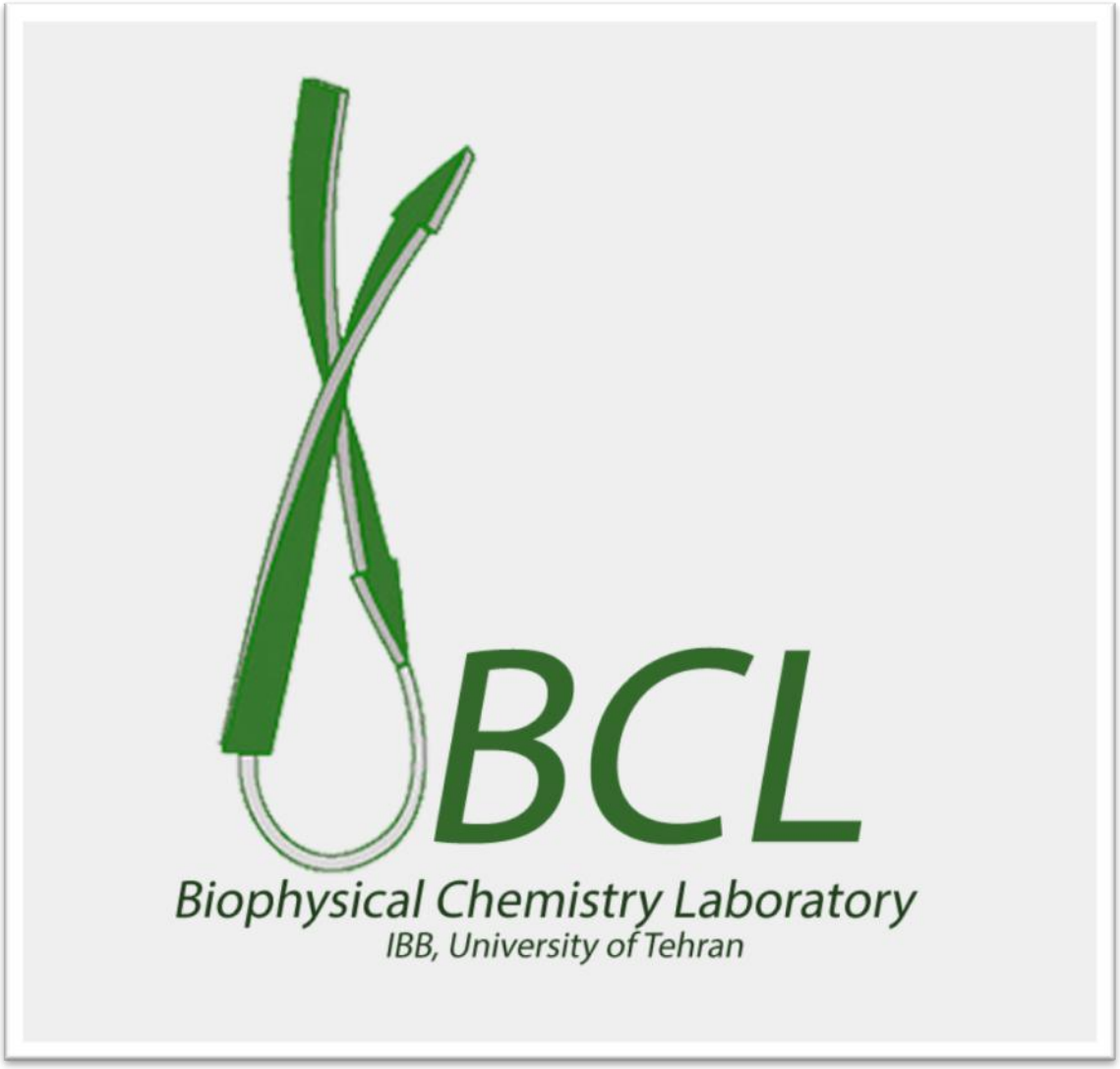
BIOPHYSICAL CHEMISTRY LAB

ANNUAL REPORT 2017



Institute of Biochemistry and Biophysics
Tehran, Iran

http://bcl.ut.ac.ir/

CONTENTS

FOREWORD

The Biophysical Chemistry Laboratory (BCL) was established in 1986 in the Institute of Biochemistry and Biophysics (IBB) as a main base and the mother of Biophysical Chemistry in Iran. BCL is famous worldwide in the research area of Thermodynamics of Protein Denaturation and Biomacromolecular Interaction.

This laboratory enjoys from advanced facilities and it is equipped with advanced apparatuses for the research. BCL is equipped with Nano Differential Scanning Calorimeters (DSC); Nano Isothermal Titration Calorimeters (ITC); modern Circular Dichroism (CD) Spectropolarometry, Sensitive Densitometer and Tensiometer; Fluorescence and Uv-vis Spectrophotometers, Microviscometers and Biochemical and Biophysical methods as well as and Computational facilities.

BCL is an appropriate place for the promotion of the research and science in the field of Biochemistry, Nanobiophysics, Biotechnology and Biophysical Chemistry. BCL is a suitable laboratory for training PhD students and postdoctorate researchers, associate researchers and sabbatical leaves for faculty members at national and international levels. Faculty members, postdoctorates, students and foreign research associates using the facilities of this laboratory which have published hundreds of full research articles in international prestigious journals. BCL is an appropriate laboratory for supporting and promoting the research of scientists and researchers at national and international levels.

BCL is advanced nano-laboratory with accurate equipment, skilled technicians and capable of serving linked with Nanotechnology Laboratory Network (LNN). BCL is accessible to LNN and it is ready to make a good service in various aforementioned area. UNESCO Chair on Interdisciplinary Research in Diabetes and Center of Excellence in Biothermodynamics are lined with BCL.

Biophysical Chemistry Lab

Lab Colleagues

Professor M. Shamsipur Razi University Department of Chemistry	**Professor M. Amani** Medical University of Ardebil
Professor P. Norouzi University of Tehran College of Science, Department of Chemistry	**Dr. S. Safarian** University of Tehran College of Science, Department of Biology
Professor. B. Moshiri University of Tehran Dept. of Electrical and Computational Eng.	**Dr. K. Nazari** Research Institute of Petroleum Industry, Tehran, Iran
Professor A. Niasari-Naslaji University of Tehran Department of Veterinary	**Professor M. Habibi-Rezaei** University of Tehran College of Science, Department of Biology
Professor H. Ghourchian University of Tehran Institute of Biochemistry and Biophysics (I.B.B)	**Professor M. Amanlou** Medical Science University of Tehran Department of Pharmacy
Professor M. R. Ganjali University of Tehran College of Science, Department of Chemistry	**Dr. G. Ataei** Medical Science Shahid Beheshti University Department of Premedical Science
Dr. Sh. Ariaeenejad Agricultural Biotechnology Research Institute of Iran	**Dr. M. Salami** University of Tehran College of Agriculture and Natural Resources

INTERNATIONAL COLLABORATION

★Professor L. Saso:

Department of Physiology and Pharmacology, Sapienza University of Rome, Italy.

