Efficacy of Echinacea on the Action of Cyproterone Acetate in Male Rats

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Abstract: The study aimed to evaluate the effect Echinacea extract (E) on the testicular antioxidants function in normal rats or that subjected to anti-androgenic compound, cyproterone acetate (CA). Rats were divided into 5 groups treated daily via an oral tube for two intervals 2 and 4 weeks, 1st control, 2nd E (Echinacea treated group in dose 63 mg kg⁻¹), 3rd CA (cyproterone acetate treated group in dose 25 mg kg⁻¹), 4th E+CA and 5th E as prophylactic one week before E+CA treatment with the same aforementioned E or CA doses. The body weight, testes, epididymis and vasa deferens weights were recorded. Sperm count, Nitric Oxide (NO), calcium ion (Ca²⁺) and malondialdehyde (MDA) contents in addition to superoxide dismutase (SOD), glutathione S-transferase (GST) activities were determined in testicular tissues. CA exhibited direct negative effect on reproductive organs weight and significant reducing effect on sperm count and Ca²⁺ contents. SOD and GST activities significantly decreased in addition to significant increase in NO, MDA contents reflecting the oxidative status of testis in CA treated rats. The prophylactic effect of E treatment, in time related manner, showed significant improvement in the antioxidant status of the testicular tissue which is more pronounced as compared to E+CA treatment.

Key words: Echinacea, cyproterone acetate, testis, sperm count, oxidative status, antioxidants

INTRODUCTION

The antioxidant system plays an effective role in protecting testes and other biological tissues below a critical threshold of Reactive Oxygen Species (ROS), preventing testicular dysfunction (Ochsendorf, 1999). ROS mediated oxidative stress is one of crucial reasons of infertility, decreased sperm viability and increased level of free radicals which may cause degeneration of testicular tissue (Koksal et al., 2002; Turner and Lysiak, 2003). The administration of antioxidants to normal animals, not suffering from induced oxidative stress, appears to improve testicular function, signifying oxidative stress a consistent feature of testicular physiology (Orozco et al., 2003; Juan et al., 2005). Antioxidants administered to infertile men advocate promising their use in male infertility treatment (Suleiman et al., 1996; Keskes-Abmar et al., 2003).

Cyproterone acetate is a synthetic steroidal drug which competes with testosterone and dihydrotestosterone for the androgen receptor. It is used to suppress male fertility in oral contraceptives formulations and also in the treatment of various sexual and metabolic disorders (Meriggiola et al., 1996). Cyproterone also has progesterone like activity and reduces pituitary luteinizing hormone and plasma testosterone (McLeod, 1993) and suppresses the secretion of gonadotropins thus, interferes with testosterone production (Barnardell and Faulds, 1994; Neumann, 1994; Honer et al., 2003). Due to the direct interaction with the cellular receptors CA inhibits the action of the androgens and due to this property it is used for the prostatic carcinoma treatment (Torri and Floriani, 2005).

Cyproterone is genotoxic and tumor initiating agent (Kasper, 2001) and the genotoxic effects postulated to be reduced by the use of antioxidants (Siddique et al., 2008).

Echinacea (E) is herbaceous plant genus, consisting of nine species and the current study used one of them Echinacea purpurea or purple coneflower. Echinacea (E) preparations have been marketed as possible immune stimulators or enhancers worldwide. Echinacea became popular as remedies for the common cold and rhinovirus infection (Barrett et al., 2006; Shah et al., 2007; Sumasek and Blandino, 2007). It has anti-tumor effect (Block et al., 2002). The therapeutic effect of Echinacea has been assigned to the presence of caffeic acid derivatives such as cichoric acid, echinacoside, chlorogenic acid and lipophilic polyacetylene-derived compounds, such as alkylamides, constituting isobutylamides are parts of the active principles and suitable for standardization of E. purpurea raw material and finished products (Letchamo et al., 1999). Pellati et al. (2005) reported that Echinacea roots are a good source of natural antioxidants possessing radical scavenging activity.

The objective of this study is to evaluate the physiological and antioxidant effect of Echinacea extract consumption on normal male rat reproductive system or that subjected to cyproterone acetate in addition to the prophylactic effect of Echinacea extract supplementation
by subjecting it to normal rat a week before cyproterone acetate treatment to explore its impact in reducing the postulated cyproterone related side effects.

