ANNUAL REPORT 2024

BCL
Biophysical Chemistry Laboratory
IBB, University of Tehran

BIOPHYSICAL CHEMISTRY LAB

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http://bcl.ut.ac.ir/1

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

International Collaborations

- **Professor T. Haertle**
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- **Professor F. Ahmad**
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- **Professor L. Saso:**
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Lab Assistant & Lab Researcher

- **Lab Assistant:**

Arash Agheli

- **Lab Researcher:**

Faezeh Moosavi-Movahedi

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Doctor of Philosophy (PhD)

- B. Davaeel
- N. MohebAlizadeh
- A. Amiri
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- E. Mirzaei
- S. Behjati
- Z. Haghparas
- M. Nourazaran
- R. Eshraghi
- R. Sattari
- Y. Shoshtari

Master of Science (MSc)

- M. Khodabandehloo
- M. Hariri

Alumni

PhD

Name	**Topic of Thesis**
E. Hosseini	Formation of amyloid fibrils and amorphous aggregates from insulin and its retrieval in ionic liquids medium

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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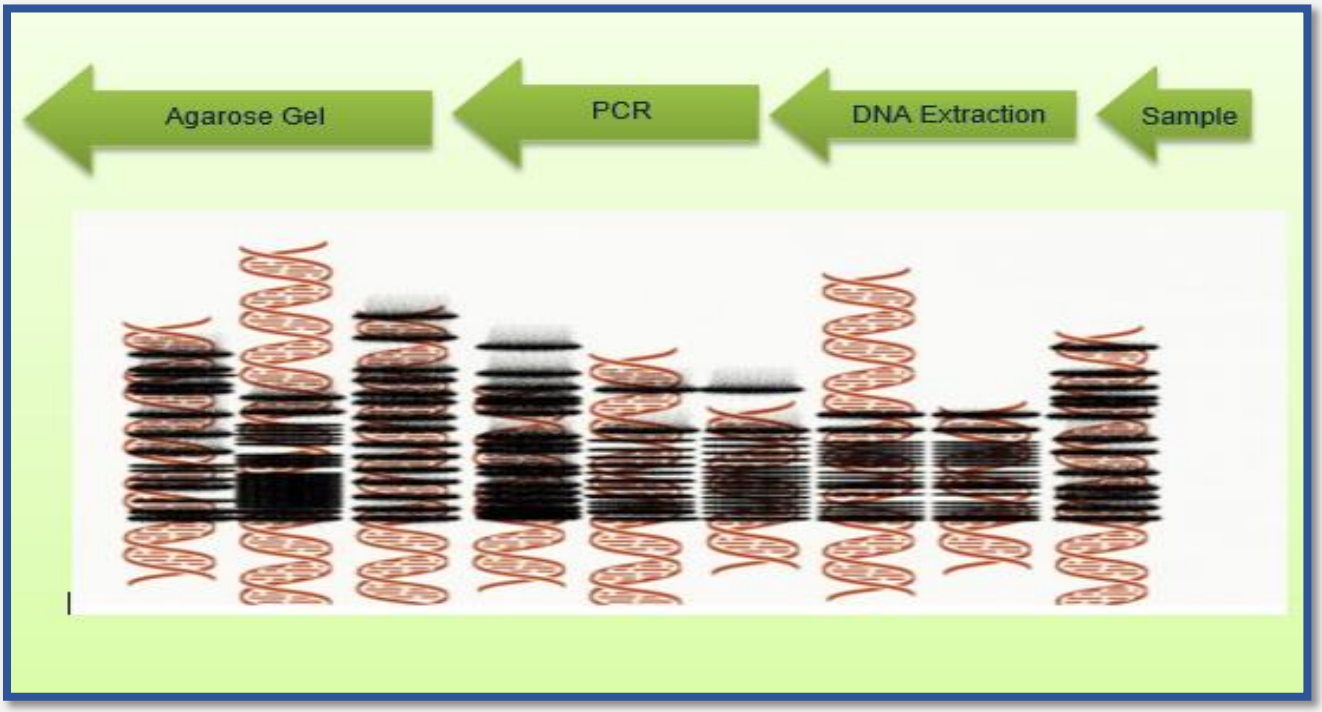

Biophysical Chemistry Kits

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

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Biophysical Chemistry Kits

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.

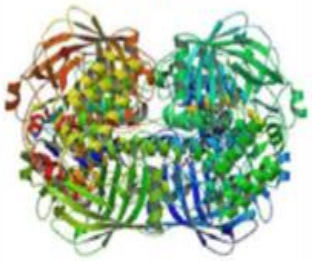
--**Textile Industry**: to remove hydrogen peroxide after bleaching and before dyeing, saving water, energy and time, not damaging the fibers and dyestuffs., and do not pollute the environment;

--**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



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Reducing the cost of catalase in industry by enzyme activation

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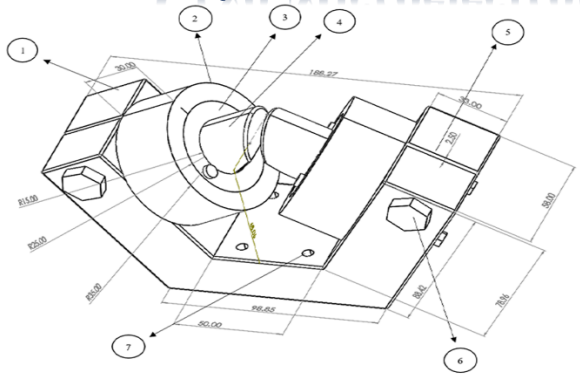
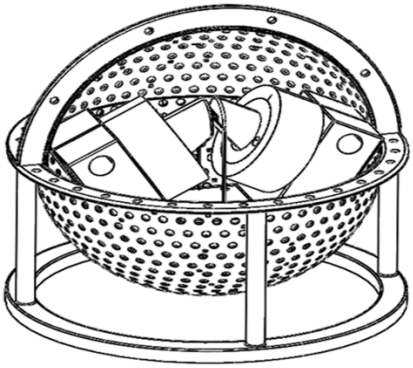
Patent

- " Cryo-microelectromagnet" Patent, No. 112450, Patent Certificate from the National Register of Real Estate, Iran, March11 2025

Cryo Microelectromagnet (CME)





Technical Description:

- Magnetic Shield: Constructed from two ABS plastic layers with embedded neodymium magnets (100 mT strength), it nullifies external magnetic fields up to 100 mT at the center, ensuring a noise-free environment.
- Electromagnet: Generates a uniform magnetic field up to 0.6 T, powered by copper coils with a water-based cooling system maintaining coil temperatures at 40°C.
- Microfluidic Chip: Features a PDMS channel with integrated microcoils (2.5 mm diameter, 20 turns) for detecting weak magnetic signals and ultrasonic wave generation (40 kHz) for inducing oscillations, reducing measurement errors to %0.01.
- Thermal Management: Thermoelectric coolers ensure precise temperature control for biological samples, critical for temperature-dependent magnetic studies.
- Innovations: Replaces traditional components with a linear variable differential transformer (LVDT) for position sensing, ultrasonic waves instead of acoustic coils, and microcoils for enhanced sensitivity.