★Professor T. Haertle

National Research Institute of Agronomique, 44316 Nantes Cedex 03, France

★ Professor F. Ahmad

Director, Centre for Interdiscipinary Research in Basic Sciences, Jamia Millia Islamia (A Central University), Jamia Nagar, NEW DELHI - 110 025, India

★Professor G. Hakimelahi

Taigen Biotechnology X, 7F, 138 Hsin Ming Rd. Neihu Dist, Taipei, Taiwan

★Dr. N. Sheibani

Department of Ophthalmology and Visual Science, University of Wisconsin, Madison, WI S370S, USA

LAB ASSISTANT:

Mrs. N. Poursasan

Associate researcher:

Faezeh Moosavi-Movahedi

POSTDOCTS

- M.R. Razbin
- M. Nourisefat
- R. Jahanbani

STUDENTS (Year 2017)

Doctor of Philosophy (PhD)	Master of Science (MSc)
❋P. Arghavan	✯N. Pishkari
❋M. Qafary	✯A. H.Lagzian
❋V. Sheikhhasani	✯M. Hajizadeh
❋L. Alaei	
❋S. Movaghati	
❋S. Hadi	
❋E. Hosseini	

Alumni (Year 2017)

PhD

Name	Topic of Thesis
E. Najd Grami	The destructive effect of methyl tert-butyl ether (MTBE) and diethylhexyl phthalate (DEHP)on human blood proteins (insulin and hemoglobin)
R. Karamzadeh	Experimental and theoretical studies of 17-β estradiol interaction with human protein disulfide isomerase
F. Mofidi-Najar	Biophysical chemical investigation of curcumin upon interaction with pure and glycated catalase using experimental and computational methods
J. Rafiei	The Study of different concentrations of deuterium depleted water on hemoglobin structure and function: gamarr adiation approach
R. Jahanbani	Extraction, partial digestion and biological evaluation of Persian walnut peptides

MSc

Name	Topic of Thesis
M. Babaei	The biophysical studies on diabetic red blood cell by optical tweezers
R. Sattari	Physicochemical studies of purified myoglobin from different slaughtering upon interaction with lead salt
E. Hosseini	The denaturation study of myoglobin by sufactants from different slaughtering methods

Technolgies:

Biophysical Chemistry Kits

Today, with the increase in production and a variety of processed foods consumed meat species, the identification of the mixed meat products should be concerned by precise technique. The companies producing meat products require the governor to set up laboratories to be able to offer their products and goods produced permission to enter the competition in the global market.
For this purpose, the detection methods and identify the species that have been used in meat production, can solve the problems in this area. In the laboratory of Biophysical Chemistry (BCL) at IBB, designed and made a new kit as BCL-Kit. The new biological methods that are used to detect meat, genetic methods were used in this kit, as well as intended for the qualitative detection of species content in raw, processed and mixed meats such as hamburger creates an even, sausage, barbecue, etc.
This product was applied to identify nine meats (cattle, sheep, chicken, buffalo, dog, cat, pig, camel, and donkey) for products and polymerase chain reaction (PCR) use the highly conserved regions of cytochrome b gen as a target sequence.
For the identification of species, it is preferable to detect DNA and extracted it from muscle.
DNA and polymerase chain reaction (PCR) use the highly conserved regions of cytochrome b gen as a target sequence. It can detect based upon PCR amplification of mitochondrial genes for species-specific detection with agarose gel electrophoresis.
The additional instructions provided inside this kit that will help the cosume for identification of meat species.

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Species Specific Identification of Meat Derivative Products by Molecular Genetic Approach (Kit)

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Walnut is a plant with economic value. In addition of food consumption, walnut is also used in traditional medicine and its healing properties have been known since many time ago. Walnut is mainly composed of protein and fatty acids. The seeds are a rich source of protein (10 to 20% of weight). Walnut contain 18 different amino acids that 8 of them are essential amino acids. Walnut also is a good source of arginine and lysine. The low proportion of lysine to arginine in walnut play an important role in serum cholesterol level. In addition, walnut has a significant amount of the amino acid tyrosine that is a semi-essential amino acid. Therefore walnut seeds can be considered as a complementary source for other foods.

Bioactive peptides normally are inactive and hidden inside the natural protein. Enzymatic hydrolysis can lead to release of these peptides. These peptides are protein fragments that have a lot of positive impact on the status and functions of the body. Bioactive peptides derived from hydrolysis of walnut protein by digestive enzymes are very important in food, pharmaceutical and nutrition industries. Because of many physiological functions, including antioxidant, anticancer and antihypertensive activity of these peptides, they can be used as ingredients in foods product, dietary supplements and nutraceutical.

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Benefits of walnut peptides in food industries as a nutraceutical

Iran, Tehran, University of Tehran, Biophysical Chemistry laboratory
Tel: 61113381
www.ibb.ut.ac.ir/bcl

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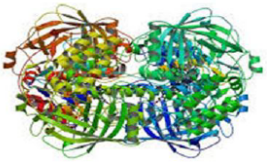
Catalase is an antioxidant enzyme with a lot of important roles in various industries. It can effectively catalyzes the transformation of residual hydrogen peroxide into oxygen and water. It can be widely used in food, textile, paper, electronics, and other industries to remove hydrogen peroxide, therefore it can lead to a significant saving of water resources and reduce energy consume.

APPLICATION FIELD & EFFICACY:

--**Food Industry:** it can remove residual hydrogen peroxide after :
using it as bleacher, preservative in food processing, eliminating the special odor of hydrogen peroxide caused by ultraviolet irradiation in production of milk, cheese and other products and leavening agent of baking food.
--**Textile Industry:** to remove hydrogen peroxide after bleaching and before dyeing, saving water, energy and time, not damaging the fibers and dyestuffs., and do not pollute the environment;
--**Papermaking Industry:** monitoring and optimizing the amount of hydrogen peroxide in bleaching process, degrading residual hydrogen peroxide after the bleaching;
--**Electronics Industry:** to remove hydrogen peroxide after eroding germanium, silicon transistors and semiconductor components; saving water, energy and time.

According to our research, the required amount of catalase enzyme can be significantly reduced by using an enzyme activator that effectively lead to low costs.

Catalase



BCL
Biophysical Chemistry Laboratory
IBB, University of Tehran

Reducing the cost of catalase in industry by enzyme activation

Iran, Tehran, University of Tehran, Biophysical Chemistry laboratory
Tel: 61113381
www.ibb.ut.ac.ir/bcl

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Commemoration of the 30th Anniversary of Biophysical Chemistry Laboratory (BCL)

Commemoration ceremony of the 30th Anniversary of Biophysical Chemistry Laboratory (BCL) was hosted by the Institute for Advanced Studies in Basic Sciences in Zanjan, with the participation of graduates and national speakers on November 4th, 2017.

The Biophysical Chemistry Laboratory (BCL) [bcl.ut.ac.ir] which is supervised by Professor Ali Akbar Moosavi-Movahedi, Professor of Biophysical Chemistry, 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 and entered the realm of serious competition with world-renowned research labs. BCL is a famous worldwide research lab in the area of thermodynamics of protein denaturation and biomacromolecular interaction affiliated at the University of Tehran. Up to now more than 150 alumni who are currently working at the universities and research institutes and industries are graduated from BCL. Researchers and students at BCL have published numerous articles in prestigious international journals and also have received numerous awards at national and international levels, i.e. International Khawarazmi Prize, International Razi Prize, National Elite Foundation Awards, International Union of Biochemistry and Molecular Biology (IUBMB) awards, top ESI (Essential Science Indicator) scientists, Fellow in The World Academy of Sciences (TWAS), Fellow in Islamic World Academy of Sciences (IAS). The Biophysical Chemistry Laboratory is one of the first admission centers for foreign and domestic post-doctoral researchers at the University of Tehran.

