Abstract No.40

The Study of Hydrogen Bonds Between Lamotrigine and some Parts of

Mitra Moosavi, Jaber Jahanbin Sardroodi, Alireza Rastkar Ebrahimzadeh*

Molecular simulations lab, Azerbaijan university of tarbiat moallem, Tabriz, IR
(E-mail: mitra3954@yahoo.com)

Nowadays, extensive studies has been done on drugs because of their importance in the human life. Many drugs including Anticonvulsant agents such as Lamotrigine (LTG) block sodium channels in a voltage_dependent manner. LTG blocks the channel in the inactivated open state. We've studied interaction between this drug with some parts of its receptors in human body by the help of Docking method and molecular dynamic simulation . These studies show that LTG binds to the excitatory amino acids such as Glutamate and Glysine in Inactivation gate and in this manner controls epilepsy.The results of this study is useful for medical scients , pharmacists , chemists and biologists.

Keywords: Drug-Protein Interaction, Lamotrigine, Voltage-gated Sodium Channel, Molecular Docking, Molecular Dynamic Simulation.

Abstract No.41

The Effects of Extremely Low Frequency Electromagnetic Fields (ELF-EMFs) on Acetylcholinesterase Activity

*Ali Afrasyabi, Gholamhossain Riazi**

Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran, IR
(E-mail: aliafrasyabi60@yahoo.com)

A serine protease Acetylcholineterase (AChE) enzyme hydrolyzes acetylcholine (ACh) to choline and acetate in the cholinergic synapses in the brain and neuromuscular junctions. Signal transmission between two neurons is a result from neurotransmitters release in the most nervous systems. Ach kind of neurotransmitters in the cholinergic system is synthesized from acetyl-CoA and choline by choline acetyltransferase enzyme. Stimulation of the pre-synaptic nerve causes the release of the ach into the synaptic cleft and bind to its receptors such as nicotinic acetylcholine receptors (nAChR) and muscarinic acetylcholine receptors (mAChR) on the post-synaptic nerve membrane for transmitting the signal to next nerve.ACh has a role in learning and short-term memory through synaptic plasticity therefore the occurrence of damage in brain cholinergic system induces disruption in memory and cognition mechanism and reduces synaptic plasticity. These effects lead to increase the rate of neurodegenerative diseases such as Alzheimer's disease. In this study we investigated the effects of Extremely Low Frequency Electromagnetic Fields (ELF-EMFs) on the synaptosomal acetylcholinesterase enzyme activty. We prepared the synaptosomes suspension from sheep brain of the left hemisphere with sucrose density gradient centrifugation based on Dodd method and measured the enzyme activity of AChE via Ellman method. The prepared synaptosome suspensions were exposed to 190 Hz and 213 Hz electromagnetic field for 30 min at flux intensity of either 0.1 mT to 1.7 mT that similar to intensity and frequency of mobile phones. Our current research aimed at the effects of ELF-EMFs on Ach concentration in synaptic cleft through AChE enzyme activity to study the Alzheimer's disease inducer parameters.

Keywords: Extremely Low Frequency Electromagnetic Fields (ELF-EMFs), Acetylcholineterase (AChE), Synaptosome.

Abstract No.42

The Effect of Sucrose and Trehalose on the Structure and Dynamics of Luciferase: Molecular Dynamics Simulation Study

Masumeh Ali Mohammadi [1], Faramarz Mehrnejad [1], Mahmoud Khadem-Maaref [2], Nader Chaparzadeh [1], Saman Hosseinkhani [3]*

1. Department of Cellular and Molecular Biology, Faculty of Science, Azarbaijan University of Tarbiat Moallem, Tabriz, IR
2. Department of Physics, Faculty of Science, Azarbaijan University of Tarbiat Moallem, Tabriz, IR
3. Department of Biochemistry, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, IR
(E-mail: asman.ma@gmail.com)

Firefly luciferase from Photinus pyralis is a 62 kDa protein which has large N-terminal domain and small c-terminal. It catalyzes a series of reactions leading to light production from substrate D-luciferin in the presence of MgATP and molecular oxygen.Over the past years, firefly Luciferase has been used in many of biological assays such as gene regulation,protein-protein interactions,cell proliferation,cell migration,chemical biology and drug discovery assays.However, the enzyme is unstable which can effect on sensitivity of those techniques.

