Biomarkers in Human and Environmental Health Risk Studies

Qasar Saleem*, Tanveer Akbar and Aqsa Salamat

Department of Chemistry, School of Science, University of Management & Technology, Lahore-54770, Pakistan

Abstract: Uncertainties in human health risk assessment, and the measuring on the impacts of contaminants have attracted great concern. Uncertainties, source-to-outcome, exposure assessment, hazard and risk characterisations are a number of techniques that have been applied to maximize results. Experts' opinions and quantitative tools have been applied to narrow the gap between data and rules for regulatory purposes. Bio monitoring information, *in vitro* data streams and computational toxicology are major areas for human health risk assessment. A need for a biomarkers data bank is of utmost need to minimize uncertainties in the toxicological environmental human health risk assessment field.

Keywords: Aflatoxins, Exposure, Susceptibility, Effects, Monitoring, Contaminants.

1. INTRODUCTION

1.1. The Case of PAHs and Benzene

The structure of Health Risk Assessment was first developed in America in order to find a link between air pollution, disease and chemicals. It deals with low-level exposure and results after effects of weak epidemiological interactions with health issues. Epidemiology cannot be handled simply, it demands a complicated methodology, and therefore has a critical position in risk assessment of environmental epidemiology. Exposure of the community to pollutants is of great concern. Generally there are two approaches to handle the issue.

1.2. The Direct Approach

This method involves monitoring a selected portion of the population. This method of monitoring can measure, the quantity of pollutant in contact with physiological barriers, for instance, tools involved in measuring air concentration, or the amount entering the body through environmental media or biological media. Indicators can be determined by analysis of blood, urine, nails or hair. Such indicators are termed as biological markers or simply biomarkers. Their measurements can reveal overall exposure regardless of their absorption routes, *i.e*., ingestion, inhalation, or skin contact.

1.3. Indirect Approach

This is the measurement or the physical modelling of pollutants in different microenvironments frequented by the community/population associated with an assessment about personal behaviour.

1.3.1. Biomarkers: A Definition

A substance, phenomenon, property, or any event which has an impact on human or environmental health by which we can gauge damage, are biomarkers.

Basically we can divide biomarkers into the following types, exposure, effect, and susceptibility. Exposure biomarkers can be further classified into biomarkers of internal and external dose. Internal dose reference the extent of exposure of the living species and external dose biomarkers refer to the extent of exposure of a target molecule, structure or cell. A substance itself, its metabolites, or its interaction with a target molecule like DNA or protein can act as both of these types of biomarkers. Hence the presence of a compound confirms the penetration and quantification establishes a relationship between environmental concentrations and biological system.

Effect biomarkers reflect the interaction between the pollutant and the human body. Measurements of biochemical changes or physical alterations lead to the establishment of a relationship between the environmental system and organism, with clinical or without clinical expressions.

Susceptibility biomarkers are the degree of sensitivity that an individual exhibits towards an external change. This can be different for any individual under the same conditions.

1.4. Selection Criteria and Biomarker Validity

Different conditions and characteristics are involved in the selection and validity of biomarkers; those that involve intrinsic characters and those that are inherent in the investigation procedure [1].

*Address correspondence to this author at the Department of Chemistry, School of Science, University of Management and Technology, Lahore-54770, Pakistan; Tel: +92 3334277152; E-mail: s2016263008@umt.edu.pk

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1.4.1. Assessment of Aflatoxin

The human exposure on individuals was evaluated from dietary aflatoxins; B1(AFB1) and M1(AFM1). Serum lysine and urinary guanine were determined as biomarkers. Workers from a university were employed and food was provided from their home. Samples were collected four times per three months. Analysis of food intake was carried out by HPLC via fluorescence detection.

Serum and urine were analysed for biomarkers by tandem mass spectroscopy. Cereals and milk contained AFB1and AFM1 28%, N = 136, 36%, N = 86 respectively. AFB1-lysine and AFB1-N7-guanine were not found in serum and urine, whereas AFM1 was 65% in urine samples. Monitoring the human exposure to food intake aflatoxin was verified by urinary AFM1 [2].

1.4.2. Biomarkers and Environmental Risk Assessment

Biomarkers have long been recognized but not routine in environmental risk assessment, whereas, clinical health risk assessment is more advanced. As biomarkers, blood pressure and serum cholesterol are common in practice usages. Biomarkers have been incorporated with health risk assessment, whereas, new techniques can include clinical end points and the measurements end points. New biomarkers are much needed in health risk assessment [3].

