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Comparative efficacy of cinnamon extract, Cinnamaldehyde, silver nanoparticles and conjugated silver nanoparticles in attenuation of cadmium induced testicular toxicity

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Abstract
Cadmium is an environmental contaminant, a known endocrine disruptor and reproductive toxicant, The present study aims to elucidate the comparative efficacy of Cinnamon Extract (CE), Cinnamaldehyde (CA), Silver Nanoparticles (AgNPs) and Conjugated Siver Nanoparticles (CAgNPs) produced by Green synthesis, in attenuating the testicular toxicity induced by Cadmium at a dosage of 200mg/Kg Bodyweight (BW) for a period of 90 days. Six Groups of 4 rats each were selected. One group given saline and treated as control, second group given Cadmium and all the rest of the groups given Cadmium along with the respective Co-administration of CE, CA, AgNPs and CAgNPs. After treatment schedule, samples were collected and biochemical parameters - Glucose, Total Cholesterol and serum Triglyceride as well as hormonal parameters – Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH) and Testosterone (TST) were evaluated along with changes in Histo architecture of Testis. Reduction in body weight (BW), Testicular weight (TW), Glucose Level, total cholesterol and FSH Levels with increase in Triglyceride as well as LH and TST Levels were observed in rats. Deleterious changes in Histopathology of Testis seems to be attenuated to near normalcy on co-administration of the above agents to a certain extent. Of the four, conjugated AgNPs seen to give an effective reversal of Cadmium induced toxic effect.

Keywords: Cinnamon, Cinnamaldehyde, silver nanoparticles, conjugated silver Nanopartcles, cholesterol, triglyceride, FSH, LH, testosterone, glucose

1. Introduction
The occurrence of chemically induced infertility appears to have a worldwide increase. Epidemiological studies have shown the correlation between heavy metal concentrations in the body and human health. One of the most toxic industrial and environmental heavy metals is Cadmium (Cd) which act as oxidative stress inducer and an endocrine disruptor in humans and rodents (Siu *et al.*, 2009) [34]. Cadmium has long been known to damage the reproductive, hepatic and respiratory systems (WHO, 1992) [40]. Cd is extremely toxic to the testicular tissues of mice, rats and several morphological and biochemical changes in mammalian testis (Acharya, 2008). Occupational exposure to Cd, such as working with Cd-containing pigments, plastic, glass, metal alloys and electrode material in nickel-cadmium batteries, and non-occupational exposure, such as food, water and cigarette smoke induces uptake of Cd from the environment into the body through pulmonary and enteral pathways (Waisberg *et al.*,2003) [39]. Cadmium accumulates mostly in the liver, kidney and spleen (Toman *et al*., 2009) [37]. Eybl and Kotyzova, (2010) [15] reported that Cd causes damage to tissues and potentially leads to carcinogenesis. Cd stimulates the production of reactive oxygen species (ROS) in association with its inhibitory effect on mitochondrial electron transport. As a result, lipids are oxidised resulting in damage to membranes (Galazyn-Sidorczuk *et al.,* 2009) [16]. Cd affects testicular spermatogenic and steroidogenic functions impairing male fertility, degrading semen quality and inducing testicular degeneration, seminiferous tubular (ST) damage and ultimately, reproductive failure (Pandya *et al.,* 2012) [27]. The pathogenesis of Cd on testicular dysfunction is a result of a complex network of causes including modulation of apoptosis and inhibition of DNA repair enzymes and induction of oxidative stress (Oguzturk *et al.,* 2012) [26]. Cadmium induced testicular oxidative stress is mediated through depletion of reduced glutathione (GSH), generation of ROS altered antioxidant enzymes and elevated lipid peroxidation (LPO) which lead to male infertility (Bu *et al.,* 2011) [10].

Currently there is a growing interest in herbal remedies due to side effects associated with chemical therapeutic agents. Spices, herbs and medicinal plants have received increasing interest as sources of beneficial antioxidants against various diseases. Among such spices that possess medicinal wonders is Cinnamon, which is an evergreen tree that is traditionally harvested in Asian countries (Jakhetia *et al.*, 2010) [19]. Cinnamon bark is widely used as a spice. It is principally used in cookery as a flavouring material. It has been reported in previous studies that various extracts of cinnamon, such as ether, aqueous, and methanolic extracts show considerable antioxidant activities. Different flavonoids isolated from cinnamon have free-redical-scavenging activities and antioxidant properties (Rao and Gan, 2014) [30]. Cinnamon has anti-inflammatory, anti-bacterial, anti-fungal, anti-viral, anti-hyperglycaemic effects and its extract is potent antioxidant and free radical scavenger (Jakhetia *et al.*, 2010) [19].