The opening of ceremony was held with a lecture entitled “Global Science Diplomacy of BCL” given by Professor Ali A. Moosavi-Movahedi, the President of Iran Society of Biophysical Chemistry, and in the following, Dr. Maryam Nourisefat was presented a lecture entitled "Scientific Achievements of BCL" and also the subject of "The Role of BCL on Advancement of Science, Culture and Innovation" was lectured by Mr. Vahid Sheikhhasani, PhD student in Biophysics and member of BCL.

After the speeches, the BCL alumni and authorities of UNESCO Chair on Interdisciplinary Research in Diabetes and ISOBC representatives in Iran and abroad were held round tables with the subject of "New horizons of ISOBC in the region".

This program was scheduled on the occasion of 30th Anniversary of Biophysical Chemistry Laboratory (BCL**)**. For more information, refer to bcl.ut.ac.ir

PUBLICATIONS 2017

1) H. Nourbakhsh, Z. Emam-Djomeh, A. Madadlou, M. E. Mousavi, A.A. Moosavi-Movahedi, S. Gunasekaran "Antioxidant Peptidic Particles for Delivery of Gallic Acid" Journal of Food Processing and Preservation 41: e12767 (2017)

2) M. H. Mehraban, S. Odooli, R. Yousefi, R. Roghanian, M. Motovali-Bashi, A.A. Moosavi-Movahedi, Y. Ghasemi "The interaction of beta-lactoglobulin with ciprofloxacin and kanamycin; a spectroscopic and molecular modeling approach" Journal of Biomolecular Structure and Dynamics 35(9), 1968-1978(2017)

3) F. Taghavi, M. Habibi-Rezaei, M, Amani, A.A. Saboury and A.A. Moosavi-Movahedi "The status of glycation in protein aggregation" International Journal of Biological Macromolecules 100, 67-74 (2017)

4) M. Chinisaz, A. Ebrahim-Habibi, A.R. Dehpour, P. Yaghmaei, K. Parivar, A.A. Moosavi-Movahedi "Structure and function of anhydride-modified forms of human insulin: In silico, in vitro and in vivo studies" European Journal of Pharmaceutical Sciences 96, 342-350 (2017)

5) F. Mofidi Najjar, R. Ghadari, R. Yousefi, N. Safari,V. Sheikhhasani, N. Sheibani and A.A. Moosavi-Movahedi "Studies to reveal the nature of interactions between catalase andcurcumin using computational methods and optical techniques" International Journal of Biological Macromolecules 95, 550-556 (2017)

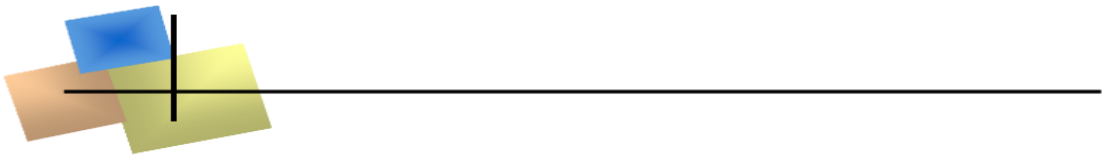
6) M. Valipour, P. Maghami, M. Habibi-Rezaei, M. Sadeghpour, M. A. Khademian, Kh. Mosavi, F. Ahmad, A.A. Moosavi-Movahedi "Counteraction of the deleterious effects of reactive oxygen species on hemoglobin structure and function by ellagic acid"
Journal of Luminescence 182, 1-7 (2017)

7) I. H. Najdegerami, P. Maghami, V. Sheikh-Hasani, Gh. Hosseinzadeh, N. Sheibani and A. A. Moosavi-Movahedi "Anti-chaperone activity and heme degradation effect of methyl tert-butyl ether (MTBE) on normal and diabetic hemoglobins" J. Mol. Recognition 30,e2596, 1-8 (2017)

8) M. Amani, A. A. Moosavi-Movahedi,B. I. Kurganov "What can we get from varying scan rate in protein differential scanning calorimetry?" International Journal of Biological Macromolecules 99, 151-159 (2017)

9) Zainab Moosavi-Movahedi, E. Salamati Kalejahi, M. Nourisefat, P.Maghami, N. Poursasan, A.A. Moosavi-Movahedi "Mixed SDS-Hemin-Imidazole at low ionic strength being efficient peroxidase-like as a nanozyme" Colloids and Surfaces A: Physicochemical and Engineering Aspects 522,233-241 (2017)

10) M. Rezaei Arjomand, Gh. Ahmadian, M. Habibi-Rezaei, M. Hassanzadeh, A. A. Karkhane, A.A. Moosavi-Movahedi, M. Amanlou ´ The importance of the non-active



site and non-periodical structure located histidine residue respect to the structure and function of exo-inulinase" International Journal of Biological Macromolecules 98, 542-549 (2017)

11) M. Mazaheri, A.A. Saboury, M. Habibi Rezaei, M. Farhadi, A.A. Moosavi-Movahedi "Curcumin, a Molecule with Multiple Forces and Biological Modulators" Iranian Journal of Nutrition Sciences & Food Technology 12(1), 121-132 (2017) [Review Paper in Persian]

12) R. Karamzadeh, M. H. Karimi-Jafari, A.A. Saboury, Gh. Hosseini-Salekdeh and A.A. Moosavi-Movahedi "Red/ox states of human protein disulfide isomerase regulate binding affinity of 17 beta-estradiol" Archives of Biochemistry and Biophysics 619, 550-556 (2017)

13) M.R. Khalesi, M. Salami, M. Moslehishad, J. Winterburn and A.A. Moosavi-Movahedi "Biomolecular content of camel milk: A traditional superfood towards future healthcare industry" Trends in Food Science & Technology 62, 49-58 (2017) [Review Paper]

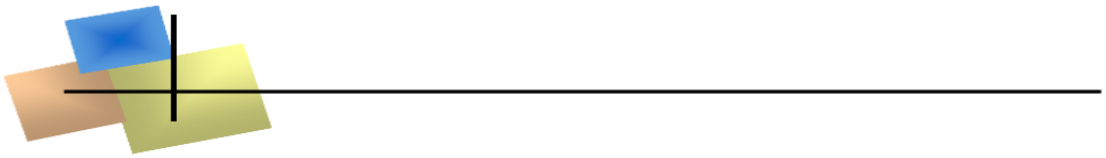
14) K. Khoshaman, R. Yousefi, A.M. Tamaddon, S. Sadat Abolmaali, A. Oryan, A.A. Moosavi-Movahedi, Boris I Kurganov "The impact of different mutations at Arg54 on structure, chaperone-like activity and oligomerization state of human αA-crystallin: The pathomechanism underlying congenital cataract-causing mutations R54L, R54P and R54C" Biochimica et Biophysica Acta (BBA)-Proteins and Proteomics 1865(5), 604-618 (2017)

15) Gh. Hosseinzadeh, A. Maghari, S. M. Famil Farniya, A. H. Keihan and A. A. Moosavi-Movahedi "Interaction of insulin with colloidal ZnS quantum dots functionalized by various surface capping agents" Materials Science & Engineering C 77, 836-845 (2017)

