Science of the Total Environment 625 (2018) 589–599

Contents lists available at ScienceDirect

Science of the Total Environment

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

Intratracheal instillation of coal and coal fly ash particles in mice induces DNA damage and translocation of metals to extrapulmonary tissues

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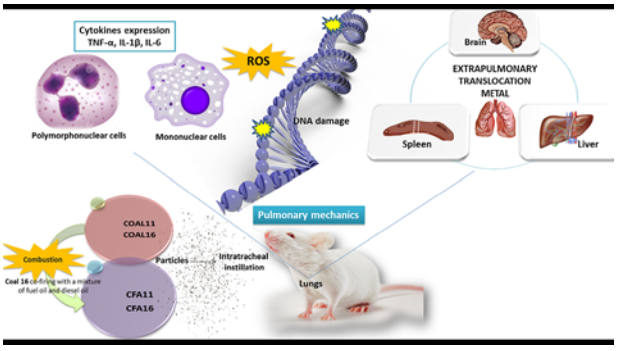
HIGHLIGHTS

- Coal particles increased lung mechanical impedance, inflammation and damaged DNA.
- The complex composition of coal and CFA particles triggers inflammatory processes.
- These effects were associated with particle composition rather than their size.
- The exposure to coal and CFA particles induced primary DNA lesions.
- Cr, Fe and Ni were efficiently translocated by the bloodstream to other organs.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 24 October 2017
Received in revised form 20 December 2017
Accepted 23 December 2017
Available online xxxx

Editor: Henner Hollert

Keywords:
Coal
Coal fly ash

ABSTRACT

Continuous exposure to coal mining particles can cause a variety of lung diseases. We aimed to evaluate the outcomes of exposure to detailed characterized coal and coal fly ash (CFA) particles on DNA, lung and extrapulmonary tissues. Coal samples (COAL11 and COAL16) and CFA samples (CFA11 and CFA16) were included in this study. Intending to enhance the combustion process COAL16 was co-fired with a mixture of fuel oil and diesel oil, producing CFA16. Male BALB/c mice were intratracheally instilled with coal and CFA particles. Measurements were done 24 h later. Results showed significant rigidity and obstruction of the central airways only for animals acutely exposed to coal particles. The COAL16 group also showed obstruction of the peripheral airways. Mononuclear cells were recruited in all treatment groups and expression of cytokines, particularly TNF-α and IL-1β, was observed. Only animals exposed to COAL16 showed a significant expression of IL-6 and recruitment of polymorphonuclear cells. DNA damage was demonstrated by Comet assay for all groups. Cr, Fe and Ni were detected in liver, spleen and

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https://doi.org/10.1016/j.scitotenv.2017.12.283
0048-9697/

Inflammatory processes
DNA damage
Metal translocation

brain, showing the efficient translocation of metals from the bloodstream to extrapulmonary organs. These effects were associated with particle composition (oxides, hydroxides, phosphates, sulfides, sulphates, silciates, organic-metalic compounds, and polycyclic aromatic hidrocarbons) rather than their size. This work provides state of knowledge on the effects of acute exposure to coal and CFA particles on respiratory mechanics, DNA damage, translocation of metals to other organs and related inflammatory processes.

1. Introduction

Coal mining, preparation, combustion, waste storage and transportation of coal cause a great number of environmental impacts. Prior to its combustion, Brazilian coal is pulverized and burned at temperatures of 1000–1300 °C (Silva et al., 2010). During this industrial process, the inorganic particles do not achieve complete combustion and particulate coal fly ashes (CFA) are produced (Burt et al., 2013; Heidrich et al., 2013; Silva et al., 2009, Silva and Boit, 2011). The reactions produced during combustion, properties and composition of the derived particles depend on the type of coal, boiler used, and combustion conditions such as the use of additional fuels as diesel oil to enhance the combustion process (Silva et al., 2010; Martinez, 2012).

When coal and CFA particles are inhaled, they trigger a broad inflammatory response. Macrophages, neutrophils and epithelial cells are stimulated and produce excessive amounts of reactive oxygen species (ROS) and cytokines. After stimulation, epithelial cells and fibroblasts can produce collagen, proteoglycans and elastic fibers, which are important components of the extracellular matrix (Schins and Borm, 1999; Sakai and Tager, 2013).