In a study, the aqueous extract of Cinnamon increased the weight of testis, cauda epididymidis and seminal vesicles in the treated male mice, explaining a possible stimulation of hormonal levels in the animals. Also, the sperm count and motility of the treated animals are significantly higher than the control group (Shah *et al.*, 1998) [2]. It has been shown earlier that ethanolic extract of cinnamon bark improved reproductive organ weight and sperm quality (Yuce *et al.*, 2012) [42]. Oral administration of cinnamon extract elevated the sperm testosterone level, improved sperm motility and alleviated testicular degenerative changes in diabetic rats (Shalaby and Mouneir, 2010). The essential oil of cinnamon bark is constituted by >80% of cinnamaldehyde and the aqueous extract of cinnamon spice has been attributed with antioxidant properties (Roussel *et al.*, 2009) [31]. Cinnamaldehyde (CA) is a bioactive compound that has been identified to have antibacterial (Ali *et al.*, 2005) [4], anti-inflammatory (Koh *et al.*, 1998) [21], hypoglycemic, anti-mutagenic (Cabelo *et al.*, 2009) [12] and anti-tumerogenic activity.

Nano biotechnology is a promising field of nano science, which extends the horizon of nano sized systems for various newer applications both in the field of biotechnology as well as in the field of nano medicine. metal nanoparticles are found to be potential therapeutic alternatives for the treatment of various diseases including cancer (Vaidyanathan *et al.*, 2009) [38]. They can cross some of the biological barriers and achieve therapeutic concentration in tissue even with less dosage of drug administration and spares the surrounding normal tissues from toxic effect. Plant extract mediated synthesis of AgNPs are significant for its rapid rate of synthesis, simplicity and eco friendliness. In this study, AgNPs are synthesized using aqueous extract of cinnamon as the reducing agent and conjugated AgNPs are also synthesized.

As Cd was reputed to exert its toxic effects by inducing ROS generation through oxidative damage, it can be hypothesized that a potent antioxidant could retard the Cd induced deleterious alterations and ameliorate its toxic effect in biological systems. In the present study, AgNPs, conjugated AgNPs and cinnamaldehyde along with aqueous extract of cinnamon were selected as ameliorating agents and the hypothesis tested as a comparative study in Cd induction of testicular toxicity and elucidating their ameliorating effects.

2. Materials and Methods

2.1 Selection of Animal Model

Albino rats, which had comparable absorption, tissue absorption, metabolism and excretion of test compound comparable to that of human beings, were selected for the present study. Wistar strain albino rats weighing about 125-250 grams were selected. The rats were procured and acclimatized to our laboratory conditions for two weeks. The animals were housed in a well ventilated, temperature and humidity controlled animal house, with a light schedule of fourteen hours and ten hours darkness. They were fed with standard diet and drinking water was made available *ad libitum.*

2.2 Preparation of Cinnamon Extract

Cinnamomum zeylanicum bark was collected from the cinnamon fields of Spices board of India, Calicut, Kerala. It was washed to remove any impurities and dried under sunlight for a week to completely remove the moisture. The bark was cut into small pieces and powdered in a mixer and then sieved using a 20-mesh sieve to get uniform size powder. The powdered cinnamon was analyzed through gas chromatography to find out the components. For the production of aqueous extract, the 100gm of Cinnamon powder was mixed with 700 ml of double distilled water. The mixed solution was kept in the water bath maintained at 90ºC for 1 hour. The filtrate was obtained by filtering with muslin cloth. The filtrate was centrifuged for 5 min at 5800 rpm for getting a clear supernatant. The clear supernatant obtained was collected and stored in refrigerator for further use.

2.3 Preparation of Cinnamaldehyde

Cinnamaldehyde was commercially purchased from Sigma Aldrich. It is a yellowish oil obtained from the bark of Cinnamon trees. Solubility of Cinnamaldehyde is that 1.42g per litre of water. For the experimental purpose 0.142g of Cinnamaldehyde is added to 100ml of water and vigorously shaken to ensure complete dissolution.

2.4 Preparation of Cadmium Chloride

Cadmium chloride was commercially purchased from Sigma Aldrich Chemicals Pvt. Ltd., Bangalore. Cadmium chloride solution was prepared by dissolving 2mg of Cadmium Chloride in 10ml of saline and injected at a dose of 0.1ml/100g BW once a week for 90 days.

2.5 Synthesis of Silver Nanoparticles

Silver nanoparticle preparation was done using the Green synthesis method. 2mM solution and 1mM solutions of $AgNO_3$ were prepared using distilled water and $AgNo_3$ was purchased from Sigma Aldrich. 5ml of plant extract were added to 10ml of 2mM and 1mM solutions. The solutions were kept in darkness for 24 hours. Then the samples were studied for identification and characterization of nanoparticles using UV- Visible Spectroscopy, Energy Dispersive X-ray (EDX), Scanning Electron Microscope (SEM) and Fourier transform infrared spectroscopy (FTIR) analysis.

