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Soldiers of Science: A Profile

PROF. OM P. MALHOTRA : SOME REFLECTIONS – FROM CHEMISTRY TO BIOCHEMISTRY TO BIOTECHNOLOGY

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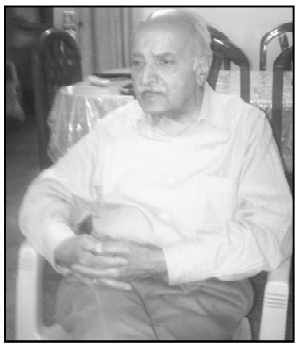
Abstract: Prof. O.P. Malhotra is a reputed enzymologist par excellence, who took research in the area of biological catalysis to great heights in India. He had a humble beginning in chemistry and moved over to biochemistry and later to biotechnology with ease. His teaching skills were also always highly appreciated. This article pays respect and admiration to the great human being, the teacher, the researcher who occupies the mind space of many lives he touched.

Keywords: O.P. Malhotra; enzymologist of repute in India; Indian biochemist.



Prof. Om P. Malhotra

Early Days of Life

Prof. Om Prakash Malhotra was born on 12 March, 1929 in Multan (Pakistan). He was a very hard-working and meritorious student since his childhood. He completed his B.Sc. Hons (Chemistry; first rank) and M.Sc. (Chemistry) from East Panjab University (now called Panjab University, Chandigarh). He was awarded with scholarships at all the University examinations he appeared.

Life in Banaras Hindu University

Soon after M.Sc., he joined chemistry department, Banaras Hindu University as lecturer in 1951. He was awarded Ph.D. degree in chemistry from Banaras Hindu University in 1957, while he fulfilled his teaching duties as well. During the same year he got fellowship (1957-59) from Indo-German Industrial Cooperation for higher studies and research in West Germany and worked with Professor Dr. K. Wallenfels of Albert Ludwig University, Freiberg on kinetic and mechanistic aspects of glucosidases and galactosidases. This work earned him his second doctoral degree, Dr. rer. nat (Biochemistry with Microbiology) with "Sehr Gut" (very good) remarks. Several papers came out of his work, including the seminal one in *Advances in Carbohydrate Chemistry* on β-Galactosidase, which were very well-received (Wallenfels and Malhotra, 1960; Wallenfels and Malhotra, 1961). After his return to India, his work was mainly focused on a variety of enzymes. Dr. Malhotra was promoted to Reader in 1961 (Chemistry/Biochemistry) and to full Professor in 1971 (Chemistry/Biochemistry) for his outstanding achievements. After superannuation in 1989, he continued as Emeritus Scientist of Council of Scientific and Industrial Research (CSIR), New Delhi from 1990 till 1995.

Honours and Awards

During his 40 years of active service, he made notable research achievements for which he was

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felicitated with various awards and fellowships. To the best of my knowledge he is a unique person who had the responsibility to Chair three different departments. He was Head, Chemistry Department (1974-78), Biochemistry (1983-86) and Coordinator of School of Biotechnology (1986-89), since its inception in 1986 till his superannuation. At least for Biochemistry and Biotechnology, he was instrumental in developing these new programs. During his active service he made numerous visits to various countries. To name a few, University of Oregon, USA (1966-68 & 1979-80), Technical University of Denmark, Denmark (1984-85), California State Polytechnic University, Pamona, USA (1988), where he had both teaching and research assignments. Prof. Malhotra was the Fellow of National Academy of Sciences (India) and recipient of prestigious Alexander von Humboldt Fellowship. He was also a UGC National Fellow (1987-89).

Research Activities

Prof. Malhotra published over 100 papers in peer-reviewed journals, which included research articles, some book chapters, and reviews.

