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# ARNOLD KENT BALLS

# 1891—1966

A Biographical Memoir by W. Z. HASSID

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Biographical Memoir

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# ARNOLD KENT BALLS

April 2, 1891–May 25, 1966

# BY W. Z. HASSID

A RNOLD KENT BALLS was born in Toronto, Canada, on April 2, 1891. He was the son of Alfred Z. and Amelia C. (Arnold) Balls. When he was young his family emigrated from Canada, settled in Philadelphia, and became naturalized American citizens. Young Arnold Kent attended the Philadelphia Central High School, where he exhibited a high aptitude for science. He graduated with a gold medal for writing the best scientific essay. He then entered the University of Pennsylvania, from which he obtained his B.S. degree in chemistry in 1912.

After graduation he joined the U.S. Department of Agriculture, where he worked as an assistant chemist in analytical chemistry. Being imaginative and interested in fundamental science, Balls was not satisfied with daily routine work. Thus, he left his position in 1914 and entered Columbia University the following year, where he worked under the guidance of Professor William J. Gies. He presented a doctoral dissertation entitled "The Occurrence of Aluminum, and Its Absorption from Food, in Dogs," and received his Ph.D. degree in 1917. During that period he also served as instructor and was associated with Hans Zinsser, head of the Department of Bacteriology. When Zinsser was away on leave, Balls was left in charge of the bacteriological work in the department. In 1917 he enlisted in the army as a private, and after two months was promoted to the rank of second lieutenant. From the beginning of his military service he worked in a scientific unit as a bacteriologist. Upon his discharge from the army in 1919, he entered private business as a research and consulting chemist in the yeast industry. In 1921 he obtained a position as associate chemist in the Department of Pharmacology at the University of Pennsylvania, where he remained until 1928.

In 1922 Dr. Balls married Elizabeth Charlotte Franke, a biochemist, who obtained her Ph.D. degree at Columbia University and later collaborated for three years with Professor Stanley Benedict.

Balls's work in the yeast industry and at Columbia University and the University of Pennsylvania brought him in close contact with the subject of enzymology, which at that time was still in the embryonic stage. Enzymes were considered to be fantastically specific catalytic agents that occurred in all living cells and had an important function in metabolic processes. However, none of the numerous investigations led to the knowledge that would enable anyone to classify an enzyme as belonging to a definite group of chemical substances. Endowed with an exceptionally keen native intelligence and intellectual curiosity, Balls became intrigued with the chemical nature of enzymes and the mechanism of their action. This subject became his lifework.

Enzymology had its beginning in Europe in the last century, and was vigorously pursued in the first quarter of this century in a number of laboratories, especially those of Buchner, Willstätter, and Waldschmidt-Leitz. Balls decided to go to Europe and devote himself to the study of this subject. In 1928 he and his family left for Germany, where he first spent a few months in the north learning to speak the German language. He then joined Professor Waldschmidt-Leitz, who had just moved his laboratory from Munich to Prague, Czechoslovakia. This laboratory was considered one of the most active centers of research in enzymology. After several months he went to Professor Pregl's laboratory in Graz for a brief period to learn microchemical methods applicable to his enzyme researches. When he returned to Prague, Balls was already proficient in the German language and soon became a very active collaborator of Waldschmidt-Leitz.

In 1930 he submitted another Ph.D. thesis entitled "Über das Wesen der Enzymwirkung: Mechanismus der Enzymatischen Peptidspalting." This thesis (*Habilitationsschrift*) gave him the title of *Privatdozent* with the privilege of lecturing students interested in enzyme chemistry, which he did very successfully in 1931.

Soon, in collaboration with Professor Waldschmidt-Leitz and other research workers in the laboratory, he published a series of papers dealing with the specificity and mode of action of peptidases on proteins.

While important resemblances between the proteases of animal and plant origin had already been recognized, the corresponding peptide-splitting enzyme systems appeared to be quite different. Balls and collaborators showed that the so-called erepsin (extracts of the animal intestinal tract and many animal tissues) is a mixture of two independently acting enzymes, a polypeptidase and a dipeptidase, and that the two enzymes are absolutely distinct in their behavior toward different substrates. He further found that peptides with more than three amino acids and polypeptide esters are readily hydrolyzed by peptidases, as shown in the accompanying formula (see p. 4).

About the same time he also obtained a specific  $\alpha$ -amino acid amidase from the "ereptic enzymes." In addition, he was one of the first investigators to show that peroxidase is an important biological oxidizing agent in living cells.



This scheme shows the various ways in which a polypeptide may be hydrolyzed by peptidases. Thus leucine \*a or tyrosine \*d may be split off first, or a hydrolysis into di- and tripeptide may take place (\*b and \*c).

His researches provided the impetus for much of the intensive research in enzyme mechanisms. He was responsible to a large extent for bridging the gap between the primitive knowledge of enzymology and the modern sophisticated achievements of this most important area of biochemistry.

