

BIOCHEMISTRY OF THE ELEMENTS
Series Editor: Earl Frieden

Biochemistry of the Lanthanides

C. H. Evans

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BIOCHEMISTRY OF THE ELEMENTS

Series Editor: Earl Frieden

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For Lillian Rose Bioletti

Preface

By a happy coincidence, the completion of this text coincided with the 200th anniversary of the discovery of gadolinite, the mineral with which the lanthanide story begins. For a group of elements which occur in only trace amounts biologically, and which have no known metabolic role, the lanthanides have spawned a surprisingly large biochemical literature. Serious interest in the biochemical properties of these elements can be traced to concerns about the safety of radioactive lanthanides toward the end of World War II. As recent events at Chernobyl indicate, this concern remains topical. However, the literature on lanthanide biochemistry predates the atomic era, beginning with sporadic, medically motivated studies in the latter part of the 19th century. Much of the present biochemical activity involving the lanthanides centers around their ability to provide important information on the interactions of Ca^{2+} with macromolecules and with eukaryotic cells. With the increasing industrial use of the lanthanides, their toxicological properties will need to be examined more closely. Rare earth pneumoconiosis has already been identified as a disease produced by industrial exposure to lanthanides. Several of the biochemical properties of the lanthanides are of relevance to modern medicine. Already cerium-based ointments are used to treat burn wounds, while paramagnetic lanthanides find application in nuclear magnetic resonance imaging.

This book is an attempt to collate and to present in reasonable detail existing knowledge of lanthanide biochemistry before the literature becomes unmanageable. The information it contains should be of value to those engaged in inquiry at the postgraduate level into all aspects of lanthanide biochemistry. Because the subject matter encompasses such a wide range of subdisciplines, it has not been possible to explicate the underlying principles of each topic. For those seeking further information, I have included an appendix listing all the review articles I could find on the various aspects of lanthanide biochemistry. The attempt to be comprehensive will make certain sections of the book tedious for those whose main interest lies elsewhere. However, this volume is not intended as

bedtime reading to be read from start to finish; rather it should serve as a repository to be dipped into for the purposes of retrieving specific information.

The problems associated with covering such an array of different disciplines in one volume have been many. *Rare earth metals* did not appear as a key phrase on the MEDLINE information retrieval system until 1975. Since much of the older literature on the lanthanides remains pertinent today, I have had to fall back on traditional methods of literature searching for the years before this. Much of the early work on the metabolism of the lanthanides was published in the reports of private laboratories and government agencies, rather than in the normal scientific journals, and some of these reports have been hard to obtain. I apologize in advance for any omissions, and would welcome any additional information. A second challenge has been the broad span of topics covered, ranging from inorganic chemistry, via molecular and cellular biochemistry, to physiology, toxicology, and medicine. In covering this spread, I have had to trespass into areas of knowledge with which I ordinarily do not deal. I trust that the specialists in these fields will forgive my intrusions and look leniently upon any inaccuracies. Again, I would gladly receive any criticisms or supplemental information.

ACKNOWLEDGMENTS. So many have contributed to the writing of this book that this risks being the longest section of the entire volume. Without the respect for and desire to search for knowledge instilled in me by my parents, Mr. and Mrs. Idwal Evans, such an undertaking would not even have been contemplated. Their constant support and concern have been invaluable and are deeply appreciated. My wife Mindy has been a "book widow" now for many months, a circumstance she has endured with good humor and understanding. Had it not been so, this book would still be uncompleted.

I owe my introduction to the lanthanides to my good friend Dr. Roderic Bowen, someone whose generosity far exceeds that normally attributed to a *Cardi: Diolch yn fawr iawn, 'was; 'r wy'n mewn dyled mawr iti*. Mr. Vernon Westcott provided my first opportunity to work with the lanthanides, and has remained a valued friend, colleague, and advisor. My intellectual life of the last eight years or so has been greatly enriched through the friendship of Dr. Tony Russell, one of the most creative of individuals. His collaborations with me on lanthanide biochemistry have always been stimulating, productive, and, above all, enjoyable.

