Abstract No.291

Lys Therapy of Diabetes: from in vitro Studies to the Animal Models of Diabetes and Type 2 Diabetic Patients

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Hyperglycemia is one of the most important reasons of diabetic complications. It causes the biomacromolecules, especially protein glycation which in order result in protein conformational change. Here the effect of glycation on the structure and function of several important proteins from various comportments e.g. plasma, extracellular medium, cytosol and nuclei is presented. Then, the effect of Lys, as a chemical chaperone from amino acid family, on the non-enzymatic glycation of many proteins and its inhibitory effect on this process that was investigated in our Lab. will be discussed. In addition, our in vivo results showed that Lys administration in the animal model of diabetes of both types 1 and 2, as well as the type 2 diabetic patients result in the decrease in serum glucose, increase in insulin secretion and decrease insulin resistance, increase serum antioxidant capacity, improve the lipid profile and HDL functionality, induce HSP70 production, reduce fibrin activity due to correction of its folding, stop the progression of cataract, etc. In conclusion, the obtained data by our team in the in vitro and in vivo studies indicate the beneficial effects of Lys therapy on reduction of diabetic complications thus it is suggested as a complement therapy for diabetes.

Keywords: Diabetes, Animal Model, Hyperglycemia, Antioxidant.

Abstract No.292

Molecular Dynamics Simulation on the Protein Structure

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The protein structure changes in the presence of different denaturants such as temperature and chemicals. These variations can be followed by different techniques such as X-ray, NMR, CD, IR and so on. There are some complementary methods same as molecular dynamics (MD) simulation and homology modeling that used in the structure determination so that some of PDB codes in protein data bank were exclusively obtained by MD. On the other hand X-ray crystallography only obtains the crystal structure of macromolecules but not solution. NMR spectroscopy investigates both liquid and crystal structures while CD and IR determine secondary structure in solution phase. The first two methods are precise and rigorous but very expensive. On the other hand MD is a powerful method in determination of tertiary structure of macromolecules specially in homologues proteins. MD methods use the classical and statistical mechanics theorem for movement and interaction of molecules. So it is an approximation method that dose not consider electron interaction in its calculations. It makes atoms to move in different direction based on Newtonian laws subsequently thermodynamic parameters. In this study, I report some applications of molecular dynamics in biology. Structural parameters such as solvent accessible surface area, hydrogen bond, CD222nm, radius of gyration and radial distribution function were obtained for enzyme by molecular dynamics and compared with experimental data.

Keywords: Molecular Dynamics Simulation, Tertiary Structure, Accessible Surface Area, Hydrogen Bond.

Abstract No.293

New Strategies in Structure-function Relationship Study of Peptides

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Peptides play significant roles in biological world especially in human life. There are a great number of peptides and proteins which are used as therapeutics and more are under development as pharmaceutical targets. However, design and prediction of their activity remain one the most challenging area in life sciences due to large amount of arrangement possibilities. Quantitative sequence-activity model (QSAM), employs quantitative structure-activity relationship (QSAR) strategies to quantify biosequence-activity/function relationship for the peptides, proteins and nucleic acids, becomes an attractive and active area in peptide researches. Therefore, a lot of efforts were done in the past to model the relation between the peptide structure/sequence with its biological activity. On the basis of QSAR concept, functions and structures of peptides or proteins are resolved by the information enclosed in the amino acid arrangements. In this methodology, a set of

descriptors is calculated for each amino acid and they are put together to produce a descriptor data matrix for a set of peptides.
Very recently, in our research group we have been involved in the definition of some new amino acid indices (AAI) for use in QSAM study of peptides. We employed the concept of atom in molecule and used the quantum topological molecular similarity (QTMS) descriptors to suggest some new AAIs. In addition, we employed the Moreau and Broto autocorrelation function on the QTMS descriptors of amino acids to extend the QTMS-based AA indices and generate some other novel indices. In another work, to increase the quality of the QSAR models reported for peptides, we proposed here the application of segmented principal component regression (SPCR) method to define more relevant sources of AA indices. Finally, using of multi-way data analysis methods in QSAM study of peptides will be explained. The suggested methods were validated by analysis of some different peptide data sets of relevant biological activities.

Keywords: Amino acid indices, Peptide, Biological activity, Structure-function.

Abstract No.294

A Possible Role of Peroxidase Activity of "heme-ferritin" Complex in Development of Neurodegenerative Diseases

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Ferritin is a ubiquitous protein for the sequestration, storage and release of iron in animal and plant cells. It has been previously shown that each ferritin molecule can bind to 15 - 17 heme moieties. Heme and sometimes heme-protein complexes possess peroxidase activities which cause irreversible damages in cells. In the present study, we reported the peroxidase activity of "heme-ferritin" complex using several oxidizable substrates. First, the ferritin was purified from liver homogenate of sheep by ammonium sulphate precipitation and DEAE ion-exchange chromatography. The peroxidase activity of "heme-ferritin" complex was then measured by using H_2O_2 or t-BHP as oxidant substrates and TMB, L-Dopa or DOPA as a reductant substrates. Results showed that the non-specific peroxidase activity of the "heme-ferritin" system can oxidize the neurotransmitters with high catalytic efficiency. According to the literature, the concentration of ferritin, free heme, and peroxide species increase in neurodegenerative diseases such as AD. There is this possibility that the peroxidase activity of "heme-ferritin" complex play a significant role in development of oxidative damage within involved cells. We will discuss the importance of our observations.

Keywords: AD, Peroxidase Activity, Ferritin, Neurodegenerative Diseases.

Abstract No.295

Interaction of a Novel Photochromic Molecule with Human Serum Albumin Studied by UV-vis Absorption, Fluorescence Spectroscopy, and Docking Calculation

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Photochroism is the phenomena that of reversible transformation between two forms (open and close form) that have different spectra by photo-irradiation. In this work, the interaction of a new photochromic molecule, 2,2-biphenyl-4-yl-2-methyl-6(4-nitrophenyl)-4-phenyl-1,3-diazobicyclo[3.1.0] hex-3-en, with human serum albumin (HSA) has been investigated by UV-vis absorption, fluorescence spectroscopy and docking calculations. 0.1 μM HSA was used in the presence of 0 to 1.47×10^{-5} M photochromic molecule. The interaction of photochromic molecule with HSA causes fluorescence quenching of HSA. The addition of photochrome to a solution of HSA induces quenching of the protein fluorescence and binding constant of interaction was also obtained about 7. 5 μM^{-1}. In other investigation the photochromic molecule absorbance was studied by a UV-Vis spectrophotometer model Perkin Elmer. The photochromic reaction was studied upon variation of time irradiation by UV-vis spectrophotometer. Absorption spectra of photochromic molecule and HSA were obtained as the time of irradiation increase from 0 to 70 s. Absorbance intensity was increased due to the close form of molecule that turn in to the open form. Rate constant of reaction was obtained from absorption spectra about 0.026 s^{-1}. In order to estimate the