Kaohsiung Journal of Medical Sciences (2011) 27, 382–389

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journal homepage: http://www.kjms-online.com

REVIEW ARTICLE

Arsenic speciation in biomedical sciences: Recent advances and applications

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Received 6 September 2010; accepted 18 November 2010
Available online 8 July 2011

KEYWORDS
Advance;
Application;
Arsenic speciation;
Biomedical science

Abstract Speciation analysis of trace elements is an important issue in biomedical and toxicological sciences because different elemental species have different effects on health and the environment. For humans, arsenic (As) is a toxic element; the toxicity of As compounds is highly dependent on its chemical form. Although inorganic As compounds are human carcinogens, organic arsenicals are relatively less toxic. This article deals with recent advances and applications of methods for As speciation in biomedical sciences, with emphasis on the specimens commonly encountered in biomedical laboratories.

Introduction

Arsenic (As) is well known as a toxic element for human beings. The International Agency for Research on Cancer has classified As and its inorganic compounds as "carcinogenic to human" (Group 1); the organic arsenicals monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) are classified as "possibly carcinogenic to humans" (Group 2B); arsenobetaine (AsB) and other organic compounds that are not metabolized in humans are "not classifiable" (Group 3) [1,2]. Chronic As poisoning is a serious public health problem worldwide; long-term exposure to inorganic As from drinking water is associated with skin lesions and malignant diseases [3–5].

As is a ubiquitous element that ranks 12th in abundance in the human body. Despite its notorious reputation as a poison, As has been used as a therapeutic agent for more than 2000 years [6]. Recently, As compounds have been examined extensively as potential anticancer agents toward some malignant diseases, especially for the treatment of acute promyelocytic leukemia (APL) [7,8], where low doses of arsenic trioxide was found to induce complete remission in individuals with APL who had a relapse, suggesting that induction of cell apoptosis might be one of the mechanisms of the therapeutic effect of arsenic trioxide. Because of the different toxic effects induced by different As species, speciation analysis is critical when evaluating

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1607-551X/$36
doi:10.1016/j.kjms.2011.05.005

the therapeutic efficiency of arsenic trioxide for treating individuals with APL.

Measurement of essential or toxic elements has traditionally been performed using atomic spectrometry techniques, most notably flame atomic absorption spectrometry (AAS), electrothermal AAS, inductively coupled plasma atomic emission spectrometry, and inductively coupled plasma mass spectrometry (ICP—MS). ICP—MS is one of the most common analytical techniques for the determination of trace elements because of its multi-element analysis capability and its high sensitivity for most elements of interest [9]. For separation, high-performance liquid chromatography (HPLC) has the advantages of greater versatility and good reproducibility relative to other chromatographic separation methods (e.g. gas chromatography or capillary electrophoresis) [10]. The combination of HPLC with suitable detection systems for As speciation in biomedical sciences is the most attractive and most established approach. Ion-exchange chromatography is the most widely used separation technique, whereas ICP—MS is the most commonly used detection method.

The low levels of As species in biomedical matrices make obtaining sensitive and reliable measurements a true challenge. ICP—MS provides a low detection limit and good sensitivity for the detection of trace element species; combined with the ease of coupling most HPLC systems with the ICP—MS, it is an excellent detection method for As speciation analysis. Table 1 lists the common As species found in biological materials. Because of the complexity of the sample matrix and the diversity of As species, the search for suitable analytical methods is a key issue for As speciation analysis in the field of biomedical sciences; this article focuses on some significant findings in the area, focusing on relevant reports published in the calendar years 2005—2009.

Advances and applications of As speciation analysis in biomedical matrices

Table 2 lists some selected recent (2005—2009) applications of As speciation in commonly used biomedical matrices. The analytical systems that have been used for As speciation in biomedical matrices, mainly from human beings, have typically combined chromatographic separation with elemental or molecular mass spectrometric detection. Among these analytical systems, HPLC coupled with ICP—MS has been the most widely used method for determining As species in biomedical matrices. In the following sections, we describe the recent applications of As speciation analysis in urine, blood, hair and nail, and other biomedical matrices.

As speciation in urine

Most of the method developments and applications of As speciation analysis in biomedical research have focused on the analysis of urine, which is generally considered a suitable sample for evaluating As metabolism. Notably, however, most medical laboratories measure only the total As concentration in urine, presumably because the practitioners are unaware that a high total-As concentration requires further speciation analysis, which might not be possible because of the lack of rapid and reliable methods. For high-throughput speciation in a medical laboratory, Heitland and Köster [23] developed and validated a method using HPLC coupled with ICP—MS for the determination of five As species in human urine. They applied this method to compare urinary As speciation for various medical cases [22], suggesting that real concentration data for As species in urine are helpful for toxicologists and hygienists to understand the impact of As species in different situations. HPLC—hydride generation (HG)—ICP—MS, HPLC—HG—atomic fluorescence spectrometry (AFS), and HG—AAS are the three most commonly used analytical methods for determination of inorganic As and its metabolites in urine. From a comparison of the performance of these three methods, Lindberg et al. [18] suggested that, because of its considerably lower costs, HPLC—HG—AFS might be a good alternative in laboratories where the high cost of ICP—MS is not justified in relation to the intended use of the instrument.

Occupational and environmental exposure to As compounds is associated with the increased prevalence of various kinds of diseases. Analytical methods for monitoring occupational or environmental exposure have focused on the determination of As metabolites in urine. Morton and Mason [54] developed an anion-exchange-based method coupled with ICP—MS that they subsequently used to

Table 1 Arsenic species commonly found in biological materials

Name	Abbreviation	Chemical formula
Inorganic arsenic species		
Arsenite (arsenious acid)	As(III)	$As(OH)_3$
Arsenate (arsenic acid)	As(V)	$AsO(OH)_3$
Organic arsenic species		
Monomethylarsonous acid	MMA(III)	$CH_3As(OH)_2$
Monomethylarsonic acid	MMA(V)	$CH_3AsO(OH)_2$
Dimethylarsinous acid	DMA(III)	$(CH_3)_2AsOH$
Dimethylarsinic acid	DMA(V)	$(CH_3)_2AsO(OH)$
Arsenobetaine	AsB	$(CH_3)_3As^+CH_2COO^-$
Arsenocholine	AsC	$(CH_3)_3As^+CH_2CH_2OH$
Trimethylarsine oxide	TMAO	$(CH_3)_3AsO$
Tetramethylarsonium ion	Me_4As^+	$(CH_3)_4As^+$