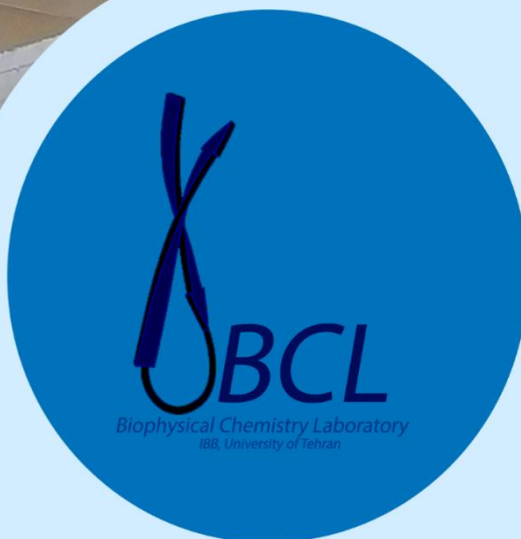




ANNUAL REPORT 2025



BIOPHYSICAL CHEMISTRY LAB

Institute of Biochemistry and Biophysics,
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<http://bcl.ut.ac.ir>

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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**
National Research Institute of Agronomies, 44316 Nantes Cedex 03, France
- **Professor F. Ahmad**
Director, Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia (A Central University), Jamia Nagar, NEW DELHI - 110 025, India
- **Professor L. Saso:**
Department of Physiology and Pharmacology, Sapienza University of Rome, Italy.
- **Professor N. Sheibani**
Department of Ophthalmology and Visual Science, University of Wisconsin, Madison, WI S370S, USA

Lab Assistant & Lab Researcher



- **Lab Assistant:**

Arash Agheli

- **Lab Researcher:**

Faezeh Moosavi-Movahedi

Postdocs



-
- Dr P. Arghavani



Doctor of Philosophy (PhD)

- ✧ N. MohebAlizadeh
- ✧ A. Amiri
- ✧ E. Rezaei Pajouhesh
- ✧ E. Mirzaei
- ✧ M. Nourazaran
- ✧ R. Eshraghi
- ✧ R. Sattari
- ✧ G. Khordadpour

Master of Science (MSc)

- ☆ B. Ahmadi
- ☆ M.R. Hariri

Alumni



PhD

Name	Topic of Thesis
Z. Haghparas	Investigating the effect of the navigating forces behind albumin aggregation in a microfluidic chip
B. Davaeil	Loading of bortezomib into human serum albumin nanoparticles and study of albumin drug interaction and NAB-BTZ biological activity
S. Behjati Hosseini	Biophysical study of soy protein microsphere for optimal release of curcumin for diabetic foot ulcer

MSc

M.H. Khodabandeloo	Investigating On the Reaction of Insulin and Heme Under the Static Magnetic Field (SMF) Exposure
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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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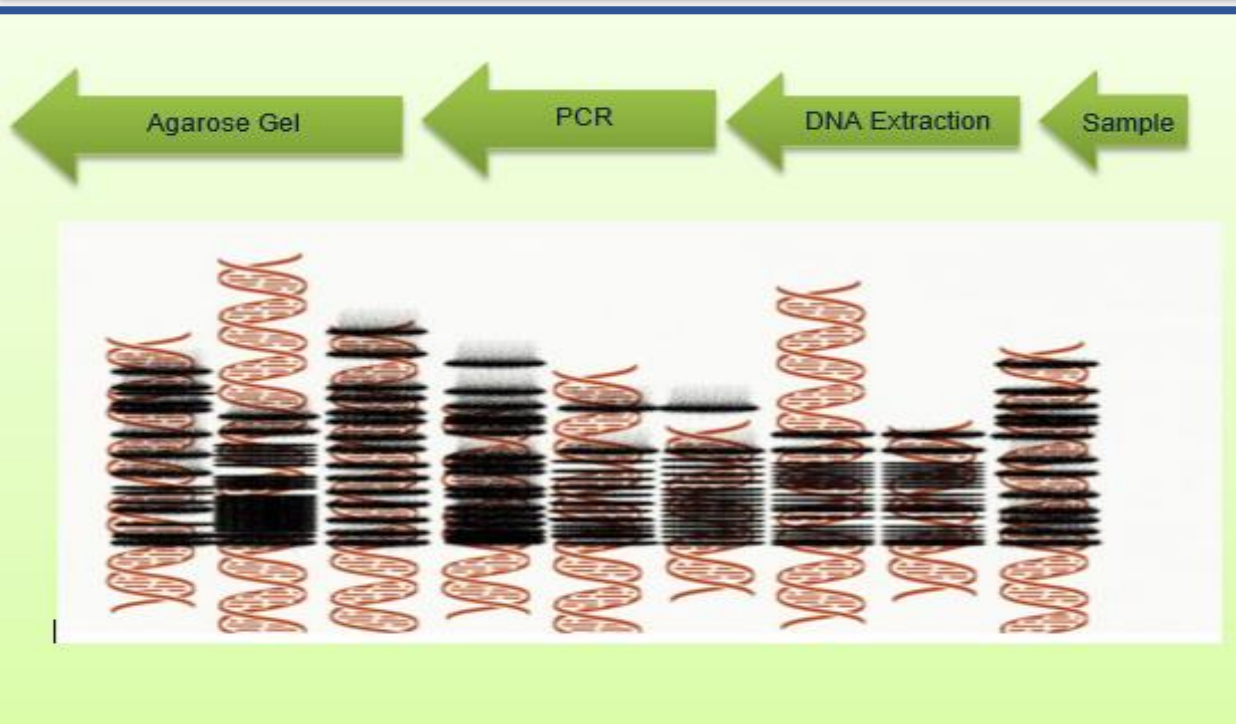