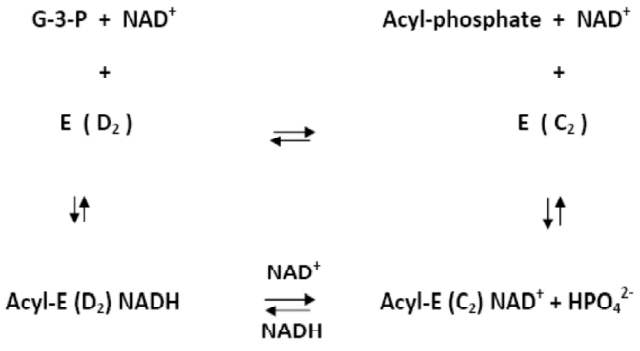
Prof. Malhotra worked on the mechanism of action of several enzymes. I do not have access to all his publications/research but some of the significant contributions made by him are briefly described below:

1. He and his students carried out extensive studies on the kinetics and mechanistic aspects of several hydrolases, namely urease, α-glucosidases, β-glucosidases and galactosidases.
2. One of the most intriguing questions relevant to biology was how identical subunits of oligomeric proteins exhibit functional asymmetry. Two different models were proposed. One championed by Daniel Koshland, which invoked that binding of a ligand induces the asymmetry. Prof. Malhotra, Sydney Bernhard and Francois Seydoux held an opposite view and proposed that the asymmetry can pre-exist because of topological arrangement of the subunits (Malhotra and Bernhard, 1973; Seydoux *et al.*, 1974). Using simple physical techniques like thermal denaturation, his group demonstrated that some of these enzymes can exist in two inter-convertible conformations (of different quaternary structure symmetry). Different substrates and coenzyme ligands exhibit preferential affinity for one or the other enzyme conformations. Their data showed that the two conformations catalyze different steps. Thus, both the conformations are catalytically relevant and enzyme conformational transformation constitutes an obligatory step in the catalyzed reaction.

The role of protein conformational isomerization in the GPDH-catalyzed reactions may be represented as in Scheme I, where E (D_2) and E (C_2) stand for one active site of the enzyme in the D_2 and C_2 symmetry conformation, respectively.

Among the two steps of the catalyzed reaction, half site reactivity has been reported mostly for the group transfer step (right hand vertical column in the Scheme I) where the obligatory effector (NAD^+) stabilize the C_2-symmetry conformation of the enzyme. All of the sites reactivity is generally observed for the redox reaction (left hand vertical column of the Scheme I) in which the aldehyde substrate (which has a higher affinity for the mung bean enzyme than NAD^+) and the reduced coenzyme product (NADH) stabilize the D_2-symmetry conformation (Malhotra *et al.*, 1978; Malhotra and Bernhard, 1981; Malhotra *et al.*, 1983).

3. Studies on PEP-Phosphatase: Our discovery of PEP-Phosphatase from plants is an example of serendipity (Malhotra and Kayastha, 1990). Prof. Malhotra had



Scheme I

suggested the author to work on pyruvate kinase (PK) from germinated mung beans. After purification of the enzyme, during kinetic studies the enzyme catalyzed hydrolysis of phospho*enol*pyruvate (PEP) but did not have any effect of ADP, which really concerned both the student and the supervisor. It turned out that by accident, author had purified a new enzyme PEP Phosphatase, which has a role during plant starvation and is often regarded as an impurity in plant PK crude extract preparations. The first report on this enzyme was acknowledged by Enzyme Commission of IUBMB (1992) and an EC number was assigned and our first two papers on this enzyme were highly cited (Malhotra and Kayastha, 1990; Malhotra *et al.*, 1995). Later, Dr. P.K. Ambasht purified PK and characterized it from germinated mung bean (Ambasht *et al.*, 1996). This clearly proved that these are two different enzymes and not two different activities residing on the same protein.

Association of Author with Prof. Malhotra

Prof. Malhotra has been an excellent teacher and has inspired generations of his students. He used to teach during M. Sc. Biochemistry (1980-82), a paper on "Biological Macromolecules" and a paper on "Enzymes". His teaching style impressed me a lot during my M.Sc. days and I decided to continue attending his classes even as Ph.D. student and as Lecturer, with his kind permission. I joined him for Ph.D. after my M.Sc. Biochemistry. Soon I realized that he is an excellent supervisor and mentor. Though he was a hard-task master, he gave us enough liberty to come up with newer ideas. He also taught us to work with limited facilities and resources. We recycled used alcohol and acetone and prepared enzyme grade ammonium sulfate and aldehyde free absolute alcohol in the laboratory. Prof. Malhotra was a cricket lover and would sometimes bring a pocket transistor to listen to running commentary.