Applications:

- Biomedical Research: Studying magnetic properties of proteins, cells, DNA, and nanoparticles for diagnostics and drug development.
- Nanotechnology: Analyzing nanomaterials and nanostructures under controlled magnetic and thermal conditions.
- Medical Diagnostics: Enabling point-of-care testing and magnetic resonance imaging (MRI) applications.
- Industrial Uses: Supporting research in electronics, energy transfer, and space technologies.

Implementation Method:

- Fabricate the PDMS microfluidic chip per standard protocols.
- Assemble the magnetic shield, ensuring neodymium magnets are correctly placed for zero-field center.
- Mount the microfluidic chip and ultrasonic source on the electromagnet.
- Connect the electromagnet to a power source, calibrate the magnetic field (up to 0.6 T) using a teslameter, and set the ultrasonic frequency.
- Introduce biological samples via inlet valves, apply magnetic field and ultrasonic waves, and process induced magnetic signals using MATLAB to generate M-H curves.
- Adjust thermoelectric coolers to maintain desired sample temperature.

Conclusion:

The Cryo Microelectromagnet represents a significant advancement in microfluidic-based magnetic analysis, offering unparalleled precision, sensitivity, and versatility. Its ability to operate in controlled thermal and magnetic environments makes it a powerful tool for biomedical, nanotechnology, and industrial applications, addressing limitations of prior systems with innovative design and functionality.

Publications

- Barati, L. Rezaei Somee, M. B. Shahsavani, A. Ghasemi, M. Hoshino, Jun Hong, A. A. Saboury, **A. A. Moosavi-Movahedi**, G. Agnetti, R. Yousefi "Insights into the dual nature of αB-crystallin chaperone activity from the p. P39L mutant at the N-terminal region" Scientific Reports 14 (1),7363 (2024)

- M. R. Ashrafi-Kooshk, F. Norouzi, A. Zare Karizak, Sh. Ahmadian, **A. A. Moosavi-Movahedi,** Gh. Riazi "Crosstalk between tau protein autoproteolysis and amyloid fibril formation" International Journal of Biological Macromolecules 262(2) 129953 (2024)

- M Nadimifar, W Jin, C Coll-Satue, G Bor, PJ Kempen, **AA Moosavi-Movahedi**, L Hosta-Rigau "Synthesis of bioactive hemoglobin-based oxygen carrier nanoparticles via metal-phenolic complexation" Biomaterials Advances, 156, 213698 (2024)

- L Alaei, M Ashengroph, **AA Moosavi-Movahedi** "Sulfonamides stimulate ROS formation upon glycation of human carbonic anhydrase II"International Journal of Biological Macromolecules,255, 128294 (2024)

- M. Edrisi, H. Daneshgar, N. Rabiee, P. Arghavani, F. Moosavi-Movahedi, A. Zare Karizak, A. Khatibi, Jun Hong, M. Bagherzadeh, **A. A. Moosavi-Movahedi**" Doxorubicin bioavailability to human hemoglobin and cancer cells via MOF-A520" Journal of Molecular Liquids, 394, 123724 (2024)

- F. Salmani, M. Mohammadi, R. Seif, S. H. Khatami, Sh. Noori, H. Sepasi Tehrani, Gh. Riazi, S. Balalaie, **A. A. Moosavi-Movahedi**, A. Moghadam Fard, K. Mahnam, A.A. Keramatinia, A. Tafakhori, V. Aghamollaei, A.R. Haghbin Toutounchi, M. R. Shahmohammadi, S. Karima "Lysine ε-aminolysis and incorporation of sulfhydryl groups into human brain tau 4R/1N and 306VQIVYK311 enhances the formation of beta structures and toxicity" International Journal of Biological Macromolecules 263(1) 130223 (2024)

- H. Abadijoo, R. Shakibi, F. Rostami Pouria, N. Manoochehri, Sh. Moharamipour, M. Hasanloo, M.R. Ghaderinia, **A. A. Moosavi-Movahedi**, M. Abdolahad, M. A. Khayamian " Charged for Destruction: Advancing Cancer Treatment with Triboelectric Nanogenerators-State of the Art and Prospects" Nano Energy, 120, 109157 (2024)

- M. Hosseini Jafari, M, B, Shahsavani, M, Hoshino, Jun Hong, A, A, Saboury, **A. A. Moosavi-Movahedi,** R, Yousefi "Unveiling the structural and functional consequences of the p. D109G pathogenic mutation in human αB-Crystallin responsible for restrictive cardiomyopathy and skeletal myopathy" International Journal of Biological Macromolecules 254(3),127933 (2024)

- L. Rezaei Somee, A. Barati, M. B. Shahsavani, M. Hoshino, Jun Hong, A. Kumar, **A.A. Moosavi-Movahedi**, M. Amanlou, R. Yousefi "Understanding the structural and functional changes and biochemical pathomechanism of the cardiomyopathy-associated p. R123W mutation in human αB-crystallin" Biochimica et Biophysica Acta (BBA)-General Subjects 1868(4) 130570 (2024)

- Faezeh Moosavi-Movahedi, A. A. Saboury, A. Ghasemi, M. Pirhaghi, F. Mamashli, M. Mohammad-Zaheri, P. Arghavani, R. Yousefi, **A. A. Moosavi-Movahedi** "Exploring the significance of potassium homeostasis in copper ion binding to human αB-Crystallin" International Journal of Biological Macromolecules 263(1) 130261 (2024)

- F. Nasiri, P. Ebrahimi, M. B. Shahsavani, A. Barati, I. Zarei, Jun Hong, M.Hoshino, **A.A. Moosavi-Movahedi**, R. Yousefi "Unraveling the impact of the p. R107L mutation on the structure and function of human αB-Crystallin: Implications for cataract formation" Biochimie 222, 151-168 (2024)
- M.R. Ghaderinia, H. Abadijoo, A. Mahdavian, E. Kousha, R. Shakibi, S. M. R. Taheri, H. Simaee, A. Khatibi, **A. A. Moosavi-Movahedi**, M. A.Khayamian "Smartphone-based device for point-of-care diagnostics of pulmonary inflammation using convolutional neural networks (CNNs)" Scientific Reports 14,6912 (2024)

- F. Molaabasi, A. Kefayat, M. Sarparast, B. Hajipour-Verdom, M. Shamsipur, A. Seyfoori. **A. A. Moosavi-Movahedi**, M. Bahrami, M. Karami, M. Dehshiri "Bioelectrocatalytic Activity of One-Dimensional Porous Pt Nanoribbons for Efficient Inhibition of Tumor Growth and Metastasis" ACS Applied Materials & Interfaces 16(23) 29581-29599 (2024)

