Science of the Total Environment 574 (2017) 1054–1074

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Review

A critical review of approaches and limitations of inhalation bioavailability and bioaccessibility of metal(loid)s from ambient particulate matter or dust

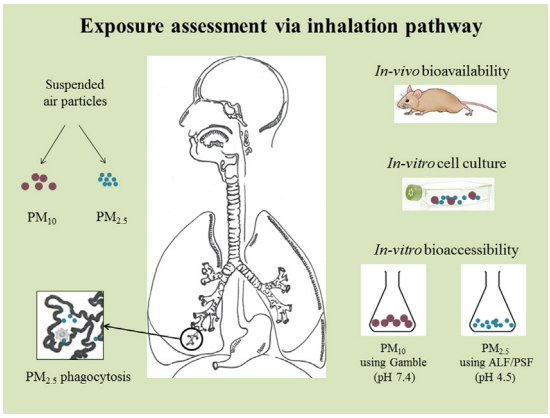
Farzana Kastury *, Euan Smith, Albert L. Juhasz

Future Industries Institute, University of South Australia, Mawson Lakes Campus, Adelaide, SA 5095, Australia

HIGHLIGHTS

- Methods for assessing metal(loid) inhalation bioaccessibility lack consistency.
- Simulated lung fluids (SLF) vary considerably.
- Particle sizes utilised are often not relevant for human inhalation exposure.
- Comparative studies illustrating the extraction efficiency of SLF are lacking.
- *In vitro* assays require *in vivo* correlation to determine predictive performance.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 1 August 2016
Received in revised form 6 September 2016
Accepted 8 September 2016
Available online xxxx

Dr. J Jay Gan

Keywords:
Ambient particulate matter
Inhalation bioaccessibility
Inhalation bioavailability
Simulated lung fluid
Gamble
Metal(loid)

ABSTRACT

Inhalation of metal(loid)s in ambient particulate matter (APM) represents a significant exposure pathway to humans. Although exposure assessment associated with this pathway is currently based on total metal(loid) content, a bioavailability (*i.e.* absorption in the systemic circulation) and/or bioaccessibility (*i.e.* solubility in simulated lung fluid) based approach may more accurately quantify exposure. Metal(loid) bioavailability-bioaccessibility assessment from APM is inherently complex and lacks consensus. This paper reviews the discrepancies that impede the adoption of a universal protocol for the assessment of inhalation bioaccessibility. Exposure assessment approaches for *in-vivo* bioavailability, *in-vitro* cell culture and *in-vitro* bioaccessibility (composition of simulated lungs fluid, physico-chemical and methodological considerations) are critiqued in the context of inhalation exposure refinement. An important limitation of bioavailability and bioaccessibility studies is the use of considerably higher than environmental metal(loid) concentration, which diminishing their relevance to human exposure scenarios. Similarly, individual metal(loid) studies have been criticised due to complexities of APM metal(loid) mixtures which may impart synergistic or antagonistic effects compared to single metal(loid) exposure. Although a number of different simulated lung fluid (SLF) compositions have been used in metal(loid) bioaccessibility studies, information regarding the comparative leaching efficiency among these different SLF and comparisons to *in-vivo* bioavailability data is lacking. In addition, the particle size utilised is often not representative of what is deposited in the lungs while assay parameters (extraction time, solid to liquid ratio, temperature

* Corresponding author at: Future Industries Institute, University of South Australia, Building X, Mawson Lakes Campus, Adelaide, SA 5095, Australia.
E-mail address: farzana.kastury@mymail.unisa.edu.au (F. Kastury).

http://dx.doi.org/10.1016/j.scitotenv.2016.09.056
0048-9697/

and agitation) are often not biologically relevant. Research needs are identified in order to develop robust *in-vitro* bioaccessibility protocols for the assessment or prediction of metal(loid) bioavailability in APM for the refinement of inhalation exposure.

Contents

1. Introduction

Despite a growing interest over the last two decades, assessment of metal(loid) exposure from ambient particulate matter (APM) or dust *via* inhalation is inherently complex and lacks consensus on many levels. APM is a complex mixture of liquid droplets, dust particles, soluble ions, metal(loid)s, elemental/organic carbon, microorganisms, spores, plant fragments, pollens, and endotoxins (Seinfeld and Pankow, 2003, Madsen et al., 2012, Mukhtar and Limbeck, 2013b, USEPA, 2015). In addition to natural sources (*e.g.* volcanic eruption or dust storm), numerous anthropogenic activities introduce APM into the atmosphere, such as, biomass/fossil fuel combustion, mining/smelting and vehicular exhaust emission (Mukhtar and Limbeck, 2013b).

Several epidemiological studies have shown that chronic environmental exposure to APM or dust may be the principal cause of elevated concentrations of metal(loid)s in blood and urine (Landrigan and Baker, 1981; Díaz-Barriga et al., 1997). Certain metals in APM have been associated with specific negative health outcomes, such as, decreased pulmonary and renal function by inhalation of Zn and Cd (Anthony et al., 1978; Nogué et al., 2004), lung cancer by inhalation of As (Smith et al., 2009), damage to DNA by Pb and Cd inhalation (Palus et al., 2003). Animal studies have also confirmed that metal exposure *via* inhalation may affect the cardiovascular system (Campen et al., 2001, 2002; Kodavanti et al., 2005; Lippmann et al., 2006; Wallenborn et al., 2008), the reproductive system (Veras et al., 2010) and act as endocrine disruptors (Iavicoli et al., 2009). As APM may remain buoyant for many days, toxic metal(loid)s in air may accumulate over time (Schaider et al., 2007; Mukhtar and Limbeck, 2013b), and be trasported rapidly over long distances (Csavina et al., 2012). Thus, metal(loid)s in APM may exert toxic effects *via* inhalation in areas that are far from the source of emission (Csavina et al., 2012; Mukhtar and Limbeck, 2013b).

The trend in exposure assessment methods is currently shifting away from total metal(loid) content analysis and towards assessing the fraction of metal(loid)s that are released from particles after coming into contact with biological fluids. The description of interstitial lung fluid composition in Gamble (1967) initiated the formulation of several SLFs and prompted the development of multiple *in-vitro* inhalation bioaccessibility models. Bioaccessibility testing is becoming an increasingly popular exposure assessment method because of its simplicity and cost effectiveness. However, a lack of consensus in the protocol, SLF composition, and most significantly, absence of strong *in-vivo* correlation, makes data interpretation and comparison between methodologies challenging.

The aim of this review is to critically analyse *in-vitro* methods for metal(loid) bioaccessibility assessment from APM/dust to highlight the inconsistencies that prevent the development and adoption of a universal protocol. To achieve this aim, the respiratory system is briefly described, then *in-vivo* and *in-vitro* methods commonly used for metal(loid) exposure assessment *via* the inhalation pathway are addressed, highlighting the studies that are noteworthy in the development of simulated lung fluids that are currently used in bioaccessibility methods. The origin and composition of different SLFs