SUMMARY AND CONCLUSIONS
The present study was undertaken to evaluate the combined effects of lead and lithium treatments on liver, brain and thyroid functions and also on blood using rat as an experimental model:

1. To elucidate the combined effects on various blood parameters viz: TLC, DLC, Hb, status of different elements and serum marker enzymes viz: alkaline phosphatase, SGOT, SGPT with reference to liver function.

2. To evaluate the effects on thyroid functions which involve the uptake and retention of I-131 and quantitation of circulating hormones.

3. To investigate the effects on liver functions by various parameters viz: alkaline phosphatase, GOT and GPT; Biological half-life of I-131 Rose Bengal with regard to its clearance pattern. To elucidate the combined effects of lead and lithium on glutathione system (GSH and GST) and various enzymes such as Cyt P450 and Cyt b5 were undertaken. Assessment of the interactions between lead and lithium with various essential and non-essential elements. {Fe, Cu, Zn, Br, Rb and K}.

4. To investigate the combined effects of lead and lithium on brain functions by estimating various parameters like acetylcholine esterase, neurotransmitters, SDH, Na⁺/K⁺ ATPase, in vitro uptake of radiolabelled nutrients and disposition of various elements.
   
   To assess various parameters involved in different functions with regards to different organs, Female Porton rats of the institute colony, weighing 130-150 g were used in the study. The rats were fed with pelleted diet and water ad libitum.

   To evaluate combined effects on various tissues, rats were divided into four main groups viz: control, lead treated, lithium treated and lead + lithium treated groups. Lead treated and lead + lithium treated rats were further divided into sub-groups according to two low and high doses of lead (50 mg/kg
body wt and 100mg/kg body wt). All the main groups were further divided depending upon the various periods of treatment i.e. 1, 2, 3 and 4 months.

The rats in lithium treated groups were given lithium carbonate in diet (1.1g/kg diet) for specified periods and lithium levels were estimated using flame photometer and were found to be in the therapeutic range (0.4-0.7 meq/L). Lead was given orally, daily by gavage, in the form of lead acetate (50 and 100 mg/kg body wt).

To carry out various haematological investigations and other parameters with regards to liver or thyroid functions, blood samples were drawn out at different time intervals i.e. 1, 2, 3 and 4 months.

To determine the thyroid uptake and biological half-life of I-131 in thyroid, the rats were held above the suitably shielded NaI (TI) gamma detector and the counting was done upto 10 days.

To assess the in vivo liver function using I-131 Rose Bengal, a special technique was designed for counting so as to find its biological half-life following different treatments. Other parameters such as liver marker enzymes were also included.

To evaluate the brain functions, estimations of acetyl choline esterase activity and neurotransmitter levels were done. The status of various elements in blood, liver and brain was determined by using X-ray Fluorescence Technique (EDXRF).

The investigations of various parameters revealed:

1. No statistical change in body weights following lithium treatment was seen whereas the rats treated with both the doses of lead indicated a significant decrease at all the time intervals. However, the treatment with high dose of lead resulted in pronounced decrease in body weights.

2. Lead administration to experimental rats for long duration increased the contents of Zn, Br, As and Rb, whereas lithium treatment reduced the contents of K, Fe, Cu, Zn and Rb. An antagonistic behaviour of lead
and lithium is noticed in relation to Zn and Rb, because the levels of these elements are elevated following lead treatment and are decreased with lithium treatment. This antagonistic behaviour is not visible with respect to any element except, in the context of combined lead and lithium treatment, where an appreciable decrease in its levels is noticed.

3. Lead treatment at high dose has significantly reduced the Hb contents at 2, 3 and 4 months. However, treatment with high dose of lead has resulted in a significant decrease in its levels after one month. Lithium treatment could result in a significant decrease of Hb contents only at 4 months of treatment. The combined treatment with lead and lithium indicated the same trend as was observed in lead treated groups.