2.6 Synthesis of Conjugated Silver Nanoparticles

Nano conjugation of biosynthesized nano particle with cinnamon extract was done. The prepared Silver nanoparticles which is dispersed in 250µl of Phosphate Buffer and 250µl of Cinnamon extract is centrifuged at 12000 rpm for 20 minutes. Silver nanoparticles were collected as pellet. To the pellet 250µl of cinnamaldehyde extract added. The said solution was incubated at room temperature for 24 hours and then centrifuged at 4500 rpm again to separate the conjugated

pellet and resuspended in phosphate buffer and store it for further use.

2.7 Experimental Design

To achieve the ultimate goal of this study, healthy male albino rats were divided in to 6 groups of 4 animals which received the following regimen of treatments.

Group A: Animals received normal saline 1ml/100gm BW once in a week for 90 days and used as Normal control.

Group B: Animals were injected Cadmium Chloride 0.1ml/100g BW once a week for 90 days subcutaneously.

Group C: Animals were injected Cadmium Chloride 0.1ml/100g BW and crude extract of Cinnamon 0.2 ml/100g BW once in a week for 90 days subcutaneously.

Group D: Animals were injected Cadmium Chloride 0.1ml/100g BW and Cinnamaldehyde 0.2 ml/100g BW once in a week for 90 days subcutaneously.

Group E: Animals were injected Cadmium Chloride 0.1ml/100g BW and Silver nanoparticles 0.2 ml/100g BW once in a week for 90 days subcutaneously.

Group F: Animals were injected Cadmium Chloride 0.1ml/100g BW and crude extract of Conjugated Silver nanoparticles 0.2 ml/100g BW once in a week for 90 days subcutaneously.

All treatments were given between 9:30 to 10:00 hours in the morning. At the end of the treatment protocol, animals were anesthetized with ether and sacrificed by decapitation. Blood was collected and allowed to clot for four hours at room temperature centrifuged at 3000 rpm for 10 minutes to separate serum and stored at-20˚c until analysis. This was then used to determine the assay of hormones and lipid profile in blood. All animals were dissected and its Testis were rapidly excised, washed with saline, blotted with a piece of filter paper and weighed. A bit of tissue from the region of Testis was fixed in 10% formalin and used for histological studies.

2.8 Assay of Biochemical and Hormonal Parameters

1. Estimation of Glucose level was done by the Anthrone method. (Morris, 1948) [24].
2. Estimation of Cholesterol was done by the method of Tietz, 1963 [36].
3. Estimation of Triglyceride was done by the method of Bowers, 1988 [9].
4. Assay of Follicle stimulating Hormone (FSH) was done by the method of Midglay and Jaffe, 1971 [23].
5. Assay of Luteinizing Hormone (LH) was done by the method of Singh *et al.*, 1984 [33].
6. Enzyme Immunoassay for quantitative determination of Testosterone hormone concentration in serum based on the method of Tietz, 1995 [35].

2.9 Histological Studies

Formaldehyde – fixed samples were to be embedded in paraffin and then sliced (section thickness 4-5µm). They were to be differentiated with xylol and histological observation to be performed after staining with haematoxylin-eosin and Green masson's trichrome methods (Luna, 1968). For histological study, the sections were to be observed under a magnification of 40 X in the microscope.

2.10 Statistical Analysis

Results obtained were tabulated. Statistical analysis was carried out using Dunnetts "t" test. Any significant variation between the control and treated groups were recorded **(**Steele and Torrie, 1960).

3. Results

3.1 Effect on Body Weight

When compared to normal control, a significant decrease in weight gain can be observed in Cadmium (Cd) induced group. A significantly increased weight gain can be seen to be brought about by supplementation with Crude Extract of Cinnamon (CE), Cinnamaldehyde (CA), Silver Nanoparticles (AgNPs) and conjugated Silver Nanoparticles (CAgNPs), the highest weight gain being caused by AgNPs supplementation to Cd induced groups, when compared to Cd induced control (Figure.1)

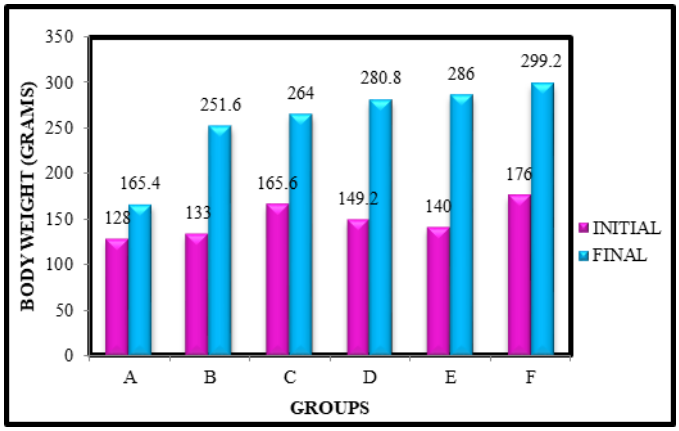

Fig 1: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in Body weight of Albino Rats

