

Contents

<i>Preface</i>	v
<i>Acknowledgment</i>	vii
<i>Contributors</i>	xv
1. Copper and Copper Alloys	1
<i>Harold T. Michels</i>	
Introduction	1
Copper: Properties of the Element	1
Pure Copper	2
Copper Alloys	2
Properties of Copper Alloys	2
Copper Alloy Families	4
The High Coppers	4
Conclusions	6
2. Corrosion Chemistry of Copper: Formation of Potentially Skin-Diffusible Compounds	7
<i>Jurij J. Hostýnek</i>	
Introduction	7
Electron Configuration and Reactivity of Copper	8
Corrosion of Copper in the Environment	8
Corrosion of Copper in Physiologic Media	9
Conclusions	15
Glossary	16
Abbreviations	16
References	16

3. Basics of Metal Skin Penetration:	
Scope and Limitations	21
<i>Jurij J. Hostýnek and Howard I. Maibach</i>	
Introduction	21
Structure of Skin and Its Function as Diffusion Barrier	23
Descriptors of Dermal Absorption	25
Permeant Categories and Paths of Diffusion	28
Compounds Formed by Metals in Contact with the Skin	31
Variables Determining Skin Diffusion of Metal Compounds	35
Methods for Measuring Percutaneous Absorption	45
Analytical Methods for Metal Detection	53
Summary and Conclusions	56
Abbreviations	57
References	58
4. Percutaneous Absorption of Copper Compounds	67
<i>Jurij J. Hostýnek and Howard I. Maibach</i>	
Introduction	67
Qualitative Diffusion Data	68
Semiquantitative Data	70
Quantitative Data	71
Discussion and Conclusions	73
Limitations in Measuring Copper Absorption In Vivo	74
Interdependence of Systemic Copper and Zinc Levels	75
Recommendations for Research to Fill Existing Data Gaps	76
Conclusions	77
Glossary	78
Abbreviations	78
References	79
5. Diffusion of Copper Through Human Skin	
In Vivo	81
<i>Jurij J. Hostýnek, Howard I. Maibach, and Frank Dreher</i>	
Introduction	81
Experimental	84
Results	85

Discussion	88
Conclusions	92
Glossary	93
Abbreviations	93
References	94
6. Irritation Potential of Copper Compounds	97
<i>Jurij J. Hostýnek and Howard I. Maibach</i>	
Introduction	97
Exposure to Copper	97
Solubilization of Copper Metal	98
Incidence and Epidemiology of Irritation Due to Copper	100
Pharmacology of Copper	101
Copper Irritancy in Skin and Mucosa	103
Conclusions	111
Abbreviations	112
References	112
7. Copper Hypersensitivity: Dermatologic Aspects—Overview	115
<i>Jurij J. Hostýnek and Howard I. Maibach</i>	
Introduction	115
Metallurgy of Copper and Its Alloys, and Its Role as Sensitizer	117
Predictive Immunology Test Results for Copper	119
Diagnostic Tests for Hypersensitivity	119
Test Concentrations for Copper ACD	123
Immunogenic Potential of Copper	123
Summaries of Population-Based Studies	134
Summary of Selected Case Reports of Immune Reactions to Copper	138
Selection of Individual Reports of Immune Reactions to Copper	138
Comments	140
Conclusions	140
Abbreviations	141
References	141

8. Copper in Medicine and Personal Care:	
A Historical Overview	149
<i>Roberto Milanino</i>	
Introduction	149
The Sumeric Culture: Circa 4000–2300 B.C.	150
The Ancient Egyptian Culture	150
The Babylonian–Assyrian Culture:	
Circa 1750–539 B.C.	152
The Ancient Indian Culture: Circa 2800–1000 B.C.	152
The Ancient Chinese Culture: Circa 3000 B.C.	
to 1100 A.D.	152
The Pre-Columbian Meso- and South-American Cultures:	
Circa 600 B.C. to 1500 A.D.	153
The Ancient Greek Culture	153
The Ancient Roman Culture: Circa 600 B.C.	
to 476 A.D.	155
From the High-Medieval Age to the Early	
20th Century	156
Beginning of the Scientific Age for Copper:	
1928–1976	157
Conclusions	158
Abbreviations	159
References	159
9. The Role of Copper in Onset, Development, and	
Control of Acute and Chronic Inflammation	161
<i>Roberto Milanino</i>	
Introduction	161
Studies on Copper-Deficient, Experimentally	
Inflamed Animals	163
Laboratory Animals: Studies on “Endogenous” Copper	
Metabolism in Acute and Chronic Inflammation	170
Human Subjects: Studies on “Endogenous” Copper Metabolism	
in Acute and Chronic Inflammations, with a Particular	
Reference to Rheumatoid Arthritis	179
Effects of “Exogenous” Copper Administration on the	
Inflammatory Process	184
Copper Anti-inflammatory Activity: Hypotheses Explaining	
the Possible Mechanisms of Action	203
Conclusions	216

Abbreviations	219
References	220
10. Copper Jewelry and Arthritis	237
<i>Brenda J. Harrison</i>	
Introduction	237
The Copper Bracelet “Myth” and Hypothesis	239
The Copper Bracelet Trial	243
The Present State of the Copper Bracelets “Issue”	251
Is There Likely to Be a Future for Copper Bracelets in Arthritis Care?	256
Appendix A: Position Statements of Support Organizations, Government Agencies, Etc.	257
Appendix B: Miscellany	259
References	261
11. Role of Copper in Anti-inflammatory Therapy and the Potential for Its Transdermal Application	267
<i>Jurij J. Hostýnek and Roberto Milanino</i>	
Introduction	267
Traditional and Modern Therapies for RA and Related Disorders	268
Drug Therapy	271
Precedents in Topical Delivery of Anti-inflammatory Agents	275
Role of Copper in AI Activity	275
Past Use of Copper Chelates in the Treatment of Rheumatoid Arthritis	278
Transdermal Delivery of Anti-inflammatory Copper Chelates vs. Conventional (Systemic) Anti-inflammatory Therapy	278
Conclusions	286
Outlook	288
Abbreviations	288
References	289
<i>Index</i>	<i>295</i>