

ORIGINAL RESEARCH PAPER

## Developing Preparation Methods for Biological Samples to Determine Trace Amounts of Heavy Metals: A Review Study

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### ABSTRACT

**Introduction:** Perpetration of samples is one of the most important stages needed for trace residue analysis of biological specimens when human exposure assessment is required. The samples preparation process makes the analyte get more purified and enriched as well as more compatible to the analysis instrument systems. The present study has concentrated on a systematic review of different articles published regarding the sample preparation methodologies of human biological samples.

**Material and Methods:** In this systematic review, all articles related to the development of sample preparation for trace residue analysis of heavy metals in occupational biological samples published in English during 2009-2019, were considered. To meet the desired objective of the current study and facilitate the related articles on physiochemical sample preparation methods accessibility combined keywords of Mesh and non-Mesh, without any limitation in the type of studies, the Pubmed, Web of Science, and Scopus were considered to be searched. Noteworthy, in this study, only the articles related to the workers' biological samples were reviewed.

**Results:** Based on the obtained results, after reviewing of the keywords through websites, 2964 articles were identified. Then, the redundant papers were removed and 59 articles were remained, based on their titles and abstracts. After detailed review of selected articles, regarding the study criteria, 8 articles were selected for the final systematic review. Five articles out of 8, (62.5%) were allocated to the development of sample preparation for mercury in biological samples. It is worth mentioning that the majority of biological samples were regarded to the urine samples (75%) in the current study. Based on the obtained results, Solid Phase Extraction (SPE), applied in 37.5% of studies, was a popular method used in sample preparation.

**Conclusion:** The development of sample preparation approaches indicates a great promise for specified methods with low costs and less extraction time when separating different heavy metals from complex matrices. These sample preparation and preconcentration techniques ease the analyses processes and provide the quantitative recoveries, higher sensitivity, and lower detection limits.

**Keywords:** Sample preparation, biological sample, extraction, heavy metals

### 1. INTRODUCTION

Based on the literature, researchers have had always efforts to reduce time and costs, increase efficiency, and simplify the sample preparation and detection steps by developing and customizing different sample preparation techniques. Many studies have been conducted on developing various biological sample preparation techniques. However, a limited number of works have been performed to merely

develop human biological sample preparation methods for measuring trace amounts of heavy metals in occupational exposures. Therefore, the present structured study reviews the research conducted on developing human biological sample preparation techniques specialized for determining the trace amounts of heavy metals.

### 2. MATERIAL AND METHODS

In this study, all the English papers published from

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Table 1. MeSh and non-MeSh keywords used to search for papers in databases

("Soxhlet extraction" OR "Liquid-Liquid Extraction[Mesh]" OR "Microwave assisted extraction" OR "Solid Phase Extraction[Mesh]" OR "Immuno extraction" OR "Molecularly imprinted polymer" OR "molecularly imprinted" OR "Dispersive spme extraction" OR "SFC (Supercritical Fluid Chromatography)[Mesh]" OR "Supercritical Fluid Chromatography [Mesh]" OR "Supercritical Fluid Extraction[Mesh]" OR "Chromatography, Supercritical Fluid[Mesh]" OR "Supercritical Fluid Extraction[Mesh]") AND ("Occupational Exposure [Mesh]" OR "Exposure, Occupational[Mesh]" OR "Exposures, Occupational[Mesh]" OR "Industrial Hygiene[Mesh]" OR "Employee Health[Mesh]" OR "Health, Employee[Mesh]" OR "Occupational Groups[Mesh]" OR "Occupational Group[Mesh]" OR "Labor Force[Mesh]" OR "Labor Forces[Mesh]" OR "Precarious Employment[Mesh]" OR "trace residual analysis" OR "measurement" OR "development" OR "Analytic Sample Preparation Methods[Mesh]" OR "sample preparation" OR "sample treatment" OR "sample pretreatment" OR "Nano toxicology" OR "biochemical toxicology" OR "Supercritical Fluid Extraction[Mesh]") AND ("Metals, Heavy[Mesh]" OR "Heavy Metals[Mesh]" OR "Mercury[Mesh]" OR "Cadmium[Mesh]" OR "Arsenic[Mesh]" OR "Chromium[Mesh]" OR "Thallium[Mesh]" OR "Copper[Mesh]" OR "Selenium[Mesh]" OR "Zinc[Mesh]")

