SUMMARY

Tuberculosis (TB) is a disease of antiquity, caused by bacteria of the *Mycobacterium tuberculosis* complex, which principally affects the lungs. The first-line drugs used to treat and cure this disease are Isoniazid, Rifampicin and Pyrazinamide. These drugs act in a synergistic manner to cause a wide array of adverse drug reactions, affecting chiefly the principle organs involved in drug metabolism and excretion. Present study was based on the hypothesis that herbs namely *Phyllanthus niruri*, *Berberis aristata* and *Achyranthes aspera* either solely or in combination would be able to cure the toxicity that is caused due to co-administration of first-line anti-tuberculosis drugs namely Isoniazid, Rifampicin and Pyrazinamide when given to normal wistar rats. Different parameters namely biochemical, hematological, histopathological, chromosomal and gene expression studies were evaluated during the study.

The results of present study endorsed the fact that the anti-tubercular drugs namely isoniazid, rifampicin and pyrazinamide are potentially toxic to wistar rats when given in combination as proved by different biochemical, hematological and histopathological studies. In addition, these drugs have some genotoxic potential as has been shown by chromosomal, DNA fragmentation and gene expression studies. The gene expression study on *NAT, NR1I2, CYP2E1* and *CYP7A1* genes carried out in liver confirmed their role in hepatotoxicity caused due to administration of first-line anti-TB drugs. The present study also suggests that plant extracts play an important role in attenuating the anti-tubercular drugs induced toxicity, though their potential may vary. In the present study, plant extracts used were effective in the following order: Polyherbal formulation > *Berberis aristata* > *Phyllanthus niruri* > *Achyranthes aspera*. Finally, the present study confirmed that oxidative stress
has been an important mechanism in toxicity of anti-tubercular drugs in wistar rats and revealed that polyherbal preparation containing three tested plant extracts in equal ratio exhibit maximum protective efficacy and may be further explored for use as a dietary supplement for patients taking anti-tuberculosis medications. Hence the present study may help the industry to produce a polyherbal supplement with fewer side effects, which are affordable and more effective in the maintenance of normal hepato-renal function during treatment with anti-TB drugs.