2. GUIDING PRINCIPLES FROM THE HUMAN HEALTH FIELD

2.1. Analysis of Unmetabolized Polycyclic Aromatic Hydrocarbons

Adult urine can serve as a biomarker of environmental exposure. Polycyclic aromatic hydrocarbons (PAHs) have great carcinogenic potential and can be monitored. Their metabolites (1-hydroxypyrene) were examined in urine. Determination of 16 USEPA parent PAHs in 20 urine samples were measured, 10 from girls and 10 from boys, ages 14-16. Out of the 16 parent PAHs, nine were 95% (benzo (a) pyrene) and three were 50%. Naphthalene and fluorine have a high carcinogenic tendency towards toxicity. Some relationships between PAH and exposure were determined. Fluorine and acenaphthalene were clubbed with thyroid hormone and benzo (a) pyrene with DNA damages by comet assay. PAHs were found in urine analysis. PAHs can be used as an exposure biomarker as a monitoring technique in different combinations [4].

2.2. Biomarkers of Cardio-Metabolic Risk

These biomarkers are linked with plasma sugar within a normal non-diabetic range. Elevated cardio vascular risk is evidence for abnormal metabolic function of glucose and can be linked to diabetes. No known biomarker so far has been used to distinguish this risk. A study was carried out to associate biomarkers for atherogenesis and plasma glucose. Around 1,000 volunteers, with an age group between 35-54, having no diabetes and cardiovascular issues were engaged in this study. They were marked as a normal glucose tolerance (NGT) group. Some were categorized as having an impaired fasting glacema (IFG) and others as having impaired glucose (IGT) tolerance. Markers for both atherogenesis and plasma glucose were investigated. Both IFG and IGT had bad profiles compared to NGT with regards to cardio-vascular risk factors, although the results were as per reference. These groups varied in statistical data groups with regards to a transforming growth factor (TGF). TGF-b1and E-selectin amounts were elevated, whereas MCP-1 was lowered within quartiles of fasting plasma glucose. Association of TGF-b1, E-selectin, C-reactive protein and MCP-1 due to a slight elevation in glycemia can be taken as modifications of typical cardio-vascular risk factors [5].

2.3. Genomics-Based Biomarkers of Human Neuro-Developmental Toxicity

Neural differentiation models are very useful in the estimation of environmental compounds that have the ability to induce neuro-developmental toxicity in the human genome. Exposure effect was estimated by *in vitro* and *in vivo* methods by measuring changes in human development. Here hESC neural differentiation model systems and human embryos are potential candidate biomarkers. The developmental toxicities for neurogenesis can be assessed by these biomarkers. The NDB gene set has 304 genes that perform actively in neurogenesis. A study conducted for their role as biomarkers, for toxicogenomic analysis focused on the effects of retinoic acid, valproic acid, or carbamazepine in a neural differentiation model [6].

Toxicogenomics has a great potential to play an important future role in human health risk assessment. Use of gene expression is gearing up among regulatory authorities in human health risk assessment. Data from gene expression build some confidence in chemical evaluations, whereas a lack of expertise and data is a major handicap in the field of genomics. This current

work provides data of gene expression and its handling techniques [7].

2.4. Use of Arius Thalassinus Fish

Applying combined oxidative stress, hematology, biochemical and histopathological biomarkers, Arius thalassinus fish from a heavily polluted area was used as a reference bundle of biomarkers in sea catfish. The amount of heavy metals was found in precious organs of fish. Results were measured in terms of morphology, hematology and oxidative biomarkers followed by histopathalogical changes. From the evidence collected, it clearly shows a linear relation between biomarkers and metals bioaccumulation. A marked difference was found in the results of polluted and unpolluted sites. The most affected part were the gills of fish [8].

2.5. Lung Cancer Biomarkers in Sputum

A diagnostic technique was developed on the basis of a biomarker to detect earlier stages of lung cancer.. This technique can improve clinical interventions since spontaneous sputum was used as a metabolic biomarker for lung cancer diagnosis [9].