3.2 Effect on Testis Weight

A slight decrease in testicular weight can be observed in Cd induced group when compared to normal control. But while supplementation with CE as well as CA is seen to bring about a near normal testicular weight increase, a slight decrease on conjugated AgNPs supplementation and very significant decrease on AgNPs supplementation to Cd induced group can be observed (Figure.2)

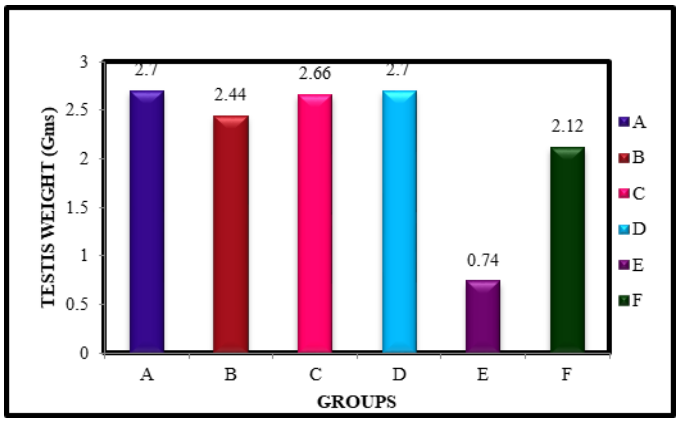

Fig 2: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in weight of Testis in Albino Rats

3.3 Effect on Hormonal Profile

Induction of Cd is observed to bring about a significant decrease in FSH level only when compared to normal control. Supplementation of CE, CA, AgNPs and CAgNPs to Cd induced groups is seen to produce a varied response. While the level of FSH and LH are observed to be significantly decreased on supplementation with CE, TST level is significantly increased. Similarly CA supplementation is also observed to bring about a significant decrease in FSH and LH levels. Supplementation with AgNPs is observed to significantly increase FSH level only, while LH level becomes decreased significantly. Conjugated AgNPs supplementation is observed to bring about a near normal increase in FSH and LH level, but a significant decrease in testosterone level, when compared to Cd induced group. (Figure. 3, 4 and 5).

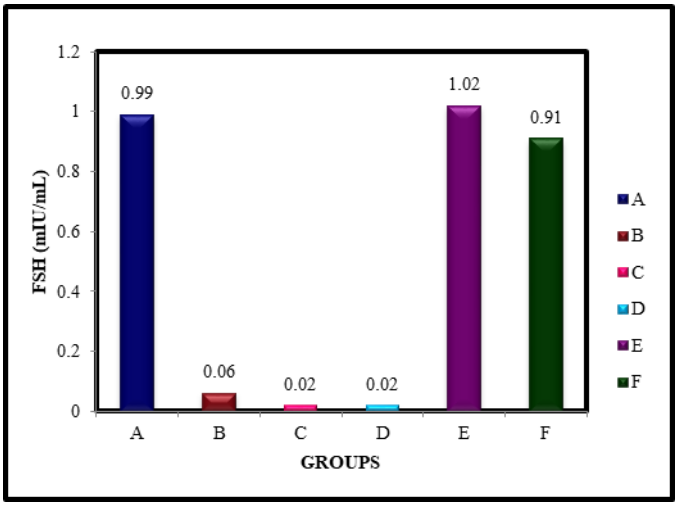

Fig 3: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in Hormonal level of Follicle Stimulating Hormone (FSH) in Albino Rats

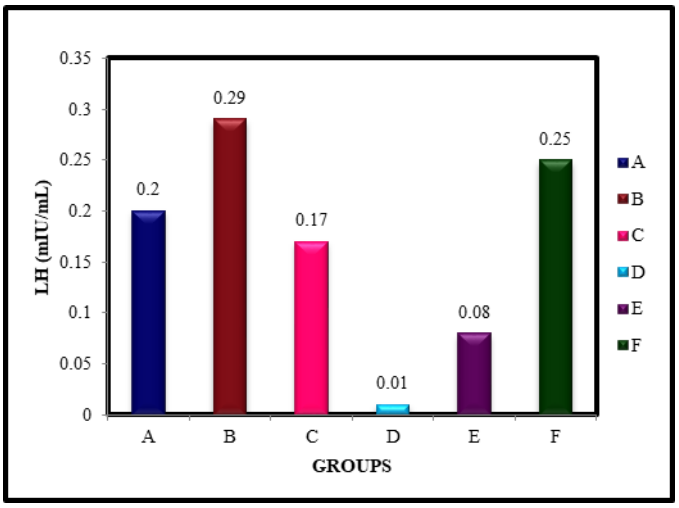

Fig 4: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in Hormonal level of Luteinizing Hormone (LH) in Albino Rats