16) S.S. Moghadam , A. Oryan , B.I. Kurganov , A.M.Tamaddon , M.M. Alavianehr , A.A. Moosavi-Movahedi , R. Yousefi "The structural damages of lens crystallins induced by peroxynitrite and methylglyoxal, two causative players in diabetic complications and preventive role of lens antioxidant components" International Journal of Biological Macromolecules 103, 74-88 (2017)

17) A. Jahanban-Esfahlan, S. Davaran, A. A. Moosavi-Movahedi, S. Dastmalchi " Investigating the interaction of juglone (5-hydroxy-1, 4-naphthoquinone) with serum albumins using spectroscopic and in silico methods" Journal of Iran. Chem. Society 14, 1527-1540 (2017)

18) M. Rahban , N. Salehi , A.A. Saboury, S. Hosseinkhani, M.H. Karimi-Jafari , R. Firouzi, N. Rezaei-Ghaleh, A.A. Moosavi-Movahedi "Histidine substitution in the most flexible fragments of firefly luciferase modifies its thermal stability" Archives of Biochemistry and Biophysics 629,8-18 (2017)



19) R. Karamzadeh, M. H. Karimi-Jafari, A. Sharifi-Zarchi, H. Chitsaz, Gh. Hosseini Salekdeh and A.A. Moosavi-Movahedi " Machine learning and network analysis of molecular dynamics trajectories reveal two chains of Red/Ox-specific residue interactions in protein disulfide isomerase" Scientific Reports 7: 3666, 1-11(2017)

20) J. Rafiei, K. Yavari, A. A Moosavi-Movahedi "Preferential Role of Iron in Heme Degradation of Hemoglobin upon Gamma Irradiation" International Journal of Biological Macromolecules 103, 1087-1095 (2017)

21)K. Khoshaman, R. Yousefi, A.A. Moosavi-Movahedi "Protective role of antioxidant compounds against peroxynitrite-mediated modification of R54C mutant αA-crystallin" Archives of Biochemistry and Biophysics 629, 43-53 (2017)

22) A. Shockravi, K. Kavousi , J. Rezania, R. Jafari, M. H. Norouzi Beirami, Sh. Ariaeenejad, Zahra Moosavi-Movahedi , P. Maghami , A. M. Mortazavian and A.A. Moosavi-Movahedi " Time-Frequency Approach in the Cluster Assignment of Amino Acids Based on Their NMR Profiles" Journal of Iran. Chem. Society 44, 2221-2228 (2017)

23) R. Yekta, Gh. Dehghan, S. Rashtbary, N. Sheibani and A.A. Moosavi-Movahedi "Activation of catalase by pioglitazone: Multiple spectroscopic methods combined with molecular docking studies" J. Mol. Recognition e2648, 1-11(2017)

24) F. Mofidi-Najjar, F. Taghavi, R. Ghadari, N. Sheibani, A.A. Moosavi-Movahedi "Destructive effect of non-enzymatic glycation on catalase and remediation via curcumin" Archives of Biochemistry and Biophysics 630, 81-90 (2017)

25) Di Li, Xiao-Lu Yang, Bao-Lin Xiao, Fang-Yong Geng, Jun Hong, N. Sheibani, A.A. Moosavi-Movahedi "Detection of Guanine and Adenine Using an Aminated Reduced Graphene Oxide Functional Membrane-Modified Glassy Carbon Electrode" Sensors 17(7) 1652 (2017)

26) M. Salami, A. Niasari-Naslaji and A. A. Moosavi-Movahedi "Recollection: Camel Milk Proteins, Bioactive Peptides and Casein Micelles"Journal of Camel Practice and Research 24(2) 181-182 (2017)

27) F. Kashanian, M. Habibi-Rezaei, A. R. Bagherpour, A. Seyedarabi and A. A. Moosavi-Movahedi "Magnetic nanoparticles as double-edged swords: concentration-dependent ordering or disordering effects on lysozyme" RSC Adv. 7, 54813–54822 (2017)

28) P. Mirmiran, A. Niasari Naslaji, A.A. Moosavi Movahedi, F. Eslami, F. Azizi " Effect of Camel Milk on Glycemic Control and Lipid Profiles of Diabetic Patients" Iranian Journal of Endocrinology and Metabolism 19(4) 223-233 (2017)

29) Gh. Hosseinzadeh, A. Maghari, S. M. Farnia, A. A. Moosavi-Movahedi "Interaction mechanism of insulin with ZnO nanoparticles by replica exchange

molecular dynamics simulation" Journal of Biomolecular Structure and Dynamics (2017) doi.org/10.1080/07391102.2017.1396254

30) M. Nourisefat and A.A. Moosavi-Movahedi "Three Decades of Continuous Records for Biophysical Chemistry Laboratory (BCL)" Biomacromol. Journal 3(1), 83-92 (2017)

Keynote speakers (2017)

1) A.A.Moosavi-Movahedi "Free Radicals: Diabetes and its Complications" Iran Academy of Science, Chemistry Symposium, Feb 2, 2017 [Keynote Speaker]

2) A.A.Moosavi-Movahedi "Medical Science and Interdisciplinary Science" Iran Medical Academy of Science, Basic Science Symposium, Feb 6, 2017 [Keynote Speaker]

3) A.A.Moosavi-Movahedi "30 Years Research on Thermodynamics of Protein Denaturation" 19th Iranian Congress of Chemistry, Shiraz, February 21-24, 2017 [plenary speaker]

4) Ali A. Moosavi-Movahedi "Nutraceutical Effect of Bioactive Peptides and Antioxidants on Diabetic Complications" International Conference on Nutrition: from Laboratory Research to Clinical Studies, September 6-8, 2017, Mashhad, Iran [Keynote Speaker]

5) A.A. Moosavi-Movahedi "Free Radicals: diabetes complications" 21st Islamic World Academy of Sciences (IAS) International Scientific Conference, Konya, Turkey October 6-11, 2017[Key Speaker].

Selected Papers (year 2017)

International Journal of Biological Macromolecules 100 (2017) 67–74

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Review

The status of glycation in protein aggregation

Fereshteh Taghavi [a,b,c], Mehran Habibi-Rezaei [d], Mojtaba Amani [e], Ali Akbar Saboury [a,f], Ali Akbar Moosavi-Movahedi [a,b,f,*]

[a] Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
[b] UNESCO Chair on Interdisciplinary Research in Diabetes at University of Tehran, Iran
[c] Faculty of Bio Science, Tarbiat Modares University, Tehran, Iran
[d] Schools of Biology, University of Tehran, Tehran, Iran
[e] Department of Biochemistry, Faculty of Medicine, Medical University of Ardabil, Ardabil, Iran
[f] Center of Excellence in Biothermodynamics, University of Tehran, Tehran, Iran

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Aggregation
Amyloid
Non amyloid

ABSTRACT

Protein crucial function and flexibility directly depend on its whole structure which is determined by the native distribution of structural elements. Any disturbances in a protein architecture leads to many kind of abnormalities and intra- or extracellular accumulation of misfolded proteins which are the basis of conformational diseases. Glycation is one of the most important unwanted post-translational modifications (PTM) which modifies protein three dimensional decoration and triggers its abnormalities. In current review, we take a look at the brief history of protein glycation, its mechanism and kinetics, glycation consequences and toxic products and its involvement in protein chemical modification, aggregation amyloids and fibril formation and different mechanisms induced by such alterations.