**Species Specific Identification
of Meat Derivative Products by
Molecular Genetic Approach
(Kit)**

Biophysical Chemistry lab.

Biophysical Chemistry lab.

Institute of Biochemistry & Biophysics



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 anti-hypertensive activity of these peptides, they can be used as ingredients in foods product, dietary supplements and nutraceutical.



**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.

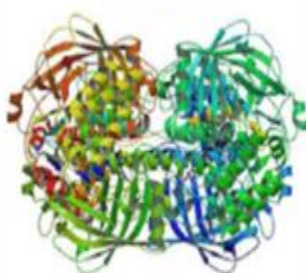
--**Textile Industry:** to remove hydrogen peroxide after bleaching and before dyeing, saving water, energy and time, not damaging the fibers and dyestuffs, and do not pollute the environment;

--**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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Biophysical Chemistry Kit & Technology

1

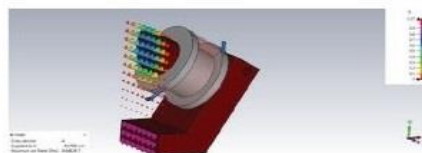
CryoMicro Electromagnet (CME)

Special conditions that govern the Vibrating Sample Magnetometer (VSM) device

1. Generating a magnetic field strength adequate for saturating the material under exposure.
2. A uniform magnetic field across the entire sample space.
3. The stability of the magnetic field, free from fluctuations, noise, and errors
4. Accurate control of experimental parameters, including the frequency and amplitude of vibration, and ensuring the reproducibility of measurements
5. Minimizing interference from external sources in the vicinity of the device

2

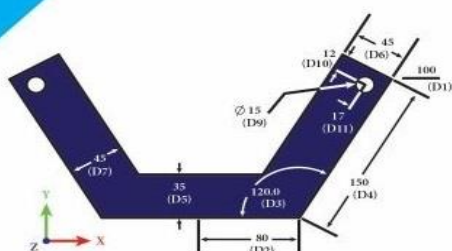
Magnetic field and magnetic intensity when the separation between two cores is one centimeter =
Approximately 600 milliTesla



Force and torque exerted on each iron core during the magnetization process.

Device Dimensions

3



Iron yoke with dimensions as depicted in the figure, measured in millimeters.



Iron core with a height of 161.70 and a diameter of 60 millimeters

Vibrating Sample Magnetometer (VSM)

4

Special conditions that govern the Vibrating Sample Magnetometer (VSM) device

1. Generating a magnetic field strength adequate for saturating the material under exposure.
2. A uniform magnetic field across the entire sample space.
3. The stability of the magnetic field, free from fluctuations, noise, and errors
4. Accurate control of experimental parameters, including the frequency and amplitude of vibration, and ensuring the reproducibility of measurements
5. Minimizing interference from external sources in the vicinity of the device
6. Temperature control to minimize any impact on the magnetic properties of the sample



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Keynote Speakers



- **A.A. Moosavi-Movahedi**, "Proteins: Marvelous Natural Intelligence of Life" 6th Conference on Proteins and Peptides Science and Technology" Shahid Beheshti University, November 19-20, 2025. Published in Biomacromolecular Journal, Vol 11(2), page 264, 2025. (Plenary Lecture)

