GENERAL DISCUSSION
Silicon containing particulate inorganic compounds such as quartz, asbestos, mica and clay are released into the environment during mining, transporting or processing of ores. Chronic inhalation of dust-laden air leads to a wide variety of lung diseases involving decreased physiological capacity and deposition of fibrous proteins in the lung; for example, asbestos dust causes damage to the macrophages (cytotoxicity), deposition of proteins on fibers (asbestos bodies), breaking of red blood cell membranes (haemolysis), calcified regions in the lung (pleural plaques), and cancer of the respiratory system. Quartz produces severe fibrosis which can lead to secondary complications. These problems which miners and industry workers face have received considerable attention and the physiological, pathological and biochemical aspects are very well studied.

However, it was a baffling question always that how could a chemically, physically and biologically inert material like silicon cause serious toxic effects. To answer
this problem, it is essential to understand the bioinorganic processes involved. From time to time, it has been implicated that silicic acid dissolving out of the dust may play a major role in dust toxicity especially in fibrosis and damage to membranes. The results from present investigations clearly indicate that silicic acid could get dissolved out from the dust on prolonged stay in the lungs and interact with vital proteins. By studying Si-protein interactions by taking bovine serum albumin as model protein, the chemical binding has been explained. The fluorescence data show that the binding could involve specific inorganic residues, thus altering the properties of proteins. Such a conclusion has been derived from the observation that trypsin activity is altered when Si combines with either BSA or trypsin. If such a binding takes place with other functional proteins including membrane components, the membrane damage due to Si-containing dust can be explained. It is also likely that the peroxidative decomposition of membrane lipids by molecular oxygen could be enhanced by Si interacting with membrane components. Since lung has got abundant $O_2$ supply, there is a constant threat of this type of damage. Also, maintenance of dust potential equilibrium in lung through regulation of mitochondrial mechanism is very vital in lung physiology and pathology, the present results along with other data from this laboratory clearly support this. Apart from explaining the inorganic processes involved in dust toxicity through protein
binding, the present studies also raise the possibility that protein bound Si in blood may serve as an index of dust exposure. However, the exact significance in the detection and prevention of dust toxicity can be ascertained by clinical studies. Protein binding could also serve as a means of elimination of dust from lungs through blood and urine. Protein-Si interaction also may be involved in other biological effects of silicon such as, diatom physiology, essential nutrient role of Si in animals and plants, stone formation in plant tissue and in the blood-flow characteristics of arteries in heart diseases.

Another important area of dust toxicity where not much is known, is the combined effect of multiple factors. How far the presence of dust in lungs affects the biological action of organic substances is of importance, since in occupational environment such combined effects are common. For example, organic vapours could get adsorbed on dust and enter lungs, or a dust exposed person inhaled organic compounds. In such cases, the capacity of a dust-laden lung to deal with organic compounds may be different from that of a normal lung. The present studies with dust and aniline exposed animals have clearly revealed the significance of such a condition where there was a decrease in the aniline hydroxylase activity on exposure to both quartz dust and aniline vapour, even though earlier observations with animals exposed to aniline vapour alone had shown an increase in the enzyme
activity. The introduction of a hydroxyl group to organic compounds at the expense of molecular oxygen is a usual body defense mechanism to render the compound more polar and thus easily removable. Sometimes, the process can lead to activation, producing a more toxic compound. Any change in this biotransformation mechanism in lung can lead to marked changes in the toxicity and the period of stay in lungs of the organic compound. From the present study, it is clear that the presence of dust could alter the toxicity of organic compounds.

Hydroxylation of organic compounds as a part of biotransformation has been very well studied in liver, which is the main site of metabolism. However, lung which is the entry point of air-borne xenobiotics has comparatively not received much attention. The present investigation has led to a clear understanding of hydroxylation of aniline in lungs through microsomal monoxygenases. It was interesting to observe from radioactive tracer studies that the induction of aniline hydroxylase activity on single exposure to aniline may also be due to synthesis of additional proteins. The involvement of hemoprotein, cytochrome P-450, in converting aniline and oxygen into \( p' \) and \( o' \)-aminophenols has been established. The hydroxylation system in lung is quite different from liver in many aspects as evident from the study. The results of the developmental studies of aniline hydroxylase showed that
pulmonary tissue acquires the capacity to deal with foreign compounds fairly early in life. It is also interesting to note that there is a possible interrelation between oxygen mediated free radical formation and their biological effects with the toxicity of both organic compounds and dust. Other bioinorganic processes likely to be effected in toxicity include transport of cations across membranes. The transport of radioactive Ca$^{45}$ into mitochondria, the swelling and mitochondrial changes of the organelle and alterations in oxidative enzyme activity could lead to disturbance in redox equilibrium in lungs. These redox changes also may have a significance in the toxicity of inhaled compounds. The mixed function oxidase can hydroxylate and dispose a wide variety of organic compounds so that the present observations of aniline are applicable to other organic pollutants also. Thus apart from the basic interest in the characterization of biotransformation in lungs, the present results also have applied importance of explaining multiple factors in toxicity.

Dust-organic compound interaction can alter the toxicity also by the dust sequestering the compounds for longer periods in lung and even converting them chemically. From the present data, it is clear that in the presence of oxygen and a reducing agent, the dust could introduce a OH group into aniline. The mechanism could be similar to Fenton reaction. Such non-enzymatic hydroxylation of organic compounds may also have a bearing in their toxicity. This could be a clear
example of a bioinorganic interaction between a dust and a xenobiotic. Introduction of OH group into proline of protocollagen, steroids and several other compounds have already been reported in vitro to be mediated by Si containing dusts. If such processes are to take place in vivo as well, they may influence the biological effects too. Thus, it becomes clear from the present studies that Si compounds cannot be considered biologically inert and the bioinorganic interactions involving silicic acid play a major role in dust toxicity.