Mrs. Diana Montgomery could not have predicted the enormity of the task that lay before her upon agreeing to type the several drafts of

the manuscript. Even with a word processor, it turned out to be a monstrous undertaking. I am very grateful for her perseverance. Much of the reference section owes its existence to Mr. David Obi, a tireless, good-natured postgraduate student with remarkable stamina. Our bibliographic efforts would have been far less fruitful without the efficient yet cheerful assistance of Mrs. Margaret Norden and her colleagues at the Falk Library, whose staff must have had cause to put in overtime during our periods of peak activity. The writing of this book was greatly expedited when Dr. Norman Curthoys permitted me to colonize a vacant laboratory in the Biochemistry Department. My "book room" became an indispensable island of retreat. Several chapters were improved immensely through critical review by Dr. Tony Russell, Dr. Jimmy Collins, and Dr. Rex Shepherd. Any remaining flaws are my own responsibility.

One of the biggest contributions to the successful completion of the book was the patience and understanding of the members of the Ferguson Laboratory for Orthopaedic Research, which has been running on autopilot for so long now. These individuals, too numerous to mention by name, have been wonderful. My expressions of gratitude to Dr. Albert B. Ferguson have been left until last not owing to lack of importance but, on the contrary, because his support, encouragement, and friendly guidance have sustained the past decade of my research in his department. Without "Ferg" this book would not exist.

C. H. Evans

Note Added in Proof

Well over a thousand publications on lanthanide biochemistry have appeared since completion of the text. While it is impossible to incorporate all such new information into this book, wherever possible some of the more important new findings have been added at the proofing stage. However, none of the recent data alter the underlying concepts of lanthanide biochemistry described in this volume.

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Contents

1. Historical Introduction	1
1.1 Opening Remarks	1
1.2 The Identification of the Lanthanides	1
1.3 Biochemical Studies on the Lanthanides	5
References	8
2. Chemical Properties of Biochemical Relevance	9
2.1 Introduction	9
2.2 Electronic Configurations and Their Consequences	10
2.3 Bonding and Coordination Chemistry	15
2.4 Radiocolloid Behavior	24
2.5 Ca^{2+} and Ln^{3+} Ions Compared	25
2.6 Catalytic Properties of Lanthanides	31
2.7 Methods of Quantitative Analysis	32
2.7.1 Introduction	32
2.7.2 Spectrophotometry	32
2.7.3 Titrimetry	33
2.7.4 Luminescence Techniques	34
2.7.5 Atomic Absorption Spectroscopy	35
2.7.6 Atomic Emission Techniques	35
2.7.7 Neutron Activation Analysis	36
2.7.8 Other Methods	37
2.8 Practical Considerations	37
2.9 Summary	41
References	42
3. Biochemical Techniques Which Employ Lanthanides	47
3.1 Introduction	47
3.2 Nuclear Magnetic Resonance Spectroscopy	47
3.3 Luminescence Spectroscopy	51
3.4 Other Spectroscopic Methods	59
3.4.1 Spectrophotometry	59
3.4.2 Electron Paramagnetic Resonance Spectroscopy	60
3.4.3 Mössbauer Spectroscopy	60
3.4.4 Magnetic Circular Dichroism	61

