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It is generally accepted that the variability of crystalline silica hazard stems from differences in surface properties among the various dust sources. However, the extent at which a given surface property governs the biological response elicited, is still a matter of debate. A tentative assignment of the various physico-chemical properties to the subsequent events taking place in the lung following the deposition of a quartz particle, in the alveolar space has been proposed (Fubini, 1998b; Fenoglio et al., 2000; Fubini et al., 2001; Fubini and Hubbard, 2003).

In this thesis a study on four commercial samples, selected on the basis of their different *in vitro* r esponses of macrophages, was performed in order to correlate the surface properties to the biological responses. An important role in silica toxicity is ascribed, in this case, to metal contaminants that can modify the hydrophilicity/hydrophobicity degree and surface charge of the quartz dusts. In fact, if metal ions, usually 1% wt maximum, are dispersed at the surface of quartz may govern the biological responses. It is known since the beginning of the last century that aluminum ions are able to reduce the toxicity of silica. The differences in biological responses among the 4 samples may be ascribed to a different amount of Al and other metal contaminants. Since the surface impurities acquire an importance in silica toxicity it becames evident that two 'pure' quartz dusts most employed as positive reference in experimental work (DQ12 in EU and Min-U-Sil in USA) were far from being pure and were the most fibrogenic and genotoxic quartz dusts. This high variability of quartz toxicity indicates a strong requirement for real model samples of silica particles with controlled surface properties. The samples used in the previous studies (Elias et al., 2000; Fubini et al., 2001; Elias et al., 2002b,a) differed one from each other by several physico-chemical properties so that a clear correlation between a single property and cellular response was difficult to achieve. The crucial role played by the metal contaminants suggested the requirement on the one hand, to study pure silica samples and on the other one to study the role of a single metal impurities at the surface. The study on pure silica sample was perfomed on one crystalline and one amorphous specimen in order to confirm the role of impurities at the surface of silica and to understand the role of crystallinity in the development of the silica toxicity. We have also investigated the role of metal ions at the surface of quartz dusts which are able to enhance or inhibit the biological responses to quartz dusts. This effect depends upon their oxidative and coordinative state. Different metal ions (Al, Fe or Cu) were deposited at the surface of quartz dusts and the samples obtained characterize for their physico-chemical properties and biological activity. The variability in silica toxicity has also been found among amorphous specimens. Diatomaceous earth, as original material, is usually amorphous and undergoes different working steps. The most important step is the calcination in air at high temperature that transforms amorphous material into a partially crystalline one (cristobalite). A study on the amorphous material and the effect of the thermal treatment is therefore required to clarify the conditions in which the transfomation to cristobalite occurs during the calcination step.