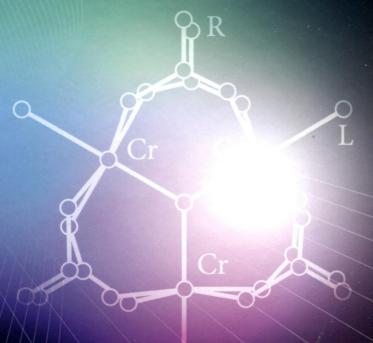


BIOINORGANIC CHEMISTRY OF CHROMIUM





The Bioinorganic Chemistry of Chromium

John B. Vincent

Department of Chemistry, The University of Alabama, Tuscaloosa, Alabama, USA This edition first published 2013 © 2013 John Wiley & Sons, Ltd

Registered office

John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, United Kingdom

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com.

The right of the author to be identified as the author of this work has been asserted in accordance with the Copyright, Designs and Patents Act 1988.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by the UK Copyright, Designs and Parents Act 1988, without the prior permission of the publisher.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book. This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is sold on the understanding that the publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The publisher and the author make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of fitness for a particular purpose. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for every situation. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of experimental reagents, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each chemical, piece of equipment, reagent, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the publisher nor the author shall be liable for any damages arising herefrom.

Library of Congress Cataloging-in-Publication Data

Vincent, John B. (John Bertram)

The bioinorganic chemistry of chromium / John B. Vincent.

p. : cm.

Includes bibliographical references and index.

ISBN 978-0-470-66482-7 (cloth)

I. Title.

[DNLM: 1. Chromium-chemistry. 2. Chromium-therapeutic use.

3. Chromium-toxicity. QV 290]

615.2532-dc23

2012022691

A catalogue record for this book is available from the British Library.

Cloth ISBN: 9780470664827

Typeset in 10.5/13pt Sabon by Aptara Inc., New D

Printed in Malaysia by Ho Printing (M) Sdn Bhd

Contents

Preface			ix
A	knov	vledgements	xiii
1	Introduction – The Current Status of Chromium(III)		
	Refe	erences	5
2	Is C	hromium Essential? The Evidence	7
	2.1	'Chromium-Deficient' Diet Studies with Rats	9
	2.2	Total Parenteral Nutrition	11
	2.3	Chromium Absorption Versus Intake and the	
		Transport of Chromium by Transferrin	12
•	2.4	Chromium Movement Related to Stresses	21
	Refe	erences	25
3	The Story of Glucose Tolerance Factor (GTF)		
	3.1	The 'Identification' of GTF	31
	3.2	Brewer's Yeast 'GTF'	35
	3.3	Biological Activity Assays	39
	3.4	Porcine Kidney Powder 'GTF'	40
	3.5	Other Questions Regarding 'GTF'	40
	3.6	Conclusions about GTF	41
	3.7	The Race to Synthesize a Model of 'GTF'	42
	3.8	Related Animal Studies	43
	Refe	erences	10

vi CONTENTS

4	Is Chromium Effective as a Nutraceutical?						
	4.1	1 Chromium Picolinate Absorption					
	4.2	History of Chromium Picolinate as a Nutritional					
		Supple	ement	57			
	4.3	Chron	Chromium Picolinate Toxic Effects?				
	4.4	Inorga	anic Chemistry of Chromium Picolinate	73			
	Refe	erences		75			
5	Is Chromium(III) Effective as a Therapeutic Agent?						
	5.1	Huma	nn Studies	85			
		5.1.1	Type 2 Diabetes	85			
		5.1.2	Subjects with Insulin Resistance or Glucose				
			Intolerance	98			
		5.1.3	Other Forms of Diabetes	98			
		5.1.4	Atypical Depression and Related				
			Conditions	99			
		5.1.5	HIV and PCOS	101			
	5.2	Rat Studies					
	5.3	5.3 Conclusion					
	References						
6	Biochemical Mechanisms						
	6.1	6.1 The Insulin Signalling Pathway					
	6.2	Chron	nium Transport and Excretion	127			
	6.3	LMW	Cr/Chromodulin	132			
	6.4	Synthe	etic Models of LMWCr	144			
	6.5	Propo	Proposed Mechanisms of Chromium Action				
		6.5.1	Direct Chromium Binding to Insulin				
			Receptor	149			
		6.5.2	Akt	151			
		6.5.3	Cholesterol	152			
		6.5.4	Chromate	152			
		6.5.5	Cytokines	154			
		6.5.6	Insulin Receptor Number	155			
	6.6	arison of Cell Culture Studies by Cell Type	155				
		6.6.1	Skeletal Muscle	155			
		6.6.2	Hepatocytes	156			
		6.6.3	Adipocytes	156			
	6.7 Conclusion						
	References						

O O 3 THEFT 3 THE O	••
CONTENTS	VII
CONTLINIS	. VII

CO:	NTEN	ITS		vii
7	Menagerie of Chromium Supplements			169
	7.1	Chron	nium Picolinate	169
	7.2	Chron	nium Nicotinate (or Chromium	
		Polyni	cotinate)	170
	7.3		nium Histidine	172
	7.4	Chron	nium454	173
	7.5	Chron	nium Nanoparticles	173
			nium Small Peptide Complexes (CrSP)	174
		Dinak		174
	7.8	Chron	nium(D-phenylalanine) ₃	174
			nium Nicotinate Glycinate (or Chromium	
			otinate Glycinate)	175
	7.10		nium Pidolate	175
	7.11	Chron	nium Methionine or Chromium Methionine	
		Chelat	te	176
	7.12	Cr3/K	emtrace	176
	7.13	Closin	g Thoughts	179
	Refe	rences		179
8	Pote	ntial U	se of Chromium in the Farm	
	Livestock Industry		189	
	8.1	Previo	ous Reviews	189
	8.2	Appro	oved Use of Chromium	
		Supple	ements	191
	8.3	Safety		191
•	8.4	Concl	usions	192
	Refe	rences		192
9	Tox	icology	of Chromium(III)	195
	9.1	Chron	nium Picolinate	198
		9.1.1	Ames Assays	198
		9.1.2	Cultured Mammalian Cells	199
		9.1.3	Drosophila Studies	200
		9.1.4	Mammalian Studies (Intravenous or	
			Intraperitoneal)	201
		9.1.5	Mammalian Studies (Oral)	202
		9.1.6	Neurological Effects	204
		9.1.7	In Vitro Studies	204
		9.1.8	Reconciling In Vitro and	
			In Vivo Studies	205

viii	CONTENTS
9.2 Chromium Nicotinate	207
9.3 Cr3/Kemtrace	208
9.4 Conclusions	208
References	209
Conclusion	215
Index	217