- M. Ghahramani, M. B. Shahsavani, S. H. Khaleghinejad, A. Niazi, **A. A. Moosavi-Movahedi,** R. Yousefi " Efficient expression in the prokaryotic host system, purification and structural analyses of the recombinant human ACE2 catalytic subunit as a hybrid protein with the B subunit as a Hybrid Protein with the B Subunit of Cholera Toxin (CTB-ACE2), The Protein Journal 43,24-38 (2024)

- Amiri, S. Abedanzadeh, B. Davaeil, A. Shaabani, **A. A. Moosavi-Movahedi** "Protein click chemistry and its potential for medical applications" Quarterly Reviews of Biophysics 57,e6 (2024)

- M. Javid, A. R. Shahverdi, A. Ghasemi, **A. A. Moosavi-Movahedi**, A. Ebrahim-Habibi, Z. Sepehrizadeh "Decoding the Structure–Function Relationship of the Muramidase Domain in E. coli O157.H7 Bacteriophage Endolysin: A Potential Building Block for Chimeric Enzybiotics" Protein Journal 43, 522-543 (2024)

- P. Arghavani, S. Behjati Hosseini, F. Moosavi-Movahedi, S. Karami, M. Edrisi, M. Azadi, S. Azadarmaki, and **A. A. Moosavi-Movahedi** "In Situ Nanoencapsulation of Curcumin in Soy Protein Isolate Amyloid-like Aggregates for Enhanced Wound Healing" ACS Applied Materials & Interfaces 16(24) 30997-310 (2024)

- E. Hosseini, P. Arghavani, M. Torabi, M. A. Zolfigol, A. Sharifi, M. Mirzaei, F. Moosavi-Movahedi, A. Amiri, R. Yousefi, M. Habibi Rezaei, **A. A. Moosavi-Movahedi** "Inhibiting insulin aggregation by chaperone-like green cholinium-based DESs as additives" Journal of Molecular Liquids 407,125274 (2024)

- S. Abdalbage, Bao-Lin Xiao, Xin-Xin Ma, Yang-Yang Li, Jian-She Wei, **A. A. Moosavi-Movahedi**, R. Yousefi, Jun Hong" Catalase immobilization: Current knowledge, key insights, applications, and future prospects" International Journal of Biological Macromolecules 276, 133941(2024)

- S. Ghareghomi, P. Arghavani, M. Mahdavi, A. Khatibi, C. García-Jiménez, and **A. A. Moosavi-Movahedi** "Hyperglycemia-driven signaling bridges between diabetes and cancer" Biochemical Pharmacology Journal 229, 116450 (2024)

- N. Golestannezhad, A. Divsalar, F. Badalkhani-Khamseh, M. Rasouli, A. Seyedarabi, B.Ghalandari, Xianting Ding, F. Goli, S. Bekeschus, **A. A. Moosavi-Movahedi**, M. Eslami Moghadam "Oxali-palladium nanoparticle synthesis, characterization, protein binding, and apoptosis induction in colorectal cancer cells" Journal of Materials Science: Materials in Medicine 35(1),4 (2024)

- S. Abedanzadeh, Sh. Ariaeenejad, B. Karimi, **A. A. Moosavi-Movahedi** Revolutionizing protein hydrolysis in wastewater: Innovative immobilization of metagenome-derived protease in periodic mesoporous organosilica with imidazolium framework" International Journal of Biological Macromolecules 278(4) 134966 (2024)

- N. Khosravi, M. Zarabi, M. M. Dehghan, S. Farzad-Mohajeri, H.Aminianfar, M. Shafie, N. Shadmehri, P. Houshmand, N. Samiei, **A. A. Moosavi-Movahedi**, M. Habibi-Rezaei "Bioinspired wound dressing: Investigating coelomic fluid-enhanced chitosan/polyvinyl alcohol nanofibers" International Journal of Pharmaceutics 666, 124765 (2024)

- S. Rostaminasab, A.R. Esmaeili, F. Moosavi-Movahedi, S. Memarkashani, H. Rezaei Rudmianeh, M. Shourian, M. Shafiee Ardestani, **A. A. Moosavi-Movahedi**, S. M. Asghari "Enhanced antitumor activity of lapatinib against triple-negative breast cancer via loading in human serum albumin" International Journal of Biological Macromolecules 282(2), 136760 (2024)

- S. Behjati Hosseini, P. Arghavani, Jun Hong, H. R. Rahimi, S. Azad-Armaki, Reza Yousefi, **A. A. Moosavi-Movahedi** "Curcumin-loaded Pickering Emulsions Based on Soy Protein Isolate Aggregates Enhance Diabetic Wound Healing" Journal of Drug Delivery Science and Technology 101, Part B, 106279 (2024)

- B. Davaeil, A. Saremipour, F. Moosavi-Movahedi, S. M. Asghari, **A. A. Moosavi-Movahedi** "Differential scanning calorimetric domain dissection for HSA upon interaction with Bortezomib: Unveiling the binding dynamics" International Journal of Biological Macromolecules 283(2), 137728 (2024)

- Kexin Xu, Linlin Ma, Yujie Chen, Yuying Li, Sanad Abdalbage, **A. A. Moosavi-Movahedi**, R. Yousefi, Jun Hong, Baolin Xiao "A biosensor based on MWCNTs-BSA and TiO2-Laccase nanocomposite modified glassy carbon electrode for sensitive detection of luteolin in traditional Chinese Medicine" Microchemical Journal 207, 112103 (2024)

- Lin-Lin Ma, Ke-Xin Xu, Bao-Lin Xiao, S. M. Abdalsadeg, Yu-Jie Chen, Yu-Ying Li, Jun Hong, **A. A. Moosavi-Movahedi** " An electrochemical sensor based on NH2-MWCNTS-CMC and ZIF-67 peroxidase-like nanocomposite for sensitive luteolin detection" J Iran. Chem. Society 21,2873-2886 (2024)

- Yu-Ying Li, Yu-Jie Chen, S. M. Abdalsadeg, Ke-Xin Xu, Lin-Lin Ma, **A. A. Moosavi-Movahedi**, Jun Hong, Bao-Lin Xiao " Biosensor Based on ZIF-67-HRP and MWCNTs Nanocomposite Modified Glass Carbon Electrode for the Detection of Luteolin in Vegetables" Langmuir 40(39) 20495-20504(2024)

- F. Adhami, S. Salmani Zarji, Kh. Nazari, A. Mahmoudi, **A. A. Moosavi-Movahedi,** N. Mohammadian Tabrizi "Biotransformation of t-butyl phenols by micellar nanoreactors of peroxidase/ionic surfactants at mild conditions: nanobiocatalyst performance and kinetic analysis" Journal of Dispersion Science and Technology (2024)

Keynote Speakers

- **A. Moosavi-Movahedi** “Conceptual view on protein functionality” Iran 5th Conference on Protein and Peptide Science, University of Tehran, May 8-9, 2024. Published in Biomacromolecular Journal, Vol 10(2), page 102, 2024 (Plenary Lecture)