Even after his official assignment in the University was over, I invited him to School of Biotechnology to deliver invited guest lectures. I knew I cannot find a better and experienced teacher than him to teach enzymes. Similarly, he was invited to deliver a series of lectures in Aligarh Muslim University and University of Delhi, South Campus for many years, till he moved to USA for good. When he was leaving Banaras Hindu University he called me to present his precious collection of books, some of which are now out of print and not available in the market. Two of these books are still my favorite viz., Enzymes by Dixon and Webb (3rd Ed, Longman Group, 1979) and Chemistry and Control of Enzyme Reactions by Scrimgeour (Academic Press, NY, 1977).

Family and Activities

Professor Malhotra was lucky enough to find Mrs. Mohini Malhotra (nee Vaswani) in the campus of Banaras Hindu University. We students got much of love and affection from her during our stay as Ph.D. students and even after we moved away. She not only published her Indian recipes in the form of Books, which were published from USA but would also dish out excellent recipes to her guests. She would often call us for lunch and tea parties. All Ph.D. students used to acknowledge her for the moral support they got during Ph.D. tenure. Much later to my surprise, I discovered that even Prof. Malhotra was a great cook. Prof. Malhotra is a completely down to earth person; he would seldom use vehicles and often walk to department and markets.

Prof. Malhotra has one son, Dr. Ajay, working as medical consultant in USA (he cleared both IIT and Medical in his first attempt but finally opted for Medical), two very talented daughters (Neelam settled in U.S.A. and Varsha in Canada). Personally, I know that Prof. Malhotra would have liked to stay for the rest of his life in 'Kashi' but due to strong family bonds, he is now staying in Virginia, USA. Since he is far away from India, I still love to hear from him and facilitate him with his petty problems, back home. I consider myself to be very fortunate to be associated with Prof. Malhotra, whom I consider as one of the great Enzymologists of the country. He is still a great source of inspiration for the author and many of his Ph.D. students who travel long distances to

see him whenever he is in India. Whenever I send him some of my reprints, he would find time to go through them and make his specific comments/suggestions. I wish him long and healthy life and seek his guidance.

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References

Ambasht, P. K., Malhotra, O. P., and Kayastha, A. M. (1996). Purification, characterization and steady state kinetic properties of cytosolic pyruvate kinase free of PEP phosphatase activity from germinating mung beans (*Vigna radiata* L.) Indian J. Biochem. Biophys. *33*, 184-194.

Malhotra, O.P. and Bernhard, S.A. (1973). Activation of a covalent enzyme-substrate bond by non-covalent interaction with an effector. Proc. Natl. Acad. Sci. (USA) *70*, 2077-2081.

Malhotra, O.P. and Bernhard, S.A. (1981). Role of NAD^+ as an effector in the formation and reaction of acyl glyceraldehydes 3-phosphate dehydrogenase. Biochemistry *20*, 5529-5538.

Malhotra, O. P. and Kayastha, A. M. (1990). Isolation and characterization of phospho*eno*lpyruvate phosphatase from germinating mung beans (*Vigna radiata*). Plant Physiol. (USA) *93*, 194-200.

Malhotra, O. P., Prabhakar, P., Sen Gupta, T., and Kayastha, A. M. (1995). Phosphoglycerate kinase-glyceraldehyde-3-phosphate dehydrogenase interaction: Molecular mass studies. Eur. J. Biochem. *227*, 556-562.

Malhotra, O. P., Singh, L. R., and Srivastava, D. K. (1983). Molecular asymmetry in alkaline phosphatase of *E. coli*. Arch. Biochem. Biophys. *220*, 519-529.

Malhotra, O. P., Srinivasan, and Srivastava, D. K. (1978). Kinetics of inactivation and molecular asymmetry of *Pisum sativum*. Biochim. Biophys. Acta *526*, 1-12.

Seydoux, F., Bernhard, S. A. and Malhotra, O. P. (1974). Half site reactivity. CRC Crit. Rev. Biochem. *2*, 227-257.

Wallenfels, K. and Malhotra, O. P. (1960). β-Galactosidase. In The Enzymes (P.D. Boyer, H. Lardy and K. Myrbäck eds.), 2nd Ed, Vol. IV, p. 409, Academic Press, New York.

Wallenfels, K. and Malhotra, O. P. (1961). The galactosidases. Adv. Carbohyd. Chem. *16*, 239-298.