**MATERIALS AND METHODS**

**Experimental animals:** This study was carried out on adult male albino rats (Wistar strain). Sixty animals were obtained from the farm of National Organization for Drug Control and Research (NODCAR) in 2008. Their weights were (130.2±18.5 g). Male rats were housed in iron mesh cages, each cage contained six rats. Animals were kept under controlled temperature of 21±2°C and 12 h light/12 h dark cycle throughout the experiment. A commercial pelleted diet was used during the experiment and allowed with water ad libitum. The animals were allowed to adapt to the laboratory conditions for two weeks before the beginning of the experiment.

**Drugs:** Cyproterone acetate (C_{22}H_{23}ClO_{4}) was obtained from Schering, Germany as ANDROCURE tablets each containing 50 mg active ingredient Cyproterone acetate (6-chloro-17-hydroxy-4alpha,2alpha-methylene-pregn-4,6-diene-3,20-dione-acetate) (LOT NO. 481A). *Echinacea purpurea* dry extract was supplied by MEPACO (Arab Company for Pharmaceutical and Medicinal Plants), Egypt as capsules each containing 175 mg from dry extract.

**Experimental design:** Animals divided into five groups using random selection each of twelve rats treated oral daily as 1st Normal control (C) received 0.1 mL of 0.5 g/100 mL carboxymethyl cellulose, (CMC) for each 100 g b.wt. 2nd Echinacea treated group (E) received 63 mg kg\(^{-1}\), 3rd Cyproterone acetate treated group (CA) received 25 mg kg\(^{-1}\), 4th Echinacea+Cyproterone acetate treated group (E+CA) received 63 mg kg\(^{-1}\) (E) + 25 mg kg\(^{-1}\) (CA) and 5th Echinacea (week) + Cyproterone acetate treated group (E w + CA) received 63 mg kg\(^{-1}\) Echinacea for 1 week before 63 mg kg\(^{-1}\) (E) + 25 mg kg\(^{-1}\) (CA) treatment. All groups were treated daily for either two or four consecutive weeks from the beginning of the experiment. These doses used calculated equivalent to the human therapeutic dose (Reagan-Slaw et al., 2008). The groups treated with E+CA received cyproterone acetate first followed by E, after 3.5 h as the peak plasma concentration of CA is being achieved in 3 to 4 h from the gastrointestinal tract (Sweetman, 2005). The animal experiments in relation to maintaining and handling animals were strictly conducted in accordance with the internationally agreed guidelines.

**Fingerprints of Echinacea extract:** Chromatographic identification of Echinacea caffeic acid derivatives: one capsule was extracted with methanol: water (80:20; v/v) with 15 min ultra-sonication at room temperature. Cafiaric, chlorogenic and chichoric acid in addition to echinacoside active ingredients of *Echinacea* extract (Fig. 1) was determined by HPLC, UV detector at 330 nm wavelength according to the method of Liu and Murphy (2007).

*Echinacea* extract by GC-MS analysis according to the method described in Song et al. (2000). Phytosterols identified by their fragmentation pattern while scanning the mass range m/z 50-700 and retention times and the representation of the analysis included in Fig. 2 (B1, B2 and B3).

**Biochemical analysis:** Body weight of the rats recorded weekly throughout the duration of the experiment. After two and four weeks of treatment, rats sacrificed 12 h following the last dose by rapid decapitation. Testis, epididymis and vas deferens dissected out, cleaned and weighed. Testis tissues were used for the measurement of

![HPLC chromatogram of *Echinacea purpurea* extracts active ingredients separation](image)

**Fig. 1:** HPLC chromatogram of *Echinacea purpurea* extracts active ingredients separation
enzyme activities of superoxide dismutase (SOD) according to Minami and Yoshikawa (1979) and Glutathione transferases (GST) according to the method of Habig et al. (1974) and Asnain et al. (1993). In addition to Malondialdehyde (MDA) was determined by HPLC according to the procedure of Karatas et al. (2002), nitric oxide (NO) (nitrites/nitrates) was determined according to the method of Papadopoulos et al. (1999) by HPLC and calcium ion was determined by colorimetric assay kit according to Ladenson (1980), Bradley and Selhann (1984) and Woo and Cannon (1984). Testicular sperm count was performed according to Blazak et al. (1993).