- **A. Moosavi-Movahedi** “Human Imitation of Extremophiles and Resilient Organisms: Tardigrades” 18th Conference of Iran Society of Biophysical Chemistry, Dec 25-266, 2024, University of Hormozgan, Bandarabbas, Iran. (Plenary Lecture)

Selected Papers

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Synthesis of bioactive hemoglobin-based oxygen carrier nanoparticles via metal-phenolic complexation

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ARTICLE INFO

Keywords:
Binding mechanism
Hemoglobin-based oxygen carriers
Manganese ions
Metal-phenolic assembly
Tannic acid

ABSTRACT

The transfusion of donor red blood cells (RBCs) is seriously hampered by important drawbacks that include limited availability and portability, the requirement of being stored in refrigerated conditions, a short shelf life or the need for RBC group typing and crossmatching. Thus, hemoglobin (Hb)-based oxygen (O_2) carriers (HBOCs) which make use of the main component of RBCs and the responsible protein for O_2 transport, hold a lot of promise in modern transfusion and emergency medicine. Despite the great progress achieved, it is still difficult to create HBOCs with a high Hb content to attain the high O_2 demands of our body. Herein a metal–phenolic self-assembly approach that can be conducted in water and in one step to prepare nanoparticles (NPs) fully made of Hb (Hb-NPs) is presented. In particular, by combining Hb with polyethylene glycol, tannic acid (TA) and manganese ions, spherical Hb-NPs with a uniform size around 350–525 nm are obtained. The functionality of the Hb-NPs is preserved as shown by their ability to bind and release O_2 over multiple rounds. The binding mechanism of TA and Hb is thoroughly investigated by UV–vis absorption and fluorescence spectroscopy. The binding site number, apparent binding constant at two different temperatures and the corresponding thermodynamic parameters are identified. The results demonstrate that the TA-Hb interaction takes place through a static mechanism in a spontaneous process as shown by the decrease in Gibbs free energy. The associated increase in entropy suggests that the TA-Hb binding is dominated by hydrophobic interactions.

1. Introduction

The transfusion of donor blood is a mainstream clinical procedure used to save lives in the context of traumatic injuries, surgical procedures, or for patients suffering from cancer, anemia, and bleeding disorders [1,2]. Despite its relevance, the use of donor blood is accompanied by important drawbacks such as limited availability, risk for disease transmission or immunological reactions. Furthermore, before blood can be transfused, there is a need for blood group typing and matching, which can result in critical delays in emergency situations [3,4]. Additionally, donor blood special storage requirements (in refrigerated conditions) and short storage lifetime (i.e., of 3–6 weeks in the refrigerator) makes it impossible to create large stockpiles when severe catastrophes take place (e.g., earthquakes, plane crashes, terrorist attacks). Thus, in an attempt to overcome these important limitations, hemoglobin (Hb)-based oxygen (O_2) carriers (HBOCs), which do not display blood type and can be stored as a freeze-dried powder for long periods of time, are currently being developed [1,4]. As highlighted in their name, HBOCs make use of Hb, which is the main component of biological red blood cells (RBCs) and the responsible protein for O_2 transport. While HBOCs have been formulated as chemically modified Hb suspensions (i.e., polymerized Hb [5,6] Hb or polyethylene glycol (PEG) conjugated Hb [7,8]), Hb encapsulation within micro- and nanosized delivery vehicles has gained a lot of attention over the past years [4,9]. Such an approach prevents Hb's extravasation from the blood vessels and avoids the dissociation of the protein tetramer with the subsequent loss of functionality. Due to these advantages, Hb has been already encapsulated within different carriers which include liposomes [10], polymersomes [11], polymer capsules [12–16] or metal-organic frameworks [17–19].

However, a challenge when designing HBOCs is to achieve a high Hb loading which is needed to attain an O_2-carrying capacity similar to that of blood. Actually, biological RBCs lack a cell nucleus and most

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Doxorubicin bioavailability to human hemoglobin and cancer cells via MOF-A520

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Drug-Hemoglobin interaction

ABSTRACT

Cancer is one of the most serious and challenging issues in the life sciences, with complicated and multifactorial mechanisms making it difficult to manage. With this complexity comes various strategies for attacking tumors, including using nanomaterials to target tumor cells, bioavailability and deliver anticancer drugs directly. Doxorubicin (DOX) is a well-known and powerful anticancer drug, but its high toxicity limits its application. Intending to reduce the cytotoxic effects of DOX on normal cell line and deliver it to cancerous cell line, the present study attempts to design and synthesize a modified metal–organic framework (MOF) named A520 and a composite containing DOX (A520@DOX). The synthesized MOFs were characterized using X-ray diffraction (XRD), electron microscopy (TEM and FESEM), and FTIR. Subsequently, the toxicity of DOX was assessed at the cellular and molecular levels using MTT assays (for the cell lines MCF −10A and MCF-7) and various biophysical assays targeting human hemoglobin (Hb). Following expectations, free DOX was highly cytotoxic and strongly affected Hb structure (converting it into methemoglobin species), while the toxicity was significantly reduced in the A520@DOX composite form. It is important to mention that DOX released from the A520@DOX was significantly pH-sensitive, so it was more pronounced in acidic pH 5 (resembling a cancerous pH environment). Furthermore, the effect of DOX released from A520@DOX resulted in more oxyHb and deoxyHb species as functional Hb species. The present study used an effective DOX delivery and bioavailability nanosystem to control cytotoxicity and ensure slow drug release.

1. Introduction

A high risk of cancer and the side effects of anticancer drugs [1] (high toxicity and production of reactive oxygen species) has prompted using some types of cost-effective nanomaterials as drug delivery vehicles to minimize the toxicity [2]. Metal-organic frameworks (MOFs) are nanomaterials that can be synthesized in a wide range of sizes with green chemistry features, consisting of functional surfaces [3]. Each MOF has two components: the metal cluster as a metal center group and multidentate organic acid as a linker [4]. These characteristics allow MOFs to be designed to load various molecules for diverse purposes [5]. Applications can be used to multiple biomedical fields, including drug bioavailability [6] and delivery [7,8], gene modification [9], biosensing [10], catalysis [11], pollution absorption and delivery of biomolecules and nutrients [9]. Therefore, MOFs, particularly those with sizes under 100 nm [12], are well-suited for specialized drug delivery systems (DDS) [13].