4. Total leukocyte counts were found to get depressed at all the intervals following lead treatment (both doses). On the contrary, lithium treatment has resulted in raising the level of TLC at 1 and 2 months and prolonged treatment up to 3 and 4 months showed a decreasing trend in TLC when compared with controls. However, combined treatment showed the same trend as was seen in lead treated group at 1 and 2 months. Moreover, further treatment up to 4 months showed a pronounced decrease.

5. Lymphocyte counts have been investigated to decrease with both doses of lead treatment throughout the study and the decrease was more pronounced with high dose. No significant change was noticed in the lymphocyte counts following 2 months of lithium treatment and thereafter a significant decrease was observed which continued up to 4 months. The combined treatment could result in pronounced decrease in the lymphocytes count at 2 months which continued up to 4 months.
6. The levels of monocytes were found to decrease with 1 and 2 months of treatment with low dose of lead whereas 3 and 4 months of treatment with lead raised the number significantly. Treatment with high dose could result in the increased monocyte, levels throughout the study. On the contrary, lithium treatment did not show any change upto 2 months whereas continuation of treatment thereafter indicated an increased levels of monocytes. Combined treatments showed the same trend as was seen in lead treated group upto 3 months. However at 4 months of combined treatment there was more pronounced increase.

7. Lead treatment has caused a significant reduction in eosinophil counts upto 2 months whereas further treatment resulted in a significant increase. However, lithium treatment showed a significant decrease at 4 months of treatment. Combined treatment with lead indicated a pronounced decrease in eosinophils at all the treatment durations. On the contrary, the high dose at 3 and 4 months resulted in pronounced increase rather than decrease.

8. Both the dose levels of lead resulted in a significant decrease in Basophils at all durations while no significant change was found following lithium treatment and combined treatment witnessed the same trend as was seen in lead treated group.

9. Protein contents were found to be significantly decreased with administration of both doses of lead for upto 4 months. Lithium treatment however did not show any change. Combined treatment showed the same trend as was seen in lead treated group but at one month there was a pronounced decrease at one month.

10. No significant change was seen in SGOT and SGPT levels upto 1 month of treatment whereas continuation of treatment for upto 4 months resulted in a significant elevation. However lithium treatment
showed a reduction in GPT levels after 3 and 4 months whereas there was no change in SGOT throughout the study. Similar trend was seen in GOT and GPT levels in combined treatment group as was seen in lead treated group.

11. Serum alkaline phosphatase activity was found to be decreased up to 4 months of lead treatment with both the doses. However, the increase was more pronounced with the high dose. Lithium treatment could indicate a significant decrease only at 3 and 4 months. The combined treatment resulted in more pronounced decrease at 3 and 4 months.

12. 2 and 24 h I-131 uptake was found to be elevated significantly following both doses of lead at all treatment intervals. On the contrary, a significant decrease in uptake was found following lithium treatment at all the intervals. Further combined treatment has shown a more pronounced increase in uptake values at all the durations.

13. Pb and Li treatment given separately indicated a significant increase in thyroidal biological half-life of I-131 throughout the study, whereas a pronounced increase was obtained following combined treatment throughout the study.

14. A progressive decrease was seen in circulating T3 and T4 levels following lead and lithium treatment separately. However, combined treatment indicated a further decrease in the serum hormone levels.

15. Lead treatment at both the doses resulted in a significant reduction in the liver contents of K, Cu, Br whereas the levels of Fe were enhanced. The levels of Rb were decreased with low dose of lead whereas the levels remain unaltered with the high dose when estimated at 1 month of its supplementation. Zn levels were noticed to increase significantly with lead (both the doses) only at 4 months of its administration. Long term lithium treatment reduced the levels of K, Cu and Rb, whereas the Zn
contents were enhanced only after 1 month of treatment. The Br levels were retarded after 4 months of treatment only. During the combined treatment (long and short term) the K and Rb levels were reduced as compared to the levels in the only lead treated group. Whereas Fe contents were lowered only after 1 month of treatment. Zn levels were raised whereas Br levels were reduced at 1 month of combined treatment when compared with the lead treated reference group. Br levels were noted to be retarded only at 1 month of combined treatment.