Statistical analysis: Statistical analysis was evaluated by one-way ANOVA. Once a significant F test was obtained, LSD comparisons were performed to assess the significance of differences among various treatment groups. Statistical Processor System Support SPSS for Windows software, Release 10.0 (SPSS, Chicago, IL) was used.

RESULTS

Figure 1 represents the HPLC analysis of the Echinacea purpurea extract and identified the active ingredients of the root extract which possesses the antioxidant potential. Figures 2a-c represent the gas chromatographic separation using the mass spectrum detector to identify the persistence of the vegetative sterols in the extract.

Testes weights in Table 1 showed significant decrement at p<0.05 in CA, E+CA and E w+CA groups treated rats after two or four weeks in comparison with the corresponding control weights, while rats treated with E exhibited not statistically different decrease and increase in testes weights as compared to the control values throughout the experimental periods.

Testes/body weight ratio decreased significantly after 4 weeks of treatments in CA and E w+CA groups as compared to the control or the 2 weeks of treatment values. The ratio in E+CA groups decreased significantly throughout the 2 periods as compared to that of the
Fig. 2: Continued
control. While in E treated groups in 4 weeks of treatment
the ratio significantly increased in comparison with that of
the 2 weeks of treatment without statistical difference
comparing to control values.

The data depicted in Table 1 showed that epididymis
weights decreased significantly at p<0.05 in CA, E+CA
and E w+CA treated rats after two or four weeks in
comparison with the corresponding control weights. In
contrast, not statistically different decrease in epididymis
weight in E treated rats after two weeks of treatment,
followed by a significant decrease after the four weeks as
compared with the corresponding control value.
A significant reduction in vas deferens weight reported in Table 1 in CA, E+CA and E w+CA treated groups of rats after two and four weeks of treatments in comparison with the corresponding control weights at the two periods. However rats treated with E showed a significant decrease after two weeks followed by not statistically different decrease in vas deferens weight after four weeks of treatment as compared with that of control.

The data in Table 2 revealed that CA treatment throughout the two experimental periods exhibited significant decrease in the testicular SOD and GST enzyme activities and sperm counts and calcium ions contents. In addition to the significant increase in the MDA and nitric oxide (nitrites/nitrates) concentrations as compared with the corresponding control or E treated groups' values.

Rats treated for two weeks in E groups showed significant increase in GST activity and nitric oxide values and significant decrease in sperm counts and calcium ions contents in comparison with the control values of the two week duration. While treatment with E for four weeks significantly affected the decrease in SOD and GST activities and the MDA, sperm counts and calcium ions contents comparing to four weeks control values.

**Table 1: Effect of Echinacea (E) and/or cyproterone acetate (CA) supplementation on the organs weights (g) of male rats**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Groups</th>
<th>Duration (weeks)</th>
<th>Control</th>
<th>E</th>
<th>CA</th>
<th>E+CA</th>
<th>E w+CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testes weight</td>
<td>2</td>
<td>2.05±0.07</td>
<td>1.87±0.12</td>
<td>1.59±0.15</td>
<td>1.32±0.17</td>
<td>1.70±0.14</td>
<td></td>
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<tr>
<td></td>
<td>4</td>
<td>2.12±0.12</td>
<td>2.13±0.11</td>
<td>0.95±0.16</td>
<td>1.56±0.17</td>
<td>1.38±0.14</td>
<td></td>
</tr>
<tr>
<td>Testes/b.wt. ratio</td>
<td>2</td>
<td>1.25±0.08</td>
<td>1.12±0.05</td>
<td>1.16±0.10</td>
<td>1.02±0.10</td>
<td>1.36±0.13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.19±0.08</td>
<td>1.35±0.17</td>
<td>0.68±0.16</td>
<td>0.78±0.14</td>
<td>0.74±0.09</td>
<td></td>
</tr>
<tr>
<td>Epididymis</td>
<td>2</td>
<td>1.67±0.05</td>
<td>1.55±0.05</td>
<td>1.31±0.11</td>
<td>1.08±0.15</td>
<td>1.10±0.12</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.90±0.14</td>
<td>1.50±0.10</td>
<td>0.94±0.06</td>
<td>0.94±0.19</td>
<td>1.38±0.11</td>
<td></td>
</tr>
<tr>
<td>Vas deferens</td>
<td>2</td>
<td>0.88±0.03</td>
<td>0.90±0.01</td>
<td>0.88±0.10</td>
<td>0.86±0.11</td>
<td>0.66±0.04</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.78±0.14</td>
<td>0.70±0.01</td>
<td>0.70±0.06</td>
<td>0.70±0.10</td>
<td>0.70±0.01</td>
<td></td>
</tr>
</tbody>
</table>