Modulating the side effects of pharmaceuticals has become a significant challenge for specific drug delivery to targeted tissues [14]. DDS mainly implies a broad spectrum of carriers at nano-scale dimensions [15]. MOFs exhibit a remarkable combination of attributes, including a high surface-to-volume ratio, substantial porosity, adjustable pore sizes [16–18], and the ability to accommodate a diverse array of compounds due to their broad range of physicochemical characteristics, whether

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Exploring the significance of potassium homeostasis in copper ion binding to human αB-Crystallin

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ABSTRACT

αB-Crystallin (αB-Cry) is a small heat shock protein known for its protective role, with an adaptable structure that responds to environmental changes through oligomeric dynamics. Cu(II) ions are crucial for cellular processes but excessive amounts are linked to diseases like cataracts and neurodegeneration. This study investigated how optimal and detrimental Cu(II) concentrations affect αB-Cry oligomers and their chaperone activity, within the potassium-regulated ionic-strength environment. Techniques including isothermal titration calorimetry, differential scanning calorimetry, fluorescence spectroscopy, inductively coupled plasma atomic emission spectroscopy, cyclic voltammetry, dynamic light scattering, circular dichroism, and MTT assay were employed and complemented by computational methods. Results showed that potassium ions affected αB-Cry's structure, promoting Cu(II) binding at multiple sites and scavenging ability, and inhibiting ion redox reactions. Low concentrations of Cu(II), through modifications of oligomeric interfaces, induce regulation of surface charge and hydrophobicity, resulting in an increase in chaperone activity. Subunit dynamics were regulated, maintaining stable interfaces, thereby inhibiting further aggregation and allowing the functional reversion to oligomers after stress. High Cu(II) disrupted charge/hydrophobicity balance, sewing sizable oligomers together through subunit-subunit interactions, suppressing oligomer dissociation, and reducing chaperone efficiency. This study offers insights into how Cu(II) and potassium ions influence αB-Cry, advancing our understanding of Cu(II)-related diseases.

1. Introduction

αB-Crystallin (αB-Cry) is a well-known member of the small heat shock protein (sHSP) family. This functional oligomeric protein has a unique structure and is abundant in the mammalian eye lens, as well as other tissues like the brain, heart, kidney, lung, and skeletal muscle. As a molecular chaperone, αB-Cry protects other proteins from irreversible aggregation due to environmental stress through its ATP-independent holdase activity [1–4]. αB-Cry forms highly dynamic, polydisperse, and flexible complexes, lacking a well-defined quaternary structure. These complexes exhibit significant alterations in response to changes in the external environment and perform a diverse range of functions [5,6]. However, dysfunction of αB-Cry has been linked to various diseases, including cataracts, neurodegenerative diseases like Parkinson's, Alzheimer's, and multiple sclerosis, as well as cardiomyopathy and cancer [1,7].

Human αB-Cry has three main domains: the α-crystallin domain (ACD), the N-terminal region (NTR), and the C-terminal region (CTR). The ACD, a key feature of the sHSP family, consists of seven antiparallel β-sheet structures. Two monomers join in an antiparallel fashion *via* ACD domains, forming a dimer with an extended β-sandwich structure through the "AP" (antiparallel interface). This interface features conserved Arg, His, and Glu amino acids, promoting stable electrostatic interactions. The CTR anchors oligomer formation and determines environment-specific sizes, while the hydrophobic, dynamic NTR domain is responsible for oligomer assembly and distribution [8–10]. Environmental stress, such as heat, triggers the enhancement of subunit dynamic, leading to the exposure of hydrophobic surfaces to the solvent and an increase in chaperone activity. It takes 22 h at 37 °C and 20 min at 48 °C for all subunits within oligomers to be exchanged [11].

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Review

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Protein click chemistry and its potential for medical applications

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Abstract

A revolution in chemical biology occurred with the introduction of click chemistry. Click chemistry plays an important role in protein chemistry modifications, providing specific, sensitive, rapid, and easy-to-handle methods. Under physiological conditions, click chemistry often overlaps with bioorthogonal chemistry, defined as reactions that occur rapidly and selectively without interfering with biological processes. Click chemistry is used for the post-translational modification of proteins based on covalent bond formations. With the contribution of click reactions, selective modification of proteins would be developed, representing an alternative to other technologies in preparing new proteins or enzymes for studying specific protein functions in different biological processes. Click-modified proteins have potential in diverse applications such as imaging, labeling, sensing, drug design, and enzyme technology. Due to the promising role of proteins in disease diagnosis and therapy, this review aims to highlight the growing applications of click strategies in protein chemistry over the last two decades, with a special emphasis on medicinal applications.

Introduction

Chemical modification of proteins has become a valuable tool for developing modified proteins. Playing complementary roles to genetic techniques, we have a broad toolkit that allows us to create an almost unlimited number of protein constructs with natural or synthetically modified residues using chemical modifications (Stephanopoulos and Francis, 2011). The ideal requirements for such reactions include functional group tolerance/compatibility, water as a reaction medium, selectivity, high reaction rates, neutral pH and room temperature (or up to 40 °C), nontoxic reagents, and low reactant concentrations. Reactions must be designed and implemented to achieve high modification efficiencies without the need for tedious and inefficient purification/characterization protocols. For in vivo studies, chemical modification methods involving those listed above are appropriate since they do not interfere with normal cell function (Boutureira and Bernardes, 2015). Protein modifications have a significant impact on signaling, migration, differentiation, and trafficking as important cellular processes through sulfation, phosphorylation, methylation, acylation, ubiquitination, glycosylation, farnesylation, and so on (Walsh et al., 2005).

Posttranslational protein modifications (PTMs) are commonly thought to be responsible for the vast biodiversity found in nature today (Boutureira and Bernardes, 2015). These modifications usually occur after protein translation. In this regard, considering the characteristics of the natural modification of proteins, it can be concluded that the efficient and controlled reproducing of PTM provides a valuable tool in the study and precise function of proteins. In addition to the facilities provided by (bio)orthogonal methods; it allows precise and site-selective modification of proteins, making it a valuable tool for in vivo and in vitro studies (Bernardes et al., 2010; Kee and Muir, 2012). Considering the various methods used for chemical modification, it will now be feasible to choose the target residue and modification type to provide the required property/function such as chemical affinity probes, fluorophores, reactive tags, and so forth. Despite the enormous progress made in the bioconjugation of proteins, there are still many serious challenges, not only from a synthetic point of view but also in manufacturing, processing, stability, and safety. Some types of proteins can be modified using methods that are not appropriate for all kinds of proteins (Boutureira and Bernardes, 2015). Therefore, there is still a need for the development of complementary reactions for site-selective modifications of proteins that are efficient, robust, and mild. The various aspects of protein synthesis have been discussed in detail (Bernardes et al., 2010), from general chemical ligation strategies (Hackenberger and Schwarzer, 2008; Kent, 2009; Siman and Brik, 2012), endogenous amino acid modification (Baslé et al., 2010), to click modification protocols (Lallana et al., 2011; Van Berkel et al., 2011; Palomo, 2012; Tasdelen and Yagci, 2013), which are more specialized on specific PTMs, including glycosylation

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In Situ Nanoencapsulation of Curcumin in Soy Protein Isolate Amyloid-like Aggregates for Enhanced Wound Healing

