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Studies on Biochemical Processes for Elucidation of Disease Mechanisms and Ensuring Food Security

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Biochemistry & Analytical Biochemistry is focused on publishing Research articles, Reviews, Editorials, Case studies, relative to the biological and chemical properties and activities of biomolecules, including the qualitative and quantitative analysis of key biocomponents.

The approached themes by Research articles, Reviews and Editorials were various, the main focus being the concern for human health: the fight against oxidative-stress related pathologies like cancer, diabetes or cardio-vascular diseases, or against various pathogens, the gene-expression profiling for enhancing the understanding of disease mechanisms, as well as the preoccupation for food safety problems.

The increasing interest in antioxidants, particularly in those intended to prevent the deleterious effects of free radicals and to prevent the occurrence of degenerative diseases, has lead to the reviewing of the mechanisms of action of antioxidants, in delaying or inhibiting the action of reactive oxygen species, as well as of accurate, fast and sensitive methods of total antioxidant activity determination (chromatographic, spectrometric, electrochemical), and of their performances. These techniques are able to offer a complete profile of the antioxidant content of foodstuffs, as presented in the above described Review [1].

Antioxidants reduce the possibility of occurrence of coronary diseases due to hypercholesterolemia, as stressed upon by the Authors of the Research Article dedicated to the role of natural antioxidants intake in reducing hypercholesterolemia. High serum LDL-Cholesterol levels represent a major risk factor for coronary artery disease and thus for myocardial infarction and stroke, increasing the death rate of coronary artery patients. The use of antioxidants is the most preferred way to inhibit lipid oxidation, special attention being drawn to natural antioxidants. Due to its antioxidant properties, walnut leaf has useful effects on cholesterol and lipid profile in hypercholesterolemic rats, and it could be used for reducing cardiovascular risks disease. These properties have been attributed to the presence of phenolic antioxidants which act by neutralizing free radicals, chelating transitional metals, quenching singlet and triplet oxygen molecules or decomposing peroxides [2].

Another research is dedicated to the relationship between lipid levels and breast cancer risk. The study reveals primarily significantly elevated total serum cholesterol and HDL cholesterol levels, in patients with carcinoma breast, compared with those of controls. Nevertheless, LDL cholesterol levels and triglycerides did not present any significant variation between the studied cases and the controls. It is highly recommended that people should reduce weight and control blood cholesterol levels in order to reduce risk of breast cancer [3].

The free radicals being also implicated in the etiology of diabetes and in its complications, the search for effective cell protective natural antioxidants is vital in the amelioration of the oxidative stress related to this degenerative disease. Magnifera indica – sourced antioxidants (phenols, flavonoids and tannins) found in Vimang tablets, as well as terpenoids and polyunsaturated fatty acids excerced a corrective action of the oxidative stress in diabetic children, the main evidence being a dramatic decrease of the oxidized LDL level, as evidentiated in the respective research [4].

The rich composition in polyphenols of coffee and the ability of cardamom oil to enhance glutathione production and increase antioxidant enzyme level, has been confirmed as being the source of amelioration of biochemical parameters related to oxidative stress in gamma-irradiated rats. The research results confirmed a significant increase in lipid peroxidation and reduction in both glutathione concentration and superoxide dismutase activity, due to exposure of rats to γ-irradiation. Moreover, the Authors proved that the effect of both coffee and cardamom resulted in significantly reducing the damaging effect induced by γ-irradiation. The observed improvement in the antioxidants' content, liver functions, lipid profile and level of testosterone and insulin in irradiated rats suggested a radioprotective effect of the mixture of coffee and cardamom, which was attributed to the phenolic compounds and essential oil contents. These possess antioxidant potential and can reduce the oxidative stress induced by γ -irradiation exposure [5].

The research investigation of a suitable drug formulation against typhoid fever has been related to the antioxidant status of the respective molecules, and to the host defense function of nitric oxide against *Salmonella*. The capacity of NO to act against oxidative processes is linked to its ability to reduce the ferryl heme. L-arginine intake increases NO production, as stressed upon by the Authors of this research. Nevertheless, the endogenous substrate is insufficient for the production of the required NO amounts. Thus, a suitable formulation consists in oral administration of L-Arginine as NO donor, along with low doses of antibiotic [6].