At the end of 1931 Dr. Balls returned to the United States, where he accepted a position in Washington, D.C., as Head Chemist in charge of the Enzyme Research Laboratory of the Bureau of Agricultural and Industrial Chemistry of the U.S. Department of Agriculture. He was invited to organize this laboratory because of the increasing realization that a fundamental understanding of the chemistry of enzymes and their mode of action was essential to future developments in the food industry. In 1943 Balls's Enzyme Research Laboratory was transferred to the Western Regional Research Laboratory in Albany, California. During his twenty years of service with the U.S. Department of Agriculture he conducted outstanding research for that department in both basic and applied aspects of food enzymes.

Balls and his associates developed methods of purifying and crystallizing enzymes. R. Willstätter found that papain was capable of hydrolyzing a synthetic peptide, but his observation was not generally accepted because it did not agree with the prevailing notions of protease action. This problem was clarified when Balls and Lineweaver succeeded in crystallizing the enzyme from fresh papaya latex. They showed that crystalline papain, like the crude enzyme preparation, was activated by  $H_2S$ , HCN, and other reducing agents and inactivated by iodoacetate,  $H_2O_2$ , and other oxidants. They also observed that hippurylamide and carboxy-L-isoglutamine were hydrolyzed by this enzyme. At present, papain is among the group of crystalline proteolytic enzymes which are intensively studied with respect to structure, mechanism of action, and the relation of structure to activity.

Chymopapain was later crystallized from papaya latex in collaboration with E. F. Jansen. They found this enzyme to be similar to papain in activation requirements and specificity, but, in contrast to papain, very stable to acid.

Balls's investigations of the effects of diisopropyl fluorophosphate and related compounds on the proteolytic and esterolytic enzymes was a major breakthrough in the identification of active centers. The diisopropyl fluorophosphate was found to undergo a stoichiometric reaction with a single serine at the active site of chymotrypsin, trypsin, and other related enzymes. The pioneering work was followed by intensive studies on "serine enzymes" in laboratories throughout the world. He later added a new major development in the area when he crystallized acetyl chymotrypsin and showed that the acetyl group is transferred to alcohols, indicating that chymotrypsin may act as an important transacetylating agent.

In 1946 Balls, Thompson, and Walden crystallized sweet potato  $\beta$ -amylase. They showed that this crystalline enzyme has a molecular weight of 152,000 and contains arginine, tyrosine, cystine and cysteine, and amide nitrogen (15.1 percent total N). The sulfur occurs mainly as masked SH groups. Three years later, in collaboration with S. Schwimmer, Balls crystallized  $\alpha$ -amylase from barley malt. The crystallization of  $\alpha$ - and  $\beta$ -amylase proved to be of value in fundamental studies of the mechanism of starch degradation.

Throughout his long and productive scientific career, Balls's prime interest was the understanding of the chemical nature of enzymes and their mechanisms of action. He very successfully applied the basic knowledge toward improvement and preservation of food products and other agricultural commodities. Thus, the knowledge gained from his work on the action of papain found wide practical application in the tenderizing of meat. His work on the oxidation-reduction of the proteinases of flour has provided useful information for the processing of wheat and to the baking industry in general. The investigations on the changes occurring in egg white contributed important knowledge pertaining to the problem of egg preservation. Application of the information obtained from the basic research of enzyme action by Balls and his coworkers resulted in more than twenty industrial patents in the area of food technology.

In 1951 the U.S. Department of Agriculture adopted a policy that the research of the four regional laboratories should be entirely devoted to work on agricultural products of the particular region in which the laboratory was located. Although the many patents pertaining to agricultural food products were a direct consequence of Dr. Balls's fundamental enzymological researches, there was strong objection to the basic work with which his laboratory was primarily concerned. As a result, Balls resigned from the U.S. Department of Agriculture and accepted a position as Professor of Biochemistry at Purdue University in Lafayette, Indiana. There he taught biochemistry and conducted research until his retirement in 1961, when he became Professor Emeritus. He and his family then returned to Berkeley.

The head of the Western Regional Laboratory provided

him with a laboratory and an office, where, with the support of a grant from the U.S. Public Health Service and the help of an assistant, Balls continued his researches. During this time, he was invited to return to Purdue University on a part-time basis to direct research of graduate students and to complete some unfinished projects. For three or four summers he returned to the Purdue campus for several months. In spite of his advanced age he spent several hours every day at the laboratory bench. After suffering a hemorrhage in one eye, Dr. Balls was unable to drive his car. Mrs. Balls then chauffeured him to and from the laboratory where he continued to work. His brain was fertile with ideas and unimpaired until the very end. During the last three years of his life he published eight papers on the mechanism of enzyme action of trypsin and chymotrypsin.

Dr. Balls belonged to a number of scientific societies. He was a member of the American Society of Biological Chemists (of which he was Secretary, 1941-1946, and Councilor-at-Large, 1946-1949); the American Chemical Society; the Society for Experimental Biology and Medicine; and the Institute of Food Technologists. He also served on the editorial board of the Journal of Biological Chemistry and the editorial committee of the Annual Review of Biochemistry (1950-1955).

