CONCLUSION
CONCLUSIONS

In the present study four anti-tubercular drugs have been studied in three different combinations during intensive phase and one combination during continuation phase to evaluate their mutagenic and clastogenic potential of these drug combinations. Based on the results the following conclusions can be drawn:

- The study for the first time has shown that Mycobacterium tuberculosis, the causative organism of Tuberculosis can induce genetic damage in the affected individuals, which is manifested in the form of increased chromosomal aberrations, SCEs and depressed cell cycle kinetics and mitotic index.

- Anti-tubercular drugs in combination (2 SHRZ, 2 HRZ, 2 H2R2Z2 and 4 H2R2) act synergistically and induce chromosome damage in the patients. This synergistic action could be between the metabolites of the drugs, since most of these drugs are non-mutagenic individually.

- The anti-tubercular drugs cause chromosome damage probably by interfering with the DNA repair mechanisms of the cells.
- The triple drug combination 2 H2R2ZZ given twice weekly was least effective in terms of chromosome damaging action. This combination induced only chromosomal aberrations but not SCEs.

- The study further strengthens the assumption that mechanisms of formation of chromosomal aberrations and SCEs are different. SCEs though considered to be a highly sensitive parameter, are not good indicators for at least some kinds of chromosome damage.

Since the study has conclusively shown that the anti-tubercular drugs do cause chromosome damage, they should be used with utmost care. However harmful the drug effects are, it is not possible to withhold the treatment to the patient as it could be fatal. Hence, selection of drug combination that are less harmful in terms of genetic damage, but equally effective in the treatment of Tuberculosis should be considered (for Eg: drug combinations like 2 H2R2ZZ). As the present study clearly indicates that the duration of these drugs also plays a vital role, it is necessary that the duration and dosage of these drugs be kept at the minimum possible level, without compromising on their effectiveness in the treatment of Tuberculosis.