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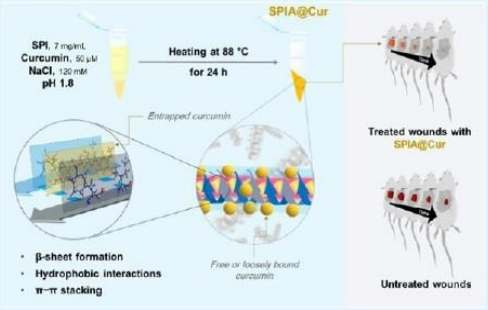
ABSTRACT: The importance of amyloid nanofibrils made from food proteins is rising in diverse fields, such as biomedicine and food science. These protein nanofibrils (PNFs) serve as versatile and sustainable building blocks for biomaterials, characterized by their high β-sheet content and an ordered hydrogen bond network. These properties offer both stability and flexibility, along with an extreme aspect ratio and reactive functional groups. Plant-derived amyloid nanofibrils, such as soy protein isolate (SPI) PNFs, are increasingly favored due to their affordability and sustainability compared with animal proteins. This study aimed to explore the formation and application of SPI amyloid-like aggregates (SPIA) and their nanoencapsulation of curcumin (Cur) for biomedical purposes, particularly in wound healing. Under specific conditions of low pH and high temperature, SPIA formed, exhibited an amyloid nature, and successfully encapsulated Cur, thereby enhancing its stability and availability. Spectroscopic and microscopic analyses confirmed structural changes in SPIA upon the incorporation of Cur and the fabrication of SPIA@Cur. The obtained results indicate that in the presence of Cur, SPIA forms faster, attributed to accelerated SPI denaturation, an increased nucleation rate, and enhanced self-assembly facilitated by Cur's hydrophobic interactions and $\pi-\pi$ stacking with SPI peptides. In vitro studies demonstrated the biocompatibility, biodegradability, and antioxidant properties of SPIA@Cur along with controlled release behavior. In vivo experiments in male Wistar rats revealed that both SPIA and SPIA@Cur significantly accelerate wound closure compared with untreated wounds, with SPIA@Cur showing slightly better efficacy. The histological analysis supported enhanced wound healing, indicating the potential of SPIA@Cur for biomedical applications.



KEYWORDS: *soy protein isolate, protein aggregation, amyloid nanofibrils, curcumin, wound healing*

INTRODUCTION

Food protein-based amyloid nanofibrils (5−10 nm wide) are quickly becoming the versatile and sustainable building blocks of biomaterials for an outspread of applications from food/pharmaceutical industries to material science and environmental science.[1−4] Protein/peptide monomers form hydrogen bonds between themselves and establish an extremely ordered network, resulting in the fabrication of nanoscale amyloid-like fibrillary aggregates[5,6] known as protein nanofibrils (PNFs). These attractive materials provide high stability and flexibility along with a remarkable aspect ratio (length: width ≈ 1000) as well as serving various reactive functional groups on their surfaces.[7−10] Self-assembled amyloid fibrils were discovered early on in human neurodegenerative diseases.[11] Later, it was substantiated that fibrillogenesis and amyloid formation are universal traits of all proteins. Goldschmidt et al. conducted a thorough genome survey and found that proteins invariably possess at least one short sequence that triggers amyloid fibril formation[12] so-called aggregation-prone regions (APRs). Functional fibrillary amyloids have also been characterized in different living kingdoms, from bacteria to humans, that perform key functional biological roles.[3] On top of that, fibrillization is thought to be an efficient approach to improving and enriching food protein functionality.[13] Fabricated PNFs made from food proteins are becoming more and more popular as starting materials and building blocks because of their affordable price and sustainability. Additionally, the aggregation and induction of fibrillogenesis in plant-based protein sources are more appealing since plant proteins are not as functional and can only be used in food science sparsely compared to animal proteins.[3] Nonetheless,

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Review

Hyperglycemia-driven signaling bridges between diabetes and cancer

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ABSTRACT

Growing epidemiological evidence indicates an association between obesity, type 2 diabetes, and certain cancers, suggesting the existence of common underlying mechanisms in these diseases. Frequent hyperglycemias in type 2 diabetes promote pro-inflammatory responses and stimulate intracellular metabolic flux which rewires signaling pathways and influences the onset and advancement of different types of cancers. Here, we review the provocative impact of hyperglycemia on a subset of interconnected signalling pathways that regulate (i) cell growth and survival, (ii) metabolism adjustments, (iii) protein function modulation in response to nutrient availability (iv) and cell fate and proliferation and which are driven respectively by PI3K (Phosphoinositide 3-kinase), AMPK (AMP-activated protein kinase), O-GlcNAc (O-linked N-acetylglucosamine) and Wnt/β-catenin. Specifically, we will elaborate on their involvement in glucose metabolism, inflammation, and cell proliferation, highlighting their interplay in the pathogenesis of diabetes and cancer. Furthermore, the influence of antineoplastic and antidiabetic drugs on the unbridled cellular pathways will be examined. This review aims to inspire the next molecular studies to understand how type 2 diabetes may lead to certain cancers. This will contribute to personalized medicine and direct better prevention strategies.

1. Introduction

Cancer is the second [1] and diabetes the ninth [2] the leading cause of mortality worldwide. The history of the identification and occurrence of these diseases and the association between diabetes and cancer dates many years ago [3]. Further studies identifying the mechanisms of these diseases have been a challenge all these years. The high prevalence of these diseases is a matter of concern that highlights the need for detailed studies. Lifestyle changes and sedentarism during the past decades are effective drivers for the development of obesity and associated diseases including type 2 diabetes (T2D) and various cancers [4,5]. T2D is reaching pandemic dimensions and is a serious threat to human health,

Abbreviations: AKT, Ak strain Transforming or Protein Kinase B; ROS, reactive oxygen species; T1D, type 1 diabetes; T2D, type 2 diabetes; AGEs, advanced glycation end-products; MAPKs, mitogen-activated protein kinases; PI3K, phosphoinositide 3-kinases; PKC, protein kinase C; AMPK, AMP-activated protein kinase; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B; HO-1, heme oxygenase-1; NQO-1, NAD(P)H- quinone oxidoreductase-1; HIF-1, hypoxia-inducible factor 1; c-AMP, cyclic adenosine mono phosphate; IGF-1, insulin-like growth factor-1; PPARγ, peroxisome proliferator-activated receptor-γ; TXNIP, thioredoxin interacting protein; PDK1, pyruvate dehydrogenase kinase 1; EMT, epithelial-to-mesenchymal transition; MMPs, matrix metalloproteases; PTEN, phosphatase and tensin homologue; GSK3, glycogen synthase kinase 3; FoxO1, forkhead box protein O1; PGC1α, peroxisome proliferator-activated receptor-coactivator 1α; PEPCK, phosphoenolpyruvate carboxykinase; SREBP, sterol regulatory element-binding proteins; FFA, free fatty acid; S6K1, S6 kinase 1; mTOR, mammalian target of rapamycin; LKB1, liver kinase B1; CaMKKβ, calmodulin-dependent protein kinase kinase β; TAK1, TGF-b-activated kinase-1; CDKN1A, cyclin-dependent kinase inhibitor 1A; CDKN1B, cyclin-dependent kinase inhibitor 1B; GLUT4, glucose transporter type 4; OGT, O-GlcNAc transferase; OGA, N-acetyl-glucosaminidase; HBP, hexosamine biosynthetic pathway; GFAT1, glutamine: fructose-6-phosphate aminotransferase; CDK1, cyclin-dependent kinase 1; ACs, adenylyl cyclases; TCF7L2, transcription factor 7-like 2; LRP5/6, lipoprotein receptor-related protein 5/6; TCF, T cell factor; LEF, lymphoid enhancer factor; SGLT2, sodium-glucose linked co-transporter-2; SU, sulfonylureas; AGIs, α-Glucosidase Inhibitors; TZDs, thiazolidinediones; GLP-1 RA, GLP1 Receptor Agonists; DPP4-i, DPP4 Inhibitors; SGLT2-i, SGLT2 Inhibitors.

