Chapter VII

General Discussion

In present work 50mg rifampicin per kg body wt. was administered orally for 30 days. The histological architecture of the liver and kidney both revealed that it resulted in fatty degeneration of liver as already studied (Sodhi *et al,* 1997b) and also in the degeneration of proximal and distal tubular cells coupled with stagnancy of blood in kidney. Present results indicated that in rats rifampicin is toxic to kidney also. The experimental studies in this project were designed to study the influence of mandur bhasma an Ayurvedic medicine, which is also recommended in Ayurveda to treat the 'yakshma' *i.e.* TB. Mandur bhasma had shown hepatoprotection against CCl4 hepatotoxicity (Devarshi *et al,* 1986) in male albino rats. The protection against CCl4 was studied by the function of different lipases which revealed that CCl4 induced fat accumulation was removed through lysosomal degradation and the fatty acids were used as energy source for tissue rebuilding. It had been also showed that mandur bhasma is capable of curing induced CCl4 hepatotoxicity and liquid paraffin toxicity simultaneously curing the kidney (Kanase *et al*

1997) in male albino rats. The studies also revealed that mandur bhasma decreased lipid peroxidation and increased glucose-6-phosphatase activity. For this reason it was decided to use mandur bhasma against the rifampicin-induced hepatotoxicity. Mandur bhasma was administered simultaneously with the rifampicin treatment. The liver and kidney function - tests showed that it also protects liver and kidney against the rifampicin toxicity. The histological architecture also confirmed these results. To study the probable alterations in other toxicity related parameters; the lipid peroxidation, glutathione, formaldehyde and protein oxidation were also studied in liver and kidney. In present results lipid peroxidation increased in rifampicin induced toxicity and was coupled with the hepatocyte degeneration and increased serum enzyme levels (AST, ALT and Alkaline phosphatase) that are indicators of hepatocyte damage. Similarly the histologically evident kidney tubular damage with rifampicin toxicity was also coupled with the elevation of the serum urea and creatinine indicating the interference in the filtering activities of the kidney. As the results indicate lipid peroxidation, formaldehyde, and protein oxidation were reduced and glutathione was increased in liver and kidney by simultaneous treatment of mandur bhasma in refampicin treated rats. Lipid peroxidation is micorosomal cytochrome P-450 mediated process that continues to damage the microsomal membranes that was decreased

simultaneously indicating majority of the hepatocytes in normal condition in histological pictures and also the normal cells of the renal tubules. These results were also coupled with the reduced serum levels of the liver function and kidney function indicating enzymes. Since glutathione was simultaneously increased in the liver and the kidney. It seems that liver and kidney are relieved from the oxidative stress by the increased glutathione. It was also increased in the only mandur bhasma treated rats also. It seems that Mandur bhasma is stimulating glutathione production. These results also indicate that mandur bhasma stimulates the natural path of the relief that is used to clear the product of routine oxidative processes. This was also observed in earlier results where mandur bhasma stimulated lysosomal lipid degradation (Devarshi *et al,* 1986). The another parameter that also directly relates with the oxidative stress is protein oxidation. It is also studied in present project. Rifampicin treatment increased the protein oxidation in liver and kidney and simultaneous treatment of mandur bhasma decreased the protein oxidation confirming the relief of liver and kidney from the oxidation stress. Attempt was also made to study the influence on rifampicin accumulation in some important soft organs of the body and its daily fecal clearance. In rifampicin + mandur treated rats the fecal clearance in general was $1/5^{th}$ of that was recorded in the refampicin treated rats though there were some variations in the daily clearance.

Similarly except oesophagus all the organs studied showed decrease in accumulation.

Though the present study showed protection of liver and kidney by oxidative stress relief and keeps the stress at least in the range that can maintain the histological architecture of liver and kidney. But this work is preliminary and probable mode/s of action can be made out in detail. Still a question remains whether the mandur bhasma will behave the same way in presence of tuberculin infections also? There is need that the curative effects of mandur bhasma be studied that may be helpful to the post-toxicity relief.