THE IMPACT OF MIMOSA PUDICA ON THE HISTOARCHITECTURE OF HYPOTHALAMIC-PITUITARY-TESTICULAR AXIS IN CADMIUM TREATED RATS

Article *in* WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES · October 2015

CITATIONS
4

READS
157

5 authors, including:

Enye Linus Anderson
Afe Babalola University
15 PUBLICATIONS **63** CITATIONS

SEE PROFILE

Oladunni Kunlere
Afe Babalola University
1 PUBLICATION **4** CITATIONS

SEE PROFILE

WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 5.210
Volume 4, Issue 10, 163-179. Research Article ISSN 2278 – 4357

THE IMPACT OF *MIMOSA PUDICA* ON THE HISTOARCHITECTURE OF HYPOTHALAMIC-PITUITARY-TESTICULAR AXIS IN CADMIUM TREATED RATS

***Edem Edem Ekpenyong[1], Enye Linus Anderson[1], Towobola Adewale Abdullateef[1], Akingbade Adebanji Modupe[1], Kunlere Oladunni Eunice[1]**

[1]Department of Anatomy, College of Medicine and Health Sciences,
Afe Babalola University, Ado Ekiti, Nigeria.

Article Received on
22 July 2015,

Revised on 20 Aug 2015,
Accepted on 10 Sep 2015

***Correspondence for Author**
Edem Ekpenyong Edem
[1]Department of Anatomy, College of Medicine and Health Sciences, Afe Babalola University, Ado Ekiti, Nigeria.

ABSTRACT

Background: Cadmium is a known environmental and industrial pollutant with an enormous neuroendocrine disrupting potential. *Mimosa pudica* Linn is a creeping annual or perennial herb known to possess antiasthmatic, antiepileptic, antitumour, aphrodisiac, analgesic, antidepressant properties and a strong radical scavenging activity. This research was aimed at investigating the impact of *Mimosa pudica* on the histoarchitectural integrity of the hypothalamic-pituitary-testicular axis in cadmium-treated rats. **Materials and Methods:** Twenty five mature wistar rats (Rattus rattus norvegicus) were employed in the study. These animals were divided into five groups - 5 Rats/Group; Control, Cadmium Toxicity, *Mimosa pudica* Extract, Protection and Therapeutic Groups. The Control Group was orally administrated with distilled water. **Result:** Toxicity was achieved with 1.2mg/kg body weight for forty days with apparent histological abnormalities and alterations to the axis components. Administration of *Mimosa pudica* (200mg/kg) body weight with cadmium in both the Protection and Therapeutic Groups showed remarkable histological improvements and markedly reduced tissue damage when compared with Cadmium Toxicity Group. **Conclusion:** Results of this study demonstrate that *Mimosa pudica* possesses protective, therapeutic as well as restorative capacity on the histoarchitecture of hypothalamic-pituitary-testicular axis components in cadmium-treated rats.

KEYWORDS: Cadmium, *Mimosa pudica*, histoarchitecture, hypothalamic-pituitary-testicular axis, toxicity.

INTRODUCTION

Mimosa pudica Linn is a creeping annual or perennial herb found to possess anti-asthmatic, aphrodisiac, analgesic, and antidepressant properties. It is known to possess sedative, emetic, and tonic properties, and has been used traditionally in the treatment of various ailments including alopecia, diarrhea, dysentery, insomnia, tumor, and neurological disorders like epilepsy, convulsions, and various urogenital infections. Phytochemical studies on *M. pudica* have revealed the presence of alkaloids, non-protein amino acid (mimosine), flavonoids C-glycosides, sterols, terpenoids, tannins, and fatty acids (Genest *et al.*, 2008).

The hypothalamus is that portion of the brain that maintains the body's internal balance (homeostasis). The hypothalamus is the link between the endocrine and nervous systems. The hypothalamus produces releasing and inhibiting hormones, which stop and start the production of other hormones throughout the body (Dindyal *et al*., 2007).

Pituitary gland is a pea-sized gland that sits in a protective bony enclosure called the sella turcica. It is composed of three lobes: anterior, intermediate, and posterior. This endocrine structure consists of ductless glands, distinct clusters of cells within certain organs of the body, and diffuse neuro-endocrine cells, regulates metabolic activities in certain organs and tissues of the body, thereby helping to bring about homeostasis brought about by chemical substances called hormones, which are released into the bloodstream to influence target cells at remote sites. Cadmium is recognized as an endocrine disruptor that modifies, among other secretions, prolactin (PRL) secretion in a number of species including humans. Cd is readily absorbed and retained in the pituitary gland of rats and affects lactotroph cell activity causing biochemical, genomic and morphological changes (Jiménez *et al*., 2012).

The testes (or testicles) are a pair of sperm-producing organs that maintain the health of the male reproductive system. In addition to their role in the male reproductive system, the testes also have the distinction of being an endocrine gland because they secrete testosterone—a hormone that is vital to the normal development of male physical characteristics (Shackelford *et al.*, 2007).

Cadmium (Cd) is ranked eighth in the top 20 hazardous substances; it is released into water as a by-product of smelting, into air by combustion of coal and oil, and into soils as impurities. In human populations, cadmium exposure occurs primarily through dietary sources and drinking water as well as cigarette smoking. Its main uses are for nickel–cadmium battery manufacture, pigments and plastic stabilizers (Jarup & Akesson, 2009). Cadmium is recognized as an endocrine disruptor that modifies, among other endocrine secretions, prolactin (PRL) secretion in a number of species including humans. Cd is readily absorbed and retained in the pituitary gland of rats and affects lactotroph cell activity causing biochemical, genomic and morphological changes, which invariably affects the different endocrine structures influenced by the pituitary gland in other parts of the body, example, testis, thyroid, etc. (Jiménez *et al*., 2012). Based on its nervine and reproductive benefits, *mimosa pudica* is being investigated in the present study to determine its protective as well as its therapeutic role on the histoarchitecture of hypothalamic-pituitary-testicular axis in cadmium-treated adult rats.

MATERIALS AND METHODS

Animals

All experiments were designed in strict adherence to the guidelines of the Afe Babalola University's Animal Ethics Committee. Twenty-five male healthy Wistar rats weighing between 98-132g of the same specie *Rattus norvegicus* was purchased from the Department of Biochemistry, Afe Babalola University, were used for the research Work. They were housed in well ventilated plastic cages, kept and maintained under laboratory condition of temperature, humidity and light. At the time of purchase, they weighed between 77 - 117g. They were allowed to acclimatize for a period of two weeks and fed with growers Mash. The rats were also given tap water at pleasure using water bottles. At the end of two weeks, the rats were weighed and were randomly assigned to five different groups A as the control group B, C, D and E as the experimental groups.