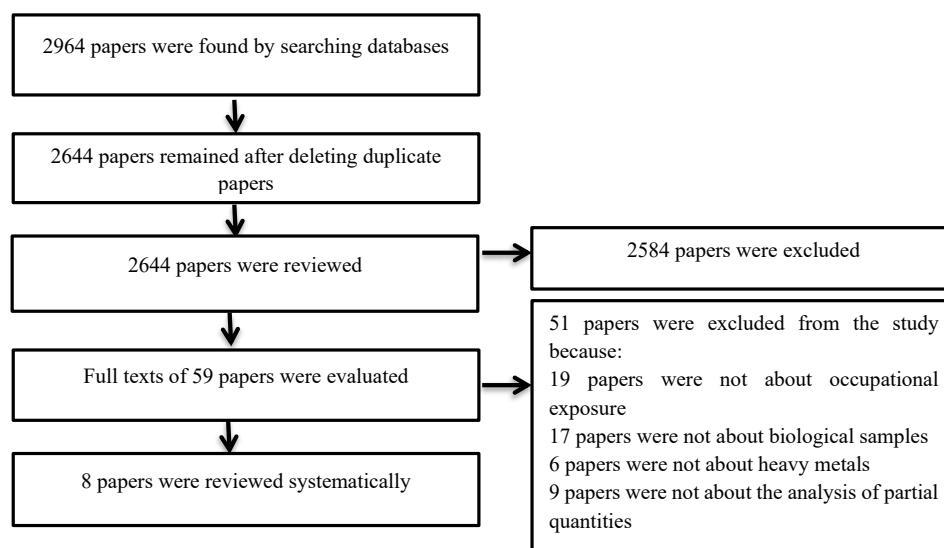


Fig. 1. Flowchart of paper selection process

2009 to 2019 on analyzing trace amounts of heavy metals or developing a method for the analysis of these metals among workers in all the occupations were searched based on a combination of MeSH terms and other keywords without any restriction on the type of study in four databases of PubMed, Web of Science, Scopus, and Embase, and then reviewed. All the 2964 papers found were entered into EndNote software (version X7, for Windows, Thomson Reuters, and Philadelphia, PA, USA). Duplicate papers were first removed to identify the relevant papers and, then, two researchers independently excluded those papers that were not related to the purpose of the study based on their titles and abstracts. The full texts of the remaining papers were reviewed to identify the papers that fully met the inclusion criteria. Data such as the name of the corresponding author, year of publication, place of study, preparation method, chemicals and devices used, and type of biological sample and metal were extracted from the studies.

### 3. RESULTS AND DISCUSSION

Out of 2964 papers collected, 300 papers were duplicates and, therefore, removed from the study. After reviewing them, 2584 papers were excluded from the study based on their titles and abstracts. The full texts of the remaining 59 papers were carefully reviewed, 51 of which were deleted due to non-compliance with the inclusion criteria. Finally, the full texts of the remaining 8 papers were reviewed and analyzed.

Based on the results, mercury or its compounds (with 62.5%) and urine samples (with 75%) had the highest rates of application among the studied heavy metals and human biological samples used to measure trace amounts of heavy metals, respectively. Among the techniques examined for sample preparation in this study, SPE was proposed as the most frequently used sample preparation technique, since it is quick and easy to perform and is widely used to extract environmental and biological samples.

First author (publication date)	Country	Metal species	Type of biological sample	Sample preparation	Apparatus	Sensors/ Absorbents
Schlathauer, M. (2017) (35)	Germany	mercury (Hg)	urine	SPE <sup>1</sup>	TEM <sup>2</sup> , AFS <sup>3</sup> , CV AFS <sup>4</sup> , CVAAS <sup>5</sup>	active Nano gold coated silica material
Khadem, M. (2010) (1)	Iran	Cobalt (II)	urine, hair, nail	SPE	FAAS <sup>6</sup>	Chromosorb 102 resin
Sommer, Y. L. (2014) (36)	USA	Hg, MeHg, EtHg	Blood	SPME <sup>7</sup> (& optimized headspace extraction	ELAN DRC <sup>8</sup> ICP MS, PerkinElm Clarus 500 Gas Chromatograph	Fiber coated with 100 µm PDMS
Matusiewicz, H. (2010) (37)	Poland	total and inorganic mercury	CRMs <sup>9</sup>	Microwave assisted decomposition method & three ultrasonic extraction procedures	CV AAS	Hydrochloric acid (HCl), tetramethylammonium hydroxide (TMAH) and formic acid (HCOOH)
Khadem, M. (2014) (38)	Iran	nickel	urine, hair and nail samples	SPE	Polarographic technique (Metrohm 757 Computrace VA voltameter)	XAD 7 & Chromosorb 102 resin
Fernandez, E. (2016) (39)	Spain	mercury	Urine	Vortex assisted DLLE <sup>10</sup> and microvolume back extraction	SPCEs <sup>11</sup>	Screen printed electrodes modified with gold nanoparticles
Sabouri, A. (2016) (40)	Iran	total mercury	urine	FI-CV AAS <sup>12</sup>	Varian AA220 AAS <sup>13</sup> (Australia)	Varian mercury hollow cathode lamp
Takeuchi, A. (2012) (41)	Japan	Inorganic arsenic [As(III) & As(V)], monomethylarsonic acid (MMA)	urine	Liquid-Liquid Extraction	GC-MS <sup>14</sup>	GC MS equipped with a capillary column

<sup>1</sup>Solid-Phase Extraction

<sup>2</sup>TEM: Transmission Electron Microscopy

<sup>3</sup>AFS: Atomic Fluorescence Spectrometry

<sup>4</sup>CV-AFS: Cold Vapor - Atomic Fluorescence Spectrometry

<sup>5</sup>CV-AAS: Cold Vapor- Atomic Absorption Spectrometry

<sup>6</sup>FAAS: Flame Atomic Absorption Spectrometry

<sup>7</sup>SPME: Solid-Phase Micro Extraction

<sup>8</sup>DRC: Biological Certified Reference materials

<sup>9</sup>DLLE: Dispersive Liquid-Liquid Micro Extraction

<sup>10</sup>SPCEs: Screen-Printed Carbon Electrodes

<sup>11</sup>AAS: Atomic Absorption Spectrometer

<sup>12</sup>FI-CV-AAS: Flow Injection Catalytic Cold Vapor Atomic Absorption Spectrometry

<sup>13</sup>GC-MS: Gas chromatography-mass spectrometry

#### 4. CONCLUSIONS

The results of the studies indicated that it is possible to reduce extraction time and costs, increase efficiency, and simplify the sample preparation and detection steps by developing different sample preparation techniques and making them particular for the detection of different metals. More appropriate measures can be taken to control the exposure of individuals to heavy metals by accurately determining their exposure status to various metals in different work environments. In this study, SPE was proposed as the most practical sample preparation technique due to its ease and speed of operation and widespread use for extracting environmental and biological samples. Therefore, further studies are recommended to develop sample preparation methods, which can be helpful in detecting and improving the exposure of people to heavy metals in the workplace.

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