Selected Papers





Electrochemical biosensor based on functional nanomaterials and horseradish peroxidase for the determination of luteolin in peanut shell, honeysuckle and perilla

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ARTICLE INFO

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Biosensor

Horseradish peroxidase

Luteolin

Functional nanomaterials

ABSTRACT

Constructing a biosensor to detect luteolin content accurately is essential, especially considering its specific health benefits at certain concentrations. In this work, the reaction of HRP catalyzed luteolin could be successfully applied in electrocatalytic processes, the oxidation process of electron loss and dehydrogenation occurring on the electrode replaced the hydrogen receptor role of H₂O₂ in the HRP biocatalytic process. This oxidation reaction had an apparent current response, thus achieving accurate measurement of luteolin. On this biosensor, CTAB was used to disperse MWCNTs, and BSA was used to improve the hydrophobicity of MWCNTs, which was conducive to the subsequent AuNPs fixation of HRP. Three detection methods (LSV, DPV and SWV) for the detection of luteolin were compared and showed that SWV method had a wider linear range (1×10^{-8} – 2×10^{-5} M) and lower detection limit (8×10^{-10} M). The determination of luteolin in Traditional Chinese Medicine (TCM) by high performance liquid chromatography (HPLC) and biosensor was almost identical. Therefore, this biosensor could successfully replace HPLC in detecting luteolin in TCM.

1. Introduction

Luteolin (3',4',5,7-tetrahydroxyflavones) is a joint flavonoid compound found in nature [1], the appearance presents a yellow crystalline shape, which exists in various vegetables and Traditional Chinese Medicines (TCMs), such as celery, peanut shell and perilla [2,3]. Luteolin exhibits diverse pharmacological effects, including anti-inflammatory, anti-cardiovascular, anti-allergic and anti-tumor properties. It is commonly employed in the management of chronic bronchitis and cardiovascular conditions [2,4,5]. Its chemical formula is C₁₅H₁₀O₆, and its structural formula was shown in Fig. S1 (Supplementary materials). Flavonoids are common polyphenols in plants, and relevant reports have confirmed that they are beneficial to human health at specific concentrations [6,7]. At 0.5–50 μM, luteolin has a protective effect on oxidative damaged venous endothelial cells

[8]. At 80–160 μM, luteolin has an inhibitory effect on the proliferation of human colon epithelial cells [9]. Therefore, it is imperative to establish a speedy, elementary and handy approaches for the determination of luteolin content [10].

At present, the qualitative and quantitative analysis methods for luteolin in relevant reports include capillary electrophoresis, spectrophotometry and high-performance liquid chromatography (HPLC). However, these methods have the demerits of cumbersome pretreatment process, expensive instruments and long detection time [11,12]. In contrast, electrochemical method has the merits of simple operation, low cost, quick response, real-time detection and so on [10,13]. In the period of prevalence of coronavirus disease 2019 (COVID-19), rapid and reliable detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody can provide immunological evidence in addition to nucleic acid test for the early diagnosis and on-site screening of

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Modeling the navigating forces behind BSA aggregation in a microfluidic chip†

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Payam Arghavani,^a Soroush Behjati Hosseini,^a Majid Badieirostami,^{b*}
Mehran Habibi-Rezaei^c and Ali Akbar Moosavi-Movahedi^{a*}

Microfluidic chips are powerful tools for investigating numerous variables including chemical and physical parameters on protein aggregation. This study investigated the aggregation of bovine serum albumin (BSA) in two different systems: a vial-based static system and a microfluidic chip-based dynamic system in which BSA aggregation was induced successfully. BSA aggregation induced in a microfluidic chip on a timescale of seconds enabled a dynamic investigation of the forces driving the aggregation process. This study employed a combination of experimental approaches, including biophysical and microscopic methods, and computational simulations using MATLAB and COMSOL Multiphysics. Obtained results revealed that Brownian movement, advective mixing, and laminar flow applied in favor of the formation of amyloid-like aggregates through the entire pathway. Furthermore, heating provided the necessary energy for the initial BSA's partial unfolding. In the following, space restriction and the cumulative effects of repulsive electrostatic and attractive van der Waals forces contributed to forming BSA clusters as a partially unfolded intermediate in the first few seconds of the aggregation process. Consequently, the synergistic effects of hydrodynamic forces (including shear force), hydrophobic interaction, and space restriction resulted in the deposition of larger aggregates on the channel sidewalls. Due to the elevated local concentration of BSA clusters alongside the strong shear force toward the channel sidewalls, the deposited structures underwent a structural conversion to form amyloid-like aggregates within a few seconds. In this study, we not only elucidated the molecular mechanisms underlying BSA aggregation but also highlighted the forces driving the aggregation process in microfluidic systems, explaining how it occurs within a timescale of seconds.