Collection and Preparation of aqueous extract from the leaves of *Mimosa pudica*

Fresh, healthy leaves of *Mimosa pudica* after identification were harvested and properly washed in tap water and then rinsed in sterile distilled water to remove dirt and possible mycotoxins. The leaves were air dried for three days and then pulverized into fine powder using an electric blender. Sixty (60) grams of the powder was extracted in 300ml of distilled water and left to stand for 48 hours at room temperature. The extract was filtered through

cheese cloth and the resulting filtrate was concentrated on steam bath until a semisolid residue (green black paste) which weighed 4.5g was obtained. The percentage yield was calculated and equivalent amount of the residue was separately reconstituted in 100ml of normal saline to give the required doses of 200mg/kg body weight.

Induction of Toxicity

Induction of toxicity was achieved by the oral administration of cadmium at 1.2kg/kg body weight. The induction was done orally using syringe and canula.

Treatment

The aqueous extract of leaves of *Mimosa pudica* was given orally at the dose of 200mg/kg for 40 consecutive days.

Experimental Design

The rats were grouped into 5 of five animals per group according to the weight of the rats. Group A weighing 114g served as the Control group; Group A - Control Group; Group B - Cadmium Toxicity Group; Group C- Mimosa Pudica Extract Group; Group D - Protective Group; and Group E-Therapeutic Group. The *Control Group* animals received distilled water only through the 40 days duration of the experiment. Rats in the *Cadmium Toxicity Group* were given 1.2mg/kg body weight for 40 days of the experiment. *Mimosa pudica Extract Group* rats were administered with 200mg/kg body weight of aqueous extract of *Mimosa pudica* for 40 days. *Protection Group* rats were given 1.2mg/kg body weight of cadmium and 200mg/kg body weight of aqueous extract of *Mimosa pudica* simultaneously for 40 days. Wistar rats in the *Therapeutic Group* received 1.2mg/kg body weight of cadmium for the first 20 days and 200mg/kg body weight of aqueous extract of *Mimosa pudica* for the remaining 20 days of the experiment.

Sacrification

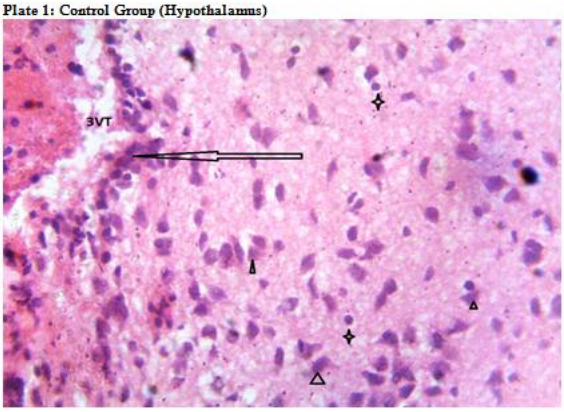
At the end of the experiment, the rats were sacrificed. This was done by cervical dislocation. The whole brain was collected and fixed in 10% formal saline and the same was done for the pituitary gland. The testes were collected and fixed in Bouin's fluid.

RESULTS

At the end of the histological analysis, marked morphological alterations were observed in cadmium-treated rats; and varying degrees of regenerations and cellular restorations were

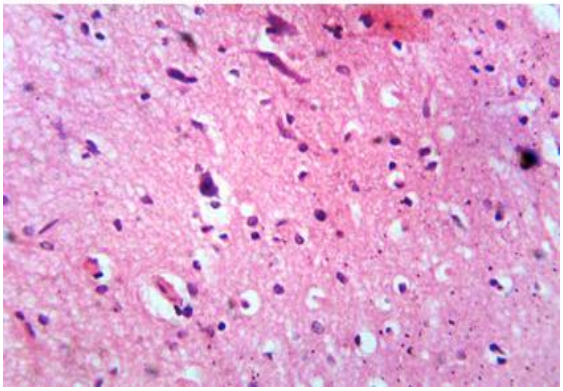
noticeable in animals treated with *Mimosa pudica* after toxicity induction with cadmium, as presented below.

Plate 1: Control Group (Hypothalamus)



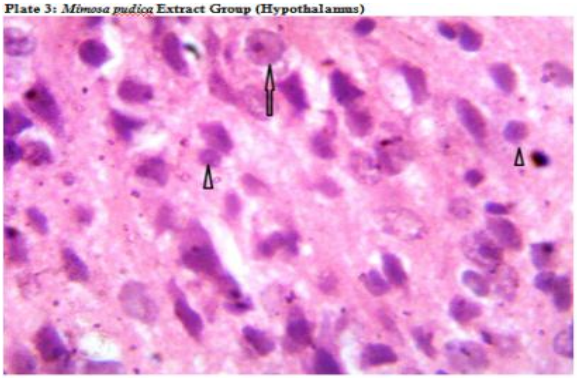
Micrograph (x400) of hypothalamus given distilled water shows section cluster of hypothalamic nuclei (arrow head), ependymal layer (arrow); lining the third ventricle (3VT).The parenchyma appears compact and the neurons have a spherical nucleus with scattered heterochromatin, the glia (star) cells appear essentially unremarkable.

Plate 2b: Cadmium Toxicity Group (Hypothalamus)



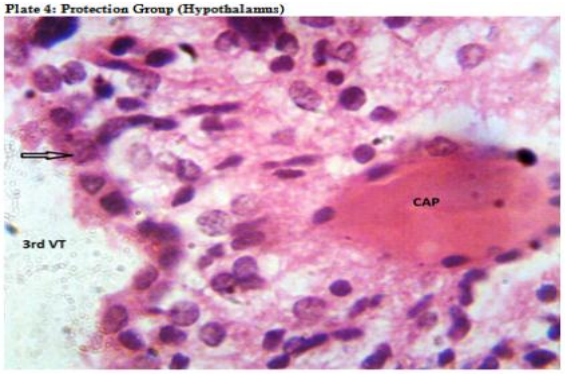
Micrograph (x400) of hypothalamus treated with 1.2mg/kg body weight of Cadmium for 40 days reveals ghost neurons characterized by oval empty spaces (vacuolizations) indicative of neurodegeneration

Plate 3: *Mimosa pudica* Extract Group (Hypothalamus)