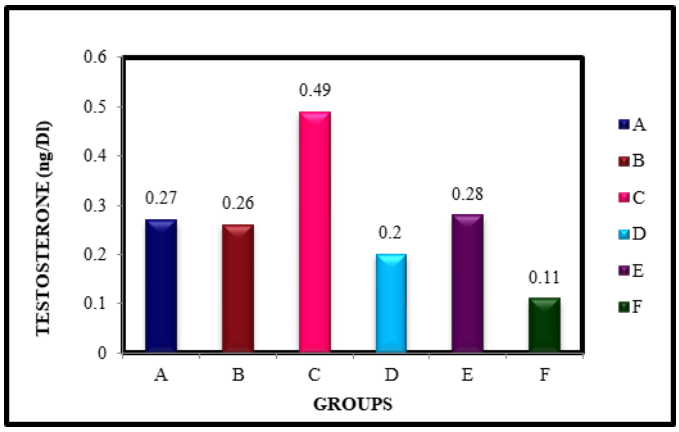

Fig 5: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in Testosterone level in Albino Rats

3.4 Effect on Lipid Profile

While compared to normal control, the level of cholesterol is significantly decreased while triglyceride level is increased on induction of Cd. On comparison with Cd induction, all the four supplementation groups expressed a significant decrease in cholesterol level, while a significant increase in triglyceride level can be observed on AgNPs and Conjugated AgNPs supplementation. (Figure. 6 and 7).

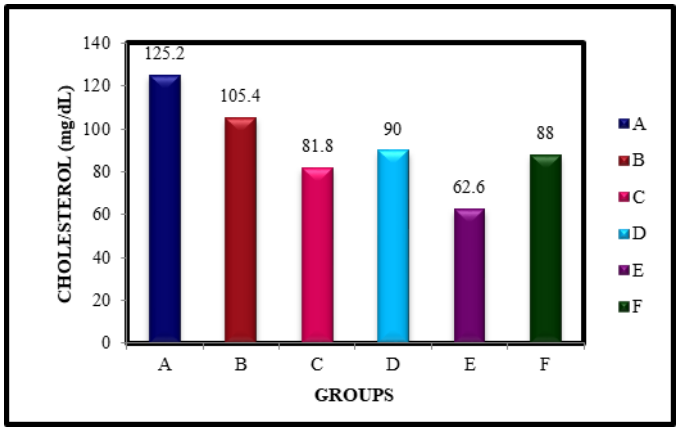

Fig 6: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in Level of Cholesterol in Albino Rats

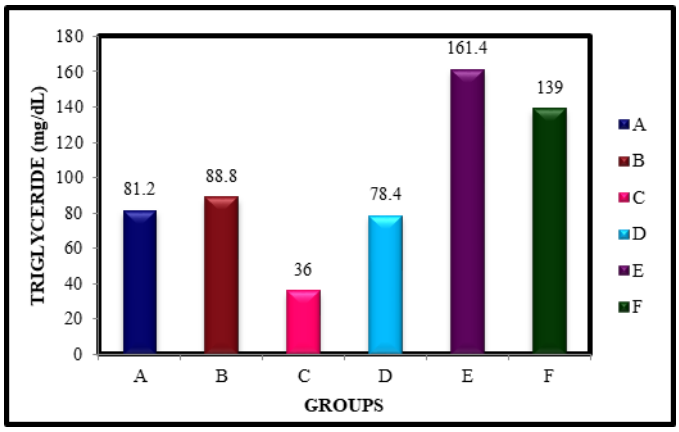

Fig 7: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in Level of Triglyceride in Albino Rats

3.5 Effect on Blood Glucose

A slight reduction in glucose level can be observed in CD induced group on comparison with control group. When compared to Cd induced group, while crude cinnamon extract supplementation seems to cause no significant change, supplementation with CA, AgNPs and Conjugated AgNPs to Cd induced group was observed to drastically reduce the level of glucose (Figure. 8).