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1. Introduction

Proteins are crucial molecules that perform essential functions in our cells. Their three-dimensional, tertiary structures are achieved through a complex folding process driven by the sequence of amino acids and the surrounding water molecules.^{1–3} However, this folding process can sometimes be disrupted, forming misfolded proteins.⁴ These misfolded proteins can aggregate into amyloid fibrils characterized by a crosslinked β -sheet structure. Amyloid fibrils are implicated in a variety of diseases, including neurodegenerative disorders like Parkinson's, Alzheimer's, and Huntington's, as well as type 2 diabetes.^{5–8}

Albumin, a crucial water-soluble protein, is the major plasma protein synthesized in the liver and plays a significant role in transferring a broad spectrum of molecules, including water, salts, vitamins, hormones, and especially fatty acids, into the bloodstream.⁹ Bovine serum albumin (BSA) is composed of a chain comprising 583 amino acids, featuring 17 cysteine residues arranged into eight disulfide bonds and one unbound thiol group, resulting in a molecular mass of 66.4 kDa.¹⁰ Despite a dominant helical structure of multi-domain BSA, it has the propensity to aggregate in response to various stressors such as alterations in pH, elevated temperatures, ionic strength, agitation, and others.^{11,12} BSA aggregation kinetics transpires swiftly, taking only a few hours, without a lag phase, leading to the formation of fibrillary aggregates with elevated β -sheet content and disordered structures.¹¹ BSA's propensity to develop fibrous structures renders it a valuable model for experimental investigations on protein aggregation.^{11–13}

The primary focus of protein aggregation research has centered on bulk systems, allowing us to investigate the influence of various physical and chemical parameters on the

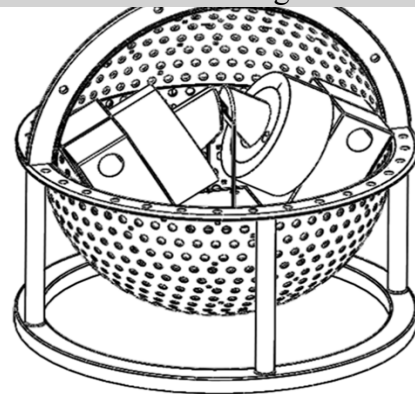
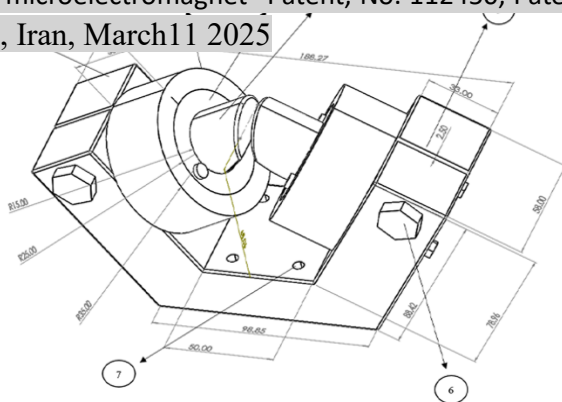
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† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d4sm01148a>

" Cryo-microelectromagnet" Patent, No. 112450, Patent Certificate from the National Register of Real Estate, Iran, March 11 2025



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.

Nanoparticle Albumin-Bound Bortezomib: Enhanced Antitumor Efficacy and Tumor Accumulation in Breast Cancer Therapy

Anita Saremi Poor, Bagher Davaeil, Marziyeh Ramezani-pour, Mehdi Shafiee Ardestani, Ali Akbar Moosavi-Movahedi, and S. Mohsen Asghari*



