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Research Article

Can *Taraxacum officinale* (Dandelion) Extract be an Alternative of Paracetamol in Inflammatory and Painful Cases? An Evaluation with Regard to Biochemical and Reproductive Parameters [1]

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Abstract

The aim of this study was to investigate the usage of *Taraxacum officinale* extract (TOE) in inflammatory and painful cases as an alternative to paracetamol (PRC) through the assessment of biochemical and reproductive parameters. Totally, 30 male Sprague Dawley rats aged eight weeks old, were used in this study. The animals were obtained from Atatürk University Experimental Research and Application Centre and kept under standard laboratory conditions. Commercial pellet chow and fresh drinking water were available *ad libitum*. Rats were divided into five groups: Group I (n= 6); referred as control. Group II (n=6); referred as TOE150 (150 mg/kg). Group III (n=6); referred as TOE200 (200 mg/kg). Group IV (n=6); referred as TOE250 (250 mg/kg). Group V (n=6); referred as Paracetamol (PRC) (2 g/kg). The treatment was performed for consecutive 8 days. The animals were tranquilized and sacrificed on 9th day of study. Blood samples, cauda epididymal semen samples and testes tissues were collected. Routine semen examinations were performed and oxidative stress levels of testicular tissues were assayed. Reproductive organ weights [total testes weight (TTW) and total cauda epididymal weights (TCEW)] were recorded. Motility in TOE250 group was significantly higher when compared to the other groups (P<0.05). Velocity of sperm cells in PRC group was significantly lower when compared to the other groups (P<0.05). Dead sperm rate in control group was significantly higher when compared to the other groups (P<0.001). On the other hand, the lowest TCEW was in TOE150 group (P<0.05). There were no differences in terms of TTW among all groups. Malondialdehyde (MDA) level of PRC group was significantly higher than the treatment groups (P<0.05). Besides, glutathione peroxidase (GPx) levels of PRC group were lower than the other groups (P<0.001). Superoxide dismutase (SOD) level of PRC group was significantly lower than the treatment groups (P<0.001). The lowest catalase (CAT) level was in PRC group and the highest glutathione (GSH) level was in T200 group (P<0.001). In conclusion, it was observed that TOE could use as alternative of PRC and hence can be avoided from negative effects of PRC on biochemical and reproductive parameters.

Keywords: *Taraxacum officinale, Paracetamol, Reproduction, Rat, Biochemical parameters*

Karahindiba Ekstresi Yangılı ve Ağrılı Durumlarda Parasetamolün Alternatifi Olabilir mi? Biyokimyasal ve Reprodüktif Parametreler Yönünden Bir Değerlendirme

