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Octacalcium Phosphate

Volume Editors

L.C. Chow, E.D. Eanes, Gaithersburg, Md.

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In Memory of Dr. Walter E. Brown (1918–1993)

Walter E. Brown was born in Butte, Mont. He graduated from high school in Aberdeen, Wash., and attended Grays Harbor Junior College. He received his BS (1940) and MS (1942) in chemistry from the University of Washington. Following his graduation from the University of Washington, Dr. Brown was employed by the B. F. Goodrich Company, Akron, Ohio, as a research physicist. In 1945 he returned to graduate school where he was a teaching fellow in physical chemistry and a tutor in Leverett House, Harvard University. He received his PhD in chemical physics from Harvard in 1949. From 1948 to 1962, Dr. Brown was a research chemist with the Tennessee Valley Authority, studying the crystallography and physical chemistry of calcium phosphates. In 1958, he conducted research at the University of Amsterdam as a Rockefeller Foundation Special Research Fellow.

In 1962 Dr. Brown moved to the Washington, D.C. area, where he was a research associate of the American Dental Association Health Foundation at the National Institute of Standards and Technology (NIST, formerly the National Bureau of Standards). He directed research on the solubility characteristics and crystal chemistry of mineralized tissues and dental calculus. In 1967 he was appointed the director of the American Dental Association Health Foundation Research Unit (now the Paffenbarger Research Center) at NIST, in Gaithersburg, Md. He served in that capacity until his retirement in 1983. As director emeritus, he remained active at the Paffenbarger Research Center, and at the time of his death he was principal investigator on one National Institutes of Health (NIH) grant and consultant on two others.

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Preface

This book is dedicated to Walter E. Brown, a leading scientist in the field of calcium phosphate chemistry. Although the central role of calcium phosphates, especially apatite, in biological mineralization has been recognized for nearly a century, it was not until Dr. Brown's pioneering studies in the 1960s on the physicochemical properties of calcium phosphates that the foundation was laid for much of the modern, current-day, research on biomineralization, dental caries, topical fluoride treatments, and calcium phosphate biomaterials.

All of the contributing authors of this book knew Walter Brown for many years as a colleague, a mentor, or a close friend, and his work has had a significant impact on the research of these authors. A unique area of Dr. Brown's research, that was especially influential in this regard, was octacalcium phosphate (OCP). His seminal study on the structure of OCP, which he began at the University of Amsterdam in 1958 while on a Rockefeller Foundation Fellowship, led him to postulate that OCP is a critical intermediate in the formation of bioapatites. Despite his strong conviction that OCP plays an extremely important role in biomineralization, the elusive highly transient nature of this calcium phosphate in biological tissue escaped the attention of most researchers in this field for many years. It was only since his death in 1993 that a great many studies have confirmed OCP to be the first mineral phase to form in many mineralized tissues and to be an integral precursor to bioapatites.

Dr. Brown started to edit a book on OCP in the early 1990s, but illness prevented him from carrying out the project beyond developing the chapter outlines. The present book, although the result of a separate effort to compile and assimilate the most up-to-date information on calcium phosphate research, closely adheres both in spirit and subject matter to that which he envisioned for the book. This is the first book to provide an extensive review of the OCP literature, and although it is much broader in scope, covering a range of calcium phosphate topics, it is fully appropriate to dedicate this book entitled *Octacalcium Phosphate* to Dr. Brown.

Each chapter covers a different aspect of calcium phosphate chemistry. As the reader will discern, the authors of some of the chapters use OCP as the focal point for their coverage while others provide a more general overview of their subject matter. Nevertheless, we hope that, taken together, the different perspectives offered by each of the chapters will enable the reader to obtain a better appreciation of the importance of this dynamic phase in understanding calcium phosphate chemistry both under laboratory conditions and in biological systems.

The first chapter describes the crystal structures of the major calcium phosphate salts. Although special consideration is given to the structures of OCP and apatite and their relationship to each other, detailed descriptions of the mono- di- and tricalcium phosphate structures are also presented. As the authors clearly point out, such structural considerations of all the major classes of calcium phosphates are important for the reason that the chemical, physical and biological properties of these salts depend not only on their compositional make-up but equally on how the constituent ions within them positionally relate to each other.

The second chapter summarizes the extensive work done by the author on the crystal growth of OCP in synthetic aqueous solutions. Described in this chapter are two experimental model systems designed to study the hypotheses that tooth enamel crystals initially grow as thin OCP ribbons and that subsequent lateral growth into mature apatite-like crystals is controlled by calcium ion diffusion from the surrounding amelogenin matrix. The author also discusses her work on OCP growth in and on collagen matrices in vitro.

The third chapter provides a thorough review ot the literature on OCP in biological systems. The chapter summarizes the often frustrating attempts to firmly establish experimentally the biological roles first proposed by Walter Brown for OCP, the study of which in vivo has been made difficult by its apparently transient nature as an intermediate phase in biomineralization processes. The authors conclude that, with the possible exception of the direct detection of OCP in some pathological mineral deposits, the most compelling evidence for OCP as a biological precursor is found in the early stages of enamel mineralization.

The fourth chapter discusses the unique capability of OCP to incorporate small organic molecules within its structure. In particular, the chapter describes how various carboxylate ions can substitute for acid phosphate groups in the hydrated layer of OCP. The authors provide an in-depth review of the preparation, characterization and special chemical, physical, and structural properties of these carboxylate-substituted OCP (OCPC) salts. The author also discuss the reasons why some carboxylates can easily incorporate into OCP while others cannot. The importance of some of these former carboxylates in cellular respiration suggests to the author possible physiological roles for OCPC salts in non mineralizing as well as mineralizing processes in vivo.

The fifth chapter covers solubility, one of the most important properties of calcium phosphate salts. Emphasis is given in this chapter to establishing a clearer conceptual framework for understanding solubility behavior based on fundamental principles governing solid-solution equilibrium processes and to using solubility phase diagrams. Also described is a model for better understanding the variable solubilities of biologically relevant apatites employing the concepts of metastable equilibrium solubility and dissolution-governing surface complexes.

The sixth chapter presents a comprehensive overview of the surface properties of calcium phosphate salts and the importance of these properties in establishing interfacial behavior. Particular emphasis is given to surface composition, charge and energy, and the roles they play in crystallization, dissolution, adsorption and biological interactions. As stressed by the authors, elucidating the surface properties and interfacial behavior of calcium phosphate salts is critical to understanding mineral formation, maintenance, and destruction in hard tissues, as well as in establishing how these minerals affect hard tissue properties, processes, and diseases.

The seventh chapter discusses the structure, morphology, composition, and solution properties of amorphous calcium phosphate (ACP), a unique calcium phosphate phase in that it lacks long-range crystalline order. The author also provides an assessment of the presence and function of ACP in biological systems. Special attention is given to the relationship of ACP to OCP and how this relationship may provide clues as to the origin of OCP as an intermediate phase in certain biocalcification processes.

The eighth chapter reviews recent studies on calcium phosphate cements (CPC), a new type of calcium phosphate biomaterial. Discussions are focused on cement setting reactions, the products formed, the effects of the products on the properties of the cement, the in vivo characteristics, and clinical applications of CPC. The combination of self-hardening capability and high biocompatibility makes CPC a unique biomaterial. Near perfect adaptation of the cement to the tissue surfaces in a defect, and a gradual resorption followed by new bone formation are some of the other distinctive advantages of this biomaterial. The chapter ends with a discussion of ongoing efforts aimed at further improvements of CPC for a wider range of clinical applications.

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