On the other hand, Sucrose and Trehalose are natural osmolytes stored in cells of organisms in order to adapt them to environmental stresses. In vitro, osmolytes decrease protein instability and force partially unfolded structures to refold. In this study, we have done Molecular dynamics simulations of firefly Luciferase in pure water and sucrose and trehalose to investigate the molecular basis of the stabilizing effect. Our results show that sucrose and trehalose mainly interact with protein main chain and water preferentially interacts with protein side chain. Also as sucrose and trehalose H-bonds with solvent decrease,their H-bond with main chain and side chain of protein increase. In addition comparison of pure water with these osmolyte solutions shows some difference in root mean square fluctuation and secondary structure of protein. As well the simulation data indicates that presence of osmolytes influence water structure and make it more ordered. Thus, these findings suggest that osmolytes probably by indirect interactions prevent protein thermal unfolding.

Keywords: Luciferase Enzyme, Co solvents, Molecular Dynamics Simulation, Protein Structural Stability.

Abstract No.43

Molecular Modeling and in Vitro Studies on Proposed Inhibitor of Bacterial Alpha-amylase

Mohammad Reza Malek [1], Parichehreh Yaghmaei [1], Bagher Larijani [2], Azadeh Ebrahim-Habibi [2]*

1. Department of Biology,Science and Research Branch ,Islamic Azad university,Tehran,Iran
2. Endocrinology and Metabolism Research Center, Tehran University of Medical Sciences, Tehran, IR
(E-mail: malek_mrn@yahoo.com)

Normal flora of the oral cavity have a role in the formation of dental caries, which occur by fermentation of carbohydrates. As so, bacterial alpha-amylase enzymes, such as Streptococcus mutans and Streptococcus sanguinis enzymes can be considered as suitable targets to prevent this event.In this study, for each bacterial enzyme, 11 models were built by Moe software. After quality evaluation, best models were selected for further studies. Potential inhibitor compounds were docked into the structures with the use of Autodock Vina. In the experimental part ,the effect of gibberellic acid was studied on Bacillus amyloliquefaciens alpha-amylase, as a model of bacterial enzyme, with the use of Bernfeld method.Blast and Clustal W2 programs showed more than 70% similarity between bacterial and human salivary α-amylase sequences. Comparison of metal ion binding sites and active sites showed acceptable similarity between the target and template structures. The results of docking showed a high affinity between gibberellic acid and bacterial enzyme. In experimental study, gibberellic acid was able to inhibit enzyme activity up to 15% at concentration of 20μM.Gibberellic acid could be further studied as to its inhibitory potential on other bacterial amylases.

Keywords: Alpha- Amylase, Molecular Modeling, Inhibitor.

Abstract No.44

Investigation of His-His interaction on the TMGS stability

Malihe Mohammadi [1], Khosro Khajeh[1], Manoochehr Mirshahi [1], Mona Atabakhshi [1], Reihaneh Mirhassani [2], Mahdieh Hadi [2]*

1. Department of Biochemistry, Faculty of Biological Science, Tarbiyat Modares University,Tehran, IR
2. Department of Biotechnology, College of Science, Tehran University, Tehran, IR
(E-mail: malihe_mohammadi@ymail.com)

Methylglyoxal synthase is a homohexameric protein that catalyzes an elimination reaction that converts dihydroxyacetone phosphate (DHAP) to form orthophosphate and methyglyoxal, which very applicable in industry. For this reason, MGS study and improved its stability is important. Recently, a gene encoding MGS from Thermus sp. GH5 (TMGS) was cloned, overexpressed and its structure has been studied by X-ray crystallography. These studies showed that TMGS gene was composed of 399 bp which encoded a polypeptide of 132 amino acids with a molecular mass of 14.3 kDa. The crystal structure of TMGS revealed that His23, Arg22 and Phe19 are in closed distance and forming a loop. On the other hand our recent study has shown that His-His interaction may be important in protein stability. To further explore this phenomenon, in this survey two modified enzymes were produced with site directed mutagenesis (SDM), one of them, one histidine and another, two histidine inserted between Arg22 and His 23. After sequencing, expression and purification, thermal stability measurements performed and the data exhibited that the thermostabilities of both mutants improved compared native TMGS. These mutagenesis data supporte this hypothesis that the interactions between like- charged amino acid residues can improve protein stability.

Keywords: Methylglyoxal Synthase, Thermophile, His-His Interaction, Stability.
