CHAPTER V

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The present study was carried out with special reference to the following:

1. To investigate the effects of aluminium on the structure and functions of reproductive organs and some other tissues of mice.
2. To study the effect of aluminium on fertility rate.
3. To evaluate the possible therapeutic effects of calcium and Vitamins (C, D, E) in mitigation of aluminium toxicity.
4. To study the effects of aluminium on SCE and Chromosome aberrations.

The work was divided into four major parts.

PART I: STUDIES ON EFFECTS OF ALUMINIUM CHLORIDE INGESTION ON REPRODUCTIVE FUNCTIONS AND SOME OF THE TISSUE FUNCTIONS OF MALE MICE.

Healthy adult male albino mice (Mus musculus) were administered aluminium chloride at a dose of 200 mg/Kg body weight for 30 and 60 days and 400 mg/Kg body weight for a single dose (15 days) to investigate the change in testis, cauda epididymis, vas deferens, seminal vesicle, muscle, liver, kidney, blood and serum. The untreated control and AlCl₃ treated animals were maintained on a standard chow and water ad libitum. The treated animals were sacrificed on the 31st day (30 days treatment), 61st day
(for 60 days treatment) and 16th day (for Single dose treatment) along with the control animals and utilised to study various parameters.

1. AlCl₃ was effective from the 30th day, as well as after 60 days and single dose treatment.
2. The treatment brought about structural alterations in the testis, cauda epididymis and vas deferens leading to change in its function.
3. Ultrastructural studies revealed alterations in the reproductive organs.
4. The analysis of aluminium levels in testis, cauda epididymis, vas deferens, kidney and serum of AlCl₃ treated mice revealed significant enhancement, which indicates that the aluminium accumulates in these tissues and would affect their structure and metabolism.
5. The treatment resulted in a significant decline of cauda epididymal sperm motility and live : dead ratio of sperms.
6. The significant decrease observed in protein levels in all organs investigated might be due to changes in its synthesis and / or metabolism.
7. The activity of SDH was significantly decreased in testis, cauda epididymis and muscle suggesting that the oxidative metabolism was altered.
8. The treatment led to a significant decrease in ATPase activity in cauda epididymis and muscle suggesting alteration in energy metabolism. A decrease in muscle ATPase would also affect its contractility.
9. The decreased levels of sialic acid found in cauda epididymis indicate alterations in sperm maturation and its structure.
10. The treatment brought about accumulation of glycogen in the vas deferens, muscle, liver and kidney and decrease in blood glucose with inhibition of phosphorylase activity affecting carbohydrate metabolism.

11. Unaltered levels of Fructose in AlCl₃ treated mice indicate that its metabolism was not affected by the treatment.

12. The treatment caused a significant hypercholesterolemic effect in the testis suggesting that its metabolism might be disturbed which could be correlated with inhibition of testicular 3β and 17β hydroxysteroid dehydrogenase (HSD) activities affecting testicular steroidogenesis. However, serum testosterone levels did not show much alterations.

13. The treatment also resulted in a significant enhancement in the DNA and RNA levels in testis, cauda epididymis and muscle. This probably suggests an alteration in nucleic acid metabolism.

14. Decreased levels of SGOT and SGPT indicate impairment in liver function as the levels of these enzymes are considered as markers for the same.

15. The decreased levels of Na⁺ observed in the kidney reveal alteration in the electrolyte balance of the body due to aluminium ingestion. The levels of K⁺ in the kidney did not show any change after the treatment.

16. The above results elucidate that aluminium has a definite role in reproductive organs. The fertility rate and implantation sites in females mated with treated male were also significantly decreased.
PART II : WITHDRAWAL STUDIES ON ALUMINIUM INDUCED TOXIC EFFECTS

Aluminium chloride (AlCl₃) was orally administered to three different groups of animals.

(i) The first group of animals were orally administered AlCl₃ at a dose of 200 mg/Kg body weight for 30 days. The treatment was withdrawn after 30 days and the animals were maintained on standard diet and water *ad libitum* for another 30 and 60 days to study the reversibility of induced effects, if any.

(ii) The second group of animals were orally given AlCl₃ at a dose of 200 mg/Kg body weight for 60 days. The treatment was withdrawn after 60 days and the animals were maintained on standard diet and water *ad libitum* for another 60 days.

(iii) The third group of animals were orally administered AlCl₃ at a dose of 400 mg/Kg body weight for 15 days, the animals were maintained for 15 days (as a period of withdrawal) on standard diet and water *ad libitum* to study the reversibility of induced effects.

The results of all groups revealed that the withdrawal of treatment produced a partial recovery in comparison with treated mice in all AlCl₃ induced effects. However, carbohydrate and nuclei acid metabolism, and testicular cholesterol metabolism in 30 and 60 days withdrawal groups showed significant recovery after withdrawal of aluminium treatment.
PART III : BENEFICIAL EFFECTS OF ASCORBIC ACID (AA), CALCIUM , VITAMIN D AND VITAMIN E

1. The results revealed that administration of the therapeutic agents manifested significant recovery in all the parameters studied.

2. The mechanism of action of ascorbic acid seemed to be mainly by virtue of detoxification and active sequestration of aluminium from the body and reducing its burden, because AA is a powerful reducing agent which participates in oxido-reduction reactions and acts as a supplementary source of electron energy, thereby activating several metabolic processes.

3. Ascorbic acid is also known to activate adenyl cyclase and inhibit phosphodiesterase (PDE) resulting in high C-AMP levels.

4. Calcium is known to activate several enzymes. Calcium is also recognised as a potent inhibitor of PDE.

5. The recovery might also be due to their inhibitory action on phosphodiesterase (PDE) which is a known inhibitor of C-AMP. The increased levels of C-AMP might lead to recovery of all parameters studied.

6. Vitamin D promotes the absorption of calcium and phosphorus and increases tissue citrate levels which acts as a chelator of aluminium.

7. Vitamin E is known for its possible therapeutic role especially in oxidation related events and is the most potent biological antioxidant form of Vitamin.
8. Administration of Vitamins D and E alone and in combination, revealed significant recovery from aluminium induced toxic effects.

PART IV: IN VITRO STUDY

$\text{AlCl}_3$ was incorporated at the doses 100 $\mu$g/ml, 200 $\mu$g/ml and 300 $\mu$g/ml in human blood samples which were cultured for 72 hours.

1. The study revealed an insignificant increase in the sister chromatid exchanges (SCE) / plate (SCE/Plate) and sister chromatid exchanges / chromosome (SCE / Chromosome) in the study group as compared to the control.

2. The results also revealed an increase in the frequency of chromosomal aberrations.

Thus, in conclusion, aluminium chloride has definite effect on reproduction and other body metabolisms. The present study elucidate that $\text{AlCl}_3$ induced effects are by and large, transient and reversible. The study also elucidates that dietary factors such as calcium and Vitamins (C, D, E) could ameliorate the toxic effects of aluminium.