Elimination of silicosis: to eliminate which silica?

ABSTRACT

International and national programmes to eliminate silicosis have been initiated with the inference that exposure to quartz is associated with silicosis. Experimental evidence is presented by numerous investigators to indicate that pathogenicity of the polymorphs of silica is related to their crystalline structure, origin, and various surface properties. As a result, in the risk assessment process, silica cannot be dealt with as a single hazard entity. Accordingly, if elimination of silicosis is to be achieved in South Africa, standard values for quartz, the main crystalline form of silica polymorphs, should be adopted which will be protective enough against the species with the greatest adverse activity existing in the South African working environment.

INTRODUCTION

A global programme by the ILO/WHO Joint Committee on Occupational Health to eliminate silicosis by 2030 was launched in April, 1995.1 Subsequently, a National Silicosis Programme in South Africa co-ordinated by the Department of Labour was launched in June 2004.2 In addition, similar programmes have been initiated on this topic by Safety in Mines Research Committee (SIMRAC).3 Understandably, the identification and the measurement of the levels of quartz associated with silicosis featured prominently in all these programmes.

Research in the last two decades has shown that quartz is a variable substance and consequently cannot be dealt with as a single hazard entity.4 This conclusion is based on research findings showing that many chemical and physical factors alter the toxicity and fibrogenicity of...
silica. These include modification of surface properties by coating, grinding and metal binding. As a result, the importance of the surface chemistry of crystalline silica in relation to its pathogenicity was strongly emphasized.

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moganite are rarely observed in nature and are formed under very high pressures.\textsuperscript{30,33}

Non-crystalline or amorphous forms of silica exist when the silicon dioxide molecules are randomly arranged. Amorphous silica can be either of non-biogenic or biogenic origin. The former includes volcanic glasses and various manufactured glass fibres, powders, gels and soils. The latter includes living matter such as diatoms, diatomaceous earth, sponges and plants such as hulls of rice seeds and sugarcane.\textsuperscript{24,35}

Silica (both amorphous and crystalline) can transform under conditions of unusual, extreme heat and slow cooling; amorphous silica can be transformed into crystalline silica and crystalline silica can transform into different crystalline forms. The presence of trace elements in the silica affects the transformation rates. Therefore, exposure to crystalline polymorphs of silica may occur during the processing of the diatomaceous earth which involves heating (calcining) at temperatures as high as 1100°C in the presence of sodium carbonate. These conditions favour the production of cristobalite.

**Factors affecting the biological activities of different silica polymorphs**

Mineralogical characteristics such as structure, composition, crystallinity, chirality, dissoloution of elements, particle size and shape, and surface properties of silica polymorphs can affect their biological activities.\textsuperscript{21,26} It is important to note that the structure of mineral surfaces differs from the structure of the bulk material. For example, in some instances the surfaces of crystalline quartz may be largely amorphous but are less common on tridymite and cristobalite.\textsuperscript{37} Techniques employed to study the surface structure of silica polymorphs include atomic-force microscopy, electron microscopies and spectroscopies, and X-ray spectroscopies, to name a few.

Because the properties of mineral surfaces determine their interaction with biological fluids and cellular membranes, this interaction, may in turn, determine their toxicity. This was confirmed by a number of investigations showing that minerals with the same chemical composition and crystal structure have different pathological potentials when their surfaces possess certain desirable properties\textsuperscript{21} or when their surfaces are modified by a variety of treatments.\textsuperscript{11,38}

The following are some of the mineralogical characteristics of silica polymorphs that were studied in relation to their biological activities:

1. **Crystalline structure:** Crystalline structure affects the pathogenic potential of silica.\textsuperscript{38,40} Quartz, tridymite and cristobalite having more irregular surfaces with protruding oxygens induced more pathogenic effects compared to coesite, a more box-like crystal.\textsuperscript{8} The pathogenic effects included the ability to lyse red blood cells and to induce pulmonary inflammation and fibrosis. The clearance kinetics by the lung macrophages was different when exposed to two quartz samples from different sources and cristobalite. Cristobalite accumulated to a greater extent compared to the quartz samples and elicited an early, sustained cellular response and increased lung hydroxyproline content in the exposed animals. Moreover, the two quartz samples tested, did not elicit identical responses.\textsuperscript{40}

Differences in toxicity between crystalline and amorphous forms of silica also exist. For example, variability in the activation of the fifth component involved in the chemotactic attraction of polymorphonuclear leukocytes was reported between different amorphous silicas compared to crystalline silica.\textsuperscript{18} Also, inhalation of crystalline and amorphous silica resulted in human pulmonary inflammation but only the inhalation of crystalline silica led to silicosis.\textsuperscript{41} Contamination of amorphous silica with polymorphs of crystalline silica may be responsible for pneumoconiosis observed in workers exposed to diatomaceous earth, a naturally occurring amorphous silica.\textsuperscript{50} This was confirmed by animal studies where animals were exposed to one of three amorphous silicas (Aerosil 200, Aerosil R 974 and Sipernat 22S) or to quartz. Although all 4 silicas produced inflammation, only quartz exposure caused silicosis.\textsuperscript{45} The differences were attributed to the ability of quartz to cause the production of surfactant protein D at much higher levels than amorphous silica and thus induce pulmonary tissue injury.\textsuperscript{46} In addition, crystalline silica and amorphous silica differ in their cytotoxicity and ability to up-regulate early inflammatory mediators.\textsuperscript{47,48} Finally, the ability of crystalline silica to induce apoptosis in human alveolar macrophages may initiate an inflammatory response resulting in fibrosis.\textsuperscript{49}

