PREFACE

Disease is a disturbed function, not merely disordered structure, for pathology in modern sense is physiology gone wrong. Pathological physiology is the main fortress of medicine. We are aware of the fact that the picture of disease is changing before our eyes. Old diseases are passing away as a result of the assaults of modern therapy, but new ones are continually taking their place. Many of these diseases are iatrogenic in nature, that is to say, they are the result of the well-meant but injudicious use of therapeutic agents. In these days when tranquilizers take the place of baby-sitters, or indiscriminate and often needless exposure to ionizing radiation for diagnostic or therapeutic purpose has become so universal, it is small wonder that the old maladies are replaced by new man-made ones. We should never forget "what is powerful for good can be potent for evil", but this is true for so many situations created by modern therapy. Though routine testing of different therapeutic agents for their various physiological effectiveness is the main objective of modern pharmaceutical research programmes, toxicological side effects are certainly not taken into consideration with the same weightage. Our knowledge on genotoxic and cytotoxic side effects of different therapeutic agents are again extremely limited.

A large number of people particularly living in the coastal belt of India suffer from the dreaded tropical diseases like leprosy and filaria, and are exposed therapeutically to
antileprosy and antifilarial drugs which are recommended for long term use, specially the formers. Although there are a few publications on the possible genotoxic effect of the antileprosy drugs most of the works are concerned with either in vitro analysis or bacterial system. The antifilarial drug has not been so far attended to in this respect.

Keeping all these in view in the present investigation an attempt has been made to evaluate potential genotoxic and cytotoxic effects of two widely recommended antileprosy drugs, viz., Clofazimine and 4'-4 diaminodiphenyl sulfone (Dapsone), and the antifilarial drug-diethyl carbamazine (the only drug of choice) in mouse in vivo system. For antileprosy drugs we have conducted a battery of assay systems such as metaphase chromosome analysis and micronucleus test in bone marrow cells, micronucleus test in regenerating hepatocytes, spermatocyte chromosome analysis sperm morphology test and sperm count assay to have a reasonably comprehensive idea on their effects on mitotic, meiotic and post-meiotic cells. But for want of time the antifilarial drug was tested by using only metaphase chromosome analysis and micronucleus test in bone marrow cells.

The works have been presented in six chapters. The 'Introduction' chapter includes in addition to introduction to the subject and literature review, an introduction to different protocols employed here. Chapter 2 includes materials and methods in general. Chapter 3 deals with the effect of mitomycin C used here as reference chemical to standardize some protocols and to
fix up some criteria for scoring different aberration types. Effects of antileprosy drugs following separate and combined treatments have been presented under 3 sections in chapter 4. Similarly chapter 5 deals with the effects of antifilarial drug. The work has been summarized in Chapter 6.