

Three Decades of Continuous Records for Biophysical Chemistry Laboratory (BCL)

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ABSTRACT

The Biophysical Chemistry Laboratory (BCL)[bcl.ut.ac.ir] was established in 1986 at Institute of Biochemistry and Biophysics (IBB), University of Tehran as a first biophysical chemistry laboratory in Iran. The main scientific career of BCL has been mostly marked on thermodynamics of protein denaturation especially by surfactants, protein folding/unfolding, protein glycation, artificial enzyme and bioactive peptides. Protein denaturation is a key technique to obtain the stability of protein in solution and understanding the protein function-structure relationship. The terminology of "hydrophobic salts" is theoretically documented in the literature for surfactants at low concentrations upon interaction with protein in BCL for the first time and also extensively involved on biophysics of molecular diabetes on the area of protein glycation. Various physical techniques such as: isothermal titration calorimetry (ITC), differential scanning calorimetry (DSC), UV-Vis and fluorescence spectrophotometries, circular dichorism, densimetry, viscometry, tensiometry, temperature scanning spectrophotometer, cyclic voltametry, atomic force microscopy, transmission electron microscopy, dynamic light scattering, electrophoresis systems and computer facilities have been applied for aforementioned research works. It has also access to equilibrium dialysis technique and macromolecular interactions theories as well as chemical and biochemical procedures if required. Researchers at BCL have published numerous books in Persian language and also articles in prestigious international journals and also have received numerous awards at national and international levels. Due to mentioned activities, constituted Center of Excellence in Biothermodynamics, UNESCO Chair on Interdisciplinary Research in Diabetes is linked with BCL. This recollection, provides a review of the thirty years activity of biophysical chemistry laboratory.

Keywords: Biophysical Chemistry Laboratory (BCL), Protein thermodynamics, Artificial enzyme, Hydrophobic salts, UNESCO Chair on Interdisciplinary Research in Diabetes

INTRODUCTION

The Biophysical Chemistry Laboratory (BCL) was established in 1986 at Institute of Biochemistry and Biophysics (IBB), University of Tehran as the main base and the mother of biophysical chemistry in Iran. BCL is a famous worldwide research lab in the area of thermodynamics of protein denaturation and biomacromolecular interaction. The first student that joined BCL was MSc student in 1987, while the laboratory was in development. Despite the limited features, the results of his study on the thermodynamic analysis of the interaction between surfactants and H1 histone was published in

Thermochimica Acta as the first outlet of the BCL in 1989 [1]. This was the initiate for internationalization of science in BCL with the support of thought, sacrifice, and perseverance. This way was led to achieving the main goal of the establishment of the laboratory with the big goals for the advancement of science, wisdom, and innovations.

In the following, in 1990, because of the results of the student studies and international publications, BCL awarded the International Khawrazmi Prize entitled "Physical chemistry of the interaction of histone proteins with surfactant". A wide range of results on histone proteins were published in international journals (referred to ibb.ut.ac.ir/~moosavi [a]).

In 1990, BCL received an invitation letter from Late Professor Zafar Zaidi, a prominent Pakistani scientist from

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the H.E.J Research Institute of Chemistry, University of Karachi, for attending the International conference entitled "Protein Structure-Function Relationship" which was held every two years. In this conference along with acquainted with the important international scientists, including the Nobel prize winners, also publishing the international advanced book has been done. The invited speaker wrote a chapter of book for publishing the advanced book named "Protein Structure-Function Relationship" which was published by TWEL, London [2].

In 1992, the first graduate course entitled "Biophysical Chemistry" was held at the Institute of Biochemistry and Biophysics (IBB). Also, the first Ph.D. student joined to BCL In 1993 and the first graduate course entitled "Biothermodynamics" was held at IBB.

In 1993, the collaboration of BCL with Professor Gholam Hossein Hakimelahi at Shiraz University started in order to investigate the interaction of the adenosine deaminase with a series of synthesized nucleoside derivatives. The results of this research were published in international journals [3,4], further studies lead to the first US Patent in 1998 [5].

The Biophysical Chemistry Laboratory has always been the originator of the first in this field. In this regard, presenting educational articles (using classroom content) can be mentioned as a novel way of analyzing and presenting the theoretical subject, for the presentation of theories and ideas besides the laboratory and research activities. This kind of Theory-Educational articles was published first in international journals by BCL [6-8]. In this method, a good question in educational course "Biothermodynamics" was solved by students. For Example; the title "surface stability factor" (SSF) as a new scientific term was coined in the literature via class students and published internationally [9].

