Therapeutic effects of date palm (*Phoenix dactylifera* L.) pollen extract on cadmium-induced testicular toxicity

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**Summary**
Cadmium (Cd) is a well-known testicular toxicant. This study was designed to explore the long-term effects of a single low dose of Cd on spermatogenesis, and testicular dysfunction and oxidative stress, and the therapeutic potential of date palm pollen extract (DPP) in averting such reproductive damage. Adult male Wistar rats received a single intraperitoneal injection of CdCl₂ (0 or 1 mg kg⁻¹). Twenty-four hours later, they started receiving DPP (0 or 40 mg kg⁻¹) orally, once daily for 56 consecutive days. Cd exposure caused significant reproductive damage via reduced weight of the reproductive organs, which includes spermatological damage (decreased sperm count and motility and increased rates of sperm abnormalities), increased oxidative stress (increased malondialdehyde and decreased reduced glutathione levels), histological alterations (necrosis, inefficient to completely arrest spermatogenesis and a reduced Johnsen’s score) and decreased serum testosterone level. DPP restored spermatogenesis and attenuated the toxic effects of Cd on the reproductive system to the levels observed in the control animals. These findings support the hypothesis that the testis is particularly sensitive to Cd, which can cause testicular damage and infertility. Treatment with DPP can ameliorate the deleterious effects of Cd, probably by activating testicular endocrine and antioxidant systems.

**Introduction**
Cadmium (Cd) is one of the most toxic industrial and environmental heavy metals. It acts as an endocrine disruptor and oxidative stress inducer in humans and rodents (Takiguchi & Yoshihara, 2006; Siu *et al.*, 2009). Cadmium has long been known to damage the hepatic, respiratory and reproductive systems (WHO, 1992). It has been demonstrated that Cd is extremely toxic to the testicular tissues of rats and mice, and several morphological and biochemical changes in the mammalian testis (Acharya *et al.*, 2008; Siu *et al.*, 2009). Cadmium has also been reported to affect testicular spermatogenic and steroidogenic functions, impair male fertility, degrade semen quality and cause testicular degeneration, seminiferous tubular (ST) damage and ultimately, reproductive failure (El-Demerdash *et al.*, 2004; Thompson & Bannigan, 2008; Siu *et al.*, 2009; Pandya *et al.*, 2012). These studies illustrate the vulnerability of the testis to Cd toxicity, although the underlying mechanisms remain poorly understood. It seems that the pathogenesis of testicular dysfunction following Cd exposure is likely the result of a complex network of causes including induction of oxidative stress, modulation of apoptosis and inhibition of DNA repair enzymes (Thompson & Bannigan, 2008; Obianime & Roberts, 2009; Bu *et al.*, 2011; Kalender *et al.*, 2012; Oguzturk *et al.*, 2012). Cadmium-induced testicular oxidative stress is mediated through generation of reactive oxygen species (ROS), depletion of reduced glutathione (GSH), elevated lipid peroxidation (LPO) and altered antioxidant enzymes, which can ultimately result in male infertility (Sen Gupta *et al.*, 2004; Kara *et al.*, 2005; Siu *et al.*, 2009; Bu *et al.*, 2011). Supplementation with vitamin E, vitamin C, α-lipoic acid and beta-carotene, which act as antioxidants and free radical scavengers, has been found to be effective against...
Cd-induced testicular damage (El-Demerdash et al., 2004; Obianime & Roberts, 2009). Therefore, it is conceivable that antioxidant agents might prevent or at least reduce Cd-induced testicular toxicity.

Herbal medicines are increasingly being used worldwide. In traditional medicine, a suspension of date palm (Phoenix dactylifera L.) pollen (DPP) grains is a herbal therapy that is widely used as a folk remedy for curing male infertility (Zaid, 1999; Zargari, 1999; Khare, 2007). Approximately, 1000 tons of DPP are produced every year by millions of palm trees grown in the Arabian region. DPP differs from bee pollen in that it is of a known source; it is homogeneous, pure and easily standardised. DPP was reported to elicit gonad-stimulating activities (Soliman & Soliman, 1958) and to promote fertility in women in ancient Egypt (Bajpayee, 1997). DPP and male palm flowers were traditionally regarded as aphrodisiacs and fertility enhancers (Zaid, 1999; Khare, 2007). DPP extracts contain oestrogenic compounds, oestrones – gonad-stimulating compounds that can improve male infertility and elicit gonadotrophin activity in rat models (Dostal et al., 1996; Bajpayee, 1997). Reports have also identified microelements contained within DPP that contain sterols and other agents that might influence male fertility (Bennet et al., 1966; Bajpayee, 1997). In regard to these components, some snack foods have been supplemented with date pollen to improve male infertility (Abde-el-Mageed et al., 1987). Pollen mixed with honey has been eaten as an aphrodisiac since ancient times (Kikuchi & Miki, 1978). However, the fertility effects of DPP, as used in traditional medicine, are not widely scientifically supported, with the exception of one experimental study that elucidated beneficial effect of a suspension of DPP on semen quality in normal male rats (Bahmanpour et al., 2006).