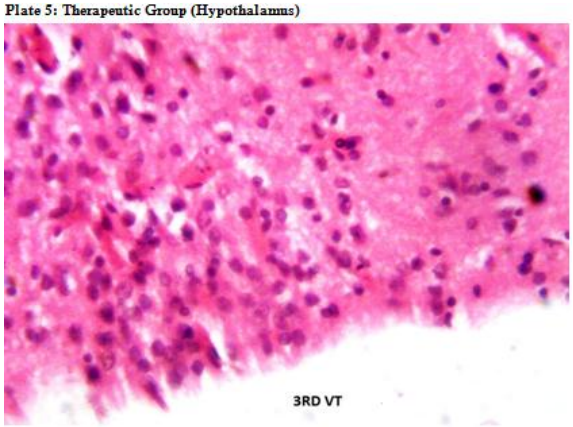
Micrograph (x400) of hypothalamus treated with 200mg/kg body weight of aqueous extract Mimosa pudica for 40 days shows cluster of hypothalamic nuclei with scattered heterochromatin, the neuroglia (arrow head) appear normal, no congestion or inflammatory cells seen

Plate 4: Protection Group (Hypothalamus)



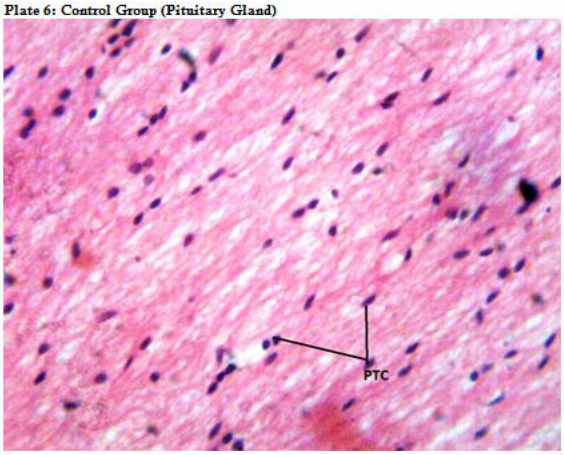
Photomicrograph (x1000) of hypothalamus treated with 1.2mg/kg body weight of cadmium and 200mg/kg body weight of Mimosa pudica simultaneously for 40 days shows the nuclei of ependymal cell (arrow) lining the third ventricle (3^{rd}vt), and a congested capillary (CAP). Neuronal recovery remarkable

Plate 5: Therapeutic Group (Hypothalamus)



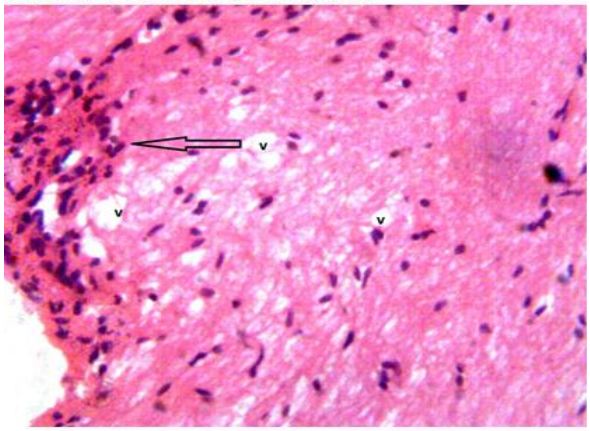
Micrograph (x400) treated with 1.2mg/kg body weight of Cadmium for 20 days and 200mg/kg body weight of Mimosa pudica for the remaining 20 days reveals eosinophillic collections (evidence of regeneration after degeneration). No inflammatory cells seen. Cellular restoration evident.

Plate 6: Control Group (Pituitary Gland)



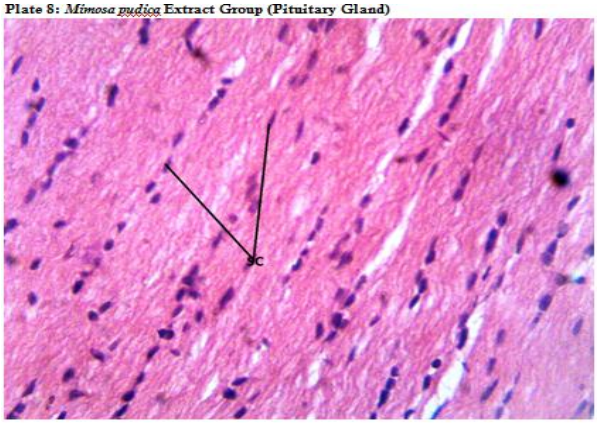
Photomicrograph (x400) given distilled water shows section of the posterior pituitary (pars nervosa) showing axons of nerve fibers, the Schwann cells and pituicytes. Micromorphology appears remarkable.

Plate 7: Cadmium Toxicity Group (Pituitary Gland)



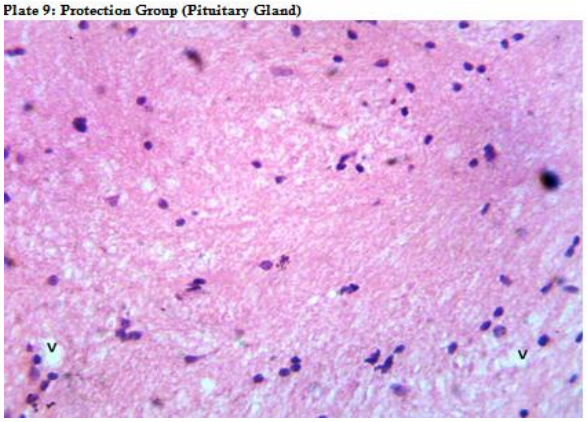
Photomicrograph (x400) of Pituitary Gland treated with 1.2mg/kg body weight of Cadmium for 40 days. Section shows perivascular inflammatory cells (arrow) and vaculoation (V) within the stroma.

Plate 8: *Mimosa pudica* Extract Group (Pituitary Gland)



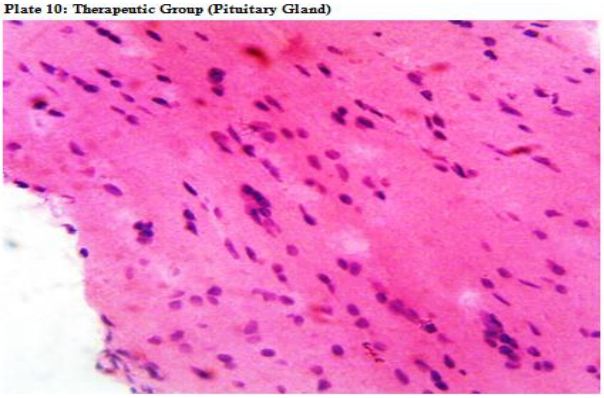
Micrograph (x400) of Pituitary Gland treated with 200mg/kg body weight of Mimosa pudica for 40 days shows section of the posterior pituitary (pars nervosa) showing axons of nerve fibers, the Schwann cells (SC) and pituicytes. Micromorphology appears remarkable.