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Curcumin-loaded pickering emulsions based on soy protein isolate aggregates enhance diabetic wound healing

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ABSTRACT

Wound healing in diabetic patients is more complex and prolonged in comparison to nondiabetic persons, and dealing with this problem has attracted considerable attention from researchers. According to its anti-inflammatory and anti-infective properties, Curcumin has a valued place in therapeutics, including wound healing. Still, its low stability and poor bioavailability are significant barriers to using its desirable properties. Hence, various biocompatible and biodegradable delivery systems have been developed to address this issue. In this study, Pickering emulsion (PE) prepared from soybean oil containing curcumin and modified SPI solution at 85 °C at pH 2.0 with 130 mM NaCl for different durations were used as a delivery system for curcumin. Changes in SPI properties were analyzed using fluorescence spectroscopy, Fourier transform infrared spectroscopy, and tensiometry methods. The prepared PEs were studied using microscopic techniques. Curcumin loading efficiency by PE was measured by UV–visible spectroscopy, and the impact of curcumin-loaded PE on wound healing was tested in diabetic rats. Spectroscopic studies and microscopy images revealed SPI amyloid-like aggregates suitable for stabilizing oil-in-water PEs. Tensiometry and creaming stability studies indicated that at least 6 h of heating ($HSPI_6$) is necessary for optimal stability. Curcumin encapsulation efficiency was 95.7 ± 2.1 %. Curcumin-loaded PE-$HSPI_6$ increased the healing rate of diabetic wounds in male Wistar rats by 1.46-fold. This study presents an approach for using biocompatible and biodegradable PEs to deliver hydrophobic compounds like curcumin for accelerating diabetic wound healing.

1. Introduction

Diabetes mellitus is a chronic metabolic disease, and Hyperglycemia in diabetic patients is the primary cause of delayed or impaired wound healing, which causes chronic wounds, especially diabetic foot ulcers [1]. The slow healing of diabetic wounds occurs due to complexities such as decreased levels of growth factors, impaired cell proliferation and migration, the occurrence and progression of hypoxia, reduced angiogenesis, dysfunctional macrophages, and chronic inflammation and infections [2–4]. Controlling inflammation and infection is an essential approach for treating and preventing the spread of diabetic ulcers [5]. Up to now, various dressing methods have been used for diabetic wound healing, including nanofibers, films, foams [6], and hydrogels [7], but emulsions, especially Pickering emulsions (PEs), have received less attention in this regard.

Emulsions, which are extensively employed in the food [8] and pharmaceutical [9] industries, are mixtures of two or more immiscible liquids in which a discrete phase is dispersed in a continuous phase [10]. Emulsions are thermodynamically unstable due to their high interfacial energy. Traditionally, emulsion stabilization relies on chemical emulsifiers. However, a newer approach suggests using surface-active solid particles as a physical barrier between the oil and water phases to address this challenge [11]. The emulsions produced by this method are called Pickering emulsions (PEs) [12], which have attracted significant interest due to their low toxicity [13] and enhanced biocompatibility resulting from the utilization of colloidal particles instead of surfactants [14]. The key point in forming PEs is ensuring that the solid colloidal particles are partially wetted by both phases while insoluble in both.

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Bioinspired wound dressing: Investigating coelomic fluid-enhanced chitosan/polyvinyl alcohol nanofibers

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ABSTRACT

The electrospun mats consisting of integrated coelomic fluid (CF) and chitosan (Chs) into polyvinyl alcohol (PVA) nanofibers were produced and evaluated for use as wound dressings. CF was obtained from earthworms (*Eisenia andrei (Fetida)*) using an electric shock method, while Chs was chemically produced from shrimp chitin and then characterized using titration, Fourier transform infrared (FT-IR) spectroscopy, and viscometry. The wound dressings with different CF contents were evaluated for their antibacterial, antioxidant, and cell viability properties. The dressings infused with CF showed significantly higher antibacterial and antioxidant activity, as well as improved cell viability compared to the control without CF. *In vivo* studies using adult Wistar albino rats showed that the Chs/PVA/CF wound dressings promoted wound healing and re-epithelialization. Moreover, histological examinations of the injuries coated with Chs/PVA/CF displayed improved re-epithelialization. These results suggest that the Chs/PVA/CF nanofiber has the potential for use as a wound dressing material.

1. Introduction

Biomimetics is a scientific discipline that uses inspiration from nature's designs and processes to address problems and improve the quality of human life (Blok and Gremmen, 2016). It has led to significant accomplishments, such as the development of biocompatible and biodegradable products, which have reduced waste, saved research costs, and mitigated threats to natural resources (Miran et al., 2021). Biomimetic properties such as biocompatibility, biodegradability, and non-toxicity are of paramount importance when designing nanofiber dressings. Consequently, researchers have recently been interested in using nanoparticles and natural products (Chs, curcumin, honey, and essential oils) for antibacterial wound dressings. For numerous years, Chs has been extensively used in the medical field for its heightened antibacterial and wound-healing attributes (Singh et al., 2017). The escalation of microbial resistance in a globalized world has led to a decline in new antibiotic research efforts (Ge et al., 2017). Efforts have been made to incorporate various natural materials into scaffolds to enhance their antibacterial, antioxidant, and wound-healing properties.

Biopolymers like chitin ($C_8H_{13}O_5N$) (Cht) and chitosan ($C_6H_{11}O_4N$) (Chs) in conjunction with proteins such as collagen, silk, and elastin, are used in creating nature-inspired composite scaffolds that are of great interest today (Lapidot et al., 2012). Cht and its main derivative Chs have properties including biocompatibility, biodegradability, lightweight, stability, acceptable mechanical and physical properties (Miran et al., 2021), and the ability to be converted into various forms of fibers, hydrogels, sponges, membranes, and films (Muxika et al., 2017).

