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The effect of aluminium and sodium impurities on the *in vitro* toxicity of cristobalite: implications for silica regulations

Abstract *

Exposure to crystalline silica (SiO_2), in the form of quartz, tridymite or cristobalite, can cause respiratory diseases, such as silicosis. However, the observed toxicity and pathogenicity of crystalline silica is highly variable. This has been attributed to a number of inherent and external factors, including the presence of impurities. In cristobalite-rich dusts, such as volcanic ash and diatomaceous earth, ubiquitous substitutions of aluminium (Al) for silicon (Si) in the cristobalite structure, and impurities occluding the silica surface, have been hypothesised to decrease its toxicity. This is tested here through the characterisation and *in vitro* toxicological study of synthesised cristobalite (from a silica sol-gel) with incremental doping of Al and sodium (Na).

Al-only doped or Al+Na co-doped cristobalite contained between 1 and 4 oxide wt.% structural Al and Na. Co-doped samples also had grown Al/Na-rich phases, such as albite. Doping reduced cytotoxicity to J774 macrophages and haemolytic capacity compared to non-doped samples. Al-only doping was more effective at decreasing cristobalite reactivity than Al+Na co-doping. The reduction in the reactivity of cristobalite is attributed to both structural impurities and a lower abundance of crystalline silica in doped samples. Neither non-doped nor doped crystalline silica induced production of the pro-inflammatory cytokine TNF-α in J774 macrophages.

Impurities can reduce the toxic potential of cristobalite, which helps to explain the low reactivity of some cristobalite-rich dusts. Whilst further work is required to determine if these effects translate to altered pathogenesis, the results have potential implications for the current blanket regulation of crystalline silica exposures.

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