Depending on the dosage and duration of the exposure, previous studies have demonstrated that both short- and long-term exposure to low or high doses of Cd were sufficient to induce testicular injury at the interstitial and tubular levels (Hew et al., 1993; Blanco et al., 2007; de Souza Predes et al., 2010). Conversely, to our knowledge, the long-term effects of a single low dose of Cd on male fertility remain obscure. We therefore sought to investigate this issue using sperm characteristics as an indicator of semen quality, Johnsen’s criteria to clarify the effects on spermatogenesis, histopathological studies for the assessment of testicular structure and lastly, measurement of testicular oxidative status and serum testosterone assays. Furthermore, we aimed to assess the anti-infertility effects of DPP on Cd-induced male reproductive toxicity.

Materials and methods

Chemicals and reagents

Cadmium chloride (CdCl₂) and 5,5-dithiobis-(2-nitrobenzoic acid) (DTNB, Ellman’s reagent) were purchased from Sigma Chemical Co. (St. Louis, MO, USA). GSH and thiobarbituric acid (TBA) were purchased from Fluka (Buchs, Switzerland). All other reagents used were of the best available pharmaceutical grade.

Collection and extraction of DPP

The DPP sample was obtained from a local herbal market in Damietta Governorate, Egypt, and authenticated at the Herbarium of the Biology Department, Faculty of Science, Alexandria University. One hundred grams of DPP powder was extracted with 80% ethanol using a 300VT Ultrasonic Homogeniser (BioLogics, Inc. Manassas, VG, USA) at a temperature below 25 °C. The extract was evaporated under reduced pressure, lyophilised to give 15 g of a yellow semi-solid residue and protected from light at 4 °C until use.

Animals and experimental procedures

Thirty-two healthy adult male Wistar rats aged 10 weeks and weighing 150 ± 20 g were obtained from a closed random-bred colony at the Medical Research Institute of Alexandria University. All rats were housed in gang cages under standard laboratory conditions (12 h light–dark cycle and 24 ± 3 °C) and fed a standard commercial laboratory-pelleted diet (Damanhur Feed Co., Al-Buhkeyra, Egypt). Food and water were provided ad libitum. The animal experiments were performed in accordance with the Guidelines for the Care and Use of Laboratory Animals of the National Institutes of Health (NIH), and the study protocol was approved by the local authorities. All efforts were made to minimise the number of rats used and their suffering. After 10 days of acclimatisation, the rats were randomly divided into four experimental groups of eight rats per group. The individual groups received vehicle, CdCl₂ (1 mg kg⁻¹ body weight [bwt], i.p.), DPP (40 mg kg⁻¹ bwt, p.o.) or CdCl₂ plus DPP respectively. Isotonic saline (0.3 ml kg⁻¹ bwt, i.p.) and distilled water (0.1 ml kg⁻¹ bwt, p.o.) were the vehicles used to administer CdCl₂ and DPP respectively. Isotonic saline and CdCl₂ were administered only once, and 24 h after dosing, the distilled water and DPP were administered daily for 56 consecutive days. The dose of CdCl₂ was based on the lowest dosage that is known to induce testicular toxicity in rats (Hew et al., 1993; de Souza Predes et al., 2010). The dose of DPP was determined based on a pilot study conducted in our laboratory. The
56-day treatment period was chosen based on the time necessary to complete a spermatogenic cycle in rats (Russell et al., 1990).