Dr. Balls's contributions to biochemistry were widely recognized, as evidenced by the many awards he received. He was the recipient of the Superior Service Award in 1949 and the Distinguished Service Awared in 1953, both presented by the U.S. Department of Agriculture. In 1959 he was given the McCollum Award for outstanding biochemical research beyond the age of sixty. In 1962 he received the Nicolas Alpert Award for preeminence in and contributions to the field of food technology, and in the same year the Spencer Award for distinguished achievements in agricultural and food chemistry. He was elected a member of the National Academy of Sciences in 1954. He was also a recipient of the Patriotic Service Award from the U.S. Army. Balls was among the first scientific investigators who followed American troops into occupied Germany during World War II to find out about the scientific activities which were going on in that country.

Balls was a man devoid of any prejudices. He valued people for their human and intellectual qualities, regardless of color, race, or religion. He and Mrs. Balls were exceedingly hospitable and generous people. They lavishly entertained guests in their spacious home for days or weeks. Often when a guest from Japan, China, or any other country arrived, they drove to the airport to meet him and brought him to their home where he would stay until the end of his visit.

To those who knew him, Balls was more than a prominent scientist. He was one of those rare personalities whose kindness and affection for his fellow men dominated his whole nature. His abiding faith in goodness and his cheerful outlook toward life were no doubt the qualities responsible for gaining him the affection of a large circle of friends. Dr. Balls was a man with a subtle sense of humor. He was adaptable and felt equally at ease with people of any stratum of society, regardless of whether the person was a waiter, truckdriver, or European nobleman.

True to his New England tradition, he believed in the unhurried, self-sufficient scholarship respected for its own sake, as contrasted with the constant pressure for rapid results and external recognition so prevalent in modern academic life. His scientific papers are models of conciseness and clarity. They show a flash of human feeling, excitement, a trace of self-effacement, and even a touch of humor.

With his tremendous capacity for work went a huge enjoyment of life. He loved good food, good wine, good company, and displayed a gay, exuberant character with his many friends. He was an enthusiastic fisherman. Frequently when he was living in Berkeley, he and his colleagues would spend the entire day salmon fishing on the San Francisco bay.

He was a person of winning charm and manners, and possessed tact with all societies. Beneath his amiable surface lay an inexhaustible energy. He had an intellectual curiosity which constantly drove him into many avenues of human learning. Although his specialty was enzymology, he was interested and well informed in history, comparative religion, literature, mythology, and political science.

He was a classicist, with a knowledge of Latin and Greek, and had a deep interest in history, especially ancient history, and the Greek philosophers. His knowledge in the fields of history and philosophy surprised even experts. He assiduously read Arnold Toynbee's ten volumes of the *Study of History* and *An Historian's Approach to Religion*, and liked to indulge in discussions of current events, interpreting them in the light of the past. He was not averse to setting his mind against that of others; and he was a skillful conversationalist, quick, logical, and incisive. But he had humor and kindliness. Very few people knew that he liked to read and write poetry.

In the memorial resolution for Professor Balls adopted by the Faculty of the School of Agriculture at Purdue University on November 2, 1966, the following quotations aptly characterize his personality:

"He was an aristocrat among men and he knew it. He played the true gentleman on the outside, but he truly lived the role on the inside. His concept of noblesse oblige imposed standards of behavior on him that most men would be taxed to meet. He was kind and considerate to everyone. He could neither be rude nor show indignation even to those who richly deserved it."

"All who knew Kent Balls well loved him, often with a

touch of awe, but with a deep and lasting sincerity. He was a fortunate man because he knew how his friends felt about him. His friends were fortunate because he knew and reciprocated their feelings with warmth."

His memory is treasured in the hearts of many friends.

He is survived by his widow, Elizabeth, and their only son, Dr. Kent F. Balls, a physician in Pennsylvania.

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## KEY TO ABBREVIATIONS

- Ann. Rev. Biochem. = Annual Review of Biochemistry
- Ber. = Berichte der deutschen chemischen Gesellschaft
- Cereal Chem. = Cereal Chemistry
- Fed. Proc. = Federation Proceedings
- Food Res. = Food Research
- Food Technol. = Food Technology
- Fruit Prod. J. = Fruit Products Journal
- Ind. Eng. Chem. = Industrial and Engineering Chemistry
- J. Am. Chem. Soc. = Journal of the American Chemical Society
- J. Assoc. Offic. Agr. Chemists = Journal of the Association of Official Agricultural Chemists
- J. Biol. Chem. = Journal of Biological Chemistry
- J. Wash. Acad. Sci. = Journal of the Washington Academy of Sciences
- Naturwiss. = Die Naturwissenschaften
- Proc. Nat. Acad. Sci. = Proceedings of the National Academy of Sciences
- Z. physiol. Chem. = Hoppe Seyler's Zeitschrift für physiologie Chemie

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