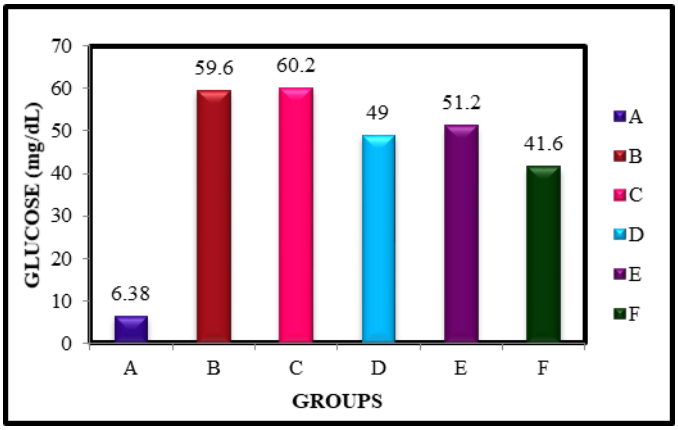

Fig 8: The Effect of Cinnamon extract, Cinnamaldehyde, Silver Nanoparticle and Conjugated Silver Nanoparticles on the Cadmium induced changes in Glucose Level of in Albino Rats

3.6 Effect on Testis Histology

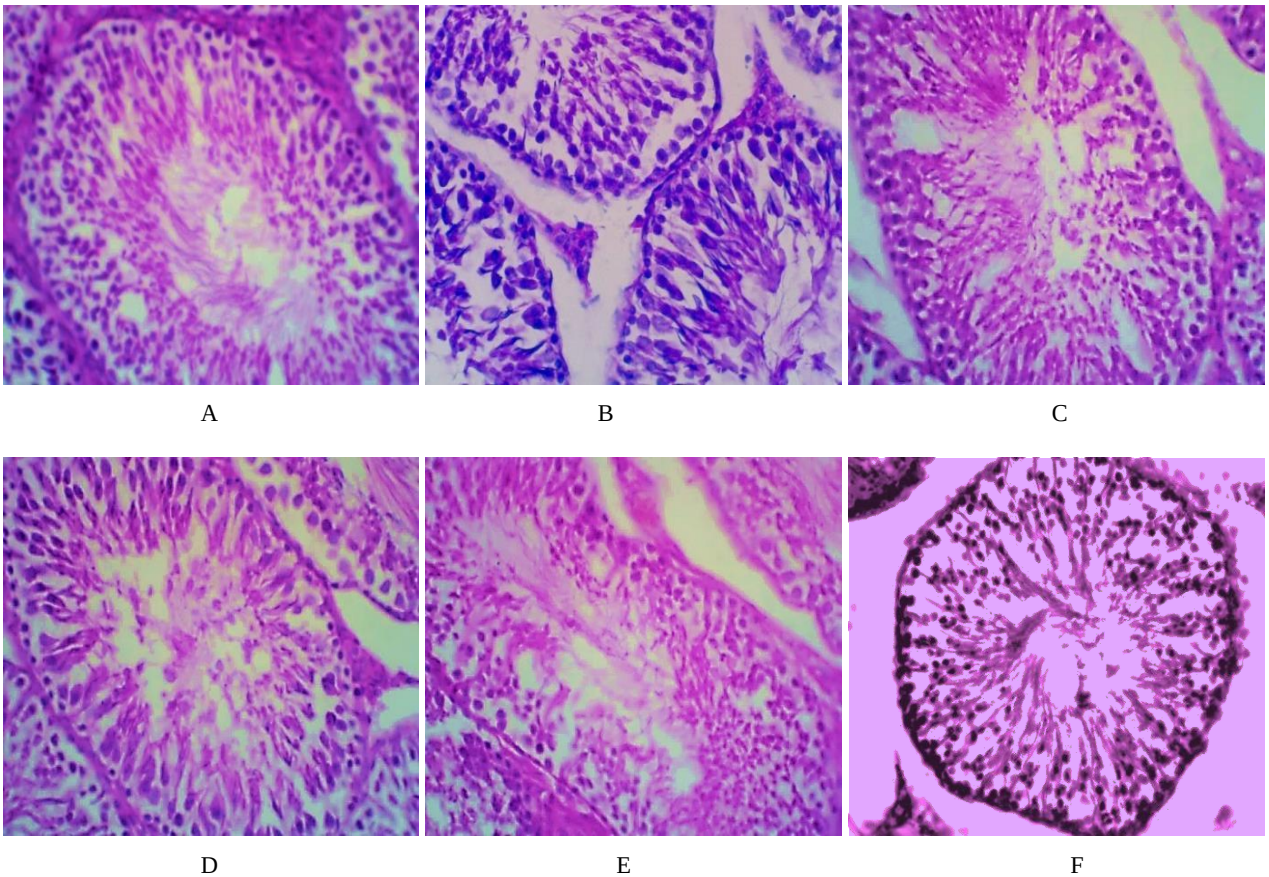

Fig 9: (A) Normal Testis section shows seminiferous tubules lined by stratified germinal epithelium with aggregations of sperm in the lumen. (B) Cd induction was observed to cause shrinkage of seminiferous tubules and diminished germinal epithelial layer. (C) Supplementation with crude cinnamon extract seen to cause slight congestion and vacuoles within the seminoferous tubules as well as increase in interstitial space. (D) Supplementation with Cinnamaldehyde observed to cause slightly shrunken tubules but spermatogenic cells are well maintained with sperm production in lumen. (E) Silver nanoparticle supplementation also seen to bring about slight dearrangement of tubular epithelium and spermatogenic cell development. (F) Conjugared Silver Nanoparticle supplementation observed to cause shrinkage of seminiferous tubule but spermatogenesis process seems to be maintained as seen by occurrence of sperm in lumen.