The search for common drug targets against bacterial pathogens is a field of interest in the treatment of life-threatening microbial infections, such as *Legionella pneumophila*. MurB reductase, one of the important enzymes involved in the biosynthesis of a peptidoglycan component of cell wall, was identified as responsible for infective endocarditis including *Legionella pneumophila*. Therefore, designing potential inhibitors targeting MurB reductase, would lead to osmotic-lysis of the bacterial pathogen. The exploration of the FAD binding site of MurB reductase was performed by the Authors. The search for a potential inhibitor involves the investigation of its mechanism of binding to the MurB reductase allosteric site. Checking the stability of the enzymeinhibitor complex is also necessary, as revealed by the Authors of this research [7].

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The Editorial on the methods of gene expression profiling is a topic to approach, as it is related to various physiological and pathological topics. The various recent high through put techniques, such as DNA microarray, applied for the purpose of human genome sequencing, are mentioned by the Authors. Genome-wide gene expression profiling helps to enhance the understanding of disease mechanisms, as explained by the Author; however, it is also reminded that the major piece of information linking a gene to its function is missing-protein expression, as proteins are the functional molecules carrying out the biological tasks of genes [8].

Studies performed on focal cerebral ischemia have identified a series of key molecular events and a number of changes in gene regulation following infarct. These studies revealed changes in the transcriptional activity of a variety of genes related to stress response, inflammation, acute- and delayed cell death. The great clinical benefit in using whole genome transcriptomics, for identifying targets in cerebrovascular disease basic neurobiological mechanisms underlying post-stroke CNS recovery, are stressed upon in the respective Editorial [9].

The Editorial on biomarkers research and development is important, as biomarkers are essential for the success of clinical trials (e.g. the elevated LDL cholesterol as clinical endpoint for dyslipidemia and measurable biomarker for coronary artery disease diagnostication,). The pharmaceutical industry has incorporated biomarkers into their preclinical and clinical studies [10].

Novel fluorescent materials like quantum dots or new organic dyes have proven to be a progress in the analysis of biomolecules, functioning as labels, without the shortcoming of activity loss of biomolecules. Luminescence-based detection or its combination with fluorescent one can cope to the increasing demand of accuracy in the analysis of complex samples (blood, serum, tissue). The respective Editorial stresses also on the widespread applications, such as the detection of cancer biomarkers, and probing of human serum [11].

The Review on the functional heterogeneity of membrane glycolipids stresses upon their ability to undergo extensive intralipid hydrogen bonding via glycosyl head groups, therefore imparting structural integrity to the membranes of the organisms. Glycolipids in the cell membranes play an important role in recognition and signaling events in a variety of biological phenomena, are potent inducers of apoptosis and differentiation in melanoma cells, regulating cell growth by interacting through growth factor receptors, concentrated receptors and effectors on both sides of the membrane, thus speeding up binding during signaling and preventing inappropriate crosstalk between pathways [12].

Most of interest biomolecules have protein structure, functioning as biocatalysts (enzymes), hormones, antiporters, signal transducers, or regulate neurotransmitter activity. Thus, many Studies have been dedicated to their structure and activity, from here benefiting clinical studies and food security ensuring.

The Editorial focused on the protein liability and lose native structure under the action of physical and chemical factors, acquire special actuality because protein structural alterations are involved in so called "conformational diseases": Alzheimer's and Parkinson's diseases, Huntington's disease, Machado-Joseph's disease (spinocerebellar ataxia), prion encephalopathies, Charcot's disease (amyotrophic lateral sclerosis), systemic amyloidosis and cystic fibrosis [13].