Plate 9: Protection Group (Pituitary Gland)



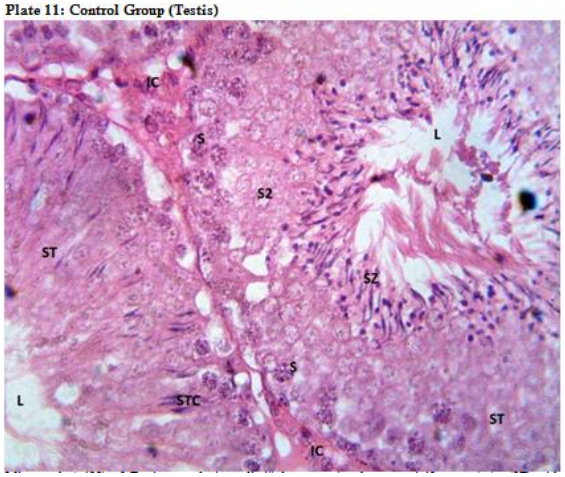
Micrograph of Pituitary Gland treated with 1.2mg/kg body weight of Cadmium and 200mg/kg body weight of Mimosa pudica simultaneously for 40 days. Section shows perivascular inflammatory cells (arrow) and vaculoation (V) within the stroma. Mild restorative activity seen with reduced vacuolations

Plate 10: Therapeutic Group (Pituitary Gland)



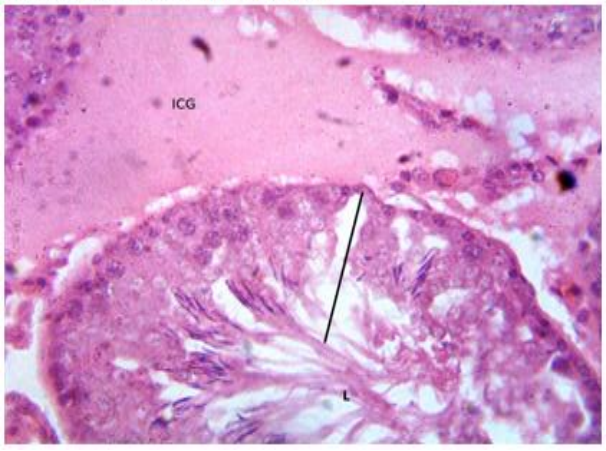
Micrograph (x400) of Pituitary Gland treated with 1.2mg/kg body weight of Cadmium for 20 days followed by 200mg/kg body weight of Mimosa pudica for the remaining 20 days. Section of the posterior pituitary (pars nervosa) shows axons of nerve fibers, the Schwann cells (SC) and pituicytes. Remarkable restored micromorphology

Plate 11: Control Group (Testis)



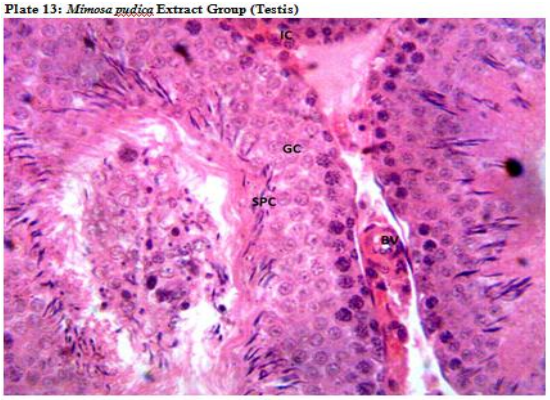
Micrograph (x400) of Testis given distilled water only, shows seminiferous tubules (ST) with defined lumen (L), composed spermatozoa (SZ). Tubules are composed of germ cells (S2) at different levels of maturation, the sertoli cells (STC) and interstitial cells (IC). Normal testicular cytoarchitecture intact

Plate 12a: Cadmium Toxicity Group (Testis)



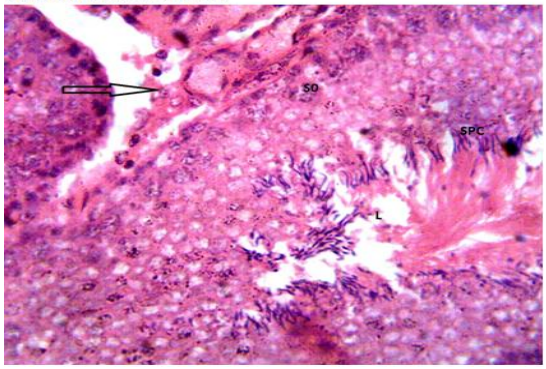
Micrograph (x400) of Testis treated with 1.2mg/kg body weight of Cadmium for 40 days shows outstanding testicular alteration; seminiferous tubules with reduced spermatogenic cells (line) within the lumen (L), also seen is marked congestion of the Interstitium (ICG) .

Plate 13: *Mimosa pudica* Extract Group (Testis)



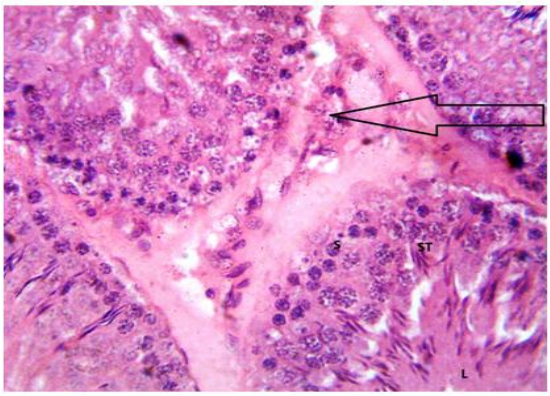
Micrograph (x400) of Testis treated with of 200mg/kg body weight of Mimosa pudica aqueous extract for 40 days. Section shows seminiferous tubules filled with germinal cells, the germinal epithelium is composed of germ cells (GC) and varying degree of maturation, within the Interstitium lies blood vessels (BV) and interstitial cells.