Özet

Bu çalışmanın amacı, biyokimyasal ve reprodüktif parametreleri değerlendirmek suretiyle karahindiba ekstresinin (*Taraxacum officinale extract, TOE*) parasetamole bir alternatif olarak yangılı ve ağrılı durumlarda kullanımını araştırmaktı. Çalışmada sekiz haftalık yaşta toplam 24 adet erkek Sprague Dawley rat kullanıldı. Hayvanlar Atatürk Üniversitesi Deneysel Araştırma ve Uygulama Merkezi'nden temin edildi ve standart laboratuvar koşullarında tutuldu. Ticari pelet yemi ve taze içme suyu *ad libitum* olarak verildi. Ratlar beş gruba bölündü: Grup I (n= 6) kontrol grubu olarak adlandırıldı. Group II (n=6) TOE150 (150 mg/kg) olarak adlandırıldı. Grup III (n=6) TOE200 (200 mg/kg) olarak adlandırıldı. Grup IV (n=6) TOE250 (250 mg/kg) olarak adlandırıldı. Grup V (n=6) parasetamol (PRC) (2 g/kg) olarak adlandırıldı. Tedavi ardışık 8 gün boyunca uygulandı. Çalışmanın 9. gününde hayvanlar trankilize edilerek kesildi. Kan örnekleri, kauda epididimal sperm örnekleri ve testis dokuları toplandı. Rutin sperma muayeneleri yapıldı ve testis dokularının oksidatif stres düzeyleri ölçüldü. Reprodüktif organ ağırlıkları [toplam testis ağırlığı (*TTW*) ve toplam kauda epididimis ağırlıkları (*TCEW*)] kaydedildi. Diğer gruplarla karşılaştırıldığında motilite TOE250 grubunda anlamlı olarak yüksekti (P<0.05). Diğer gruplarla karşılaştırıldığında velosite PRC grubunda anlamlı olarak düşüktü (P<0.05). Diğer gruplarla karşılaştırıldığında ölü sperm oranı kontrol grubunda anlamlı olarak yüksekti (P<0.001). Diğer taraftan en düşük total kauda epididimal ağırlık (*TCEW*), TOE150 grubundaydı (P<0.05). Bütün gruplar arasında total testis ağırlığı (*TTW*) açısından fark yoktu. Malondialdehit (MDA) düzeyi PRC grubunda tedavi gruplardan anlamlı olarak yüksekti (P<0.05). Bunun yanında, glutatyon peroksidaz (GPx) düzeyi PRC grubunda diğer gruplardan düşüktü (P<0.001). Superoksit dismutaz düzeyi (SOD) PRC grubunda tedavi gruplarına göre anlamlı olarak düşüktü (P<0.001). En düşük katalaz (CAT) düzeyi PRC grubunda ve en yüksek glutatyon (GSH) düzeyi T200 grubundaydı (P<0.001). Sonuç olarak, TOE'nin PRC'nin alternatifi olarak kullanılabileceği ve bu nedenle PRC'nin biyokimyasal ve reprodüktif parametreler üzerine olumsuz etkilerinden kaçınılabileceği gözlenmiştir.

Anahtar sözcükler: *Karahindiba, Parasetamol, Reprodüksiyon, Rat, Biyokimyasal parametreler*

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INTRODUCTION

In recent years, it is observed that the increase of comparative experimental studies in laboratory animals [1].

Paracetamol (acetaminophen or N-acetyl-p-amino phenol, PRC) is a mild analgesic, antipyretic agent and also a non-steroidal anti-inflammatory drug [2]. PRC is moderate effective drug when taken in appropriate doses and used against headache, fever, migraine, toothache, influenza infections, muscle and joint pain, middle ear pain, sinusitis, injuries and variety pains for long years [3].

Taraxacum officinale (dandelion) plant has phyto-chemical properties when analyzed as a whole in view of roots, leaves and flowers [4]. There are available studies showing TOE is a type of rich plant in view of vitamin and minerals [5]. It is an important plant in terms of A, B, C, D, vitamin E, as well as choline, inositol, lecithin, minerals and oligoelements (calcium, sodium, magnesium, iron, copper, phosphorus, zinc, manganese). In addition, dandelion, has the nutritional value, is one of the best natural sources of potassium, since it contains high levels of potassium [6,7]. TOE has been widely used as a folkloric medicine for its anti-inflammatory, anti-rheumatic, diuretic, hypolipidemic, anti-carcinogenic, antiulcer, antioxidant, antiviral, anti-allergic, anti-coagulant, anti-hyperglycemic, analgesic, prebiotic and chloretic properties. Furthermore, TOE has inhibiting effect on reactive oxygen species [8,9].

Male reproductive development is mainly regulated by testosterone, which stimulates the development of testes and reproductive tract at puberty and supports spermatogenesis and fertility in adulthood [10].

Motility is a characteristic function of mature sperm. Sperm motility is under the control of many biochemical factors such as mitochondrial function and enzyme activity [11]. Velocity expressing the position change depend on time and motion, is the primary determinant of sperm competition success [12]. The non-viable sperm term, is primarily related to the loss of integrity of the sperm plasma membrane, leading them to an irreversibly loss of homeostasis, immotility and death [13].