2. **Origin of the silica polymorphs:** Differences in pathological response between specimens of the same silica polymorph of different origin have also been observed. For example, it was shown that at equal mass, workplace quartz samples had less inflammatory potential and toxicity compared to the standard DQ12 quartz samples.\textsuperscript{52} It appears that the matrix in which the crystalline silica particles exist, e.g. in coalmine dust or fly-ash, could modify the surfaces of the crystalline silica and thereby modulate their toxicity.\textsuperscript{51} Finally, quartzes with high and low toxicities in vitro\textsuperscript{40} and in vivo\textsuperscript{14} could be identified.

3. **Various surface modifications:** Surfaces of different silica polymorphs can be altered by different physical e.g. grinding and thermal treatments and chemical processes e.g. acid and polymer treatments. Different laboratories have made the crucial observation that grinding of crystalline silica increases its toxicity. For example, it was shown that exposure of animals to freshly fractured quartz increased their risk for pulmonary diseases compared to those exposed to aged quartz particles.\textsuperscript{9,15,17} This was attributed to increased levels of surface radicals on the ground surfaces of crystalline silica (Figure 1).\textsuperscript{52} The generation of surface radicals decreased thus: cristobalite $\rightarrow$ quartz $\rightarrow$ coesite $\rightarrow$...
The reactivation of the aged quartz surfaces by the adsorption of the hydroxyl and superoxide anion radicals was also demonstrated.\(^{16}\)

Thermal treatments on the other hand, have been shown to selectively quench the radicals, decrease their hydrophilicity and thus decrease their toxicity.\(^{11,13}\) Thermal treatment can convert silanols, present on the surfaces of these crystals, to siloxanes and thus modify the surface without the involvement of the bulk of the crystals (Figure 2).\(^{11,53}\) For example, such conversion at the surface of cristobalite was shown to fully convert the surfaces to the hydrophobic state making them inert both \textit{in vitro} and \textit{in vivo}\(^{11}\) and thus confirmed the lack of toxicity of hydrophobic silicas.\(^{14}\)

Modification of surfaces can also be introduced by chemical treatments; for example, treatments with acids, surfactants, aluminium lactate or polyvinylpyridine-N-oxide (PVNO).\(^{55-57}\) Depending on type of treatment, these chemicals have either decreased the genotoxic and inflammatory properties\(^{58-60}\) or increased the toxicity\(^{8}\) of the silica surfaces.

4. **Contaminants in silica polymorphs:** Earlier work has shown that some of the contaminants in quartz change their toxicity. In general, contamination with aluminium on the surface of quartz reduces its toxicity\(^{6,61}\) and contamination with iron has the opposite effect.\(^{5,62}\)

**Conclusions**

The diversity of structures exhibited by the silica polymorphs imparts a wide range of intrinsic and surface properties to silica. These diversities affect the solubility, cleavage characteristics, morphologies and surface properties that influence its biological activities.\(^{21,63}\) The aforementioned investigations have provided ample evidence relating these properties to silica toxicity. Amorphous silica is less active than crystalline silica and within the crystalline silicas, coesite is less active than quartz, cristobalite or tridymite and stishovite is biologically inert.\(^{6,64,65}\) In addition, evidence has been presented showing that, due to variations in surface activities of crystalline silica due to grinding, origin and contaminants, different samples within the same silica polymorphs may have different pathogenicities.\(^{5,20,30,66}\)

In the risk assessment, silica cannot be dealt with as a single hazard entity.\(^{17}\) It is therefore of great relevance and should be considered in the context of elimination of silicosis in South Africa. Three crucial questions arise: (1) Is a single regulatory level protective of health taking into account all the different polymorphs and the different forms existing within the same polymorph? (2) Is the same regulatory level for quartz protective enough for all the occupational environments e.g. those that produce fractured silicas compared to those that use aged silicas? (3) Will a single regulatory level be effective where the quartz contains significant levels of contaminants such as iron as has been shown for South Africa?

Understandably, to propose different regulatory standard values for each occupational environment, producing various quartz species with different activities, will not be practical. It will, however, be possible to adopt regulatory standard values which will protect against the most active quartz species found in the South African working environment.

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**Figure 1.** Generation of surface free radicals upon grinding.\(^{11}\)

**Figure 2.** Conversion of hydrophilic surfaces with silanol groups into hydrophobic surfaces with the formation of siloxanes with thermal treatment.\(^{11}\)
environment. Therefore, if elimination of silicosis is to be achieved at all in South Africa, serious considerations should be given to regulate the correct silica polymorphs, that is, those with the mineralogical properties with greatest adverse activity. It is critical that all of these issues are considered in policy decisions in South Africa. Similar considerations have been made by international agencies in lowering their regulatory standard values.

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