Plate 14: Protection Group (Testis)



Micrograph (x400) of testis treated with 1.2mg/kg body weight of Cadmium and 200mg/kg body weight body weight of Mimosa pudica aqueous extract simultaneously shows seminiferous tubules filled with germinal cells, the germinal epithelium is composed of germ cells (GC) and varying degree of maturation, within the Interstitium lies blood vessels (BV) and interstitial cells that are not remarkable.

Plate 15: Therapeutic Group (Testis)



Photomicrograph of Testis treated with 1.2mg/kg body weight of Cadmium for 20 days and 200mg/kg body weight of aqueous extract of Mimosa pudica for 20 days. Section reveals reactive germ cells undergoing recovery from cellular damage.

DISCUSSION

The current investigation showed the efficacy of *mimosa pudica* in preventing/ameliorating the toxic effects of cadmium on the histoarchitecture of the hypothalamic-pituitary-testicular axis in adult Wistar rats. At the moment, this is the first report showing these effects.

Histopathology is considered the most reliable parameter for the detection of toxic effects on male reproduction (Creasy, 2001; Lanning *et al.*, 2002); and as such histological investigation was carried out to ascertain the extent of cellular and tissue disruption induced by cadmium on the different components of the hypothalamic-pituitary-testicular axis.

Cadmium exposure has been reported to be a risk factor for infertility and it is very dangerous on testicular function (Sarah *et al.*, 2012; Sokol, 1997). The study of the hypothalamic pituitary-gonadal axis in animals exposed to the metal is of great interest since the levels of

cadmium in air, water, soil, and foods have increased several-fold in many parts of the world as a result of emissions from industrial activities (Sebahat *et al.*, 2005).

Cd-induced neurotoxicity might be caused by impaired neurogenesis, resulting in markedly reduced neuronal differentiation and axonogenesis, leading to neuronal cell death (Chen *et al.*, 2008). The present study evaluated the histomorphological damage of cadmium on the hypothalamus, the result revealed 'ghost neurons' characterized by oval empty spaces (vacuolizations) which are indicative of neurodegeneration. Though the scope of this study did not cover hormonal analysis, the impaired cytoarchitecture is an evidence of altered plasma gonadotropin levels as shown in different studies of the hypothalamus (Lafuente & Esquifino, 1999).

Cadmium toxicity changes the general morphology of the pituitary gland. In the present study, the tissue appeared slightly atrophied in a few areas with perivascular inflammatory cells and vacuolations within the stroma. This is in conformity with the work of Favorito *et al.*, (2010). This evidence has been reported also in other glandular tissues as in the thyroid of the catfish Clarias batrachus (Jadhao *et al.*, 1994), in the testis of the cyprinid Puntius sarana (Kumari *et al.*, 1991) and of the monkey Presbytis entellus entellus (David & Ramaswami, 1971). Underlying these histological disorganizations are cadmium's inhibitory effect on the hormonal secretion of many adenohypophyseal cells, which was reported in mammals: the levels of LH, PRL and GH in serum of the rat exposed to cadmium decrease (Lafuente *et al.*, 2001; Lafuente *et al.*, 1997) as well as the levels of GTH in pig (Han *et al.*, 2006) and female rats (Pillai *et al.*, 2003). Recently it has been also reported that Cd modifies the lactotrophs activity of pituitary gland through biochemical, genomic and morphological changes, contributing directly or indirectly to the levels of serum prolactin in rat (Calderoni *et al.*, 2010).

Pituitary secretion activity has been shown to be affected by metals and this endocrine gland is a particularly sensitive target to cadmium toxicity (Lafuente *et al.*, 2001; Poliandri *et al.*, 2006; Cano *et al.*, 2007), but not very much has been reported regarding the mechanism of action of the Cd like endocrine disruptor. It is just reported that divalent cations, as Cd, inhibit in vitro release of GH and PRL from bovine adenohypophyseal secretory granules (Lorenson *et al.*, 1983). Calderoni *et al.*, (2005) report that cadmium modifies the lipid contents of pituitary gland and directly or indirectly the levels of prolactin and growth hormone in serum. Lafuente *et al.*, (2005) have reported that the inhibitory effect of cadmium

on PRL and LH secretion may be partially explained by a decrease in the content of glutamate and aspartate in anterior hypothalamus. Several studies have shown that cadmium could compete with calcium at the pituitary level (Waalkes & Poirier, 1984; Milos *et al.*, 1989), which results in altered calcium regulation. Thus it either interferes with calcium influx through the membrane channel (Kasprzak & Poirier, 1985; Cooper *et al.*, 1987) and disrupts intracellular calcium mobilization and subsequently alters the cytoarchitectural integrity of the gland. Further researches are however certainly required to define the mechanism of cytotoxic action of cadmium on the pituitary cells.

Cadmium accumulates in male reproductive organs, in both humans and animals Numerous studies have confirmed that the testis is more sensitive to cadmium than other important organs (Souza *et al.*, 2010). Histopathological observations also showed remarkable destruction of the testis in the rats poisoned with cadmium in the present study. This is consistent with the earlier works of Habeebu *et al.*, (1998); Jones *et al*., (1988) in which they showed that cadmium caused liver, kidney and testicular damage. Similarly, other agents like lansoprazole, oxolinic acid and procynidone appear to induce leydig cell damage and tumors of the testis in rats by perturbation of testosterone production and overstimulation of testicular interstitia via increase serum luteinising hormone (Fort *et al.*, 1995; Murakani *et al.*, 1995; Yamada, 1994). This indicates a reduction in normal feedback inhibition mechanism in rats by cadmium at the level of hypothalamus and/or pituitary resulting from reduced testosterone production by the testes which is critical in the formation of testicular interstitial cell tumors (Waalkes *et al.*, 1997b). Furthermore the loss of testosterone feedback can result in pituitary cell hypertrophy, hyperplasia and eventually pituitary neoplasia (Nyska *et al.*, 1998). Thus the disruption of the hypothalamic-pituitary-testicular axis may contribute to the causation of both testicular and pituitary destructions in the present study.

Exposure of animals to cadmium induced oxidative stress, stimulates the synthesis of cadmium binding proteins metallothioneins (MT) and heat proteins (Klassen *et al.*, 1999). Cadmium-induced oxidative stress has been associated with production of reactive oxygen species (ROS) comprising mainly superoxide radical anion (O2 -), hydrogen peroxide and hydroxyl radical (OH) which lead to lipid peroxidation, membrane protein and DNA damage which can also result in carcinogenesis (Bagchi *et al.*, 1996). This had been reported to cause apoptosis, necrosis and cell proliferation (Habeebu *et al.*, 2000; Stoh *et al.*, 2001). From this study, cadmium stimulated the histopathological damages which include seminiferous tubules

with reduced spermatogenic cells [line] within the lumen, with marked congestion of the Interstitium (ICG). This disorganization could be positively correlated with increase in phosphatase levels.