The results are presented as Means±SE of 6 rats. a: Significant change from the corresponding control value. b: Significant change from the E group. c: Significant change from the CA group. d: Significant change from the E + CA treated group. e: Significant change between two and four weeks with the same treatment. Significance at 0.05 level

**Table 2: Effect of Echinacea (E) and/or cyproterone acetate (CA) supplementation on testicular SOD and GST activities, MDA, calcium ions and nitric oxide contents and sperm count**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Groups</th>
<th>Duration (weeks)</th>
<th>Control</th>
<th>E</th>
<th>CA</th>
<th>E+CA</th>
<th>E w+CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD (μg g⁻¹ wet tissue)</td>
<td>2</td>
<td>318.42±3.19</td>
<td>301.71±2.66</td>
<td>218.10±11.15</td>
<td>209.38±6.64</td>
<td>279.27±10.79</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>316.41±5.12</td>
<td>269.51±2.85</td>
<td>211.57±14.29</td>
<td>287.73±16.11</td>
<td>310.52±19.41</td>
<td></td>
</tr>
<tr>
<td>GST (μmole/mg wet tissue)</td>
<td>2</td>
<td>1.38±0.09</td>
<td>1.73±0.11</td>
<td>0.85±0.04</td>
<td>1.44±0.05</td>
<td>1.17±0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>1.88±0.05</td>
<td>1.11±0.05</td>
<td>0.84±0.06</td>
<td>0.88±0.12</td>
<td>0.90±0.05</td>
<td></td>
</tr>
<tr>
<td>MDA (μmol g⁻¹ wet tissue)</td>
<td>2</td>
<td>114.07±6.36</td>
<td>98.22±4.50</td>
<td>150.21±9.11</td>
<td>146.53±7.33</td>
<td>119.29±2.84</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>112.86±5.61</td>
<td>85.85±4.02</td>
<td>143.15±1.78</td>
<td>129.14±6.22</td>
<td>112.91±8.94</td>
<td></td>
</tr>
<tr>
<td>Sperm count (10⁴ g⁻¹ wet tissue)</td>
<td>2</td>
<td>16.76±1.14</td>
<td>16.61±0.57</td>
<td>11.56±0.40</td>
<td>11.41±0.20</td>
<td>19.63±1.20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>20.19±1.10</td>
<td>17.41±1.15</td>
<td>8.89±0.79</td>
<td>16.68±0.80</td>
<td>18.81±0.56</td>
<td></td>
</tr>
<tr>
<td>Ca²⁺ (mg g⁻¹ wet tissue)</td>
<td>2</td>
<td>0.05±0.01</td>
<td>0.59±0.01</td>
<td>0.53±0.02</td>
<td>0.54±0.02</td>
<td>0.58±0.02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.66±0.02</td>
<td>0.56±0.01</td>
<td>0.52±0.02</td>
<td>0.55±0.03</td>
<td>0.56±0.02</td>
<td></td>
</tr>
<tr>
<td>Nitric oxide (mg g⁻¹ wet tissue)</td>
<td>2</td>
<td>5.54±0.20</td>
<td>6.73±0.15</td>
<td>10.27±0.38</td>
<td>11.44±0.27</td>
<td>7.11±0.15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>5.37±0.12</td>
<td>5.80±0.21</td>
<td>11.12±0.34</td>
<td>11.09±0.41</td>
<td>8.35±0.26</td>
<td></td>
</tr>
</tbody>
</table>