Free radicals are short-lived reactive atoms or molecules contain unpaired electrons in the outer orbitals. The most common radicals are hydrogen (H^+), superoxide (O_2^-), hydroxyl (^-OH), nitrogen oxide (NO) and nitrogen dioxide (NO_2). Free radicals can lead to gene mutation, aging and tissue-cell destruction caused by the molecular changes such as generated by normal metabolism. On the other hand, MDA acts on the ion-exchange through the cell membranes, leads to crosslinking of the compounds in the membrane and provokes the adverse consequences such as alteration of the ion permeability and the enzyme activity [14]. Besides, antioxidants try to prevent the free radicals and reactions [15]. There are various endogenous defense mechanisms against free radicals, such as the enzymes SOD, GSH, GPx and CAT, whose activities eliminate superoxide, hydrogen peroxide and hydroxyl radicals [16].

The aim of this study was to investigate the usage of TOE in inflammatory and painful cases as an alternative to PRC through the assessment of biochemical and reproductive parameters.

MATERIAL and METHODS

The approval of Committee for Institutional Animal Care and Use was provided from Ataturk University Local Board of Ethics (The approval number: 2013/132) before the study had been planned.

Plant Material

T. officinale L. samples were collected in September 2013 from Erzurum (Turkey) and identified by Saban KORDALI (Atatürk University, Faculty of Agriculture, Department of Plant Protection, Erzurum). A voucher specimen has been deposited in the Herbarium of Ataturk University, Erzurum (Turkey).

Preparation of the Samples

Plant materials were dried under shade and powdered coarsely before extraction. The dried *T. officinale* L samples were powdered in a blender and then 100 g of sample was extracted individually with 500 mL ethanol at room temperature. The extract was filtered and evaporated to dryness in a vacuum at 40°C with a rotary evaporator after 48 h. Filtration, the organic solvents were evaporated under reduced pressure and temperature. The dried extracts were stored at 4°C until used. The extract was dissolved in 0.5% aqueous carboxymethylcellulose (CMC) suspension in distilled water prior to intraperitonally administration to animals by using needle eight days [17].

PRC Material

2 g/kg of PRC was dissolved in 1% carboxymethyl cellulose (CMC), 1x Phosphate buffered saline (PBS) buffer [18].

Preparation of PBS Buffer

8 g NaCl, 0.2 g KCl, 1.44 g Na_2HPO_4, 0.24 g KH_2PO_4 was weighed, pH adjusted to 7.4 in 980 mL and the solution was completed to 1 L.

Animals and Experimental Procedure

In the study, 24 male Sprague Dawley rats aged eight weeks old and weighted 250-300 gr, were used. The animals were obtained from Atatürk University Experimental and Application Research Centre and housed in standard laboratory conditions. Commercial pellet chow and fresh drinking water were available *ad libitum*. Rats were divided into five groups: Group I (n= 6); referred as control, physiolo-

gical saline was administered via intraperitonally (IP) route. Group II (n=6); referred as *Taraxacum officinale* extract (TOE) 150, 150 mg/kg TOE, was given IP. Group III (n=6); referred as TOE200, 200 mg/kg TOE was injected IP. Group IV (n=6); referred as TOE250, 250 mg/kg TOE was administered IP. Group V (n=6); referred as Paracetamol (PRC), paracetamol administered animals were fasted 24 h and 2 g/kg per os (p.o.). The treatment was performed for consecutive 8 days. The animals were tranquilized and sacrificed on 9th day of study.

Preparation of Plasma

The blood samples was transferred to the vacuum tubes with coagulant and anticoagulated. Plasma and serum were separated at 3000 rpm, +4°C during 10 min by centrifugation. Samples were stored at deepfreeze, -20°C until biochemical analyzes would made.

Collection of Samples

Following decapitation procedure, the testes and cauda epididymidis of the rats were removed from the corpse and cleaned from connective tissues such adipose or connective tissues with anatomical scissors and tweezers. Cauda epididymal semen samples and testes tissues were collected. Routine semen examinations were performed and oxidative stress levels of testicular tissues were assayed. Reproductive organ weights [total testes weight (TTW) and total cauda epididymides weights (TCEW)] were recorded.