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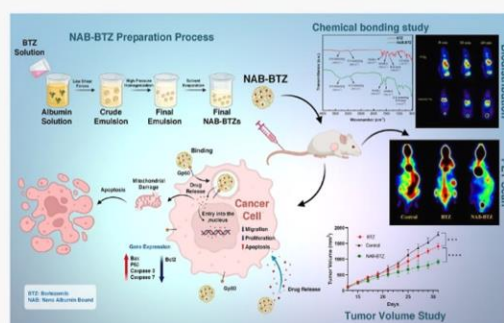
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ABSTRACT: Nanoparticle albumin-bound (NAB) formulations are emerging as a viable strategy for the intravenous delivery of poorly water-soluble drugs. This study aims to improve the therapeutic profile of Bortezomib (BTZ), addressing its low solubility and significant systemic toxicity through the development of NAB-BTZ nanoparticles. The synthesized nanoparticles exhibited an average size of 296.47 ± 10 nm and a high drug encapsulation efficiency of 75%, and a drug loading of 10%. NAB-BTZ displayed a controlled, pH-sensitive release profile, with 59% release at pH 5.4 (mimicking tumor environments) and 46% at pH 7.4 after 12 h. In vitro assays demonstrated that NAB-BTZ significantly reduced the viability of 4T1 mammary carcinoma cells in a dose- and time-dependent manner, increasing late apoptosis from 6% to 54% after 48 h, compared to 24% for free BTZ. At molecular level, NAB-BTZ induced apoptosis by upregulating p53 and Bax, downregulating Bcl-2, and activating caspases 3 and 7. In vivo tests in a murine 4T1 breast cancer model showed that NAB-BTZ substantially inhibited tumor growth, achieving an average tumor volume of 916 mm^3 by day 31 versus 1400 mm^3 for free BTZ, leading to an improved survival rate of 100% compared to 83% in the BTZ group. Technetium-99m (^{99m}Tc) labeling and SPECT imaging confirmed enhanced targeting capability, showing preferential accumulation of NAB-BTZ in tumor sites compared to free BTZ. These findings suggest that NAB-BTZ not only improves antitumor efficacy but also enhances its safety profile, underscoring its clinical potential in breast cancer therapy.

KEYWORDS: albumin, bortezomib, breast cancer, NAB technology, tumor growth



1. INTRODUCTION

Chemotherapy remains a common cancer treatment due to its extensive effectiveness; however, the lack of specificity in targeting tumor cells and the challenges in efficient drug transport to tumor sites are considerable limitations.¹ Additionally, issues such as multidrug resistance, the complexity of the tumor microenvironment, and interpatient variability further impede chemotherapy's success. To overcome these obstacles, innovative drug delivery systems, particularly those leveraging nanotechnology, are under investigation.² Nanoparticles (NPs) offer several advantages, including biocompatibility, biodegradability, controlled immunogenicity, and reduced toxicity, making them promising candidates for cancer therapy.³ NPs can be specifically engineered in terms of size, shape, and surface characteristics to enhance tissue penetration, prolong retention time at target sites, and enable surface modifications that improve therapeutic efficacy.⁴ Proteins, with their amphiphilic properties, can interact with both hydrophilic and hydrophobic drug molecules, rendering them ideal for drug delivery systems.^{5,6} Notably, albumin nanoparticles have gained prominence for drug delivery

systems due to their stability, biodegradability, nontoxicity, and low immunogenicity. In cancer treatments, albumin-based nanodevices enhance tumor penetration through selective interactions with cellular receptors, such as albumin (a 60 kDa membrane-bound glycoprotein) and osteonectin (SPARC), which are involved in albumin binding and endocytosis.^{6,7} Furthermore, albumin has a globular structure with hydrophobic pockets, allowing for noncovalent binding of small drug molecules, facilitating the design of albumin-based nanoparticles for controlled drug delivery.⁸ While albumin binding reduces the free concentration of drugs in circulation, it extends their circulation time, an advantageous property in cancer nanomedicine.⁹ One method for creating nanoparticle albumin-bound (NAB) formulations is NAB technology, which

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Monitoring the Time-Dependency of Multi-Stage Events in Thermal BSA Aggregation-Fibrillation: Electrochemical Admittance Approach

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Bovine serum albumin (BSA) thermal aggregation follows hyperbolic behavior, lacking a distinct nucleation process, suggesting spontaneous unfolding and assembly above the melting point. Common methods like thioflavin T (ThT) assay may not effectively discern initial BSA aggregation events. To overcome this limitation, advanced electrochemical approaches have been used to clarify the mechanisms of conformational changes and the overall kinetics of the process. Time domain monitoring of the BSA conformational changes under thermal aggregation using fast Fourier transform admittance measurement revealed four preliminary stages of the BSA aggregation process. These four stages were further investigated using various spectroscopic techniques, electron microscopy, ζ-potential analysis, and surface tension measurements. Temperature, as the main driving force, has different effects across different temperature ranges. Key findings included the onset of unfolding post-42 °C (0–1.25 min), assembly near the melting point (3.5 min), and the formation of aggregates and β-sheets at thermal equilibrium (after 3.5 min) based on data obtained. MD simulation of BSA showed that high temperatures accelerate the unfolding process and correspond to β-sheet formation. Electrochemical admittance findings provided valuable insights into BSA conformational changes, showcasing its promising potential to study protein misfolding-related diseases.