Biocatalysts are very important components of analytical and clinical methods and they are also utilized in various fields of life

sciences, including biochemical, physiological, and biomedical research. The overview of their importance and applications is welcome and reveals: the determination of enzyme activities (e.g. alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatinine kinase, phosphatase, amylase, cholinesterase, lipase etc.) and the enzyme-coupled determinations of metabolites (such as D-glucose, acetoacetate, creatinine, cholesterol, L-phenylalanine) as a diagnostics of various diseases, however enzymes serve also as parts of immuno-assays and biosensors. Biocatalytical sensors use enzymes to quantify local changes of ions, as well as for signaling intermediates, and metabolites in real time [14].

Biosensors represent a viable alternative to laborious and time consuming conventional techniques. They represent sophisticated analytical instruments which incorporate a biorecognition element (e.g. enzyme, nucleic acid, antibody, whole cell), in close contact to a transducer. The transduced parameter can be electrical (current intensity, potential/pH difference), optical (absorbance, fluorescence, luminiscence), thermal or piezoelectrical. Among biosensors, enzyme electrodes combine the advantages of specificity and selectivity provided by the biocatalyst, with the accuracy, sensitivity and rapidity of the physico-chemical detection and do not require laborious separation and other sample pre-treatment steps. Enzyme electrodes can use various detection techniques to detect physiologically and biochemically important analytes, such as glucose, as presented in the respective Editorial. Most glucose biosensors are either glucose oxidase or glucose dehydrogenase - based and use all types of detection (electrochemical, optical, thermal, piezoelectrical) and are applied in various fields like biomedical or food analysis [15].

Although NKA (Na $^+$, K $^+$ -ATPase) has been traditionally considered a pure energy transducing ion pump, recent evidence reveals that it is also involved in the regulation of many cellular functions including gene expression, cell growth, and cell motility. Protein-protein interactions are a major means of bridging NKA activity to signaling molecules or organelles. The Author of the Editorial dedicated to this topic asserts that the same ouabain used for the treatment of heart problems can be synthesized and released by the peripheral organ adrenal cortex and in the brain, mainly by the hypothalamus. That release of endogenous ouabain can be regulated by physical exercise, causing a rapid rise in concentration that declines rapidly upon rest [16].

The prolonged exposure (3-5 hrs) to radiofrequency electromagnetic radiation increased RBC acetylcholinesterase activity, measured using UV-VIS spectroscopy by Ellman modified method. According to the changes observed in the AChE activity, it was concluded by the Authors that the increasing duration of the electromagnetic radiation exposure causes an increase in cholinergic activity [17].

The determination of testosterone levels is useful for investigation of androgen-producing tumors, anti-androgen therapy in prostate cancer and sex assignment in newborns. For women, testosterone concentrations in circulation accounts 10-15% of men, and has physiological properties like maintaining bone mineral density. The assessment of serum testosterone performed by LC-MS/MS analysis alleviates the technical difficulties in steroid measurement especially in low concentrations which is encountered by most automated immunoassays. The Authors of this research proved that the LC/MS method allows simple, useful, analysis of low level of testosterone in short analysis time and small sampe volume [18].

The search for antidotes to food security problems has lead to the need for alternate sources rich in nutrients. Macrotermes nigeriensis is a gregarious termite rich in proteins, carbohydrates and lipids, vitamins and minerals, as presented by the Authors of this research study. This rich source of nutrients, vitamins, minerals and unsaturated fatty acids could help in fighting against protein energy related disease conditions, encountered in developing countries, as indicated in the respective Research Article [19].

The investigation of food composition in nutrients is deepened by the study of milk composition. The data obtained by the Authors confirm the composition similarity between donkey and human milk, especially with respect to enzyme content: the presence of lysozyme and lactoferrin in important amounts, along with the small amounts of lactoperoxidase. Thus, this milk can be used to feed children affected by Cow Milk Protein Allergy (CMPA), but also other subjects with CMPA, such as adults and the elderly [20].

The preoccupation of the usefulness of crops and vegetable composition was another subject approached: the glucosinolates level (which severely limits usefulness of the crop Indian mustard (*Brassica juncea* (L.) Czern. + Coss.)) and antioxidants (tocopherol) level was determined by Near Infrared Reflectance Spectroscopy and colorimetry [21].

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