Collection of blood, reproductive organs and tissue samples

On day 56, the rats were deprived of food overnight, individually weighed and anaesthetised with diethyl ether. Blood was collected from the retro-orbital plexus into anticoagulant-free test tubes, and the serum was removed and stored at −20 °C until determination of the serum testosterone level. The rats were then immediately sacrificed by cervical decapitation. The testes, epididymides and accessory sex organs (seminal vesicles and prostate glands) were excised and weighed, and the index weight (I.W.) of the excised organs was calculated as follows: I.W. = organ weight (g)/bwt (g) × 100. One testis, epididymis, prostate and seminal vesicle from each rat were removed, thoroughly washed with physiological saline (NaCl 0.9%), blotted on filter paper, rapidly fixed in modified Davidson’s fluid for 48 h and stored in 70% alcohol until further processing (Latendresse et al., 2002). The other testis was kept at −70 °C for subsequent assaying of GSH and LPO content.

Assessment of sperm production

Epididymal spermatozoa were counted using a modified method of Yokoi et al. (2003). Briefly, the epididymis was minced in 5 ml saline, placed in a rocker for 10 min and incubated at room temperature for 2 min. The supernatant was diluted 1 : 100 in a solution containing 5 g NaHCO₃, 1 ml formalin 35% and 25 mg eosin per 100 ml distilled water. Approximately, 10 μl of the diluted semen was transferred to each counting chamber of an improved Neubaur haemocytometer (Depth 0.1 mm; LABART, Munich, Germany) and was allowed to stand for 5 min before counting under a light microscope at ×200 magnification.

Evaluation of sperm motility and morphology

Sperm progressive motility was evaluated microscopically within 2–4 min of isolation from the cauda epididymis, as previously described (Sönmez et al., 2005). Fluid was obtained from the cauda epididymis with a pipette and diluted to 2 ml with Tris buffer solution. The percentage of motile sperm was evaluated at ×400 magnification. The percentage of morphologically abnormal spermatozoa was determined after staining with eosin–nigrosin stain (Evans & Maxwell, 1987): a total of 300 sperm were counted on each slide under a light microscope at ×400 magnification.

Biochemical assays

Each frozen testis was homogenised in 50 mM Tris–HCl buffer (pH 7.4) containing 1.15% KCl, and the homogenate was centrifuged at 10 000 g for 15 min at 4 °C. Aliquots of the supernatant were used for spectrophotometric assessment of the levels of GSH, using Ellman’s reagent (Sedlak & Lindsay, 1968) with a method based on the reductive cleavage of DTNB by a sulphhydryl (-SH) group to yield a yellow colour with maximum absorbance at 412 nm, and LPO, which was assayed as malondialdehyde (MDA) after the reaction with TBA (Buege & Aust, 1987). Serum testosterone was determined using an enzyme immunoassay kit (Immunometrics Ltd., London, UK).

Spermatogenesis evaluation (Johnsen’s score)

Spermatogenesis and spermatogenetic activity and organisation were graded using Johnsen’s Scoring System (Johnsen, 1970). Five different cross-sections cut at right angles to the longitudinal axis of the seminiferous tubules (STs) were evaluated under a light microscope at ×400 magnifications. In each cross-section, twenty randomly selected STs were systemically evaluated; each tubule was given a score ranging from 1 to 10 according to the presence or absence of the main cell types arranged in the order of maturity, as described by Johnsen, as follows: 10 = full spermatogenesis with normally organised tubules; 9 = many late spermatids but disorganised tubular epithelium; 8 = only a few late spermatids; 7 = no late spermatids, but many early spermatids; 6 = only a few early spermatids; 5 = no spermatids or spermatocyte, but many spermatocytes; 4 = no spermatids, few spermatocytes, and arrest of spermatogenesis at the primary spermatocyte stage; 3 = only spermatogonia; 2 = no germ cells, only Sertoli cells are present; and 1 = no semiferous epithelial cells, but tubular sclerosis is present. The mean score was determined for each group.

Histopathological examination

The fixed specimens were processed using conventional paraffin-embedding techniques. From the prepared paraffin blocks, 5-mm-thick sections were obtained and stained with haematoxylin and eosin (H&E) for light microscopic examination.

Statistical analysis

Statistical analysis was performed using SAS software (SAS Inc., Cary, NC, USA). The data were analysed using analysis of variance (ANOVA) with Duncan’s multiple range test to compare treatment means at P ≤ 0.001. All data are expressed as the mean ± standard error (SE).
Results

Generally, all experimental animals were healthy without any clinical signs of toxicity or mortality throughout the entire experimental period.