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Protein folding is a vital process in which the functional native state of the protein is secured. However, this process is error-prone, and inappropriate protein folding leads to misfolding of protein structures. Due to their lower stability, misfolded proteins can aggregate and stabilize through the formation of intermolecular β-sheets.¹ In recent decades, the mechanisms of protein aggregation have been extensively studied owing to the significant role of protein aggregation in various research fields, such as biophysics, biochemistry, biotechnology, medicine, pharmaceuticals, and even food science.^{1–6} However, due to the complexity of the process, researchers have not yet comprehensively understood the mechanism of aggregation, particularly how an α-helical protein, such as BSA, transforms into β-rich fibril-like aggregate.^{1,7} Chemical and physical parameters, such as temperature, pH, ionic strength, mechanical forces, protein concentration, and adding some chemicals that can interact with proteins including heavy metals such as Cu²⁺, Pb²⁺, Hg²⁺, as well as nanomaterials, play a critical role in inducing conformational changes followed by intermolecular interactions, resulting in protein aggregation and fibril formation.^{8–11} Thermal aggregation is a process in which a protein loses its native conformation above its melting temperature, and subsequently denatured polypeptides self-assemble into fibril-like aggregates.¹² These structural changes occur due to the exposure of hydrophobic regions, followed by the formation of nonspecific interactions through non-covalent bonds, such as hydrophobic forces, Vander Waals attraction, hydrogen bonds, and salt bridges.^{3,13} It is worth mentioning that all these intermolecular interactions occur at the very first stages of protein aggregation. Protein aggregation has been extensively studied using established methods such as circular dichroism (CD) spectropolarimetry, fluorescence spectroscopy, Fourier-transform infrared (FTIR) spectroscopy, UV absorption spectroscopy, differential scanning calorimetry, and others.^{12,14,15} These methods often involve multi-step, time-intensive, and have limitations in clarifying the mechanisms of the aggregation process, especially in the first few minutes. The investigation into the

aggregation process of proteins is crucial for understanding the initial unfolding stages that lead to fibril-like aggregation. This understanding is essential to prevent the formation of pathogenic amyloid structures associated with conditions such as anemia, diabetes, and various neurological disorders.^{1,5,10} According to the literature, the protein aggregation process can be divided into three distinct phases: the lag phase, the growth phase, and the plateau phase. The lag phase encompasses the initial events, such as monomer activation—including unfolding and, in some proteins, misfolding—which then lead to the formation of oligomeric structures.¹⁶

In this context, some globular proteins, such as albumin and lactoglobulin display distinctive characteristics that are devoid of lag time and nucleation, posing challenges for the existing literature to comprehensively delineate the multi-step events in the first minutes.¹⁷ Consequently, there is a pressing need to devise simpler, accurate, cost-efficient, highly selective, user-friendly, and real-time methods for identifying diverse protein structures during the aggregation process. Electrochemical approaches have been leveraged to tackle this challenge. Prior studies have shown that α-helical proteins such as BSA are destabilized by denaturing agents/conditions, leading to the formation of aggregates with β-sheets rich content, while these proteins do not tend to form β-structures in their native state.^{8,18} Bovine serum albumin is the key protein in plasma and has been highly studied in denaturation and aggregation studies.⁸ This carrier protein has an important task in the circulatory systems of blood.¹ The native BSA predominantly adopts an α-helical structure, with a 583-residue in the mature protein comprising a polypeptide chain with three homologous domains (I, II, III).³ At physiological pH (7.4), BSA bears a negative net charge owing to abundant negative residues on its surface.⁹ The early stages of BSA aggregation, involving the unfolding of monomeric conformers transitioning into a fibril-like state, remain obscure.⁸

Electrochemistry is a branch of chemistry that explores electron-involved chemical processes.^{19,20} Modern electrochemistry has been used to investigate the structural changes of biomolecules, especially the protein aggregation associated with human diseases.^{21–23} In biological systems, like nerve cells and proteins, electrochemistry plays a pivotal

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Scientists Collaboration for Science Development and Peace: USERN View

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Scientists play a crucial role in the development of science by proposing new hypotheses, conducting research, refining existing theories, and generating new knowledge. Their work forms the foundation for technological advancements, medical breakthroughs, and environmental solutions that shape modern society and improve the quality of life for humanity (1,2).