3.5	Luminescence Immunoassay and Enzyme Assay	62
3.6	Cytochemical Detection Techniques	63
3.7	Electron Microscopy	65
3.8	Separation and Purification Techniques	66
3.8.1	Methods Involving Extraction or Precipitation	66
3.8.2	Lanthanide Enhanced Affinity Chromatography	69
3.8.3	Magnetic Separation Techniques	70
3.9	Cellular Ca^{2+} Fluxes: The Lanthanum Method	70
3.10	Other Methods	72
3.10.1	X-Ray Diffraction	72
3.10.2	DNA Analysis	72
3.10.3	Miscellaneous Methods	73
3.11	Summary	74
	References	76
4.	The Interaction of Lanthanides with Amino Acids and Proteins	85
4.1	Introduction	85
4.2	Amino Acids and Small Peptides	86
4.3	Thermolysin	90
4.4	The "E-F Hand" Proteins	94
4.4.1	Parvalbumin	94
4.4.2	Troponin C	101
4.4.3	Calmodulin	103
4.4.4	Calbindin	106
4.4.5	Oncomodulin	109
4.5	The " γ -Carboxyglutamate" (Gla) Proteins	109
4.5.1	Prothrombin (Factor II)	109
4.5.2	Factor X (Stuart-Prower Factor)	114
4.5.3	Factor IX (Christmas Factor)	116
4.6	Factor XIII (Fibrin Stabilizing Factor)	117
4.7	Lysozyme	117
4.8	Proteins of Iron Transport and Storage	120
4.9	Trypsin and Related Enzymes	121
4.10	Elastase	124
4.11	Collagenases	125
4.11.1	Clostridiopeptidase A	125
4.11.2	Mammalian Collagenases	127
4.12	Collagen	127
4.13	α -Amylase	129
4.14	Staphylococcal Nuclease	132
4.15	$\text{Ca}^{2+}/\text{Mg}^{2+}$ -ATPase	132
4.16	Actin and Myosin	136
4.17	Hemocyanin	140
4.18	Phospholipase A_2	143
4.19	Acetylcholinesterase	144
4.20	Concanavalin A	145
4.21	Serum Albumin	146
4.22	Immunoglobulin	148

4.23	Enolase	149
4.24	Kinases	150
4.25	Other Proteins	152
4.26	Summary	155
	References	158
5.	Interactions of Lanthanides with Other Molecules of Biochemical Interest	173
5.1	Mononucleosides and Mononucleotides	173
5.2	Other Nucleotides	181
5.3	Polynucleotides and Nucleic Acids	182
5.4	Carbohydrates	194
5.5	Porphyrins	199
5.6	Other Substances	201
5.7	Summary	203
	References	204
6.	Interactions of Lanthanides with Tissues, Cells, and Cellular Organelles	211
6.1	Introduction	211
6.2	Membrane Interactions of Lanthanide Ions	212
6.2.1	Binding of Lanthanides to Artificial Phospholipid Membranes	212
6.2.2	Binding of Lanthanides to Plasmalemmae	215
6.2.3	Impermeability of Membranes to Lanthanides	219
6.3	Influence of Lanthanides on Transmembrane Fluxes of Metal Ions	223
6.3.1	General Considerations	223
6.3.2	Lanthanides and Cation Fluxes in Muscles and Nerves	225
6.3.3	Lanthanides and Cation Fluxes in Nonexcitable Cells	228
6.4	Effects of Lanthanides on Cellular Metabolism	231
6.4.1	General Considerations	231
6.4.2	Cardiac Tissue	232
6.4.3	Smooth Muscle	236
6.4.4	Skeletal Muscle	239
6.4.5	Nervous Tissue	241
6.4.6	Platelets	245
6.4.7	Mast Cells	246
6.4.8	Adrenal Tissue	248
6.4.9	Pancreas	250
6.4.10	Erythrocytes	252
6.4.11	Polymorphonuclear Leukocytes	252
6.4.12	Amphibian Bladder and Skin	253
6.4.13	Other Tissues and Cells	255
6.5	Cellular Organelles	259
6.5.1	Mitochondria	259
6.5.2	Endoplasmic Reticulum	264
6.5.3	Other Organelles	265