The results are presented as Means±SE of 6 rats. a: Significant change from the corresponding control value. b: Significant change from the E group. c: Significant change from the CA group. d: Significant change from the E + CA treated group. e: Significant change between two and four weeks with the same treatment. Significance at 0.05 level
DISCUSSION

In the present study treatment of male rats with cyprome trope acetate reduced the testes, testes-body weight ratio, epididymis and vas deferens weights during the experimental periods as expected according to the anti-androgenic action of this drug in rat (O’Connor et al., 2002; Campos et al., 2003) and in line with Aleem et al. (2005) results about CA treatment in a dose of 20 mg kg$^{-1}$ for 15 days which reduced the fertility and weights of accessory sex glands of the male rats.

The oxidative stress in testis was discernible in terms of perturbations in the activities of antioxidant enzymes SOD and GST and nitric oxide level. SOD protects against spontaneous O$_2$ toxicity and lipid peroxidation. The reduction of SOD suggests that it is involved in antioxidant defense and it has been shown to act as an alternate regulatory switch in testicular steroidogenesis (Pradeep et al., 1999). It is evident, that SOD plays an important role in scavenging of reactive oxygen species (ROS) in testes, because in comparison to rat liver, the activity of catalase and glutathione peroxidase is much lower in the testicular tissue (Peltola et al., 1992). The GST conjugates GSH with compounds containing an electrophilic center and thereby provides critical protection against products of oxidative stress. Since the GSH-conjugate is transported out of the cell, intracellular GSH is consumed irreversibly in the conjugation and thus the maintenance of intracellular GSH levels is essential for the optimal function of GST (Zhang et al., 1998). On the other hand GST significant reduced activity in CA treated groups may be explained through the tissue degeneracy, as the enzyme activities in the animal systems upon exposure to carcinogenic chemical have evolved various defense mechanisms to protect themselves from the oxidative damage. As GSTs form a part of adaptive response of germ cells to oxidative stress and are important constituents in detoxifying the products of lipid peroxidation that inhibition of GST leads to the augmentation of lipid peroxidation and resulting in germ cell apoptosis (Rao and Shaha, 2000; Yang et al., 2001).

The testicular tissue nitrate/nitrite, as an index of NO production and MDA levels were significantly elevated in rat testes in CA treated groups. The tissue NO increase in CA group may be attributed to the injury of testicular tissue in relation to abundant ROS production and consequent migration of macrophages and polymorphonuclear leucocytes to the region (Sikka, 2001). The significant increase in lipid peroxidation marker (MDA) enhanced ROS generation in testis after two and four weeks of treatment suggesting cyprome trope acetate potential to induce significant oxidative stress in the reproductive milieu of rats. The results are consistent with the possible role of reactive oxygen species for the genotoxicity previously suggested by Siddique and Afzal (2005).

NO radicals have been found to regulate multiple biological functions in inflammation and in mediating many cytotoxic and pathological events. NO has a bimodal effect on sperm motility whereby low concentrations of NO enhance sperm motility, whereas high concentrations of NO decrease it. This effect might be due to the dual nature of NO, which is a signal transduction molecule at low concentrations, while being cytotoxic at higher concentrations (Sikka, 2001; Sheweta et al., 2005). In general imbalance in peroxidant and antioxidant status could produce oxidative stress (Ong et al., 2002).

Also, the formation of free radicals and oxidative stress by CA was involved in the destruction of Sertoli cells and the azospernia occurred and this result occurred indirectly via the androgen deprivation effect of CA causing diminution of antioxidant detoxification (Tam et al., 2003).

As regard to Echinacea treatment the data in this study showed not statistically different decrease in testes and vas deferens weights but significant decrease in epididymis weight after four weeks of treatment with Echinacea. Echinacea treatment for 2 to 4 weeks showed gradual antiandrogenic activity through the effect on male sexual hormone testosterone producing organ which may be associated with the vegetative steros which are from the constituents of Echinacea extract (Skauidkia et al., 2003; 2004). The chemical structure of these compounds is very similar to cholesterol. In the digestive duct vegetative steros reduce the absorption of cholesterol, creating a certain competition between sters and cholesterol thus dietary phytosterols may reduce the risk of prostate cancer by lowering the activities of the enzymes of testosterone metabolism (Awad and Fink, 2000; Trautwein and Demonty, 2007).