Chitin (Cht) is a renewable polymer that is mostly found in

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Differential scanning calorimetric domain dissection for HSA upon interaction with Bortezomib: Unveiling the binding dynamics

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ABSTRACT

Human serum albumin (HSA), a crucial plasma protein, plays a significant role in drug interactions within the bloodstream, bearing considerable clinical relevance. Bortezomib (BTZ) is a potent anti-cancer drug for multiple myeloma (MM) and mantle cell lymphoma (MC). The mechanism of BTZ transfer in the blood remains undetermined. This study aims to investigate the binding of BTZ to HSA using the techniques of differential scanning calorimetry (DSC), circular dichroism (CD), fluorescence spectroscopy, and computational methods such as molecular docking and molecular dynamics simulations. This study presents the thermal dissection of domain I (D_I) of HSA by subjecting it to a temperature elevation of 79.2 °C (2 °C above T_m of D_I) using DSC, which provides new information on the thermal behavior of HSA domains. Furthermore, the deconvolution analysis of the HSA thermogram in the absence and presence of BTZ revealed that the drug binding site is located in D_I and impacts D_{II}. The interaction between BTZ and HSA with a binding affinity (K_b) of $7.744 \pm 0.2 \times 10^5$ M^{-1} influences protein dynamics and reduces HSA's thermal stability by almost 1 °C. This study is crucial for predicting the pharmacokinetics and pharmacodynamics of BTZ, aiding in developing safer and more effective treatments for MM and MC.

1. Introduction

Bortezomib (BTZ) is a dipeptide boronic acid that binds selectively and reversibly to the 26S proteasome [1]. BTZ was initially developed as a reversible proteasome inhibitor with anti-inflammatory properties [2,3]. Since then, it has been further developed for the treatment of multiple myeloma (MM) and mantle cell lymphoma (MCL) and subsequently investigated for its potential in treating other types of cancer [4]. The BTZ promising activity observed in early-phase clinical trials was followed by a series of clinical trials that ultimately led to FDA approval in 2003 for the treatment of patients with relapsed MM [5]. Today, BTZ has shown potent inhibition of tumor growth in various solid tumors, including pancreatic, prostate, ovarian, breast, and colorectal carcinomas [6,7]. Previous studies have explored the mechanism of action for BTZ. It suppresses the NF-κB pathway, decreases the regulation and expression of anti-apoptotic target genes, and induces apoptosis in tumor cells [8,9]. BTZ clinical application is restricted because of low solubility, high toxicity, inherent instability, and notable side effects [10–12]. Due to these limitations, low doses of BTZ are administered to patients [13]. Consequently, further studies on BTZ are necessary to enhance the drug's efficacy. It has been established that plasma proteins can transport approximately 83 % of BTZ within the concentration range of 100 to 1000 ng/mL, although the specific protein responsible for this is still unidentified [1,14]. Drug binding to plasma proteins is critical as it influences the drug's efficacy, metabolism, pharmacokinetics, and distribution within the body [15,16].

Human serum albumin (HSA), with a concentration of 35–40 mg/mL, is the most abundant protein in the bloodstream (0.6 mM, 60 % of plasma protein) [17,18]. Its structure is composed of three domains: domain I (D_I), domain II (D_{II}), and domain III (D_{III}), which are each characterized by an α-helical secondary structure [19–21]. The thermal stability varies across these domains, $D_I > D_{II} > D_{III}$ [22,23]. While D_{II} and D_{III} contribute to protein function, D_I is crucial in ensuring HSA's stability [23]. These domains are divided into subdomains A and B, each containing 4–6 α-helices [24]. The unique structure of HSA enables it to function as a blood pressure regulator, antioxidant, anti-inflammatory

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Biosensor Based on ZIF-67-HRP and MWCNTs Nanocomposite Modified Glass Carbon Electrode for the Detection of Luteolin in Vegetables

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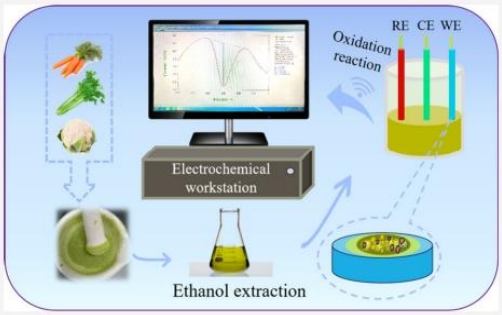
ABSTRACT: Luteolin has various pharmacological properties, including anti-inflammatory, antioxidant, and antitumor characteristics. Due to its potential value in drugs and functional foods, it is important to develop an efficient method for detecting luteolin. In this work, the poor selectivity of existing luteolin nonenzymatic sensors was solved by translating the enzyme-catalyzed reaction from bulk solution to the surface of a horseradish peroxidase (HRP) modified electrode through an electrocatalytic oxidation process. Here, we modified the surface of a glassy carbon electrode (GCE) with metal−organic frameworks (MOFs; ZIF-67 here, abbreviated as ZIF), functional nanomaterials, and HRP and finally covered it with Nafion (NF). In this case, luteolin acts as a hydrogen donor, and the electrode acts as a hydrogen acceptor; the oxidation reaction occurs on the electrode surface. The use of ZIF-67 ensured the conformational stability of HRP to ensure the selectivity and anti-interference property, and SDS-dispersed multiwalled carbon nanotubes (MWCNTs) enhanced the electrode conductivity. The use of NF avoids shedding of the electrode material during the testing process. A UV−vis spectrophotometer was used to study the selectivity of luteolin by HRP and the compatibility between HRP and ZIF. The materials were characterized and analyzed by scanning electron microscopy and transmission electron microscopy. Due to the synergistic effect of these nanomaterials, the linear range of NF/ZIF-HRP/MWCNTs-SDS/GCE was 1.0×10^{-2} to 6.0 μM, with detection limits of 25.3 nM (S/N = 3). The biosensor showed long-term stability and reproducibility, with a relative standard deviation of 4.2% for the peak current (n = 5). Finally, the biosensor was successfully used to detect luteolin in carrots, celery, and cauliflower.



1. INTRODUCTION

Luteolin is a natural flavonoid with anti-inflammatory, antitumor, antiviral, and other pharmacological properties.[1−3] It is widely distributed in the plant kingdom. In addition to common herbs, such as chrysanthemum and honeysuckle, luteolin is also found in many daily consumed foods. Studies have shown that luteolin is widely found in commonly consumed vegetables such as carrots, celery, and cauliflower.[4] It is thought to be a dietary supplement that helps lipid and carbohydrate metabolism. Generally, individuals on a healthy diet typically consume about 2−125 mg of luteolin daily.[5] This is beneficial because luteolin can scavenge reactive compounds containing nitrogen and oxygen, preventing cell damage and combating cancer. Food therapy is becoming more and more popular. Numerous luteolin dietary supplements on the market are already derived from vegetables.[6] Food safety has recently aroused widespread attention in modern society. In this context, more objective and reliable analytical tools are needed to determine food quality and safety. On-site food safety and quality assessment are always in demand for the development of sensitive and selective electrochemical sensors.[7]

Compared with spectroscopy, colorimetry, and chromatography,[8] the electrochemical method has a fast response, good selectivity, high sensitivity, good reproducibility, simple operation,[9] and is more effective in real-time analysis. Electrochemical sensors have become significant in various fields, including biotechnology and medicine, industrial applications, and environmental monitoring.[10] Of course, it is not uncommon to detect luteolin by electrochemical methods. For example, Tang et al. constructed an electrochemical sensor based on graphene quantum dot/gold nanoparticle nano-

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