Reproductive organs I.W

The I.W. of the reproductive organs (i.e. the testes, epididymides and accessory sex glands) was significantly lowered in Cd-exposed rats relative to the controls. Treatment of rats with DPP alone failed to elicit significant change in the I.W. of the reproductive organs. However, treatment of Cd-challenged rats with DPP restored the I.W. of the reproductive organs to weights similar to those in the control group (Fig. 1).

Sperm parameters

Compared with the control group, we observed a significant decrease in the sperm count in the Cd-treated rats; however, sperm count improved following treatment with DPP. The administration of DPP alone also significantly increased sperm count (Fig. 2a). Sperm motility was significantly impaired in Cd-treated rats and significantly improved following DPP supplementation, albeit not to the control level. However, it was insignificantly altered in DPP-alone-treated rats (Fig. 2b). The total number of sperm abnormalities (head and tail) was significantly increased in Cd-treated rats; however, these abnormalities were markedly improved by subsequent treatment with DPP. Moreover, there were no significant differences in sperm abnormalities between the rats treated with DPP alone and the control group (Fig. 2c).

Testicular antioxidant status

The levels of GSH and LPO, two markers of testicular oxidative stress, were significantly affected by Cd treatment; the GSH level was significantly decreased, and the

Fig. 1 Index weight of the reproductive organs (i.e., testes, epididymides and accessory glands) of rats exposed to cadmium (Cd) and/or date palm pollen extract (DPP). All values are expressed as mean ± SE, n = 5. The values indicated by different letters are significantly different among groups (P ≤ 0.001, ANOVA with Duncan’s multiple range test). Index weight = organ weight (g)/bwt (g) × 100.

Fig. 2 Sperm parameters: sperm count (a), motility (b) and incidence of abnormalities (c) in rats exposed to cadmium (Cd) and/or date palm pollen extract (DPP). All values are expressed as mean ± SE, n = 5. The values indicated by different letters are significantly different (P ≤ 0.001, ANOVA with Duncan’s multiple range test).
MDA level was significantly increased. Treatment with DPP alone significantly increased the GSH level without changing the MDA level compared with the control group. Notably, DPP significantly improved the levels of GSH and MDA in Cd-treated rats, albeit not to the levels in the control group (Fig. 3a,b).

Serum testosterone levels
Exposure to Cd resulted in a significant decline in serum testosterone levels. Treatment with DPP alone did not significantly affect testosterone levels, but did markedly improve testosterone levels in Cd-treated rats compared with the control group (Fig. 3c).

Evaluation of spermatogenesis
Based on Johnsen's scoring system, spermatogenesis was markedly worse in the Cd-treated group than in the control group. Spermatogenesis was significantly improved by the administration of DPP in the Cd-treated group, albeit not to the level in the control group. Furthermore, administration of DPP alone triggered germ cells to enter the late spermatid and maturation phases (Fig. 3d).

Pathologic findings
Compared with the testes of control rats (Fig. 4a), the rats in the Cd-treated group had firm, atrophied, greyish-white testes (Fig. 4b). The testes were of normal testicular morphology in rats treated with DPP alone or with Cd followed by DPP.

Upon microscopic examination of the testes of control animals, the STs were compactly arranged, each tubule exhibiting a narrow-to-spacious lumen that either contained sperm or was empty. The tubular epithelium was highly intact and contained Sertoli cells resting on the basement membrane, together with spermatocytes and spermatagonia. Round and elongated spermatids were embedded in or associated with the Sertoli cells at different stages of the spermatogenic cycle (Fig. 5a). The epididymides of control rats were histologically normal, and their tubules were impacted with spermatozoa (Fig. 5b). A similar histological structure was observed in the
DPP-treated group, and most of the STs were in the terminal stages (stages VII and VIII) of the spermatogenic cycle (Fig. 6).

In the Cd-treated group, all of the rats developed severe testicular lesions; these included degeneration, necrosis and atrophy of 88% of the STs (Fig. 7a). Approximately, 10% of the STs showed complete necrotic changes, hyalinisation and mineralisation, while 64% showed a Sertoli cell–only pattern with complete cessation of spermatogenesis (Fig. 7b), 14% lined with spermatogonia and exhibited severe hypospermatogenesis and 12% showed active spermatogenesis. Leydig cell aggregation was the prominently observed feature; this phenomenon resulted from the relative abundance of these cells as the tubule volume fraction had markedly declined (Fig. 7b). All of the testicular blood vessels were intact (Fig. 7c). The epididymides of Cd-treated rats were histologically normal, but the tubules were either empty or impacted with dead spermatogenic cells (Fig. 7d).