Semen Evaluation

One of cauda epididymidis was used to obtain semen sample for each animal. For this purpose, randomly selected cauda epididymidis was minced in Petri dish including 5 mL of physiological saline. To provide the migrations of spermatozoa from cauda epididymidis to fluid, 5 min incubation period was obtained on warmed stage (at 35°C). Following the incubation period, cauda epididymidis residue was removed by using anatomical tweezers from the Petri dish. The fluid remaining in the Petri dish was used as semen sample. Evaluation of semen was conducted using routine spermatological parameters including motility, velocity and dead sperm rate.

To evaluate the percentage of sperm motility and velocity, light microscope (Primo Star; Carl Zeiss, Oberkochen, Germany) equipped with the heated stage was used. Briefly, a slide was placed on a heated stage warmed up to 35°C placed on a conventional light microscope. Approximately 20 µL of semen sample was dropped on the slide. The percentage of sperm motility was detected by visual investigation of the sample. To estimate the sperm motility, randomly selected three different fields from each sample were interpreted. The average of three field estimations was calculated as the final motility score of the sample [19,20]. To determine the sperm velocity, the distance of five head positions were measured and were divided into time spent for moving such distance. Velocity of approximately 50 to 60 motile sperm was measured for each individual [21].

Sperm viability was evaluated with light microscope at 400x magnification with the help of immersion oil (immersion oil for microscopy type A, no: 1.515; Nikon, Tokyo, Japan) after eosin nigrosin staining [22]. The smear was prepared for counting. A total of 200 cells were counted and the results are presented as percentages.

Biochemical Evaluations of Testicular Tissues

For assaying MDA, CAT, SOD levels and GSH activity homogenates were centrifuged for 15 min at 1000 g at +4°C while to assay the GPx activity of testicular homogenates were centrifuged for 20 min at 9000 g at +4°C. Following the centrifuge process, the obtained supernatant was subjected to enzyme assays as soon as possible. The homogenisation of testicular tissues was carried out in Teflon-glass homogenizer with a buffer containing 1.15% KCl to obtain1:10 (w/v) whole homogenate.

The malondialdehyde (MDA) level of testicular tissues was measured by the thiobarbituric acid reaction method of Placer et al.[23]. The values of MDA were expressed as nmol/g tissue. The CAT activity of testicular tissue was determined according to the method of Goth [24]. The values of CAT were expressed as kU/g protein. The SOD activity of testes was measured as the level of decrease in the absorbance at 560 nm and SOD values of testicular homogenates were expressed as EU/mg protein. To assay superoxide dismutase (SOD) activity of testicular tissues, the method of Sun et al.[25] was used. The GPx activity of testes was determined using the method of Matkovics et al.[26] method. The GPx activity of testicular homogenates was expressed as U/mg protein. The GSH content of testicular homogenates was determined at 412 nm according to the method; described by Ball [27], Fernandez and Videla [28]. GSH levels were expressed as mmol/g tissue. The protein content of the testicular tissues was measured according to the method described by Lowry et al.[29].

Statistical Analysis

Statistical comparisons of data were analysed using General Linear Model/Repeated Measures (SPSS, Version IBM 20.0 Microsoft, Chicago, IL, USA) in-group comparisons. Data were expressed as mean ± standard error of the mean (SEM). Differences were considered significant when $P<0.05$.

RESULTS

The results of the study are presented in two tables as reproductive and biochemical parameters. As it is seen in *Table 1*, motility value was significantly higher in TOE250 group when compared to the other groups ($P<0.05$).

Velocity of sperm cells in PRC group was significantly lower when compared to the other groups (P<0.05). Dead sperm rate in control group was significantly higher when compared to the other groups (P<0.001). On the other hand, the lowest TCEW was in TOE150 group (P<0.05). There were no differences in terms of TTW among all groups. According to our findings, it was found that the T250 group was more positive effective than the other groups in terms of reproductive parameters. In *Table 2*, malondialdehyde (MDA) level of PRC group was significantly higher than the other groups (P<0.05). Besides, glutathione peroxidase (GPx) and superoxide dismutase (SOD) levels of PRC group were significantly lower than the other groups (P<0.001). The lowest catalase (CAT) level was in PRC group and the highest glutathione (GSH) level was in T200 group (P<0.001). We observed that the T200 group was more favourable than the other groups in terms of biochemical parameters. Besides, it was determined that PRC has negative impact particularly in terms of biochemical parameters.