In drug discovery, random screening as a tool in identifying new biologically active molecules has been the most productive. Free radicals are generated by both internal (cellular respiration, etc.) and external (alcohol, pollution, smoking, etc.) sources. These free radicals can damage all cellular macromolecules (proteins, carbohydrates, lipids and nucleic acids) and attribute to many disorders (Thirumalai *et al.*, 2011). However, these radicals are controlled by antioxidants, which can safely interact and terminate the chain reaction before vital molecules are damaged. There are several enzyme systems (catalase, superoxide dismutase etc.) within our body that scavenge free radicals. In addition micronutrients such as vitamin E, beta-carotene and vitamin C form dietary sources and can act as antioxidants (Sharma *et al.*, 2010; Nonita & Mylene, 2010). The present study explored the scavenging antioxidant property of *Mimosa pudica* on the cytostructural integrity of the hypothalamic-pituitary-testicular axis in cadmium treated rats.

Anti-oxidants are agents that significantly inhibit the rate of oxidative activity (Murray *et al.*, 2000). They can be generally categorized into preventive and non preventive antioxidants (Parker, 1986). Vitamin C, E and selenium are the best known preventive antioxidants (Parker, 1986). Vitamins C, E and selenium inhibited oxidation by an effect on calcium metabolism, (Stoh *et al.*, 2001), protein kinase C (Das & King, 2007) inhibition and catalysis of the reduction of hydrogen peroxide which protect biological membranes from oxidative degradation (Murray *et al.*, 2000).

The *Mimosa pudica* invites attention of the researchers worldwide for its pharmacological activities such as antiepileptic, anticonvulsant, antidiabetic, antitoxin, antihepatotoxin, antioxidant, aphrodisiac and wound healing activities. It is reported to contain alkaloid, glycoside, flavonoid and tannis. All parts of the plant are considered to possess medicinal properties and used in the treatment of biliousness, leprosy, dysentery, vaginal and uterine complaints, inflammations, burning sensation, fatigue, asthma, leucoderma, blood diseases (Chauhan *et al.*, 2009). *Mimosa pudica* leaves, which were used in this investigation is reported to be the richest in total flavonoid and total phenolic contents compared to other parts of the plants (Jing *et al.*, 2011). Flavanoids and other phenolic compounds of plant

origin have been reported as scavengers and inhibitors of lipid peroxidation (Meenakshi *et al.*, 2012).

Toxicity in the hypothalamic tissue induced by cadmium resulted in cell death with apparent 'ghost neurons' following inflammatory mechanisms. Treatment with *Mimosa pudica* in both the Protection and Therapeutic Groups showed neuronal recovery (Plate 4 and 5). This was due to its antioxidant properties which protect DNA against damage induced by the reactive oxygen species. Perivascular inflammatory cells and vaculoation within the stroma (Plate 7) observed in the pituitary gland, of the cadmium group would compromise the endocrine function of the hypothalamic-pituitary axis (Massanyi *et al.*, 2007). These changes were attenuated by 200mg/kg body weight of *Mimosa pudica* (Plate 10).

The testes are endocrine organs hence damage to the tissue will result in abnormal endocrine responses. Because the integrity of the testes is compromised histologically following cadmium toxicity, furthermore Cd is known to also directly cause destruction to the testicular organs and hypothalamus-pituitary gonadal axis thus destroying the secretory organs of hormones (Massanyi *et al.*, 2007) and compromising hormonal release. In this study, 1.2mg/kg body weight of cadmium produced cytoarchitectural alterations including seminiferous tubules with reduced spermatogenic cells [line] within the lumen and marked congestion of the Interstitium (Plate 12). This damage is believed to be brought about by the inhibition of the serum hormonal levels of FSH and LH which induce the signals for testosterone synthesis (Cooke *et al.*, 1981). An inhibition of these signals results in the time-dependent monophasic serum inhibition in testosterone levels showing reproductive dysfunction, cell death and apoptosis by cadmium (Habeebu et al 1998; Massanyi *et al.*, 2007; Stoh *et al.*, 2000) resulting in liver and accessory sex tissues atrophy such as the prostate (Waalkes *et al.*, 1997a). This will result in reproductive dysfunction.

Testis treated with 200mg/kg body weight of *Mimosa pudica* aqueous extract for 40 days showed seminiferous tubules filled with germinal cells, the germinal epithelium is composed of germ cells (GC) and varying degree of maturation, within the Interstitium lay blood vessels (BV) and interstitial cells with no apparent toxic histological evidence. At this dosage, aqueous extract is safe, and this is in agreement with Pradeep's (2012) toxicity studies on *Mimosa pudica*.

Cadmium-induced testicular toxicity is caused by the interactions between complex networks, involving the inhibition of oxidative stress, which leads to an increase in germ cell

apoptosis (Siu *et al.*, 2009; Turner & Lysiak, 2008) and/or distortion of the blood-testis barrier with subsequent germ cell loss, testicular edema, and hemorrhage (Cheng & Mruk, 2012). After prolonged exposure, damage inflicted by cadmium can be found at interstitial and tubular level (Mathur *et al.*, 2011). The present study revealed a distorted testicular histoarchitecture (Plate 12) induced by cadmium toxicity, and it confirms the above assertions. The present research revealed treatment with aqueous leaf extract of *mimosa pudica* showed reactive testicular germ cells undergoing recovery from cellular damage (Plate 15). However, *Mimosa pudica* ethanolic root extract, which is highly aphrodisiac and toxic at high dose showed decreased spermatozoa number (http://www.hillgreen.com/pdf/mimosapudica).

SUMMARY/CONCLUSION

The current research demonstrated that *Mimosa pudica* has protective, as well as restorative capacity on the histoarchitecture of hypothalamic-pituitary-testicular axis in cadmium treated rats. This confirms its ethnomedical use as a therapeutic intervention in infertility. However, caution should be taken as regards the dose administered. Moreover, I recommend that biochemical, genetic as well as histochemical investigations should be carried out in subsequent studies for a more appreciable, detailed and confirmatory result.