ROS can also be generated by independent mechanisms in addition to the cellular pathway owing to the inherent chemical properties of coal and CFA particles. An important factor that determines the ability of oxidative generation of these particles is the hazardous elements, for example metals, contained in them, which can increase ROS generation *via* Haber-Weiss reaction (Knaapen et al., 2004; Bonner, 2007). It is known that ROS lead to DNA strand break, inter- and intra-strand crosslinks, and DNA-protein crosslinks. These modifications in DNA are related to harmful events such as mutation, cancer and other diseases (Jena, 2012). Additionally, coal and CFA particles contain organic constituents such as polycyclic aromatic hydrocarbons (PAHs), and several organic nanoparticles including carcinogenic ones (Liu et al., 2008; Burt et al., 2013; Da Silva, 2016; Sanchís et al., 2013, 2015). PAHs undergo metabolic activation and form diol-epoxides that possibly bind covalently to DNA (Singh et al., 2007; Jarvis et al., 2014). Semiquinone radicals also are produced and can undergo redox cycling, leading to ROS formation (Donaldson et al., 2005; Singh et al., 2007).

The exposure to coal and CFA particles and its relationship with diseases of the respiratory tract and other target organs, including some cancers, have been under discussion for several years. Recently our research group demonstrated DNA damage induced by coal and CFA samples *in vitro,* related to oxidative stress generated by hazardous elements and PAHs (León-Mejía et al., 2016). In this context, *in vivo* studies are necessary to elucidate the complex mechanisms related to the pulmonary physiology and the translocation of particles containing hazardous elements to tissues. Additionally, the inflammatory processes triggered after exposure to chemically complex particles and their putative burden on the DNA constitute another broad area of interest deserving a closer exploration. Thus, the aim of this work was to

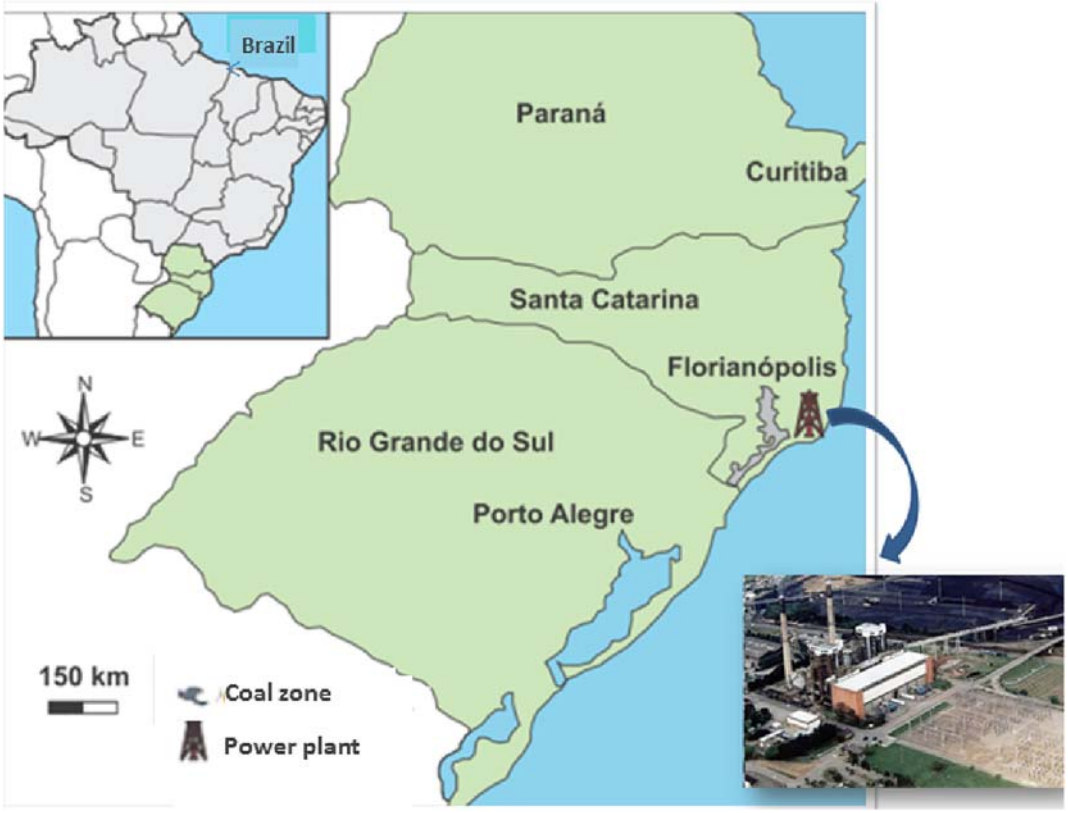

Fig. 1. Location of coal mine and power plant in the state of Santa Catarina.