4. Discussion

Body weight (BW) changes reflect the changes in the internal milien. Khaki *et al.*, (2014) [20] have reported about the significant decrease in body weight but no significant change in testicular weight (TW) on Streptozoin (STZ) induction, when compared to control group. Increase in BW to near normal levels was seen to be brought about by co-adminisration with ginger and cinnamon. Significant

reduction in BW as well as TW on STZ induction and an increase in co-administration with a herbal blend of ginger, clove and cinnamon has been reported by Abraham and Al-Shahly (2015) [17] in accordance with the prior study by Al-Amin *et al.,* (2006) [2]. Adamkovica *et al.,* (2014) [1] have also reported abut the significant difference in final BW of rats given Cd, diazinon and mixture of Cd and diazinon, but significant increase in testis weight on Cd induction as welll as simultaneous exposure to Cd and diazinon. Albasha and Azab (2014) [3] have also reported about the decrease in BW on $CdCl_2$ induction and increase on co-administration with fenugreek seeds, rosemary as well as cinnamon. In the present study also, Cd induction is observed to significantly reduce the BW and slightly reduce the testicular weight on comparison to normal group. Co-supplementation with CE, CA, AgNPs and CAgNPs were seen to significantly increase the BW to above normal level, while in the case of testicular weight AgNPs supplementation is seen to significantly reduce TW, while other supplementations are observed to increase TW of normal level.

Treatment with $CdSO_4$ caused a significant decrease in TW when compared to control in the study of Ige *et al.,* (2012) [18]. Elgawish and Ghanem (2014) [14] have also reported about a signnificant reduction in relative weight of testis on Cd induction. Therefore the reduction on BW may be due to increase of muscle wasting as well as loss of tissue protein due to cadmium. The increase on co-supplementation may be due to control of muscle wasting and formation of tissue protein.

The Blood Glucose concentration was reported to be increased on STZ treatment, which on co-administration with herbal blend of giner, cinnamon and clove reduced to near normal levels (Ibrahim and Al-Shathly, 2015) [17]. In the present study, Cd treatment is observed to bring about slight reduction in glucose level. While CE supplementation maintains near normal level of glucose, the other supplementation with CA, AgNPs and conjugated AgNPs further reduced the glucose level significantly. As cinnamon supplementation facilitates glucose dispersal in healthy hormone, this may be shifted by enhancing insulin sensitivity by increasing phosphorylation of signalling proteins as well as by insulin-sensitive glucose -4 –mediated glucose uptake into muscle cells. Methyl hydroxylchalone polymers of cinnamon are thought to be effective insulin mimetics which may activate the cell's utilization of glucose. Mahmood *et al.,* (2011) [22] have also reported about the significant decrease in blood glucose concentration on dosing with 200mg and 400mg/Kg BW of cinnamon extract to rats. The hypoglycaemic effect of Cinnamon Oil (CO) was also reported by Ping *et al*., (2010) [28] that 100mg of CO significantly decreased fasting blood glucose concentration. Therefore co-administration of CE and CA as well as AgNPs and conjugated AgNPs seems to have brought about a hypoglycaemic effect.

Cd accumulation in testis induces oxidative stress by two mechanisms by reacting with sulfhydryl groups of various proteins or by glutathione depletion. Cd toxicity alters testicular function and reduces fertility by lowering sperm count and motility (Yang *et al.,* 2006) [41]. Androgenesis in testis starts with synthesis of cholesterol followed by its transport within the steroidogenic testicular tissues and its metabolism to form steroid biosynthesis. The increased production of LH and FSH allows synthesis of Cholesterol by activating the enzymes of Cholesterol biosynthesis. LH and FSH production regulates the uptake of cholesterol esters by steroidogenic cells. The marked decrease in serum levels of testosterone is due to decreased synthesis and availability of cholesterol, thus resulting in down regulation of steroid biosynthesis (Barlow *et al.,* 2003) [6]. Following cholesterol biosynthesis, StAR transports it to the inner mitochondrial membrane. Cd induction decrease serum level of LH, as LH is responsible for steroidogenesis through StAR activation in steroidogenic cells (Fauser, 1999).