REFERENCES

1. Bagchi, D., Bagchi, M., Hassoun, E., Stohs, S. *Cadmium-induced excretion of urinary lipid metabolites, DNA damage, glutathione depletion and hepatic lipid peroxidation in Sprague-Dawley rats.* Biol. Trace. Element. Res., 1996; 52: 143-154.
2. Calderoni, A., Biaggio, V., Acosta, M., Oliveros, L., Mohamed, F., and Gimènez, M. *Cadmium exposure modifies lactotrophs activity associated to genomic and morphological changes in rat pituitary anterior lobe.* Biometals., 2010; 23: 135-43.
3. Calderoni, A., Oliveros, L., Jahn, G., Anton, R., Luco, J. and Giménez, M. *Alterations in the lipid content of pituitary gland and serum prolactin and growth hormone in cadmium treated rats.* BioMetals., 2005; 18: 213-20.
4. Cano, P., Poliandri, A., Jimenez, V., Cardinali, D. and Esquifino, A. *Cadmium-induced changes in Per 1 and Per 2 gene expression in rat hypothalamus and anterior pituitary: effect of melatonin.* Toxicol Lett., 2007; 172: 131-6.

5. Chauhan, B. and Davi, E. *Germination, emergence, and dormancy of Mimosa pudica*. Weed Biology and Management., 2009; 9(1): 38–45. doi:10.1111/j.1445-6664.2008.00316.x.
6. Chen, L., Liu, L., Luo, Y. and Huang, S. *MAPK and mTOR pathways are involved in cadmium-induced neuronal apoptosis.* J. Neurochem., 2008; 105: 251–261.
7. Cheng, C. and Mruk, D. *The blood-testis barrier and its implications for male contraception. Pharmacol.* Rev., 2012; 16-64.
8. Cooke, B., Magee-Brown, R., Golding, M. and Dix, C. *Heterogeneity of Leydig cells from mouse and rat testes, evidence for a Leydig cell cycle?* Int. J. Androl., 1981; 4: 355–366.
9. Cooper, R., Goldman, J., Rehnberg, G., McElroy, W. and Hein, J. *Effects of metal cations on pituitary hormone secretion in vitro.* J Biochem Toxicol., 1987; 2: 241-9.
10. Creasy, D. *Pathogenesis of male reproductive toxicity*. Toxicologic Pathology., 2001; 29(1): 64–76.
11. Das, E. and King, G. *The role of protein kinase C activation and the vascular complications of diabetes.* Pharmacol Res., 2007; 55: 498–510.
12. David, G. and Ramaswami L. *Changes observed in the FSH and LH cells of the adenoypophysis of Presbytis entellus entellus following cadmium induced testicular necrosis.* Experientia., 1971; 27(3): 342- 3.
13. Dindyal, S. *"The sperm count has been decreasing steadily for many years in Western industrialised countries: Is there an endocrine basis for this decrease?"* The Internet Journal of Urology., 2007; 2(1): 1–21.
14. Favorito, R., Grimaldi, M., Coppola, M. and Ferrandino, I. *Effects of Acute Cadmium Exposure on the Pituitary Gland of Podarcis sicula.* The Open Zoology Journal., 2010; 3: 30-36. 1874-3366/10 2010
15. Fort, F., Miyajima, H., Suzuki, T., Yamamoto, M., Hamashima, T., Sato, S., Kitazaki, T., *et al. Mechanism for species-specific induction of leydig cell tumors in rat by lansoprazole.* Fundam. Appl. Toxicol., 1995; 26: 191-202.
16. Genest, S., Kerr C., Shah, A., Rahman, M., Saif-E-Naser G., Nigam, P., *et al.*, *Comparative bioactivity of two Mimosa species.* Lat Am Caribb Bull Med Aromat Plants., 2008; 7: 38–43.
17. Habbeebu, S., Liu, J. and Klaassen, C. Cadmium-induced apoptosis in mouse Liver. Toxicol Appl Pharmacol., 1998; 149(2): 203-209.

18. Jadhao, A., Paul, P. and Rao, P. *Effect of cadmium chloride on the pituitary, thyroid and gonads in the catfish, Clarias batrachus (Linn.).* Funct Dev Morphol., 1994; 4(1): 39-44.
19. Jarup, L., Akesson, A. (2009)*Current status of cadmium as an environmental health prob lem.* Toxicol. Appl. Pharmacol., 2009; 238: 201-208
20. Jiménez, V., Cano, P., Fernández, P., Cardinali, P., Esquifino, I. (2012) *Cadmium as an endocrine disruptor. Correlation with anterior pituitary redox and circadian clock mechanisms and prevention by melatonin*. Free Radical Biology and Medicine., 2012; 53.
21. Jing, Z., Ke, Y., Wen-long, Z., Jian, Z. and Ping Y. *Studies on the active components and antioxidant activities of the extracts ofMimosa pudica Linn. from southern China.* Pharmacogn Mag., 2011; 7(25): 35–39.
22. Jones, M. and Cherian, M. *The search for chelate antagonists for chronic cadmium intoxication.* Toxicology., 1988; 62: 1-25.
23. Kasprzak, K. and Poirier, L. *Effects of calcium and magnesium acetates on tissue distribution of carcinogenic doses of cadmium chloride in Wistar rats.* Toxicology., 1985; 34(3): 221-30.
24. Klaassen, C., Liu, J. and Choudhuri, S. *Metallothionein: an intracellular protein to protect against cadmium toxicity.* Annu Rev Pharmacol Toxicol., 1999; 39: 267-294.
25. Kumari, M. and Gopal D. *Cadmium-induced histomorphological changes in the testis and pituitary gonadotrophic hormone secreting cells of the cyprinid Puntius sarana.* Bollett Zool., 1991; 58: 71-6.
26. Lafuente, A., Blanco, A., Márquez, N., Alvarez-Demanuel, E. and Esquifino, A. *Effects of acute and subchronic cadmium administration on pituitary hormone secretion in rat.* Rev Esp Fisiol., 1997; 53(3): 265-9.
27. Lafuente, A., González-Carracedo, A., Romero, A., Cabaleiro, T. and Esquifino, A. *Toxic effects of cadmium on the regulatory mechanism of dopamine and serotonin on prolactin secretion in adult male rats.* Toxicol Lett., 2005; 155(1): 87-96.
28. Lafuente, A., Marquez, M., Perez-Lorenzo, M., Pazo, D. and Esquifino A. *Cadmium effects on hypothalamic-pituitary-testicular axis in male rats.* Exp Biol Med., 2001; 226: 605-11.
29. Lanning, L., Creasy, D., Chapin, R. *et al.*, (2002) *Recommended approaches for the evaluation of testicular and epididymal toxicity.* Toxicologic Pathology., 2002; 30(4): 507–520.

