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Analysis of Bisphenol A in Blood and Urine Samples: A Mini Review

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Bisphenol A is constantly discharged at trace levels in food packed in metal cans with PVC linings. This is also present in bottled water. This represents a cause for concern because of potential effects of bisphenol A to human health. We compiled data on the methods used for analysis of bisphenol A in blood and urine samples published in the last 10 years.

Key Words: Blood, Urine, Bisphenol A, HPLC, GCMS.

INTRODUCTION

Bisphenol A is widely distributed and exhibits weak estrogenic activity. In contrast to bisphenol A, the corresponding glucuronide metabolite is not estrogenic. Therefore, free and total bisphenol A were determined in human urine samples to assess the significance of free bisphenol A for risk assessment[1]. Total (free plus conjugated) urinary bisphenol A is currently being used to assess human exposure to this contaminant[2].

Selection and classification of literature data: Because large data has been published over the last 10 years on the occurrence of bisphenol A in the environment, so, it is decided to set the following criteria to select and assure the quality of the compiled values. Only those papers were considered which report bisphenol A in blood and urine samples published in peer-reviewed journals. Articles reporting the limit of quantification (LOQ) of their determination method were selected. Data reported in figures were not considered because of the uncertainty of their interpretation.

The aim of this study is to establish an easy and accurate method which could be used for the determination of bisphenol A in the body liquid such as serum and urine. Two high-performance liquid chromatography systems, HPLC with electrochemical detector and HPLC with mass spectrometry using electrospray ionization (ESI) interface were used[3].

Brock *et al.*[4] reported a new approach for assessing human exposure to bisphenol A by measuring bisphenol A in urine. Authors validated this method by duplicate analyses using gas chromatography coupled to a high-resolution mass spectrometer. Authors investigated environmental exposure levels of bisphenol A in human by measuring bisphenol A glucuronide (BPA-G) in urine. Bisphenol A was extracted with diethyl ether after enzymatic hydrolysis of glucuronide substances in urine. The extract was analyzed using a column-switching HPLC system[5].

Kuklenyik *et al.*[6] developed a sensitive and robust method for measurement of bisphenol A and six nonylphenol in urine. The method was based on the use of automated solid-phase extraction coupled to isotope dilution-gas chromatography/ mass spectrometry. Limits of detection were approximately 0.1 ng in 1 mL of urine. Inoue *et al.*[7] reported an approach for assessing human exposure to bisphenol A based on measuring the glucuronide in urine sample. The detection limit was 0.1 ng mL^{-1} and the calibration curves (0.45-90 ng mL^{-1}) had correlation coefficients exceeding 0.999. The method may be applied to the detection of trace amounts of bisphenol A in human urine samples. Kawaguchi *et al.*[8] developed a new method for the determination of trace amounts of bisphenol A in river water, urine, plasma and saliva samples, based on stir bar sorptive extraction. This simple, accurate, sensitive, and selective analytical method may be applicable to the determination of trace amounts of bisphenol A in liquid samples.

Authors developed a rapid and sensitive method base on based on liquid chromatography tandem mass spectrometry, for the determination of bisphenol A and BPA-gluc in plasma and urine. Limit of quantitation (LOQ) for bisphenol A in control urine was 15 pmol/mL; LOQ for BPA-gluc was 65 pmol/mL. Volkel *et al.*[9] developed a method using isotope dilution on-line solid-phase extraction coupled to high performance liquid chromatography-tandem mass spectrometry for the determination in urine of nine environmental phenolic compounds including bisphenol A. The method can be used for quick and accurate analysis of large numbers of samples in epidemiologic studies for assessing the prevalence of human exposure to environmental phenols[10].

Liu *et al.*[11] evaluated the feasibility of electrochemical detector in combination with high performance liquid chromatography for determination several phenols simultaneously in urine. As to demonstrate the method's utility, authers determined urinary enterolactone, daidzein, genistein and bisphenol A in samples from nine children and 24 adults. Ye *et al.*[12] determined the percentage of glucuronide and sulfate conjugates of three phenolic compounds, bisphenol A, 2,5-dichlorophenol and 2-hydroxy-4-methoxybenzophenone in urine samples. Authors used a sensitive on-line solid phase extraction-isotope dilution-high performance liquid chromatography tandem mass spectrometry method. Bisphenol A is a weak estrogen. Volkel *et al.*[13] developed a rapid and sensitive method for the determination of bisphenol A and BPA-gluc in plasma and urine based on liquid chromatography-tandem mass spectrometry. Limit of quantitation (LOQ) for bisphenol A in control urine was 15 pmol/mL; LOQ for BPA-gluc was 65 pmol/mL. They found that bisphenol A was below the LOD in all except two of the samples. A high-sensitivity analytical method was developed that uses stir bar sorptive extraction with *in situ* derivatization and thermal desorption gas chromatography-mass spectrometry. This method is used for the simultaneous measurement of trace amounts of phenolic xenoestrogens, such as 2,4-dichloro phenol, 4-*t*-butyl phenol, 4-*t*-octyl phenol, 4-nonyl phenol technical isomers, pentachlorophenol and bisphenol A, in human urine samples.