DISCUSSION

It is tried to determine the usage of *Taraxacum officinale* extract (TOE) in inflammatory and painful cases as an alternative to paracetamol (PRC) through the assessment of biochemical and reproductive parameters. We observed that the administration of TOE at doses of 250 mg/kg had beneficial effects upon the reproductive parameters and 200 mg/kg of TOE had positive effects upon the biochemical parameters in present study.

Reduction of antioxidant defense causes the ROS (reactive oxygen species) production and the formation of oxidative stress [30]. The increasing of ROS production stems from very intensely oxidative modification of enzymatic proteins [31].

There are limited literature data demonstrating the efficacy of *Taraxacum officinale* extract and PRC on reproductive parameters in rats. Due to restricted literature data, our findings generally were interpreted by comparison with biochemical parameters.

PRC is widely used anti-inflammatory, analgesic and in the group of non-prescription drug [32]. Whereas in overdose, PRC can be detrimental to various tissues [20,33-34]. High dose PRC transform into NAPQI (N-Acetyl-p-benzoquinone imine) - toxic metabolite by cytochrome p450 enzymes in the biological systems. This form leads to the oxidative stress, glutathione consumption and increased lipid peroxidation taking hydrogen from polyunsaturated fatty acids [35,36]. These reactive metabolites initiates cell stress through various mechanisms such as glutathione consumption or these metabolites can be connected to enzymes, lipids, nucleic acids and other cellular structures [37]. The cause of lipid peroxidation is a great aldehyde generating polyunsaturated fatty acids in the cell membrane and

Table 1. *The values (Mean ±SEM) of reproductive parameters in male rats*
Tablo 1. *Erkek ratların reprodüktif parametre değerleri (Ortalama±* SEM)

Groups	Motility	Velocity (0 -5 Intervals)	Dead Sperm Rate	Total Testis Weight - TTW (g)	Total Cauda Epididymal Weight -TCEW (g)
Control	45.22±0.83^{a}	3.46±0.18^{b}	42.30±0.53^{c}	2860.00±52.61	408.77±9.60^{b}
TOE150	47.90±1.58^{ab}	3.20±0.20^{b}	36.94±1.94^{ab}	2631.00±47.49	345.00±25.72^{a}
TOE2OO	45.58±1.42^{a}	3.00±0.00^{b}	39.40±1.33^{bc}	2768.40±64.01	408.20±16.30^{b}
TOE250	50.80±0.00^{b}	3.00±0.00^{b}	34.98±0.74^{a}	2814.88±52.73	417.75±12.32^{b}
PRC	46.16±2.17^{a}	2.20±0.20^{a}	37.64±2.99^{ab}	2894.60±66.98	408.00±14.86^{b}
P Value	*	*	***	--	*

*$^{a-c}$ The values represented by different letters within the same row are significantly different from each other; * P<0.05, *** P<0.001*

Table 2*. The values (Mean ±SEM) of biochemical parameters in male rats*
Tablo 2. *Erkek ratların biyokimyasal parametre değerleri (Ortalama±* SEM)

Groups	MDA (µmol/g)	GSH µmol/g	CAT (kU/g)	GPx U/mg	SOD (EU/mg)
CONTROL	38.10±2.65^{b}	0.79±0.02^{bc}	294.64 ±6.27^{bc}	0.05±0.01^{b}	9.01±0.127^{a}
TOE150	31.58±2.03^{a}	0.79±0.03^{bc}	273.89±17.42^{b}	0.07±0.01^{bc}	9.61±1.15^{b}
TOE2OO	29.66±0.80^{a}	0.83±0.01^{c}	316.71±1.63^{c}	0.07±0.01^{c}	10.63±0.07^{c}
TOE250	28.90±1.84^{a}	0.76±0.02^{b}	301.23±5.92^{c}	0.07±0.01^{bc}	10.52±1.14^{c}
PRC	49.75±1.50^{a}	0.56±0.04^{a}	215.29±20.63^{a}	0.04±0.01^{a}	8.70±1.14^{a}
P Value	*	***	***	***	***