2.6. Use of Multiple Cell and Tissue Level Biomarkers

Exploration and exploitation of gas and oil is carried on worldwide especially in the sea and oceans resulting in the spillage of hydrocarbons. A combination of biomarkers and pollutants was jointly used to draw a relationship between the occurrences of a stress syndrome in mussels (mytilusgallo provincialis). An algorithm that reflects exposure gradients and temporal trends was studied. An elevated biological disturbance in sentinel organisms was recorded [10].

2.7. Eco Toxicological Potential of NSAIDs

Pharmaceutical compounds like NSAIDs (non-steroidal anti-inflammatory drugs) have limited distribution in coastal areas. So bioavailability, biomarkers and natural occurrence in mussels, mytilusgallo provincialis, can be used as biomarkers. Environmental accumulation of NSAIDs and their various effects in mussels, Mytilusgallo provincialis, shows a relationship to these target organisms. Compounds of the same class like diclofenac, were below detectable concentrations. Measurements of algae ecotoxicological biomarkers highlighted impairment of immunological parameters, such as, genotoxicity and modulation of lipid metabolism, oxidative and neuro toxic effects [11].

2.8. Solving the Complexity of Sediment Risk Assessment

The integration of multiple biomarkers and sediment geochemistry help us in solving the complexity of sediment risk assessment. For the study, a benthic fish was exposed to estuarine in the lab. Then *in situ* bioassays were conducted to assess the ecological risk. Exposure to contaminants and uncontaminated sediments by using biomarkers CYP1A and thionein were studied. Proteomic sand gene transcription investigation provided a way to understand the mechanics of toxicity. Both metabolic imbalance and impairment of defences were studied. In situ bioassays, although less expedited and more affected by confounding factors, provided data better related with overall sediment contamination [12].

2.9. Human Risk Assessment of Environmental Chemicals in the Post Genomic Era

A relationship between genomics and allied methodologies regarding human health risk assessment for environmental pollutants is of interest to an evolving toxicity mechanism. It should be a way forward to hazardous characterization by using quantitative risk assessment. It can be set by introducing exposure standards and remedial strategic values. Its purpose is in evolution of QRA for EC in the post genomic period. This can be comprised of three phases, augmentation, integration and expansion. At molecular level pathway-based biomarkers can be further developed. Statistical and *in silico* models can help further our understanding of the risk phenomenon. This approach will be more direct in understanding human health risk assessment in the environment [13].

2.10. Breakfast and Fast Food Consumption

The trend of obesity in adults is linked with skipping breakfast and opting for fast food. The trend is related to biomarkers and diabetes. Insulin resistance was studied by the modelling of anthropometrics, fasting lipids, glucose, insulin, and homeostatic. A relationship between biomarkers, controlling for calories consumed, body mass index (BMI), and demographic covariates were assessed. Breakfast intake was linked with parameters e.g. lower BMI, body fat, insulin, HOMA-IR, and metabolic syndrome (MetS). Whereas the fast food was linked with higher BMI, body fat, low-density lipoprotein cholesterol, triglycerides, glucose, insulin,

HOMA-IR, and MetS cluster score. In a sample of healthy adolescents, biomarkers for chronic disease have deep relationships to the important metabolic syndrome [14].

2.11. Urinary Micro RNA Biomarkers of Pesticide Exposure

MicroRNAs (miRNAs) are stable at room temperature and are recommended as molecular biomarkers to monitor disease and exposure status. miRNAs have been used clinically as potential diagnostic biomarkers for kidney and bladder cancers and other diseases, but their non-clinical setting has yet to be fully developed. As biomarkers of pesticide exposure and early biological response by identifying the miRNAs present in urine, farmworker/non-farmworker pairs were used to characterize the between- and within-individual variability of these miRNA epigenetic regulators. miRNAs were isolated from archived urine samples. Seven miRNAs were detected in at least 50% of the samples, and one miRNA was present in 96% of the samples. Five of these miRNA trended towards a positive dose response relationship with organophosphate pesticide metabolites in farmworkers. miRNAs may be novel biomarkers of pesticide exposure [15].

3. CONCLUSION

Biomarkers can provide authenticity and first hand information about human health risk assessment. Different biomarkers can be studied and even developed to monitor human environmental health risk assessment. The importance of biomarkers has increased as industrialization of different areas has increased the probability of exposure to different environmental chemicals and other phenomenon. Therefore, establishing a databank of biomarkers can serve humanity and the environment.

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