Contents

* Corresponding author. Fax: +98 21 66404680.
E-mail address: moosavi@ut.ac.ir (A.A. Moosavi-Movahedi).

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0141-8130/

European Journal of Pharmaceutical Sciences 96 (2017) 342–350

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European Journal of Pharmaceutical Sciences

journal homepage: www.elsevier.com/locate/ejps

Structure and function of anhydride-modified forms of human insulin: In silico, in vitro and in vivo studies

Maryam Chinisaz [a,b], Azadeh Ebrahim-Habibi [c,*], Ahmad-Reza Dehpour [d,e], Parichehreh Yaghmaei [b], Kazem Parivar [b], Ali Akbar Moosavi-Movahedi [f]

[a] Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[b] Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran
[c] Biosensor Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
[d] Department of Pharmacology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[e] Experimental Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran
[f] Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran

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Keywords:
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Anhydride derivatives
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ABSTRACT

Insulin is a therapeutic protein whose amyloid formation is reported in diabetic patients. Four anhydride compounds were used in the current study in order to experiment their potential reducing effect on insulin propensity to form amyloid fibrils. The modified forms (obtained with succinic-, 3,3-dimethylglutaric, 2-phenylglutaric-, and (2-Dodecen-1-yl) succinic anhydride), were first characterized with regard to melting temperature (Tm), changes in secondary structure percentage and hydrophobic surface. Fibril formation was then assessed by Congo red absorbance kinetics and transmission electron microscopy. Functionality was investigated with the use of an insulin tolerance test in NMRI mice. Finally, 10 ns molecular dynamics simulations were performed during which structural changes, potential energy, gyration radius, RMSD, and accessible surface area were monitored.

In all cases, α-helical structure content of the modified forms was reduced, but thermal stability and structural compactness of modified insulin were increased except in case of the dodecenylated species. All modified insulin forms undergo amorphous aggregation instead of amyloid fibrils formation, and dodecenylated insulin makes the largest amorphous aggregates. In silico results were overall in accordance with in vitro studies. Finally, only succinylated insulin was functional, although dimethylglutaric-modified insulin started to show some activity after 2 h.

1. Introduction

Formation of insoluble, distinct amyloid fibrils from soluble proteins is related to the pathophysiology of several disorders including neurodegenerative ones (Skovronsky et al., 2006), systemic diseases such as AA and AL (amyloid light-chain) amyloidosis, and even type II diabetes (Chiti and Dobson, 2006). Many other proteins with various structures and function are able to convert to amyloid fibrils in vitro (Booth et al., 1997; Chinisaz et al., 2014a), and it is now widely believed that this process is a common, intrinsic property of proteins (Chiti et al., 2002).

Several proteins, including insulin have been used as models to investigate amyloid structures properties (Arora et al., 2004; Fodera and Donald, 2010; Loksztejn and Dzwolak, 2010). Insulin is a small peptide hormone, composed of two A and B polypeptide chains which are linked by two disulfide bonds (Baker et al., 1988). In the secretary vesicles of pancreas, the predominant form of insulin is a three-dimers hexamer containing 2–4 zinc ions, but in order to become biologically active, insulin has to take a monomeric form (Derewenda et al., 1991; Zoete et al., 2004). Similarly, amyloid formation of insulin (in vitro) occurs on monomers and is influenced by low pH, high temperature and increased ionic strength (Muzaffar and Ahmad, 2011; Sneideris et al., 2015).

In vivo, insulin amyloid fibrils have been observed in diabetic patients as part of cutaneous amyloid tumors at the sites where frequent insulin injections are made, in as many various locations as shoulders,

Abbreviations: SUC, [succinic anhydride]; SUCINS, Insulin modified by SUC; DMG, [3,3-Dimethylglutaric Anhydride]; DMGINS, Insulin modified by DMG; PHG, [2-phenylglutaric anhydride]; PHGINS, PHG1INS and PHG2INS, Insulin modified by PHG; DOD, [(2-Dodecen-1-yl)succinic anhydride]; DODINS, DOD1INS and DOD2INS, Insulin modified by DOD; HI, native human insulin.

* Corresponding author at: Biosensor Research Center, Endocrinology and Metabolism Molecular-Cellular Sciences Institute, Tehran University of Medical Sciences, Shariati Hospital, North Kargar Avenue, 1411413137, Tehran, Iran.
E-mail address: aehabibi@sina.tums.ac.ir (A. Ebrahim-Habibi).

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Full Length Article

Counteraction of the deleterious effects of reactive oxygen species on hemoglobin structure and function by ellagic acid

Masoumeh Valipour [a,b,c], Parvaneh Maghami [a,d], Mehran Habibi-Rezaei [e], Mostafa Sadeghpour [f], Mohamad Ali Khademian [g], Khadijeh Mosavi [g], Faizan Ahmad [h], Ali Akbar Moosavi-Movahedi [a,b,*]

[a] Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
[b] Center of Excellence in Biothermodynamics, University of Tehran, Tehran, Iran
[c] Department of Biology, Faculty of Science, Azarbaijan Shahid Madani University, Tabriz, Iran
[d] Department of Biology, Science and Research Branch, Islamic Azad University, Tehran, Iran
[e] School of Biology, University of Tehran, Tehran, Iran
[f] Office of Health, Safety and Environment (HSE) Oil Ministry, Tehran, Iran
[g] Office of Health, Safety and Environment (HSE) Oil Ministry, Bandar Mahshahr, Iran
[h] Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, New Delhi 110025, India

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ABSTRACT

Ellagic acid (EA) has been gaining a considerable attention in recent years. The interest in non-drug and herbal base therapies is being increased. EA is a biological molecule found in different fruits and seeds, which is known to have the ability to scavenge reactive oxygen radicals. It has been observed that methyl *tert*-butyl ether (MTBE) has destructive effects on structure and function of hemoglobin (Hb), an important respiratory blood protein. This conclusion is reached from our far-UV circular dichroism, Soret band absorption, fluorescence and oxygen affinity measurements. It has also been observed from our chemiluminscence measurements that ROS production is increased in the presence of MTBE which degrades heme in Hb. The main goal of this study was to offer a way to scavenge ROS produced during MTBE interaction with Hb. We report that EA decreased the heme degradation and ROS production in Hb solutions containing MTBE.

1. Introduction

Ellagic acid (EA) is a phenolic compound found in various fruits and nuts. Pomegranate, strawberries, raspberries and grapes are examples that contain EA [1–4]. Previous studies indicate that EA performs several significant functions such as antioxidation, and anticancer, antibacterial and anti mutagenic activities [2,5–9]. Body cells are frequently exposed to different endogenous and exogenous agents. Reactive oxygen species (ROS) may be generated due to this exposure. Under diseased conditions the balance between oxidation and antioxidation is shifted toward oxidative stress and cause damages to important biomolecules [10]. In the last few years EA has gained growing interest in medicine and food science, for it exerts the ability to quench reactive oxygen species (ROS). These could protect the cell from oxidative damages [1].

As a gasoline modifier, methyl *tert*-butyl ether (MTBE) is commonly added to fuels. MTBE improves fuel combustion by increasing the oxygen content and enhancing octane numbers. Oxygenates exposure can occur during the production of oxygenate and gasoline transportation, especially at gasoline stations [11–13]. MTBE possesses properties such as high water-miscibility and slow biodegradation in groundwater. It is a volatile compound and is being produced and used worldwide in large amount. MTBE may cause diverse environmental and human health concerns [14–18]. Different studies on animals have shown that MTBE is toxic and has carcinogenic potential [19–22]. The feasible adverse effects of MTBE on individuals were examined by limited epidemiological and clinical examinations. Their sensitivity to MTBE exposure was reported by showing several symptoms including nose, eye and mouth irritation, vomiting, headache and dizziness [23–25]. However, studies on MTBE effects at the molecular level are still lacking.