*$^{a-c}$ The values represented by different letters within the same row are significantly different from each other; * P<0.05, *** P<0.001;* ***nmol/g=*** *Nanomole per gram testis tissue;* ***µmol/g=*** *mikromol/gram tissue;* ***kU/g=*** *Katalunite/gram tissue;* ***/mg=*** *Unite /miligram tissue;* ***EU/mg=*** *Enzymeunite/miligram*

results in the increasing of MDA level [38]. In PRC induced hepatotoxicity studies when toxication group in comparison with control group, it was observed significant increase in MDA level (P<0.05) in rats [39,40]. Aksu et al.[20] determined that the decreasing of GSH-px and SOD activity of testicular tissue in the PRC group when compared to the control group in rats. In present study, it is thought that the increasing in MDA level, the decreasing in GSH level, CAT, SOD and GPx activities arise from the harmful effect of PRC via NAPQI pathway.

PRC generated a reduction on sperm motility and count significantly but did not cause any pathological lesion in testis in a study in rats [41]. Aksu et al.[20] showed that PRC toxicity decreased the sperm motility. Similarly, we observed statistically significant reduction in terms of motility in the PRC group in comparison with TOE250 group in the present study. It is thought that the similar results stem from the mode of administration and toxic dose.

It might need to use anti-inflammatory and analgesic substances due to these harmful effects as alternative of PRC.

Natural antioxidants not only protect food lipids from oxidation but also provide a positive contribution on health precluding damage caused by biological degeneration [42]. Some studies clearly showed the antioxidant activity, anti-inflammatory effect and liver protection of *Taraxacum officinale* [43,44]. The antioxidant effects of TOE were determined to reduce the lipid peroxidation [45].

Astafieva et al.[46] specifed the characterization of ToHyp1 and ToHyp2 peptides from *Taraxacum officinale* flowers and exhibited antimicrobial activity of ToHyp2 against Gram-positive and Gram-negative bacteria.

There are numerous studies showing the negative effects of lipid peroxidation and bacterial contamination on reproductive parameters in biological systems [47-50].

It is thought that the mentioned physiological features of TOE can play an active role on the reproductive and biochemical parameters in present study.

Taraxacum officinale increased the antioxidant levels (glutathione and β-carotene) and the activity of antioxidant enzymes (superoxide dismutase, glutathione peroxidase, glutathione reductase) and significantly decreased the lipid peroxidation in mice [51]. It was observed the development in endogenous antioxidant profile via implementation of the roots and leaves of *Taraxacum officinale* in rats [52,53]. These findings support our results.

It can be emphasized that the antioxidant characteristic of TOE has an effect on the oxidative stress and the antioxidant parameters via suppression reactive oxygen species and prevention lipid oxidation [54].

Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acids peroxidation in the cells. An increase in free radicals causes overproduction of MDA. Malondialdehyde level is commonly known as a marker of oxidative stress and the antioxidant status in cancerous patients [55]. Sumanth and Rana [56] determined that alcohol extract of the *Taraxacum officinale* roots in dose of 100 mg/kg orally, significantly decreased the level of MDA compared to toxicity group (P<0.01). Furthermore it was observed that when toxicity group compared to the control group, the level of MDA significantly elevated (P<0.001). Similarly, we observed that the level of MDA significantly decreased in the groups of TOE administered (150, 200 and 250 mg/kg TOE). Besides, the level of MDA significantly increased in the group of PRC (P<0.05).