In Mishima et al. (2004) study, they assumed that SOD activity in peripheral blood was increased because of antioxidants such as echinacocide and caffeine acid in Echinacea purpurea (identified by HPLC) which eliminate superoxide (O$^{-}$) by a free radical scavenging effect. Pellati et al. (2004) indicate that E roots are a good source of natural antioxidants and could be used to prevent free-radical-induced deleterious effects, capable of scavenging hydroxyl radicals, nitration inhibition and to suppress the oxidation of human low-density lipoprotein, particularly at the molecular level and also transition metal chelating (Hu and Kitts, 2000; Weiss and Landauer, 2003; Masteikova et al., 2007).
These results are agreed with the results in this study as treatment with E caused a significant reduction in MDA content in testes and not statistically different change in SOD in the first two weeks. Weiss and Landauer (2003) documented a protective effect of polyphenols from E against free radical damage and a class of specific antioxidants known as caffeyl derivatives in appreciable amounts. SOD remove (O$^{-}$) generated by NADPH-oxidase in neutrophils and can play an important role in protecting spermatozoa during genitourinary inflammation (Baker et al., 1996).

In the present results CA induced a significant decrease in sperm count and this reduction was improved by using treatment with E+CA. This improvement may be due to improvement of hemoglobin levels and number of erythrocytes by Echinacea treatment (Abouelella et al., 2007).

Cypromezone acetate treatment alone or with E produced a significant reduction in testicular NO. Lue et al. (2003) suggested NO physiological role in regulation of germ cell number and in determining testicular size. Concomitant treatment with CA + E improves but did not inhibit the significant reduction of testicular NO. Endothelial production of NO is at least partially regulated by the inositol trisphosphate (IP3)-dependent calcium (Ca$^{2+}$) signalling pathway, which may be activated by ligand–receptor binding and/or wall shear stress. The elevated levels of free Ca$^{2+}$ in the cytosol reversibly bind with calmodulin, the resulting Ca$^{2+}$-calcmodulin complexes activate endothelial nitric oxide synthase enzyme, thus causing an increase in synthesis and release of NO. In addition, NO leads to increased levels of cyclic guanosine monophosphate (cGMP), this activates protein kinase. This is thought to inhibit Ca$^{2+}$ influx, thus providing a negative feedback mechanism and limiting the concentration of Ca$^{2+}$ in the cytosol. (Shen et al., 1992; Lin et al., 2000; Plank et al., 2007). Ca$^{2+}$ can directly activate antioxidant enzymes, increase the level of SOD in animal cells (Gordeeva et al., 2003) and induce mitochondrial GSH release (Brookes et al., 2004). The result in this study in this trend, there is a significant reduction in testicular SOD and intra cellular testicular Ca ions. Yan et al. (2006) studies indicated that Ca$^{2+}$ plays dual roles in regulating ROS homeostasis.

The net Ca$^{2+}$ effects on ROS generation and annihilation appear to be tissue-specific and context-sensitive, and, within a given cell, are differentially regulated in local subcellular compartments. These results give an explanation for intracellular testicular calcium ion reduction. Also, Lyng et al. (2000) suggested that the calcium signals are probably coupled to the regulation of gap junctional efficiency between Sertoli cells.

The low-affinity receptors may convey complementary androgen signals at elevated local levels such as in the testis, when nuclear receptors are (over) saturated. Androgens can also induce rapid calcium fluxes in a variety of cell types, including human prostatic cancer cells and rat sertoli cells (Steinsapir et al., 1991; Gorzymska and Handelsman, 1995; Gorzymska-Fjälling, 2004). This suggests explains the effect of CA treatment on decreasing the testicular Ca ion content.

The study suggests that Echinacea supplementation especially a week before cyproterone acetate shows improvement in the oxidative stress induced by cyproterone acetate treatment. That may be due to the Echinacea antioxidant activity. The anti-androgenic effect of E may in addition to the anti-inflammatory and immune enhancing activity add valuable for using it as a co-treatment for male contraceptives or in treatment of prostate cancer which needs more investigations.

ACKNOWLEDGMENTS

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REFERENCES