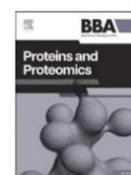
Important scientific discoveries were made by individual scientists working alone, rather than in a network. One notable example is Isaac Newton's development of the laws of motion and universal gravitation in the late 17th century. While Newton had access to the work of other scientists like Kepler and Galileo, his formulation of the fundamental principles of physics was largely done in isolation. Other examples include Albert Einstein and the theory of relativity, Marie Curie and radioactivity, Gregor Mendel and the laws of inheritance, Dmitri Mendeleev and the periodic table, and Charles Darwin and the theory of evolution (3).

It is generally better for scientists to work as part of a network rather than alone. While independent research allows for deep focus and innovation, scientific progress today increasingly depends on collaboration. Working within a network enables scientists to share expertise, resources, and data, which accelerates discovery and problem-solving. In addition, complex scientific problems, such as climate change, public health issues,

and space exploration, often require the combined efforts of expert scientists from multiple disciplines.

There are important scientific discoveries that happen only through scientific networking and collaboration among scientists. One prime example is the Human Genome Project, completed in 2003. Other notable examples include CERN and the discovery of the Higgs Boson, the development of mRNA vaccines for COVID-19, research on the International Space Station (ISS), research on global climate change, the development of antiretroviral therapy for HIV/AIDS, and many others. These examples demonstrate that in many of today's most significant scientific breakthroughs, collaboration across borders, disciplines, and institutions is essential for tackling the complexity and scale of modern scientific challenges. In line with the aim of borderless networking in science, in 2015, the first meeting for top scientists from different disciplines and nations was held to establish a network of top scientists as well as Nobel and Abel Laureates to move towards science without borders. A year after the meeting, the Universal Scientific Education and Research Network (USERN) was officially introduced and started its activities (4).

The Universal Scientific Education and Research Network (USERN) aims to foster scientific collaboration and promote education and research worldwide. Established with the concept of "Science



The role of the N-terminal p.R56Q mutation in modulating oligomerization and chaperone activity of human α B-crystallin in relation to cardiomyopathy

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ABSTRACT

α B-crystallin (α B-Cry), a critical small heat shock protein, is crucial for cellular proteostasis, especially in the heart and lens. α B-Cry mutations can disrupt its chaperone activity, leading to pathological conditions such as myopathy, cardiomyopathy, and cataracts. The p.R56Q mutation in the N-terminal domain, a region that participates in oligomerization as well as interactions with key proteins such as desmin and α A-Cry, has been associated with cardiomyopathy. However, its specific pathogenic mechanism is not well understood. This study aimed to elucidate the structural and functional consequences of the p.R56Q mutation. Recombinant p.R56Q α B-Cry was purified by chromatographic methods. Moreover, spectroscopic, microscopic, and computational techniques were employed to assess the influence of the mutation on protein function, structure, and stability. Our findings indicated that the p.R56Q mutation leads to significant alterations in human α B-Cry secondary to quaternary structures. The mutant protein was less stable and more prone to forming amyloid-like aggregates. The p.R56Q α B-Cry also formed larger oligomers and exhibited enhanced chaperone activity compared to its wild-type (WT) protein counterpart. Interestingly, it had a greater affinity for binding to desmin and α A-Cry. While increased chaperone function might be expected to have protective effects, it could interfere paradoxically with critical cellular processes, such as apoptosis, and thus enhance disease pathogenesis. This research provides new insights into the molecular mechanisms underlying α B-Cry-associated cardiomyopathy by highlighting how the p.R56Q mutation alters structural dynamics and chaperone activity.

