrial respiration, iron absorption, collagen and elastin crosslinking, and free radical scavenging.

The safe daily intake of dietary copper is 2 to 3 mg/day, while the actual requirement is only 0.8 mg/day. It is well known that copper plays a vital role in the functioning of the nervous system. The neurodegenerative phenotypes of Menkes and Wilson's diseases underscore the essential nature of this metal in nervous system development, and the consequences of disturbance of neuronal copper homeostasis. Also, inherited deficiency of caeruloplasmin is associated with progressive neurodegeneration of the retina and basal ganglia. Recent studies have also indicated the involvement of copper in the pathogenesis of Alzheimer's disease, prion-mediated encephalopathies, etc., which emphasize the need for further elucidation of the mechanisms of copper metabolism, particularly within the nervous system.

Contents



I. Copper in Mammals. Biochemistry and Molecular Biology of Copper in Mammals.
II. Copper Proteins. Biochemistry of the Wilson's Disease Protein. Biologically Relevant Properties of Copper-Containing Proteins Analyzed by Means of Semiquantitative and Quantitative Theoretical Descriptors. Molecular Modeling and Dynamics of Copper Proteins. The Prion Protein and Copper: What Is the Connection? Prion Protein: A Synaptic Cuproprotein. Cytochrome-e Oxidase. The Fet3 Protein: A Multicopper Ferroxidase Essential to Iron Metabolism in Yeast. Interaction of Copper-Binding Proteins from *Enterococcus hirae*.
III. Copper Transport. Copper Uptake in Eukaryotic Cells. The Role of PINA in Copper Transport, Circadian Rhythms, and Wilson's Disease. The Identification of Motifs Involved in the Intracellular Trafficking of the Menkes Disease Protein. Intracellular Copper Transport and ATP7B, the Wilson's Disease Protein. A Multicopper Oxidase-Based Iron-Transport System in Yeast.
IV. Molecular Pathogenesis of Diseases of Copper Metabolism. Molecular Basis of Diseases of Copper Homeostasis. Disturbances of Copper Homeostasis and Brain Function. Role of Copper and Other Transition Metal Ions in the Pathogenesis of Parkinson's Disease, Prion Diseases, Familial Amytrophic Lateral Sclerosis and Alzheimer's Disease. Molecular Genetics and Clinical Aspects of Menkes Disease and Occipital Horn Syndrome. The Meaning of Alternative Transcripts of the Menkes Disease Gene. Expression Profiling in Menkes Disease. Regulation by Copper of the Expression of Human Bis, a New Gene Involved in the Cellular Stress Response to Metals. Non-Indian Childhood Cirrhosis: Using a Founder Population to Identify the underlying Genetic Defect.
V. Copper Toxicity and Therapeutics. Biological Effects of Chronic Copper Exposure. Copper Toxicity to Tight Junctions in the Human Intestinal Caco-2 Cell Line. Cellular Responses to Copper in Aquatic Organisms: *Importance of Oxidative Stress and alteration of Signal Transduction*. Selective Removal of Copper Accumulating in the Form Bound to Metallothionein by Tetrathiomolybdate. Control of Copper in Wilson's Disease and Diseases of Neovascularization, such as Cancer. Copper-Rich Metallothionein Polymers During the Development of Fulminant Hepatitis in LEC Rats: *Effect of D-Penicillamine*.
VI. Copper Metabolism and Homeostasis. Sensory Protein Modification: *A New Feature in Copper Balancing*. Comparative Analysis of Copper and Iron Metabolism in Photosynthetic Eukaryotes vs. Yeast and Mammals. Copper and the Morphological Development of *Streptomyces*. Molecular Hardware of Copper Homeostasis in *Enterococcus hirae*. Copper Homeostasis in Plants. The Role of Copper ions in Regulating Methane Monooxygenases in Methanotrophs. Regulatory Responses to Copper Ions in Fungi.

In the book under review, Edward J. Massaro leads a distinguished panel of experts to evaluate the current status of our knowledge relating to the biochemistry of copper in general, and its role in health and disease in particular. The panel, comprising over 90 researchers, presents its views on copper pharmacology and toxicology (including copper proteins and transport), copper toxicity and therapeutics, and copper metabolism and homeostasis. The experts on the panel also investigate the molecular pathogenesis of copper in a variety of metabolic diseases such as Menkes and Wilson's diseases, as well as the role of copper in diseases such as familial amyotrophic lateral sclerosis, Parkinson's disease, prion disease, and Alzheimer's disease.

The book is divided into 6 sections (see table on left) dealing with various research areas, beginning with copper in mammals, biochemistry of copper proteins, and mechanics of copper transport, and

progressing to the molecular pathogenesis of copper-related diseases, toxicity and therapeutics of copper, and copper metabolism. Detailed discussions relating to these areas provide the reader with valuable insight into the current status of copper pharmacology and toxicology, and are well supported by recent references. Of particular interest to this reviewer are the sections on molecular pathogenesis of diseases of copper metabolism, and copper toxicity and therapeutics. In Wilson's disease, a copper toxicosis condition, and Menkes disease, a copper deficiency disorder, copper homeostasis is disturbed by genetic mutation. Wilson's disease is an autosomal recessive inherited disorder of copper metabolism resulting in accumulation of the element in many tissues and organs. The Menkes disease complex is characterized by abnormal neurodevelopment and connective tissue pathology that can precipitate premature death. Excessive intake of copper can also result in early childhood cirrhosis and idiopathic copper toxicosis. The pathophysiology of these conditions with particular reference to the role of copper has been extensively dealt with in the book. There is increasing evidence to suggest the involvement of this element in other conditions also, for example, oesophageal cancer. In fact a lot more research and study are required to delineate more clearly the role of copper in several diseases afflicting not only man, but lower animals as well. To that end, the Handbook of Copper Pharmacology and Toxicology serves as an excellent beginning that provides researchers and students with a view of the current status in this area.

Being a forensic toxicologist, this reviewer would have appreciated research work on acute and chronic toxicity of copper salts, in addition to elemental copper! While the incidence of copper salts (especially copper sulfate) poisoning has come down in recent times in India as compared to the situation that prevailed some years ago, it is still a matter of concern.

This impeccably produced book is an authoritative reference source containing all the up-to-date information needed to work on any aspect of copper biology.



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Dr.V.V.Pillay has been in the vanguard of the movement among medical professionals in India to develop the neglected field of Toxicology. He has published extensively in both the scientific and lay press on matters relating to Toxicology, as well as his chosen discipline - Forensic Medicine. Dr.Pillay has authored 6 books on Forensic Medicine and Toxicology, and has received an award for one of them (Modern Medical Toxicology), generally considered to be a trend setter among books on the subject in India. He has reviewed several books on Toxicology for the Internet Journal of Forensic Medicine and Toxicology. Dr.Pillay received a scroll of honour in appreciation of work done in the field of Toxicology from the Medicolegal Society, All India Institute of Medical Sciences, New Delhi. He has established a state-of-the-art Poison Control Centre, recognized by the World Health Organization at the institute

where he is currently employed (AIMS, Cochin). Among his most sought-after publications is a 700 page reference work on Toxicology.

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