Chapter - V

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Endocrine effects of graded doses of endocrine disrupting agent, mercury in the form of mercuric chloride (MC; HgCl₂, 2 mg and 4 mg/kg, po) was evaluated in adult male rats for 60 days. The endocrine organs were steroidogenic (Testis and adrenal) and nonsteroidogenic tissue (thyroid and pancreas). The parameters are gravimetry, steroidogenesis and metabolism related which included were proteins, phosphatases, cholesterol, serum amylase, glucose, SDH, ATPase and histology of endocrine organs. The antioxidant indices evaluated were superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR), catalase, lipid peroxidation (LPO), glutathione (GSH), total -SH groups and ascorbate of above endocrines. Accumulation of mercury in each tissue was also estimated after mercury feeding. Amelioration effect of melatonin (5 mg/kg ip.) on mercury induced disruptive effects in rats was also studied.

The data brought about a reduction in whole body absolute and relative weights of treated rats indicating toxic nature of this metal as it is known to inhibit and denature the proteins by binding with –SH groups of them. The steroidogenic enzymes like 3β and 17 β hydroxysteroid dehydrogenases (HSDs) declined gradually after mercury ingestion. Contrarily cholesterol levels increased suggesting hormone biosynthesis inhibition in these steroidogenic tissues. Androgen deficiency also caused spermatogenesis
arrest at spermatocyte level. Seminiferous tubules indicated regressive changes. Leydig cells were atrophic. Adrenal hormone production was also affected due to inhibition of enzymes involved in adrenal cortical hormone synthesis. Medullary and cortical histology also indicated shrinkage and vacuolization, showing endocrine disruptive nature of the metal.

Pancreatic amylase, proteins, cholesterol and blood glucose levels were estimated. Increased amylase, cholesterol and glucose levels indicated pancreatitis. High levels of blood glucose also indicated altered insulin production in genesis of diabetes. These were supported by histopathological alterations in it as a result of mercury intoxication. Thyrotoxicosis is evidenced by loss of its weight, loss of synthesis of thyroglobulin protein and inhibition of enzymes involved in hormone production after Hg** treatment. Follicle degeneration was also observed. Phosphatase activities in all endocrine tissues revealed gradual reduction, emphasizing mercury effect on cellular functions of endocrines. Activities of SDH and ATPase enzymes were also diminished after Hg treatment revealing its effect probably on mitochondria. Mitochondrial damage of mercury is due to its accumulation in it. Its accumulation gradually increased in low and high doses of mercury in these endocrines as observed in our study.

The antioxidant enzymes and non-enzymes components of defense system exhibited a significant reduction in their levels inducing endocrine tissue oxidative damage. It is further supported by elevated levels of LPO and further alterations in hormone receptor binding due to mercury ions. Ca++
regulating mechanism might also be altered in endocrine tissue of Hg\(^{++}\) fed rats to augment endocrine disrupting nature of mercury, which is also one of the probable mechanisms of mercury on endocrine organs.

Melatonin supplementation to mercury fed animals, most of the metabolic, steroidogenic, defence system indices and other markers of specific endocrine tissue were reversed at varied levels in comparison to control. LPO, cholesterol, glucose and Hg\(^{++}\) levels in the respective endocrines reversed partially/ fully to control levels. Histological features were also maintained to certain extent. This effect of melatonin and its metabolites is attributed to indole group and its side chains involved in destroying or neutralizing ROS and RNS produced as a result of endocrine disruptive molecules of inorganic mercury. Thus, MLT has an important application in population exposed to endocrine disrupters like mercury.

Based on the above conclusions the following future line of work needs to be undertaken:

1. Toxicity of mercury at cellular and molecular level.
2. Hormonal studies need to be studied.
3. Genotoxic effects.
4. Ultra structural studies.
5. Mechanism of mercury and other endocrine disruptive components (EDCs) and their interaction need to be further investigated.
6. These studies along with supplementation of melatonin are to be correlated with reversibility studies.
7. Effects of other antioxidants are also to be studied for comparison.

8. Antioxidant combination also needs to be done.

9. Studies on exposed human population are to be initiated.

1C. Amelioration of melatonin and other antioxidant combination is tried in these exposed populations.