1. Introduction

The α B-crystallin (α B-Cry) is expressed in various tissues, including the eye lens, brain, kidney, muscle, and heart. It plays a vital role in protecting these tissues from oxidative stress and heat by preventing the aggregation of misfolded proteins [1]. As a holdase chaperone, α B-Cry interacts with the exposed hydrophobic surfaces of misfolded or unstructured proteins, stabilizing them until they are refolded by ATP-dependent chaperones. Chaperone activity makes α B-Cry a critical

component of the protein quality control system [2]. α B-Cry also has a unique structure and domain arrangement. Being part of the small heat shock protein (sHSP) family, containing 175 amino acids and an approximate molecular weight of 20 kDa, it has three main domains. The highly conserved core α -crystallin domain (ACD, 66–148) has eight antiparallel β -sheet structures (β 2– β 9) folded similarly to immunoglobulin. Flanking the ACD are hydrophobic variable N-terminal (NTD, 1–65) and hydrophilic C-terminal (CTD, 149–175) domains [3]. Both domains possess the isoleucine-proline-isoleucine (IPI/IXI) motif in

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REVIEW

Type 2 Diabetes Mellitus Exacerbates Pathological Processes of Parkinson's Disease: Insights from Signaling Pathways Mediated by Insulin Receptors

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Abstract Parkinson's disease (PD), a chronic and common neurodegenerative disease, is characterized by the progressive loss of dopaminergic neurons in the dense part of the substantia nigra and abnormal aggregation of alpha-synuclein. Type 2 diabetes mellitus (T2DM) is a metabolic disease characterized by chronic insulin resistance and deficiency in insulin secretion. Extensive evidence has confirmed shared pathogenic mechanisms underlying PD and T2DM, such as oxidative stress caused by insulin resistance, mitochondrial dysfunction, inflammation, and disorders of energy metabolism. Conventional drugs for treating T2DM, such as metformin and glucagon-like peptide-1 receptor agonists, affect nerve repair. Even drugs for treating PD, such as levodopa, can affect insulin secretion. This review summarizes the relationship between PD and T2DM and related therapeutic drugs from the perspective of insulin signaling pathways in the brain.

Keywords Parkinson's disease · Type 2 diabetes mellitus · Insulin · Therapeutic agents

Introduction

Parkinson's disease (PD), a neurodegenerative disorder, significantly affects human health. It is caused by the death of dopaminergic cells in the dense part of the substantia nigra. The risk of PD increases with age [1]. Primary symptoms of PD include muscle rigidity, balance disorders, bradykinesia, and tremors. Patients with PD are prone to developing several other diseases, such as type 2 diabetes mellitus (T2DM), cancer [2], gastrointestinal diseases [3], vitamin D deficiency [4], peripheral neuropathy [5], and musculoskeletal disorders [6]. Among these, T2DM is among the diseases most closely related to PD. In this review, we focus on the role of insulin and its signaling pathways in PD and T2DM.

PD, or paralysis agitans, is a prevalent neurodegenerative disorder, predominantly affecting individuals over the age of 60. Characteristic symptoms of PD include bradykinesia, increased muscle tone, postural instability, and a resting tremor [7]. However, over the past few decades, researchers have gradually discovered that PD is not just a single disease but is closely associated with the occurrence of several other diseases, especially T2DM [8]. Recent studies suggest that T2DM accelerates the progression of PD through various mechanisms, such as impaired neuronal function, a damaged nervous system, and increased inflammation. Hypoglycemic drugs used for T2DM, such as metformin and glucagon-like peptide-1 (GLP-1) receptor agonists, can ameliorate symptoms of PD, indicating that medications for diabetes may offer novel therapeutic approaches for neurological disorders [9]. Therefore, it is imperative to investigate the association between PD and T2DM and explore the role of insulin in both conditions.

Notably, insulin resistance plays a significant role throughout the progression of PD. T2DM is a systemic metabolic disorder characterized by hyperglycemia, insulin

Shufen Liu and Tingting Liu contributed equally to this work.

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Converging Modern Science and Ancient Wisdom in Elucidation of the Heart Function

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Contemporary scientific evidence and research increasingly support the idea that the heart plays far more complex and significant roles than its traditional function as a mechanical pump for blood circulation. Today, more attention is being given to the broader and deeper contributions of the heart. This article aims to introduce the lesser-known dimensions of the heart by drawing on both modern experimental science and the insights of ancient wisdom. We review evidence showing how the heart influences neural processes, decision-making, and emotional regulation. The article highlights the heart's role as a sophisticated neuro-secretory and conscious center by integrating findings from neuroanatomy, neurophysiology, neuroradiology, and psychophysiology with perspectives from ancient wisdom. Bridging scientific discoveries with timeless wisdom enriches our understanding of the heart's determining role in connection with the brain, intuitive intelligence, emotional leadership, and decision-making. This convergence suggests the need to review, redefine, and expand our understanding to develop a realistic view of the universe. It also highlights ways in which modern humans can address semantic, moral, and environmental crises through wisdom-guided supervision and ethical leadership. In doing so, this approach may foster the sustainable development of human societies.

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