PREFACE

It is well established that occupational exposure to asbestos can result in a number of toxic manifestations ranging from simple inflammation to pulmonary fibrosis known as asbestosis, bronchogenic carcinoma and mesothelioma. Asbestos appears to augment the mutagenic and carcinogenic effects of chemical carcinogens. Epidemiological and experimental studies were clearly indicated a multiplicative effect of asbestos and cigarette smoke on the initiation of bronchogenic carcinoma. The development of bronchogenic carcinoma is more common among smokers exposed to asbestos than exposed non-smokers. Cigarette smoke not only helps in the development of bronchogenic carcinoma in asbestos exposed population but also develops asbestosis much faster. Several theories on the basis of experimental studies have been proposed from time to time to elucidate the mechanisms of interaction between asbestos and cigarette smoke in the development of bronchogenic carcinoma. It appears that there are various other unidentified factors exist in the working environment of an asbestos factory influencing the process of development of the disease.

This is substantiated by other findings of our laboratory that a very high incidence of asbestosis are present among the workers in a local asbestos factory established only a decade back. Indepth investigation revealed that approximately 90% of the factory workers are also exposed to kerosene vapours as they use the same for domestic lighting
and cooking as a cheaper alternate to electricity. A closer examination of the cooking stoves revealed that they emitted heavy smoke (soot). Kerosene vapours and the soot may be the predisposing factors playing important role in the augmentation of the disease observed in the asbestos factory workers in our studies. In addition to this it is also relevant to consider that a large number of manufacturing units in India also use kerosene as industrial solvent which results in kerosene vapours pollution in the atmosphere in immediate vicinity. The presence of asbestos fibers in the same atmosphere from a neighbouring unit could influence or accelerate the disease process.

The author of this dissertation, therefore, selected the problem of combined exposure to asbestos and kerosene/soot to which a large number of Indian population is exposed. As mentioned above the combination of cigarette smoke and asbestos facilitates in the development of bronchogenic carcinoma. One of the factor responsible for their carcinogenic and co-carcinogenic behaviour is polynuclear aromatic hydrocarbons (PAHs) which are present in the cigarette smoke. Kerosene and its soot also contain a large number of aliphatic and aromatic hydrocarbons besides many other organic and inorganic contaminants which causes pulmonary damage. Their co-exposure may increase the toxic manifestations. While large number of studies conducted on asbestos and cigarette smoke no report is available on the combined effect of asbestos and kerosene/soot as evident by the survey of the literature.
In the present study, therefore, the combined toxicity of chrysotile asbestos and commercial sample of kerosene and its soot were conducted using *in vitro* and *in vivo* model systems which are already established in this laboratory. This dissertation constitutes a report on the studies of co-exposure of chrysotile and kerosene/soot to isolated rat hepatocytes in order to evaluate their cytotoxicity *in vitro*. Later the *in vitro* observations were validated by the actual short term *in vivo* animal experiments using rat pulmonary alveolar macrophages. Further, the chemical, biochemical and histopathological studies were also conducted to understand the pattern of pulmonary fibrosis at different stages of exposure. In addition, alterations in the phase I and phase II drug metabolizing enzyme system following co-exposure to chrysotile and kerosene/soot were also studied to develop an insight into the mechanism of kerosene and soot metabolism in asbestos exposed rat lungs which also affects the carcinogenic response of asbestos.

The results of the present investigation provide an insight of the possible mechanisms by which higher incidence of fibrosis and bronchogenic carcinoma may develop in asbestos exposed workers who are using kerosene oil.