30. Lorenson, M., Robson, D. and Jadobs, L. *Divalent cation inhibition of hormone release from isolated adenohypophysial secretory granules.* J Biol Chem., 1983; 258(14): 8618-22.
31. Massanyi, P., Lukac, N., Slivkova, J., Kovacik, J., Makarevich, A., Chrenek, P., *et al. Mercury-induced alterations in rat kidneys and testes in vivo.* J Environ Sci Health A Tox Hazard Subst Environ Eng., 2007; 42(7): 865-870.
32. Mathur, P., Lui, W., Lee, W., Bonanomi, M. and Silvestrini, B. *Regulation of blood-testis barrier dynamics by desmosome, gap junction, hemidesmosome and polarity proteins: An unexpected turn of events*. Spermatogenesis., 2011; 105-115.
33. Meenakshi, S., Umayaparvathi, S. and Arumugam, M. (2012) *Balasubramanian seaweeds of Gulf of Mannar.* Asian pac J Trop Biomed., 2012; 566-570.
34. Milos, M., Comte, M., Schaer, J. and Cox, J. *Evidence for capital and six auxillary cation-binding sites on calmodulin: divalent cation interactions monitored by direct binding and microcalorimetry*. J Inorgan Biochem., 1989; 36: 11-25.
35. Murakami, M., Hosokawa, S., Yamada, T., Harakawa, M., Ito, M. koyama, Y., Kimura, J., *et al. Species-specific mechanism in rat leydig cell tumorigenesis by procynidone. Toxicol.* Appl. Pharmacol., 1995; 131: 244-252.
36. Murray, K., Granner, D., Mayer, P. and Rodwell, V. *Harpers Biochemistry 25th Edition*., 2000; 8: 83-85, 130-136.
37. Nonita, P. and Mylene, M. *Antioxidant and cytotoxic activities and phytochemical screening of four Philippine medicinal plants.* J Med plants Res., 2010; 4(5) : 407-414.
38. Nyska, A., Leininger, J., Maronpot, R., Haseman, J., and Hailey, J., *Effects of individual versus group caging on the incidence of pituitary and leydig cell tumors in F344 rats: Proposed Mechanism.* Med. Hypotheses., 1998; 50: 525-529.
39. Parker, L. *Oxygen radicals and antioxidants in endurance exercise: biochemical aspects of physical exercise.* Elsevier Science Publishers Amsterdam., 1986.
40. Pillai, A., Priya, L. and Gupta, S. *Effects of combined exposure to lead and cadmium on the hypothalamic-pituitary axis function in proestrous rats.* Food Chem Toxicol., 2003; 41(3): 379-84.
41. Poliandri, A., Esquifino, A., Cano, P., *et al. In vivo protective effect of melatonin on cadmium-induced changes in redox balance and gene expression in rat hypothalamus and anterior pituitary.* J Pineal Res., 2006; 41(3): 238-46.

42. Pradeep, K., Reetesh, M. and Deepak, K. (2012) *Evaluation of Analgesic and Anti-Inflammatory Potential of Mimosa Pudica Linn.* International Journal of Current Pharmaceutical Research ISSN- 0975-7066., 2012; 4(4).
43. Sarah, F., Samual B., Roland, E., Titilayo A. *Testicular toxicity and sperm quality fallowing cadmium exposure in rat: Ameliorative potentials of allium cepa.* Journal of human reproductive science., 2012; 37.
44. Sebahat, T., Bünyamin, K., Günfer, T., Gülten, E. and Osman, G. *Effects of cadmium and zinc on plasma levels of growth hormone, insulin-like growth factor I, and insulin-like growth factor-binding protein 311.* Biological Trace Element Research., 2005; 108: 197-204.
45. Shackelford, T., Goetz, A., *"Adaptation to Sperm Competition in Humans".* Current Directions in Psychological Science., 2007; 16: 47. doi:10.1111/j.1467-8721.2007.00473.
46. Sharma, R., Chaphalker, S., Adsool, A. *Evaluating antioxidant potential, cytotoxicity and intestinal Absorption of flavonoids extracted from medicinal plants.* Int J Biotechol Appl., 2010; 2(1): 1-5.
47. Siu, E., Mruk, D., Porto, C. and Cheng, Y. *Cadmium-induced testicular injury.* Toxicol. Appl. Pharmacol., 2009; 240-249.
48. Sokol, R. *The hypothalamic-pituitary-gonadal axis as a target for toxicants. Comprehensive Toxicology.* Oxford: Elsevier Science., 1997; 10: 87–98.
49. Souza, P., Diamante, M. and Dolder, H. (2010) *Testis response to low doses of cadmium in Wistar rats.* International Journal of Experimental Pathology., 2010; 91(2); 125–131.
50. Stohs, S., Bagchi, D., Hassoun, E. and Bagchi, M. *Oxidative mechanisms in the toxicity of chromium and cadmium ions. J. Environ.* Pathol. Toxicol. Oncol., 2001; 20: 77-88.
51. Thirunlalai T, Viviyan, S., Elumalai, E. and David E. *Hypolipidaemic and antioxidant effect of Enicostemma littorale Blume.* Asian pac J Tropical Biomed., 2011; 381-385.
52. Turner, T. and Lysiak, J. *Oxidative stress: a common factor in testicular dysfunction.* Journal of Andrology., 2008; 29(5): 488–498.
53. Waalkes, M. and Poirier, L. *In vitro cadmium-DNA interactions: cooperativity of cadmium, magnesium and zinc.* Toxicol Appl Pharmacol., 1984; 75: 539-46.
54. Waalkes, M., Rehm, S. and Devor, D. The effects of continuous testosterone exposure on spontaneous and cadmium-induced tumors in the male Fischer (F344/NCr) rat: Loss of testicular response. Toxicol. Appl. Pharmacol., 1997; 142: 40-46.

55. Waalkes, M., Rehm, S., Coogan, T. and Ward, J. (1997a) *Role of cadmium in the etiology of cancer of the prostrate.* In target organ toxicology series: Endocrine toxicology (J.A. Thomas and H.D. Colby, eds) pp 227- 244, Raven Press, New York.
56. www.hillgreen.com/pdf/mimosapudica
57. Yamada, T., Nakamura, J., Murakami, M., Okuno, Y., Hosokawa, S., Matsuo, M., *et al. The correlation of serum luteinising hormone levels with induction of Leydig cell tumors in rats by oxolinic acid. Toxicol.* Appl. Pharmacol., 1994; 129: 146-154.