Abbreviations: MTBE, methyl *tert*-butyl ether; EA, ellagic acid; Hb, hemoglobin; ANS, 1-anilinonaphthalene-8-sulfonic acid; CD, circular dichroism; ROS, reactive oxygen species

* Corresponding author at: Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran.
E-mail address: moosavi@ut.ac.ir (A.A. Moosavi-Movahedi).

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Red/ox states of human protein disulfide isomerase regulate binding affinity of 17 beta-estradiol

Razieh Karamzadeh [a, b], Mohammad Hossein Karimi-Jafari [c], Ali Akbar Saboury [a], Ghasem Hosseini Salekdeh [b, **], Ali Akbar Moosavi-Movahedi [a, *]

[a] Department of Biophysics, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
[b] Department of Molecular Systems Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran
[c] Department of Bioinformatics, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran

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ABSTRACT

Human protein disulfide isomerase (hPDI) is a key redox-regulated thiol-containing protein operating as both oxidoreductase and molecular chaperone in the endoplasmic reticulum of cells. hPDI thiol-disulfide interchange reactions lead to the adoption of two distinct red/ox conformations with different substrate preferences. hPDI also displays high binding capacity for some endogenous steroid hormones including 17 beta-estradiol (E2) and thus contributes to the regulation of their intracellular concentration, storage and actions. The primary focus of this study was to investigate the impact of E2 binding on functional activity of recombinant hPDI. Then, we examined the effect of E2 binding on structural alteration of hPDI red/ox conformations and its influence on affinity and position of interaction using experimental and computational analysis. Our results revealed that interaction of one E2 per each hPDI molecule led to the inhibition of hPDI reductase activity and conformational changes in both oxidation states. Mutually, E2-binding position were also redox-regulated with higher affinity in oxidized hPDI compare to the reduced form. The importance of histidine-256 protonation states in distinct binding preferences of E2 were also demonstrated in hPDI red/ox conformations. These findings might pave the way for better understanding of the mechanisms behind the redox-dependent hormone-binding activity of hPDI.

1. Introduction

Preserving cellular redox balance is strongly regulated by the thiol-containing proteins that are sensitive to redox status [1]. The human protein disulfide isomerase (hPDI) is an essential redox-sensitive enzyme, associated with maintaining cellular redox poise by possessing two couples of catalytic cysteines [2,3]. hPDI is composed of four thioredoxin-like domains, a, b, b' and a' in a U-shaped architecture. The a and a' work as the catalytic domains by accommodating pairs of cysteines in conserved CGHC- motifs. The central domains (bb') are the base of the protein, which mainly involve in substrates binding and coordination of adjacent catalytic domains [4]. Structural plasticity of hPDI is typically under the influence of disulfide bonds that leads to the formation of two distinct oxidized (ox-hPDI) and reduced (red-hPDI) states [5,6]. Red-hPDI exhibits a "closed" conformation, which provides less accessible area for substrate binding on the b' domain. By contrast, oxidized form forms an "opened" structure with more accessible cleft for target acquisition [4,7,8]. hPDI redox-associated conformational changes lead to the recognition of different substrates for further oxidation, reduction and/or isomerization reactions [2].

The balance between the concentration of ox- and red-hPDI in endoplasmic reticulum is under the influence of folding load of reduced substrates (i.e. nascent or misfolded polypeptides) that regulates the redox homeostasis [2]. During the higher rate of protein synthesis in growing cells or cellular stress, hPDI-redox balance shifts into red-hPDI for oxidative protein folding/refolding [2]. Therefore, hPDI red/ox ratio varies upon different environmental and/or internal alterations that could sense cellular state.

Apart from enzymatic and chaperone-dependent activities,

* Corresponding author.
** Corresponding author.
E-mail addresses: salekdeh@royaninstitute.org (G.H. Salekdeh), moosavi@ut.ac.ir (A.A. Moosavi-Movahedi).

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The impact of different mutations at Arg54 on structure, chaperone-like activity and oligomerization state of human αA-crystallin: The pathomechanism underlying congenital cataract-causing mutations R54L, R54P and R54C

Kazem Khoshaman [a], Reza Yousefi [a,*], Ali Mohammad Tamaddon [b], Samira Sadat Abolmaali [b], Ahmad Oryan [c], Ali Akbar Moosavi-Movahedi [d], Boris I. Kurganov [e]

[a] Protein Chemistry Laboratory (PCL), Department of Biology, Shiraz University, Shiraz, Iran
[b] Center for Nanotechnology in Drug Delivery and School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran
[c] Department of Pathology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran
[d] Institute of Biochemistry and Biophysics (IBB), The University of Tehran, Tehran, Iran
[e] Bach Institute of Biochemistry, Research Center of Biotechnology of the Russian Academy of Sciences, Leninsky Ave. 33, bld. 2, Moscow 119071, Russia

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ABSTRACT

A major part of cataractogenic mutations in human αA-Crystallin (αA-Cry) occurs at Arg residues. While Arg54 is highly conserved within different species, the cataractogenic mutations R54L, R54P and R54C have been recently identified in *CRYAA* gene, encoding human αA-Cry. The detailed structural and functional aspects, stability and amyloidogenic properties of αA-Cry were determined upon the above-mentioned missense mutations, using various spectroscopic techniques, gel electrophoresis, electron microscopy, size exclusion chromatography analyses, and chaperone-like activity assay. The different mutations at Arg54 result in diverse structural alterations among mutant proteins. In addition, the mutant proteins displayed reduced thermal stability, increased amyloidogenic properties and attenuated chaperone-like activity against aggregation of γ-Cry, catalase and lysozyme. The mutant proteins were also capable of forming larger oligomeric complexes with γ-Cry which is the natural partner of α-Cry in the eye lenses. The most significant structural and functional damages were observed upon R54L mutation which was also accompanied with increased oligomeric size distribution of the mutant protein. The cataractogenic nature of R54P mutation can be explained with its detrimental effect on chaperone-like activity, conformational stability and proteolytic digestibility of the mutant protein. Also, R54C αA-Cry displayed an important intrinsic propensity for disulfide protein cross-linking with significantly reduced chaperone-like activity against all client proteins. These mutations revealed a range of detrimental effects on the structure, stability and functional properties of αA-Cry which all together can explain the pathomechanisms underlying development of the associated congenital cataract disorders.