In 1994, the isothermal microcalorimetry "Activity Monitor" was purchased from the Swedish Company. It was set up by Ph.D. students in BCL. Also in 2005, an isothermal nanocalorimetry was purchased too. Valuable articles on isothermal calorimetric studies of proteins and enzymes have been published [10-13,a].

In 1995, designing of artificial enzymes started based on biomimetic science in the laboratory. It was the first time in Iran that the issue of biomimetic has been defined and applied. Peroxidase was the first pattern for designing the

artificial enzyme. Advanced studies on designing different artificial enzymes continued in the laboratory, and various articles were published in this field [14-17,a].

The investigation of the interaction of DNA with folded and unfolded histone and also the interaction of DNA with surfactants was started in 1995 and related research results were published in international journals [18-22].

In 1996, the thermodynamic study of avian hemoglobins was investigated with collaboration with late Prof. Zafar Zaidi, and the research continued and several doctoral students studied their thesis on this subject. The equipping BCL with the Swedish microcalorimetric device 'Activity Monitor' lead to publishing valuable papers on the thermodynamics of avian hemoglobins [23-25]. In this year, while attending the Protein Structure-Function Relationship conference in Pakistan, the possibility of scientific collaboration with the Indian Professor, Professor Faizan Ahmad was provided. In addition, participation in the conference led to the publication of part of the studies as a chapter of a book named "Protein Structure-Function Relationship", Plenum Press, New York [26].

The Biophysical Chemistry Laboratory has always hosted different scientists. The first foreign guest from China joined to BCL in 1996 as a postdoctoral position and the second foreign guest from Nigeria joined to BCL in 1997. A year after, BCL was hosted its third guest from Nigeria. All these guests were supported by the International Centre for Theoretical Physics (ICTP) project in Italy.

Institute of Biochemistry and Biophysics (IBB), has a Memorandum of Understanding with the Third World Academy of Sciences which already its new name is: The World Academy of Sciences (TWAS) and the ICTP in Italy, which researchers from developing countries can visit IBB specially BCL for their sabbatical. Scientists from Pakistan, Nigeria, joined to BCL through ICTP project and studied the effects of surfactants on natural and mutated hemoglobin which were studied and continued in the following years [27,28].

In 1997, extensive research was carried out on the suicide deactivation of catalase, peroxidase, tyrosinase via its substrates and valuable articles were published internationally [29-34].

In 1999, an article about science and spiritual technology was published in "Hamdard Islamicus" journal

with the title of "mysteries of spiritual scientific knowledge" as a valuable metaphysics article [35].

It should be noted that various speeches, lectures, and articles about the science and wisdom innovation system were performed and also published [36] and [a]. A general and popular talk was presented in World Science Day for Peace and Development in 2013, with the aim of defining the subject of science and wisdom innovation system for students, scholars and researchers.

In 1999, Micro Differential Scanning Calorimetry (DSC) was purchased for the laboratory. The device was set up by Ph.D. students with the help of Professor Potekhin, the Russian scientist and his technician from Russia. Professor Potekhin was invited by BCL and did stay at IBB for two weeks and he presented a few talks at IBB and also lectured a few titles in the course of Biophysical Chemistry and Biothermodynamics. The advanced Nano Differential Scanning Calorimetry was also purchased from the United State in 2003. The valuable papers about the investigation of proteins *via* DSC were published [37-40,a].

The international project of studying the effect of temperature on amine oxidase activity had approved in collaboration with Professor Giovina Floris from Italy in 2009. Due to this collaboration two doctoral students completed their thesis [41-43].

In 2001, the project of thermodynamic investigations of molten globule-like state for proteins in the presence of non-ionic surfactants at the basic pH was initiated in the BCL and extensive research was continued on this subject [44]. Then, a collaboration between BCL and Professor Yuji Goto, the Japanese Professor of Protein Research Center of the University of Osaka, was established. In this regard, molten globule studies of cytochrome C *via* anionic surfactants such as sodium dodecyl sulfate (SDS) has been started and the performance of anionic surfactant as hydrophobic salt in low concentrations, first was coined in the scientific literature [45-49].

Biophysical Chemistry Laboratory is one of the world's most important and well-known databases in research on the interaction of sodium dodecyl sulfate and proteins.

In 2003, an extended research on the measurement of hydrogen peroxidase and reactive oxygen species on protein denaturation and protein conformation was started. In this regards the research collaboration with Professor Shamsipur

started and the reports were published on this subject [50-53].

The relationship between BCL and British Professor Alan Cooper, the British professor of Biophysical Chemistry at the University of Glasgow, was established. The second edition of the Book of Biophysical Chemistry in Persian was republished in 2008 by University of Tehran Press. One chapter of this book was based on the book of "Biophysical Chemistry" written by Professor Alan Cooper [a].