Kawaguchi *et al.*[14] measured bisphenol A and 4-nonyl phenol isomers in urine samples from a reference population. They used isotope-dilution gas chromatography/mass spectrometry. Bisphenol A was detected in 95 % of the samples examined. This study provides the first reference range of human internal dose levels of bisphenol A and 4-nonyl phenol isomers in a demographically diverse human population[15].

Schoringhumer *et al.*[16] described the development of a simple and highly selective analytical method for the determination of free and total bisphenol A in urine samples. the LOD (S/N = 3) was 0.2 ng/mL. The method was applied to healthy adults and dialysis patients for determination of free and total urinary bisphenol A levels.

Authors found detectable levels of three phytoestrogens (enterolactone, daidzein and genistein) and bisphenol A in 21 residual amniotic fluid specimens that they collected before 20 weeks gestation. Bisphenol A was present at very low concentrations (10 % > LOD of 0.5 μg/L)[17]. Moors *et al.*[18] established method for simultaneous determination of DAI, its metabolite equol (EQ), GEN and bisphenol A by GC-MS analysis. They validated and applied this method to measure concentrations in human urine. LOD were 4, 4, 5 and 3 ng/mL urine for DAI, EQ, GEN and bisphenol A, respectively. Bisphenol A was detected in 9 of 15 urine samples ranging from 3-11 ng/mL and at 55 ng/mL in one sample. Biomonitoring results showed much higher dietary exposure to phytoestrogens than to bisphenol A in German adults. Volkel *et al.*[1] determined free and total bisphenol A in human urine samples to assess the significance of free bisphenol A for risk assessment. Limit of detection was 0.3-2.5 μg/L. Total bisphenol A was determined in 147 urine samples with concentrations between < LOD and 9.3 μg/L. This work based on microextraction of bisphenol A, prior to its determination by liquid chromatography and fluorescence detection. The procedure involves the enzymatic hydrolysis of urine. The practical detection limit was 0.197 μgL^{-1}, which is below the usual concentrations of bisphenol A in urine (ranges reported 0.4-149 μgL^{-1}). The method was successfully applied to the determination of total bisphenol A in urine from Garcia-Prieto *et al.*[2].

This review critically reported concentrations of bisphenol A in blood and urine of non occupationally 'environmentally' exposed humans. In urine samples, bisphenol A (as glucuronide) was present in average concentrations in the range of 1-3 μg/L suggesting that daily human exposure to bisphenol A is below 6 μg/person (< 0.1 μg/kg bw/day) for the majority of the population[19].

Kawaguchi *et al.*[20] described a new method for the determination of trace amounts of bisphenol A in human urine samples with gas chromatography-mass spectrometry. This simple, accurate, sensitive and selective analytical method can be applicable to the determination of trace amounts of bisphenol A in human urine samples. Mahalingaiah *et al.*[21] determined the temporal variability and predictors of bisphenol A exposure. They measured urinary concentrations of bisphenol A among male and female. They found that bisphenol A urinary concentrations among pregnant women were 26 % higher than those among the same women when not

pregnant). The urinary bisphenol A concentrations of the female and male partner on the same day were correlated (r = 0.36; p = 0.02). They found a nonsignificant increase in urinary BPA concentrations in women while pregnant compared with non-pregnant. Ye *et al.*[22] measured levels of six dialkyl phosphate metabolites of organophosphorus pesticides, a chlorpyrifos-specific metabolite (3,5,6-trichloro-2-pyridinol), bisphenol A and 14 phthalate metabolites in urine samples pregnant women. The data indicate that the Generation R study population provides a wide distribution of selected environmental exposures. Reasons for the relatively high levels and possible health effects need investigation.

The authors measured bisphenol A in saliva and urine samples collected at prescribed intervals after the sealants were placed. Isotope-dilution mass-spectrometry-based methods for bisphenol A measurements were used. Urinary and salivary bisphenol A levels in subjects who received these sealants were similar to baseline levels[23].

Conclusion

Detrimental effects of bisphenol A on human beings are possible with the constant exposure through drinking water and canned food. Indirect impact on human health from drinking water and canned food cannot be ruled out when considering the potential risk of bisphenol A. Blood and urine samples are used for bio-monitoring of bisphenol A.

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