1. Introduction

Crystallins (Crys) consist of over 90% of the total soluble proteins of vertebrate eye lenses. These highly concentrated proteins comprise a transparent matrix of high refractive index and divided into three major classes of α-, β- and γ-Cry [1–3]. As the main constituent of eye lens proteins, α-Cry is composed of two subunits (αA- and αB-Cry) with an approximate molecular mass of 20 kDa, comprising 173 and 175 amino acid residues, respectively. The αA- and αB-Cry subunits which display 57% sequence homology are capable of forming hetero oligomeric structures with age and species specific ratios of 1:1 to 3:1 [4,5]. In addition, these protein subunits assemble into the oligomers of different sizes, ranging between 300 to 1000 kDa [6,7]. While αB-Cry commonly expresses in various tissues such as eye lenses, retina, brain, heart, lungs and skeletal muscles [8], the expression of αA-Cry is mainly limited to the lens tissue [9]. As a member of vertebrate small heat shock protein family, each subunit of α-Cry contains a flexible-globular N-terminal domain and a larger C-terminal immunoglobulin fold domain which flanked by a flexible and exposed electropositive extension necessary for the interaction with client proteins [3,7,10]. In addition to their structural and refractive responsibilities, α-Cry subunits assist the folding of client proteins, thereby preventing their aggregation and precipitation in the eye lenses [3,5,7]. Also, α-Cry, by high affinity binding to copper ions, is capable of preventing the excess generation of reactive oxygen species in the lenticular tissues [11]. This

* Corresponding author.
E-mail address: ryousefi@shirazu.ac.ir (R. Yousefi).

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Interaction of insulin with colloidal ZnS quantum dots functionalized by various surface capping agents

Ghader Hosseinzadeh [a], Ali Maghari [a,*], Seyed Morteza Famil Farniya [a], Amir Homayoun Keihan [b], Ali A. Moosavi-Movahedi [b,c,**]

[a] Department of Physical Chemistry, School of Chemistry, College of Science, University of Tehran, Tehran, Iran
[b] Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
[c] Center of Excellence in Biothermodynamics, University of Tehran, Tehran, Iran

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ABSTRACT

Interaction of quantum dots (QDs) and proteins strongly influenced by the surface characteristics of the QDs at the protein–QD interface. For a precise control of these surface-related interactions, it is necessary to improve our understanding in this field. In this regard, in the present work, the interaction between the insulin and differently functionalized ZnS quantum dots (QDs) were studied. The ZnS QDs were functionalized with various functional groups of hydroxyl (−OH), carboxyl (−COOH), amine ($-NH_2$), and amino acid (−COOH and $-NH_2$). The effect of surface hydrophobicity was also studied by changing the alkyl-chain lengths of mercaptocarboxylic acid capping agents. The interaction between insulin and the ZnS QDs were investigated by fluorescence quenching, synchronous fluorescence, circular dichroism (CD), and thermal aggregation techniques. The results reveal that among the studied QDs, mercaptosuccinic acid functionalized QDs has the strongest interaction ($\Delta G^{\circ} = -31.50$ kJ/mol at 310 K) with insulin, mercaptoethanol functionalized QDs destabilize insulin by increasing the beta-sheet contents, and only cysteine functionalized QDs improves the insulin stability by increasing the alpha-helix contents of the protein, and. Our results also indicate that by increasing the alkyl-chain length of capping agents, due to an increase in hydrophobicity of the QDs surface, the beta-sheet contents of insulin increase which results in the enhancement of insulin instability.

1. Introduction

Quantum dots (QDs) are defined as luminescent semiconductor nanocrystals whose size are smaller than twice the size of their exciton Bohr radius. Because of the quantum-size confinement effect, QDs show unique optical and electronic properties [1]. Due to these novel properties, the new emerging QDs have been widely used in biomedical applications such as bioimaging [2], drug delivery [3], and therapies [4]. ZnS QDs either solely or as a shell at the surface of Cd-containing QDs, have been utilized in biomedical imaging [5], biosensing [6] and cancer diagnosis [7].

Surface capping agents are commonly used in the synthesis and functionalization of nanomaterials [8]. These materials could also be used for the stabilization and water solubilization of QDs. Surface capping agents increase the stability of QDs through electrostatic repulsion, steric stabilization, or a combination of both mechanisms [9]. In nanomaterials synthesis it is not mandatory the covalent bonding of the capping agent to the nanomaterials surface, however in functionalizing of nanomaterials by a capping agent, the capping agent must be covalently bonded to the nanomaterials surface. In the case of the synthesis and functionalization of chalcogenide QDs, sulfur-containing capping agents are the commonly used ones [6,10,11]. In such QDs, sulfur-containing capping agents are attached to the surface of the QDs through S-chalcogen bonds and their functional end group(s) determine(s) the surface characteristics of the QDs. Functional end groups of the capping agents on the surface of QDs can be further used for functionalization of the QDs or attachment of some biological agents to the surface of the QDs such as the attachment of antibodies for the target delivery purposes [12].

In biomedical applications of QDs, such as cancer diagnosis, in order to detection of various diseases the QDs as diagnostic agents are injected directly into the blood vessel and carried by blood to their targets (cancerous cells). Inside of the blood vessel, by exposure of the blood proteins to QDs, these proteins may be adsorbed on the QDs surface, leading to the formation of the protein–QDs conjugates [13–16]. The attached proteins at the surface of QDs (protein corona) undergo some

* Corresponding author.
** Correspondence to: A. A. Moosavi-Movahedi, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran.
E-mail addresses: maghari@ut.ac.ir (A. Maghari), moosavi@ut.ac.ir (A.A. Moosavi-Movahedi).

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Machine Learning and Network Analysis of Molecular Dynamics Trajectories Reveal Two Chains of Red/Ox-specific Residue Interactions in Human Protein Disulfide Isomerase

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Razieh Karamzadeh[1,2], Mohammad Hossein Karimi-Jafari[3], Ali Sharifi-Zarchi[4,5,6], Hamidreza Chitsaz[6], Ghasem Hosseini Salekdeh[2,7] & Ali Akbar Moosavi-Movahedi[1]

The human protein disulfide isomerase (hPDI), is an essential four-domain multifunctional enzyme. As a result of disulfide shuffling in its terminal domains, hPDI exists in two oxidation states with different conformational preferences which are important for substrate binding and functional activities. Here, we address the redox-dependent conformational dynamics of hPDI through molecular dynamics (MD) simulations. Collective domain motions are identified by the principal component analysis of MD trajectories and redox-dependent opening-closing structure variations are highlighted on projected free energy landscapes. Then, important structural features that exhibit considerable differences in dynamics of redox states are extracted by statistical machine learning methods. Mapping the structural variations to time series of residue interaction networks also provides a holistic representation of the dynamical redox differences. With emphasizing on persistent long-lasting interactions, an approach is proposed that compiled these time series networks to a single dynamic residue interaction network (DRIN). Differential comparison of DRIN in oxidized and reduced states reveals chains of residue interactions that represent potential allosteric paths between catalytic and ligand binding sites of hPDI.

