6. CONCLUSION

The results of this study suggest that the therapeutic modality involving simultaneous administration of drug and an immune enhancer can be used to advantage in the treatment of experimental *L. donovani* infections. BHMARB medium was satisfactorily used for parasite maintenance to obtain high yield of *L. donovani* promastigotes, which were ultimately required for antigen isolation and immunological studies. During these investigations, biochemical and immunological tests, were performed to characterize the protein and carbohydrate nature as well as the antigenicity of parasite antigens used for immunological studies. The hamsters were infected with *L. donovani* and after ten weeks of inoculation the liver and spleen were removed and the assessment of infection was carried out by making parasite counts.

Firstly, the various drug dose responses were determined alone. The 10 mg/kg body weight drug dose treatment can reduce the parasite load. After that, the effect of different doses of TDM alone and in combination with various drug concentration was determined. It has been found that 10 mg drug dose/kg body weight combined with 500 ug TDM/kg body weight significantly reduced the parasite load as compared to the treatment with drug alone. The haematological studies showed that the total leukocyte count was higher in the infected and lower drug doses. Leukocytosis was reversed by giving a combined therapy of drug and TDM.
The mean haemoglobin concentration was also reduced. The anaemic condition was controlled by using a combination of drug and TDM. In the differential leukocyte count, the lymphocytes and monocytes were found increased in the infected animals. The count was normalized by giving a combined dosages of drug and TDM. Our studies indicate that leishmaniasis causes various structural and functional alterations in different organs of host namely, liver, spleen and kidney. Our results conclude that hepatotoxicity assumes special significance in experimental infection of rodents. The above findings are supported by the fact that liver acts as the primary organ for host's homeostasis, and as such various chemical constituents and enzymes of liver including, total lipids, phospholipids, cholesterol, lipid peroxidation, proteins, DNA, RNA, liver transaminases and liver phosphatases are invariably altered. Significantly, histochemical studies were also helpful in confirming that massive biochemical changes take place during leishmanial infection. Due to liver dysfunction, changes were also observed in serum transaminase and serum phosphatase contents. The most striking feature observed in our study was that in the infected animals and in the lower drug dose treated animal groups the level of serum phosphatase and serum transaminase, which were found to be altered due to liver dysfunction, normalize in the combined therapy (drug + TDM). These results further indicate a good correlation
between host's resistance to infection and the availability of these enzymes.

The leishmanial infection adversely affected the host's vital organs such as liver, spleen and kidney. Pathological lesions in the hamster's liver infected with *L. donovani* showed alteration in the hepatic lobules. Sinusoides were dilated and filled with hypertrophied kupffer cells containing phagocyttosed L.D. bodies. Contrary to this, the animals which were treated with combined therapy of drug and TDM showed normal architecture, free from pigment deposition.

In brief, the various experiments performed during this work revealed that infected animals showed massive biochemical alterations in tissue and serum. Similar tissue alterations were also observed in histopathological examination of the infected liver and in the animals which were treated with lesser doses of drug. Such alterations were not seen when similar examinations were carried out in the animal groups which were respectively treated with a combination of drug and TDM and higher drug doses alone.

It can therefore be concluded from our results of various experiments that combined therapy of drug (lesser doses) and TDM can be used effectively to treat leishmaniasis. It minimizes the side effects seen in the case of treatment with higher drug dosages alone.