BIOCHEMISTRY OF THE ELEMENTS
Series Editor: Earl Frieden

Biochemistry of the Lanthanides

C. H. Evans

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C. H. Evans
The Ferguson Laboratory
University of Pittsburgh
Pittsburgh, Pennsylvania

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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 pneumonoconiosis 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 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: *Prasios* = green; *dymium* = twin
Neodymium	1885	Von Welsbach	From Greek: *Neo* = new; *dymium* = 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: *Dysprositos* = hard to get at
Holmium	1879	1. Soret 2. Cleve	*Holmia*, Latinized version of Stockholm
Erbium[b]	1843	Mosander	After the town of Ytterby in Sweden
Thulium	1878	Cleve	After *Thule*, 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	*Lutetia*, 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.