In the following years, thermodynamics of a molten globule state of glycated proteins by sugars and ketone bodies was extensively studied by students in BCL [54,55,a]. In 2001, Thermodynamics of protein glycation study started as the first molecular diabetic project in BCL and continued years after. The reports of thermodynamics protein glycation were published in international journals [56-66]. Also, the Book of Glycobiology was published in 2012 by University of Tehran Press.

Protein glycation research encountered the understanding of diabetes and its complications from a molecular point of view. Because of the global importance of this issue, and the widespread publications from BCL, UNESCO Chair on Interdisciplinary Research in Diabetes (ucird.ut.ac.ir) at University of Tehran was established that is linked with BCL. Already, UCIRD is one of the literature sources for publications in the biophysics of diabetes. Prof. Mehran Habibi-Rezaei and Dr. Freshteh Taghavi are the main contributors to this Chair.

In 2003, after several biophysical chemistry conferences in Iran, Iran Society Of Biophysical Chemistry (ISOBC) was established with the aim of developing and disseminating biophysical chemistry knowledge through annual meetings, organizing conferences, educational workshops and granting scientific awards (Global Scientific Contribution ISOBC Award; Moosavi-Movahedi Award; Awards for young distinguished researcher) to scientists, young Ph.D., students and researcher in the field of biophysical chemistry and related disciplines [referred to isobc.com]. ISOBC gives the scientific services to more than 200 members from Iran and other countries.

In 2005, QSAR analysis for adenosine deaminase upon interaction with a series of adenine derivatives as inhibitors was published. This work was awarded Razi Festival First

Rank Award [67,68]. Also in this year, the chemometric and thermal analysis of RNase A upon interaction with sodium dodecyl sulfate was started and carried out in collaboration with the Professor Bahram Hematinejad from Shiraz University. The years after, the chemometric research continued by postdocs [69].

In 2005, the research on "conformational lock and thermal inactivation kinetics of Euphorbia amine oxidase" was carried out and then Dr. Hong Jung, the Chinese scientist studied on superoxide dismutase when he was Ph.D. student in BCL and Microanalysis Lab at IBB. The following years, conformational lock investigations continued on other enzymes [70-73]. In 2011, an agreement was formed between the Institute of Biochemistry and Biophysics (IBB) and the School of Life Science Henan University, Kaifeng, China. After this agreement, the collaboration between this school and BCL was expanded, and common articles were published [74,75].

Since 2005, extensive research has been done on the effects of osmolytes on proteins and enzymes. Parts of this research have been done *via* collaboration with Professor Faizan Ahmad's laboratory [76-79].

Prior to 2007, protein fibrillation studies started in BCL, and since 2009 the studies of proteins fibril formation by sugars continued and antioxidants were used to reduce protein fibrillation [58,80-84]. In this regards, antioxidants define as free radicals scavenger as fibrillation agents.

The first research on mobile phone radiation effects on the human hemoglobin structure was published in 2009, and then in the following years, the research continued on luciferase [85-87]. Research has shown the impact of phone cell mobile radiation on structural changes and protein functions.

In the laboratory, extensive works have been done on the structure and function of human, birds, and fish hemoglobins, and extensive articles have been published [23,88-90].

In 2009, the first reports of camel milk proteins and their peptides were performed at BCL as a common project with Professor Thomas Haertle from INRA research center in France. The research studies on camel milk proteins and their peptides were published in a prestigious article for the first time in the world. Researches have been continued in collaboration with students and academic members until

now [91-103]. Professor A. Nisari-Naslaji and Dr. M. Salami and Dr. R. Yousefi are the main collaborators for camel milk projects.

In 2014, the first Iran patent, entitled "Production of fermented camel milk containing antioxidant and antihypertensive peptides", was registered [104].

The experiences on milk proteins were published in the book entitled "Chemistry and Application of Milk Proteins", University of Tehran Press, 2014. Meanwhile, the study of the effect of walnut peptides and its role in an effective adjustment in cancer cells was first reported in scientific literature [105].

In 2011, extensive computational studies were done on protein folding pathways with the collaboration of professor Dokuliyani's scientific group from the United States. Protein theoretical research continued and various reports published [106-110].

Since 2011, the study of the effects of Petrol contaminants on proteins started, and the research was continued by Ph.D. students. In this regard, an applicable project was approved by the petrochemical Company of Mahshahr about the effect of MTBE on blood proteins. The final report was completed in 2017. The effect of MTBE as a potent oxidizing agent on the formation of molten globule in insulin and also the effect of pomegranate (ellagic acid) on human blood protein as a moderator for the MTBE effect was reported [111-112].