Regarding lipid profile, dosage of 200mg of CE brought about slight or no remarkable change in the level of serum cholesterol, triglyceride and lipoproteins (Mahmood *et al*., 2011) [22]. The study by Blevins *et al.,* (2007) [8] reported that oral administration of Cinnamaldehyde (20mg/kg BW) decreases serum total cholesterol and triglyceride levels significantly. The results of this experimnetal study thus indicates the hyolipidaemic effect of CA. Amin and El-Twab (2009) [5] have proposed the mechanism that CE may improve the postprandial over reproduction of intestinal apo B 48-containing lipo proteins by ameliorating intestinal insulin resistance ad thus be beneficial in controlling lipid metabolism. Thus in the present study, while Cd induction significantly reduced serum cholesterol level, but increased the triglyceride level. Co-administration of CE, CA, AgNPs as well as CAgNPs were observed to significantly reduce the cholesterol level. The triglyceride levels were observed to be significantly increased on AgNPs and CAgNPs supplementation only in Cd induced groups.

Regaring hormonal control, in the present study while Cd was seen to bring about a significant decrease in FSH level only, co-administration of CE and CA were seen to further significantly reduce FSH and LH level, while AgNPs and CAgNPs supplementations were seen to significantly increase FSH level to near normalcy. Cd induction significantly increased serum LH levels and only conjugated AgNPs were effective in reverting LH levels to near normalcy. In the rats, the ultimate number of Sertoli cells in adult testis is determined by both the rate and duration of proliferative phase. So, the hormonal factors controlling the rate and duration of Sertoli cell proliferation are critical determinants of fertility. Previous studies have observed that FSH is a mitogenic factor during Sertoli cell proliferative phase (Buzzard *et al.,* 2000) [11]. But Khaki *et al*., (2014) [20] have reported about the reduction in serum LH, FSH and TST levels in STZ treated rats The administration of ginger, cinnamon and combination caused significant increase in LH, FSH and TST levels in serum of STZ treated rats.

Obianime and Roberts (2009) [25] have reported about the biphasic dose dependant increase followed by decrease of FSH and LH, which in turn induced the signals for TST synthesis (Cooke *et al.,* 1981) [13]. Inhibition of serum hormonal level of FSH and LH results in inhibition of TST levels resulting in reproductive dysfunction and cell death. Leydig cell damage and tumor of testis due to perturbation of TST production and overstimulation of testicular interstitial due to increase in serum LH also observed. This results in reduction in normal feedback inhibition in rats. The loss of TST feedback can result in disruption of Testis - pituitary axis contributing to both testicular and pituitary dysfunction.

Testis is sensitive to environmental exposure induced cellular damage. Administration of $CdCl_2$ was observed to alter testicular functions through reduction in organ weight, deckine in sperm cell concentration, increase sperm abnormality and reduction of seminiferous tubule diameter.

The marked reduction in TW may be a reflection of the reduced tubular diameter observed in other studies (Blanco *et al.,* 2007, Ponnusamy and Pari, 2011) [7, 29] inducing severe haemorrhage, edema, necrosis and atrophy of seminiferous tubules. Thus deformed serminiferous tubules, loss and regeneration of spermatogenic cells and pyknotic Leydig cells are observed on Cd induction. Disruption of seminiferous tubule structure and decrease in spermatogenic cell series has been documented by Ibrahim and Al-Shahly (2015) [17], on STZ treatment. These changes were reversed on administration of herbal blend of Cloves, Ginger and Cinnamon. Similarly in the present study, co-administration of CE is seen to bring about a reversal with appearance of normal looking seminiferous tubules and spermatogenic cells as well as, spermatids in the lumen, even though slight shrinkage of seminiferous tubules is evident. Co-administration of CA also is seen to bring about the occurence of normal looking seminiferous tubules with intact Leydig cells and normal spermatogenic process. The Seminiferous tubles of AgNPs administered groups also showed a regeneration to near normal overall appearance, but internally disorganization of spermatogenic cells is still evident. Though co-administration of CAgNPs seen to express a shrunken histoarchitecture of seminiferous tubules with wide interstitial spaces, internally the spermatogenic cells seems to have redeveloped their spermatogenic machinery, as evidenced by increase in FSH and LH which are needed for the normal sertoli cell function even though a reduced TST level is observed. Thus CE seems to be more beneficial in the reversal of Cd induced changes than conjugated AgNPs in the restoration of disrupted hormone levels.

5. Conclusion

In the present study, the eluciation of the most effective attenuation of Cadmium induced Testicular Toxicity by usage of crude extract of Cinnamon, Cinnamaldehyde (Its potent constituent), Silver Nanoparticle and Conjugated Silver Nanoparticle through study of glucose level, lipid profile, hormonal profile and histopathology of Testis has been undertaken. Of the four agents Cinnmaldehyde and Conjugated Silver Nanoparticles seem to be better attenuating agents. Further research is required to confirm a better dosage potential for reducing complication which may arise as a result of environmental and occupational exposure to such deleterious agents.

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