16. A significant increase in Tb of I-131 Rose Bengal in liver was noticed with both the doses of lead at all the treatment durations. Interestingly maximum increase was obtained at 3 months with both doses of lead. Lithium caused a significant increase at 2 months and on the contrary resulted in a significant decrease at 4 months, while no change was observed at 3 months. Combined treatment showed a pronounced increase at 4 month only.

17. GOT and GPT showed a significant reduction following lead treatment with both the doses at 3 and 4 months. On the contrary there was stimulation in their activities following lithium treatment at 3 and 4 months. Combined treatment showed a pronounced decrease throughout the study.

18. A significant inhibition of alkaline phosphatase was noticed at both the doses of lead after 4 months. On the contrary, there was elevation at 3 and 4 months of lithium treatment. However combined treatment indicated the same trend as was seen in lead treated groups.

19. Cyt bs and P₄₅₀ activities were raised at 1 month following lead treatment alone and thereafter a significant decrease was seen up to 4 months. However, lithium treatment showed a significant increase at 2 and 4
months. Combined treatment evidenced the same trend as was seen in lead treated group.

20. GSH levels increased following lead and lithium treatment individually. However pronounced increase was noticed with combined treatment only at 4 months.

21. GST activities were significantly increased following 1 month of treatment and subsequently got reduced at 4 months. Lithium treatment could result in inhibition of GST, but only at 4 months. Combined treatment showed same trend as was seen in lead treated group.

22. A stimulation in Glucose-6 phosphatase activity was seen with both the doses of lead at all the treatments periods. On the contrary a significant inhibition was noticed with lithium treatment only at 4 months. Same trend was seen in case of combined treatment as was seen in lead treated group.

23. Fe, Br and Rb were increased whereas K and Cu levels decreased following lead administration (low and high doses) for short and long terms. Zn levels were reduced at 4 months of lead supplementation at both the dose levels. The K and Rb levels decreased and Br levels reduced at 1 and 4 months of lithium supplementation. Fe levels decreased following long term lithium treatment. Cu levels were increased whereas Zn levels decreased following 4 months of its supplementation. Long term combined (lead and lithium) treatment witnessed a reduction in brain K and Rb contents when compared with lead treatment group. Br and Fe levels increased significantly after short and long term combined treatment, whereas Zn contents were raised only after long term treatment. However the Zn levels were noted to decrease at 1 month of combined treatment.
24. A significant reduction in in vitro glucose uptake of brain slices, following lead treatment (both the doses) at all duration whereas a stimulation in glucose uptake was seen with lithium treatment throughout the study. Interestingly a significant elevation in glucose uptake was seen following combined treatment thus indicating a similar trend as was seen in lithium treatment group. Alanine uptake was found to be significantly depressed following lead treatment. On the contrary, a significant elevation was seen following lithium treatment at all the durations. Combined treatment also showed a pronounced increased in uptake values at 2 and 4 months indicating the same trend as was seen in lithium group. Leucine uptake was found to inhibited significantly at all the treatment intervals following lead treatment. Lithium treatment also resulted in same trend. Interestingly combined treatment indicated a significant elevation which however was not there when compared individually with each treatment.

25. High dose of lead and lithium has resulted in increased levels of epinephrine and norepinephrine at 4 months of treatment. Combined treatment however indicated a more pronounced increase.

26. ATPase activity was seen to be inhibited significantly throughout the study (with both doses of lead). However, lithium treatment did result in decreased ATPase but only at 4 months. Combined treatment caused further reduction at 3 and 4 months.

27. A significant inhibition was obtained in SDH activity following both doses of lead throughout. Lithium has resulted in significant elevation of activity but only at 4 months. Similar trend was seen in combined treatment as was seen in lead treated group.
Both doses of lead inhibited acetylcholine esterase activity throughout. However a significant stimulation in the activity was seen at all the intervals following lithium supplementation. The combined treatment showed same trend as was seen in lead treated group.