6.6	Summary	265
	References	267
7.	The Occurrence and Metabolism of Lanthanides	285
7.1	Introduction	285
7.2	Sources and Biological Distribution	286
7.3	Microbial Interactions with the Lanthanides	293
7.4	Metabolism of Lanthanides by Invertebrates and Fish	295
7.5	Metabolism of Lanthanides by Mammals and Birds	296
7.5.1	Metabolism of Soluble Lanthanide Salts after Extravascular Administration	296
7.5.2	Metabolism of Soluble Lanthanide Salts after Intravenous Injection	303
7.5.3	Effects of Chelators on Lanthanide Metabolism	315
7.5.4	Metabolism of Insoluble Lanthanide Particles	324
7.6	Summary	327
	References	328
8.	Toxicology and Pharmacology of the Lanthanides	339
8.1	Introduction	339
8.2	Effects of Lanthanides on Microorganisms	340
8.3	Effects of Lanthanides on Plants	343
8.4	The Acute Toxicity of Lanthanides in Vertebrates	343
8.5	General Toxicological and Pharmacologic Effects of the Lanthanides ...	353
8.6	Lanthanide-Induced Calcification	359
8.7	Lanthanides and the Liver	361
8.7.1	General Considerations	361
8.7.2	The Rare Earth Fatty Liver	363
8.7.3	Drug Metabolism and Lipid Peroxidation	368
8.7.4	Hepatic Gluconeogenesis	369
8.7.5	Morphological Changes	372
8.8	Blood: The Anticoagulant Properties of Lanthanides	373
8.9	Neurological Effects of Lanthanides	375
8.10	Lanthanides and Reticuloendothelial Function	376
8.11	Summary	378
	References	380
9.	Past, Present, and Possible Future Clinical Applications of the Lanthanides	391
9.1	Introduction	391
9.2	General Historical Medical Uses of Lanthanides	391
9.3	Applications Based on Antimicrobial Properties	392
9.3.1	Historical Introduction	392
9.3.2	Cerium Salts in the Treatment of Burns	393
9.4	Lanthanides as Anticoagulants	396

9.5	Antitumor Therapy	397
9.6	Imaging and Tracer Studies	399
9.6.1	Introduction	399
9.6.2	Scintigraphic Imaging	400
9.6.3	Cisternography and Tracer Studies with Radioactive Lanthanides	404
9.6.4	Nuclear Magnetic Resonance Imaging	405
9.6.5	Computed Tomography	407
9.7	Radiosynovectomy	408
9.8	Atherosclerosis	410
9.9	Inflammation and Arthritis	413
9.10	Summary	417
	References	417
Appendix: Review Articles on Lanthanide Biochemistry		427
Index		429

Historical Introduction

1.1 Opening Remarks

In the summer of 1787, Karl Arrhenius, a lieutenant in the Swedish army, chanced upon a new mineral, which he named “ytterbite” after the nearby Swedish town of Ytterby. This book is a descendent of that discovery, which foreshadowed the identification of a new group of elements, the rare earths or lanthanides. (For a discussion of nomenclature, see Section 2.1.) The intervening 200 years have been colorful ones. Owing to the close chemical similarities between the members of the lanthanide series, they resisted easy purification and separation from one another. Numerous misidentifications, false claims, and counterclaims are scattered through the pages of this chapter of chemical history. For a number of years, the existence of the lanthanides challenged the accuracy of Mendeleev’s periodic table of the elements. Taken together, there is enough material here for an historian of science to write an instructive book on the identification of the lanthanides in its own right. For reasons to be discussed below, the biochemical properties of the lanthanides have received increasing attention over the last three decades or so. The brief historical orientation presented below sketches the intellectual route from Arrhenius’s new mineral (Arrhenius, 1788) to this book.

1.2 The Identification of the Lanthanides

The first chemical analysis of ytterbite was undertaken by the Finnish chemist Johann Gadolin. He determined that the mineral contained the oxides of beryllium, silicon, and iron, in addition to a new earth which Gadolin christened “ytterbia” (Gadolin, 1794). Ekeberg (1797) subsequently shortened its name to “yttria.” The choice of the word “earth”

was unfortunate, as it is more properly applied to the oxide of a metal, rather than the metal itself. In Gadolin's time, "earth" was taken to include "all substances which possessed the properties of alkalis, did not float and did not change on heating, were almost insoluble in water and evolved gas bubbles during reaction with alkalis" (Trifonov, 1963). Actually, the French chemist Vauquelin had concluded at the beginning of the nineteenth century that cerium was a metal and not an earth, but this finding was ignored. The true nature of "earths" was discovered in 1808 by Sir Humphrey Davy. As we shall see, the term rare earth is a double misnomer, as not only are these elements not earths, but they are also not particularly rare (Section 7.1). Indeed, some of the commoner lanthanides are more abundant on earth than, for example, lead, tin, zinc, mercury, and gold. They are also present in the sun's atmosphere, in meteorites, and on the moon, where they are relatively abundant. Nomenclature has historically proved unfortunate for the lanthanides, with misnaming, conflicts over names, and changes of name frequently leading to confusion. We have already seen that Gadolin's "ytterbia" was soon changed to Ekeberg's "yttria." The parent mineral ytterbite was subsequently renamed gadolinite in honor of Gadolin. In view of its important chemical legacy, the Finnish mineralogist Flink is said to have written that gadolinite "perhaps played a greater role in the history of inorganic chemistry than any other mineral" (Trifonov, 1963).

