CONCLUSIONS

- Lead and cadmium in isolation and in combination caused a dose and time dependent inhibition of steroidogenic enzymes, along with a change in structure of ovary and uterus, uterine protein profile in non pregnant rats without causing any change in estrous cyclicity. Accumulation of metal increases with dose and time of treatment. However, additive effect has not been demonstrated in combined treated animals with increase of dose and time of exposure. Dose of 0.05 mg/kg. body wt. for 15 days was selected as optimum dose and time of treatment respectively. For further study.
- Reproductive performance, frequency of pregnancy, placental , ovarian weights, litter size and litter weight did not demonstrate any change at 0.05 mg/kg. body wt. from premating till the end of gestation, but steroidogenic enzymes and steroid production was decreased in metal treated groups both in ovary and placenta, along with a change in placental protein profile.
- To elucidate the mechanism behind the decrease steroid production, granulosa cells were chosen as the cellular model for further study. Decreased gonadotropin binding to its receptor, along with decreased 17β Hydroxy steroid dehydrogenase activity was demonstrated at a dose of 0.05 mg/kg. body wt. for 15 days.
- In order to understand the mechanism for such biochemical effects, both "*in vivo*" and "*in vitro*" experiments were performed, metal treatment in

isolation or in combination caused an elevation in lipid peroxidation, change in membrane lipid content, decreased Na^+ K^+ ATPase activity and altered membrane fluidity, along with decreased anti oxidant status. Most of these modification were ameliorated with zinc and sulfhydryl protectants.

Ovary is coordinated with hypothalamus-pituitary axis and regulation of the entire HPG unit is essential for its function. Present study elucidates association between toxic metal concentrations and potential endocrine disruptions in steroidogenic organs i.e., ovary and placenta. Also, lead and cadmium either in isolation or in combination decreases gonadotropin binding on the granulosa cells of the ovary, leading to decreased steroid production by inhibiting the key steroidogenic enzymes during non-pregnant and pregnant stages of reproductive cycle in females. It is also clear from this study that such low level exposure with metals can also interact with transcriptional machinery, thereby causing depleted expression of important proteins that are required for steroid production or their function. It can be suggested that combined exposure to metals might not always cause additive or antagonistic effect, but it depends on the duration and concentration of metal exposure. Present study also indicates that exposure of metal toxicant at this sub-toxic level can define environmental, occupational and life style (smoking) risk factors in ovarian function during the preconception and conception period of female reproductive lifespan.