Spermatogenesis was restored in most of the STs (84%) in rats treated with Cd plus DPP. This phenomenon resulted in histological features similar to those in the control group, except for a few STs that were lined with Sertoli cells only (7%) and others that were only lined with spermatogonia (9%). Aggregation of Leydig cells neighbouring the damaged STs was rarely observed (Fig. 8a). Treatment with DPP markedly reduced the testicular lesions caused by Cd, and a normal number of epididymal spermatozoa was found within the lumen in these rats (Fig. 8b). There were no significant morphological or histopathological changes in the seminal vesicles or prostate glands of rats in any of the experimental groups compared with the control group.

**Discussion**

Our interest in the reproductive toxicity of Cd developed from observations that the testis is very sensitive to Cd, which causes profound testicular damage and irreversible infertility (Takiguchi & Yoshihara, 2006; Blanco et al., 2007; de Souza Predes et al., 2010; Oguzturk et al., 2012). In the current study, we investigated the delayed effects of a single low dose of Cd (1 mg kg⁻¹ bwt) on testicular pathophysiology as well as the therapeutic possibilities of...
DPP against Cd-induced toxicity and infertility. The present results indicate that Cd significantly reduced the relative weights of the testes, epididymides and accessory sex glands and lowered the epididymal sperm concentration, suppressed sperm motility and increased the percentage of sperm abnormalities. These effects were associated with a reduction in serum testosterone levels. Our findings, which are consistent with previous reports (Acharya et al., 2008; El-Shahat et al., 2009; de Souza Predes et al., 2010; Yari et al., 2010), confirm the organotoxic and spermiotoxic effects of Cd in rats. Cadmium has been reported to induce necrotic degenerative changes in the testes (El-Shahat et al., 2009; de Souza Predes et al., 2010), which may contribute to the reduced testicular weight and decreased sperm count and motility (WHO, 1992; Wang et al., 2007). Exposure to Cd also disrupts the tight junctions between Sertoli cells and alters Sertoli–germ cell adhesion (Hew et al., 1993) with consequent exfoliation of immature cells into the lumen of STs, leading to a reduction in viable sperm count. Furthermore, our results showed that STs containing Sertoli cells–only pattern are the predominant tubular type. Therefore, it seems likely that spermatogonial stem cells are the target spermatogenic stage for Cd pathophysiology. These spermatogonial cells were affected to a greater extent than the endothelium as there were no visible changes in the integrity of the vascular endothelium, which confirms the hypothesis that Cd damages the seminiferous epithelium at lower concentrations than are required to damage the testicular endothelium (Hew et al., 1993). Thus, it appears likely that Cd can induce STs atrophy, markedly suppress spermatogenesis and cause abnormalities in spermatozoa.

The decreases in the weight of the sex organs, sperm count and sperm motility may also be a direct consequence of LPO and altered membrane properties that lead to atrophy of the sex organs and to the death of germ cells at different stages of development (Hew et al., 1993; El-Demerdash et al., 2004; Acharya et al., 2008). Our study revealed that Cd exposure markedly increased testicular oxidative stress, as reflected by the significant depletion of GSH and concomitant increase in MDA levels, thereby leading to irreversible cell damage in the testicular tissues and deterioration of sperm characteristics. Sen Gupta et al. (2004) reported that Cd possesses a
strong affinity for the thiol groups of amino acids, particularly cysteine. Depletion of GSH levels causes an increase in ROS leading to increased LPO, altered intercellular stability, damaged DNA and cellular membranes, and consequent induction of cell death (Stohs et al., 2001; El-Shahat et al., 2009). ROS generated from metal catalysis may also increase meiotic errors and sperm deformation (Acharya et al., 2008). In our experiments, the testicular injury was confirmed by marked alterations in the histological structure of the testes. The testes of Cd-treated rats exhibited degeneration, necrosis and atrophy of almost all of the STs with incomplete to complete spermatogenic arrest, as assessed by Johnsen’s scoring system.