The human protein disulfide isomerase (hPDI), is one of the most abundant redox-regulated molecular chaperones accounting for the folding of almost one-third of proteins in cells[1]. As the first discovered protein-folding catalyst[2], hPDI works as both an enzyme and a chaperone in various cellular processes including the oxidative stress, unfolded protein response, apoptosis and viral membrane fusion, using thiol disulfide exchange reactions[3–6]. A wide range of multifunctional features of hPDI are tightly associated with its unique molecular architecture. The horseshoe-like structure of hPDI is composed of four thioredoxin-like domains named a, b, b' and a' (Fig. 1). The N- and C-terminal domains – a and a' – contain conserved cysteine residues within CGHC motifs that are responsible for the formation, breakage and rearrangement of disulfide bonds on peptide/protein substrates; whereas the b and b' domains mostly contribute to substrate binding[7]. Targeted domain rearrangements during the redox-dependent activities of hPDI lead to the formation of two distinct "opened" and "closed"

[1]Department of Biophysics, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran. [2]Department of Molecular Systems Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran. [3]Department of Bioinformatics, Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran. [4]Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran. [5]Computer Engineering Department, Sharif University of Technology, Tehran, Iran. [6]Computer Science Department, Colorado State University, Fort Collins, Colorado, 80523, USA. [7]Department of Systems Biology, Agricultural Biotechnology Research Institute of Iran, Agricultural Research, Education, and Extension Organization, Karaj, Iran. Correspondence and requests for materials should be addressed to M.H.K.-J. (email: mhkarimijafari@ut.ac.ir) or A.A.M.-M. (email: moosavi@ut.ac.ir)

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Destructive effect of non-enzymatic glycation on catalase and remediation via curcumin

Fayezeh Mofidi Najjar [a, b], Fereshteh Taghavi [c], Rahim Ghadari [d], Nader Sheibani [e], Ali Akbar Moosavi-Movahedi [b, f, *]

[a] Department of Chemistry, Shahid Beheshti University, Tehran, Iran
[b] Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
[c] Faculty of Biological Science, Tarbiat Modares University, Tehran, Iran
[d] Computational Chemistry Laboratory, Department of Organic and Biochemistry, Faculty of Chemistry, University of Tabriz, Tabriz, Iran
[e] Departments of Ophthalmology and Visual Sciences, Cell and Regenerative Biology, and Biomedical Engineering, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA
[f] Center of Excellence in Biothermodynamics, University of Tehran, Tehran, Iran

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ABSTRACT

Non-enzymatic glycation of proteins is a post-translational modification that is produced by a covalent binding between reducing sugars and amino groups of lysine and arginine residues. In this paper the effect of pathological conditions, derived from hyperglycemia on bovine liver catalase (BLC) as a model protein was considered by measuring enzyme activity, reactive oxygen species (ROS) generation, and changes in catalase conformational properties. We observed that in the presence of glucose, the catalase activity gradually decreased. ROS generation was also involved in the glycation process. Thus, decreased BLC activity was partly considered as a result of ROS generation through glycation. However, in the presence of curcumin the amount of ROS was reduced resulting in increased activity of the glycated catalase. The effect of high glucose level and the potential inhibitory effect of curcumin on aggregation and structural changes of catalase were also investigated. Molecular dynamic simulations also showed that interaction of catalase with curcumin resulted in changes in accessible surface area (ASA) and pKa, two effective parameters of glycation, in potential glycation lysine residues. Thus, the decrease in ASA and increase in pKa of important lysine residues were considered as predominant factors in decreased glycation of BLC by curcumin.

1. Introduction

For a long time, the cause of diabetic complications was an open question but today there is consensus that these complications are associated with chronic hyperglycemia. Thus, high blood sugar is recognized as a causative factor in the pathogenesis of diabetes complications [1]. Exploration of the non-enzymatic glycation theory and its relation with excessive plasma and tissue glucose reinforced that these can exert pathological effects [2]. The glycation reaction typically takes place between free ε-amino groups of some amino acid residues especially lysine, arginine and sometimes histidine of a protein and glucose. This reaction leads to formation of a Schiff base, subsequently chemical rearrangement and more complex products (Amadori products). This process eventually results in the formation of advanced glycation end products (AGE) as an important glycation toxin. Numerous studies have demonstrated that glycation can cause gradual deterioration in the structure and function of proteins [3–5]. Oxidative stress is also a widely accepted consequence of chronic hyperglycemia [6,7], which is an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense mechanisms present in biological systems [8,9]. Recent studies indicated that if this ROS is not rapidly removed, it may also affect proteins through either glycoxidation pathways [10] or lipoproxidative production of reactive aldehydes [11]. There is also a causal relationship between hyperglycemia-induced ROS generation and intracellular AGE production [12]. In addition, there are numerous studies on effective antioxidant compounds which can help lower the markers

* Corresponding author. Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran.
E-mail address: moosavi@ut.ac.ir (A.A. Moosavi-Movahedi).

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Article

Detection of Guanine and Adenine Using an Aminated Reduced Graphene Oxide Functional Membrane-Modified Glassy Carbon Electrode

Di Li [1,†], Xiao-Lu Yang [1,†], Bao-Lin Xiao [1,†], Fang-Yong Geng [1,†], Jun Hong [1,2,*,†], Nader Sheibani [3] and Ali Akbar Moosavi-Movahedi [4,*]

1 School of Life Sciences, Henan University, JinMing Road, Kaifeng 475000, China; lidi0722@hotmail.com (D.L.); xiaoluy1989@sohu.com (X.-L.Y.); arixxl@163.com (B.-L.X.); gengfangyong@hotmail.com (F.-Y.G.)

2 Institute of Biotechnology, Henan University, Kaifeng 475000, China

3 Department of Ophthalmology and Visual Sciences and Biomedical Engineering, University of Wisconsin School of Medicine and Public Health, Madison, WI 53726, USA; nsheibanikar@wisc.edu

4 Institute of Biochemistry and Biophysics, University of Tehran, Enquelab Avenue, Tehran 13145-1384, Iran

* Correspondence: hongjun@henu.edu.cn (J.H.); moosavi@ut.ac.ir (A.A.M.-M.); Tel.: +86-371-2388-7799 (J.H.); +98-21-640-3957 (A.A.M.-M.)

† These authors contributed equally to this work.

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Abstract: A new electrochemical sensor based on a Nafion, aminated reduced graphene oxide and chitosan functional membrane-modified glassy carbon electrode was proposed for the simultaneous detection of adenine and guanine. Fourier transform-infrared spectrometry (FTIR), transmission electron microscopy (TEM), and electrochemical methods were utilized for the additional characterization of the membrane materials. The prepared electrode was utilized for the detection of guanine (G) and adenine (A). The anodic peak currents to G and A were linear in the concentrations ranging from 0.1 to 120 μM and 0.2 to 110 μM, respectively. The detection limits were found to be 0.1 μM and 0.2 μM, respectively. Moreover, the modified electrode could also be used to determine G and A in calf thymus DNA.

Keywords: aminated reduced graphene oxide; adenine; guanine; electrochemical detection; glassy carbon electrode

1. Introduction

Adenine (A) and guanine (G) are vital constituents of deoxyribonucleic acids. They are very important in storing genetic information. Measuring the levels of A and G is important in bioscience and clinical diagnosis, because their quantities can act as important indicators for the diagnosis of various illnesses [1–5].

Numerous technical means are used for such analyses, including chemiluminescence [6], isotope dilution mass spectrometry [7], HPLC [8,9], capillary zone electrophoresis [10], and calorimetry [11]. Among these, the electrochemical methods have many merits compared with the traditional methods including real-time application, high sensitivity, fast response, and low cost [12,13]. However, the analytical sensitivities are usually very low, due to the irreversible adsorption and weak direct electron transfer capacity for both A and G on the surface of conventional electrodes.

In order to overcome the aforementioned shortcomings, many materials are used to modify electrodes, including the carboxylation of multi-walled carbon nanotubes [14], mesoporous carbon [15], and TiO_2 nanobelts [16]. Recently, different functional membranes, such as graphene–ionic liquid–chitosan composites [17], graphene–Nafion composite membranes [18],

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

M. Nourisefat and A.A. Moosavi-Movahedi*
Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran
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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

*Corresponding author. E-mail: moosavi@ut.ac.ir