Before 2011, Professor Luciano Saso from Sapienza University of Rome, Department of Physiology and Pharmacology, Italy began to collaborate with BCL. The oxidative stress and antioxidant mechanisms on protein were studied [113]. After that, a lot of research was done on the curcumin in BCL [114-116]. The role of curcumin in inhibition of protein fibrillation and the effect of curcumin on the activation of catalase are one of the important research at the recent years in BCL [81,117,118]. Even in 2017, a review article on curcumin and its therapeutic effects was published [119].

In general, the research activities in BCL can be divided into seven general fields: Studies of protein structure function, interaction of proteins with surfactants, Enzyme kinetics, Thermodynamic study of protein glycation, Research on camel milk peptides, Proteins and Artificial enzyme and Theoretical protein research.

One of the activities in BCL are summarized as 16 published books in Persian as follows:

- 1) Biophysical Chemistry, University of Tehran Press, 1992, 4th Edition, 2015
- 2) Physical Chemistry of Biological Macromolecules (Serial Books), vol. 1, University of Tehran Press, 1995
- 3) Enzyme Kinetic, University of Tehran Press, 1996
- 4) Chemical Thermodynamics, University of Tehran Press 1998, 2nd Edition 2007.
- 5) Biochemistry of Kombucha, Amir-Kabir Press, 1999
- 6) Methods in Biochemistry & Biophysics, University of Tehran Press 2002, 5th Edition 2014. This book selected in 80th anniversary of University of Tehran as one of 80 treasure books by University of Tehran Press dated July 12, 2015
- 7) Biological Buffers, Amir-Kabir Press, 2002
- 8) Protein Structure and Function, University of Tehran Press, 2004, 2nd Edition 2011
- 9) Handbook: A Practical Guide to International Journal, University of Tehran Press, 2008
- 10) Biothermodynamics, University of Tehran Press, 2009
- 11) Iran and Global Foundations for Cultivation of Elites, Amir-Kabir Press, 2009
- 12) Conceptual Biochemistry, University of Tehran Press, 2009
- 13) Modulation of Human Damages from Cigarette Smoke, Amir-Kabir Press, 2009
- 14) Glycobiology, University of Tehran Press, 2013
- 15) Chemistry of Milk Proteins and its Application, University of Tehran Press, 2014
- 16) Application of Fluorescence Spectroscopy in Biological Sciences, University of Tehran Press, 2016

Among other achievements of BCL, constituted Center of Excellence in Biothermodynamics in Iran (cebiotherm.ut.ac.ir), the UNESCO Chair on Interdisciplinary Research in Diabetes (ucird.ut.ac.ir), Iran Society of Biophysical Chemistry (isobc.com) and its membership in the European Biophysical Societies' Association (EBSA), the International Union of Biochemistry and Molecular Biology (IUBMB) and Union of Iranian Society of Life Sciences can be mentioned.

The Biophysical Chemistry Laboratory is one of the first admission centers for foreign and domestic post-doctoral researchers at the University of Tehran. The first post-

doctoral researcher joined BCL in 1996 via the fellowship of ICTP, Italy and until now BCL has welcomed 15 domestic and foreign postdoctoral researchers in BCL. The post-doctoral researchers was attended in BCL was from Iran and Iranian PhD from abroad, China, Germany, Nigeria and other researchers from different countries.

The BCL's relation and collaborations with other labs in Universities and Research Centers around the world, including India, Pakistan, China, Nigeria, Indonesia, Italy, France, Russia, United Kingdom, United States, Germany and etc. are confirmed.

So far, more than 69 Ph.D. students and 88 master students have been graduated from BCL. For more information see the "bcl.ut.ac.ir".

Researchers at the BCL have received numerous awards at national and international levels. For example, International Khawarazmi Prize, the International Razi Prize, the National Elite Foundation Awards, the International Union of Biochemistry and Molecular Biology (IUBMB) awards, Fellow in The World Academy of Sciences (TWAS), Fellow in Islamic World Academy of Sciences, Eminent researchers of Iran and University of Tehran and Eminent Professors of University of Tehran are the honors of the BCL Achievements. Beside this, BCL is a leading lab of the University of Tehran. These activities are part of the achievements of BCL.

Professor Ali A. Saboury is a faculty member and research partner of BCL 1993-2013 and since 2013 he continued his research activity in the Biothermodynamic lab at IBB which is always in collaboration with BCL and he is main partner for BCL

Mrs. Najmeh Poursasan is a valuable Lab Assistant in BCL who supports her kinds to students and researchers.

We thanks to all Iranian great scholars, scientists, students collaborated with BCL in this record. It is worth noting that the related further information of BCL is followed in bcl.ut.ac.ir.

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Most Research Terminologies in BCL