Biswas et al. (2001) reported that the reduction in the weight of the sex organs is a primary indicator of possible changes in androgen status. Some recent reports suggested that exposure to toxicants decreases testicular sperm count and increases sperm abnormalities (Acharya et al., 2008; Siu et al., 2009; de Souza Predes et al., 2010), which could be related to low levels of serum testosterone (Ji et al., 2010). However, the mechanism behind these antisteroidogenic effects remains largely unexplored. The reduction in circulating testosterone resulting from Cd exposure could be, in part, attributed to a reduction in the cellular levels of testicular luteinizing hormone receptor and the production of cyclic adenosine monophosphate (Gunnarsson et al., 2003). Alternatively, this reduction could result from decreased viability of Leydig cells as a consequence of the necrobiotic effects of toxicants (Yang et al., 2003).

Interestingly, the therapeutic intervention in Cd-intoxicated rats with DPP extract at a dose of 40 mg kg\(^{-1}\) bwt 24 h following Cd injection effectively attenuated the deleterious reproductive effects of Cd, restoring the weight of the reproductive organs with concomitant improvements in sperm count, sperm motility and abnormality rates, and serum testosterone levels. The observed therapeutic potency of DPP might be due to several contributing factors, primarily including the hormone-mediated effects elicited through its content of gonadotropin-like substances or steroidal components that act as gonad-stimulating compounds, improving male fertility (Zargari, 1999) and maintaining normal serum levels of testosterone. It is also known that the estradiol components of DPP play an effective role in regulating the renewal of spermatogenic cells and male reproductive tissues that possess oestrogen receptors (Miura et al., 2003). Moreover, the success of DPP therapeutic intervention in preserving testicular weight in Cd-treated rats reflects the triggering of germ cells to enter the late spermatid stage and maturation phase. Testicular size and weight are normally regulated by fluid secretion from the Sertoli cells and by the production of sperm in the STs (Biswas et al., 2001). It should be noted that unlike metal chelators such as dithiocarbamates and monoisoamyl meso-2,3-dimercaptosuccinate, which are only effective when given within 1 h of Cd administration (Kojima et al., 1992; Yan et al., 1997), and selenium, which is successful up to 2 h after Cd exposure (Jones et al., 1997), DPP was effective 24 h after Cd dosing.

Free radical-induced oxidative damage to spermatozoa has recently received considerable attention for its role in reducing sperm function and causing infertility. Factors that offer protection from such effects are, therefore, of great clinical importance. In the present study, administration of DPP exhibited an antioxidant effect, as evidenced by improved GSH and restored LPO in the testes of Cd-treated rats. Thus, DPP can ameliorate Cd-induced oxidative stress in the testicular tissues, as evidenced by the renewal of spermatogenesis in the seminiferous tubules and normalisation of the testicular histarchitecture. The mechanism by which DPP acts as an antioxidant has not been fully elucidated. In addition to augmenting GSH, the major endogenous antioxidant scavenging ROS, evidences indicate that quercetin, a bioactive flavonoid component of DPP, has free radical scavenging properties (El Ridi et al., 1952) that exert a synergistic action with Cd in increasing the expression of a stress protein, metallothionein, that offers protection against Cd toxicity and oxidative stress (Kara et al., 2005; Morales et al., 2006; Park et al., 2010). Quercetin was...
recently reported to protect spermatogonial cells from oxidative damage caused by reproductive toxicants (Mi et al., 2010; Kalender et al., 2012). Quercetin, via its antioxidant activities, blocks the production of intracellular peroxide, the occurrence of DNA ladders and the production of hypodiploid cells induced by H₂O₂ (Chow et al., 2005). The antioxidant properties of DPP may therefore reasonably explain the beneficial role of DPP in obviating the adverse effects of Cd on sperm parameters and testicular tissues.

Conclusion

In this study, we found that a single low dose of Cd (1 mg kg⁻¹ bwt) induced significant spermatological damage, oxidative stress and histopathological alterations in the reproductive tissues of male rats 56 days after exposure, ultimately resulting in infertility. Our results also indicate that spermatogonial stem cells are particularly sensitive to Cd toxicity. Remarkably, treatment with DPP (40 mg kg⁻¹ bwt) once daily for 56 days, starting 24 h after Cd injection, effectively prevented the deleterious effects of Cd. The pro-fertility properties of DPP are mainly achieved through its endocrine-mediated effects, consistent with its vital role in the antioxidant systems that protect against Cd damage, and possibly due to its prevention of oxidative damage to testicular tissues. Taken together, our findings support the hypothesis that the testis is very sensitive to Cd, which can induce testicular damage and infertility that can be blocked by the therapeutic administration with DPP.

References


Date palm attenuates cadmium testicular damage

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