Much of the subsequent hundred years was spent in isolating new lanthanides from their ores, often demonstrating in the process that preparations previously considered pure actually contained a mixture of more than one lanthanide. Most of these separations involved tedious rounds of fractional crystallization. The chemistries of these elements are so close that eons of geochemical activity had done little in the way of natural fractionization, beyond providing ores enriched in heavy or light lanthanides. Most mineral sources thus contain mixtures of several different members of the series. Some idea of the extent of the preparative problems can be gauged from the fact that, before the development of ion-exchange techniques in the mid-twentieth century, some of the rarer lanthanides required as many as 40,000 fractional crystallizations before they were really pure (Spedding, 1951).

Through the work of Berzelius and Hisinger in Sweden and, independently, Klaproth in France, cerium was the first lanthanide to be processed to a reasonably high degree of purity. It was named after an asteroid, Ceres, that had recently been discovered (Table 1-1). Thus, until 1839, two rare earths, yttrium and cerium, were known. In this year, Karl Mosander, a student of Berzelius, discovered lanthanum. Shortly thereafter, Mosander separated a new earth from lanthanum oxide. Because

Table 1-1. Discovery of the Lanthanides^a

Lanthanide	Year of identification	Discoverer	Origin of name
Lanthanum	1839	Mosander	Lanthanein; Greek for "to lie hidden"
Cerium	1803	1. Berzelius and Hisinger 2. Klaproth	Ceres, an asteroid discovered in 1801
Praseodymium	1885	Von Welsbach	From Greek: <i>Prasios</i> = green; <i>dymium</i> = twin
Neodymium	1885	Von Welsbach	From Greek: <i>Neo</i> = new; <i>dymium</i> = twin
Promethium	1947	Marinsky Glendenin Coryell	Prometheus, the Greek god who stole fire from heaven for men's use
Samarium	1879	De Boisbaudran	From its ore, samarskite, named after the Russian engineer Samarski
Europium	1889	Crookes	Europe
Gadolinium	1880	Marignac	After the Finnish chemist Gadolin
Terbium ^b	1843	Mosander	After the town of Ytterby in Sweden
Dysprosium	1886	De Boisbaudran	From Greek: <i>Dysprositos</i> = hard to get at
Holmium	1879	1. Soret 2. Cleve	<i>Holmia</i> , Latinized version of Stockholm
Erbium ^b	1843	Mosander	After the town of Ytterby in Sweden
Thulium	1878	Cleve	After <i>Thule</i> , the Roman name for the northernmost region of the inhabitable world
Ytterbium	1878	Marignac	After the town of Ytterby in Sweden
Lutetium ^c	1908 1907	1. Von Welsbach ^c 2. Urbain	<i>Lutetia</i> , Latin for Paris
Yttrium	1794	Gadolin	After the town of Ytterby in Sweden

^a Difficulties exist in determining the precise year of identification and in deciding who should be given credit for the discovery of several of the lanthanides. Thus, although Gadolin identified yttrium in 1794, he did not realize that his preparation contained a mixture of at least three lanthanides. Yttrium was not purified, as its oxide yttria, until the work of Mosander in 1843. Similarly, what Marignac called ytterbium in 1878 was shown by Urbain in 1907 to be a mixture of lutetium and "neoytterbium" or ytterbium, as it is now called. In constructing this table, I have tried to list as the discoverer the chemist who first identified the element, regardless of the state of purity then obtained. Cases of simultaneous, independent discovery are indicated in the appropriate places. Most of these elements were first identified as their oxides, in which the ending -ium is replaced by -a, e.g. La_2O_3 , lanthana; Ce_2O_3 , ceria. The discoverer of each element did not necessarily give it its modern name.

^b Terbium was originally designated element 68 and erbium, element 65. The names were reversed in 1877.

^c Lutetium is the name given by Urbain. Von Welsbach called it cassiopeium.