Glutathione (γ-glutamyl-L-cysteinylglycine, GSH) is an acidic molecule characterized by a cysteine residue and a γ-linked amino acid which provides protection against hydrolysis by cellular proteases [57]. Parmar et al.[39] determined that the decrease in GSH level of the group of PRC toxicity in comparison with the control group in rats. In other study, Park et al.[58] showed that the significantly decrease (P<0.05) in GSH level of toxicity group compared to the control group and significantly increase (P<0.05) in GSH level of the water extract of *Taraxacum officinale* leaves compared to the toxicity group in rats. In addition, Sumanth and Rana [56] administered the alcohol extract of the *Taraxacum officinale* roots in two divided doses as 50 and 100 mg/kg orally,100 mg/kg dose of TOE significantly increased the level of GSH, compared to toxicity group (P<0.001), besides it was observed that any significance is not detected in 50 mg/kg dose. According to our results, the lower GSH level was in PRC group and the higher GSH level was in TOE200 group (P<0.001). In current study, it is thought that the administration of toxic dosage of PRC led to the oxidative stress, glutathione consumption and increased lipid peroxidation by NAPQI. TOE200 group has provided improving effect in GSH level thank to the antioxidant properties.

Glutathione peroxidase (GPx), an enzyme dependent on the micronutrient selenium (Se), plays a critical role in the reduction of lipid and hydrogen peroxides [59]. Sumanth and Rana [56] observed that 100 mg/kg dose of alcohol extract from *Taraxacum officinale* roots significantly increase the GPx level compared to the toxicity group (P<0.001). Besides, they determined the significantly decrease in GPx level of toxicity group in comparison with the control group (P<0.001). There is another study evidentally the increasing level of GPx by the using of hepatoprotective plants [60]. In other study, Cho et al.[61] determined that the significant increasing in the level of glutathione peroxidase of *Taraxacum officinale* group (aqueous extract of *Taraxacum officinale* leaves) in comparison with control group. Especially TOE200 group showed the higher level compared to toxicity (PRC) group in the level of GPx in our study

(P<0.001). This result implied that the TOE200 dosage reduce the lipid peroxidation.

Catalase (CAT) is an important antioxidant enzyme in organisms which could catalyze H_2O_2 to H_2O and O_2 to maintain the redox balance [62]. Sumanth and Rana [56] determined that 50 and 100 mg/kg dose of alcohol extract from *Taraxacum officinale* roots significantly increase the CAT level compared to the toxicity group (P<0.01, P<0.001; respectively). Cho et al.[61] applicated the water extract of *Taraxacum officinale* leaves to the rats, and observed the increasing of CAT level in TOE groups. In our study, although TOE150 group is lower compared to the control group in terms of CAT, TOE200 and TOE250 groups showed the improver effect in CAT level.

Superoxide dismutases catalyze the dismutation reaction of O^{2-} and transforming it into hydrogen peroxide and oxygen for defending against ROS [63,64]. Alcohol extract of the *Taraxacum officinale* roots in dose of 50 and 100 mg/kg, significantly increased the level of liver SOD compared to toxicity group in rats (P<0.01, P<0.001; respectively) [56]. The groups of T200 and T250 showed high protective effect in terms of SOD in the present study and demonstrated conformity to the above study despite the differences of tissues.

Tahtamouni et al.[65] carried out the aqueous extract of *Taraxacum officinale* orally to adult male rats at doses of 1065 and 2130 mg/kg body weight and recorded the motility values 33.9±7.8% and 30.7±7.8%, respectively. The motility value was 85.1±6.2%. There was significantly difference between treatment groups and control group (P≤0.0001). We observed that the motility value of TOE250 group was higher in comparison with the other groups except TOE150 group (P<0.05). In terms of velocity, we determined that the lower value in PRC group when compared to the other groups (P<0.05). Besides, TOE250 group has provided protection upon sperm cells by reducing the rate of dead sperm in the present study. The administration of the aqueous extract of *Taraxacum officinale* resulted in a significant decrease in testis weight in the two experimental groups (aqueous extract of *Taraxacum officinale* at doses of 1065 and 2130 mg/kg body weight, orally) in comparison to the control group in rats [65]. In the current study, although there is no significant difference, it was observed a decrease in the total testis weight in the TOE groups. Furthermore, TOE150 group showed significantly lower value in terms of total cauda epididymal weight in comparison with the other groups (P<0.05) in the present study.

Consequently, it was observed that the especially administration of TOE at doses of 250 mg/kg had beneficial effects upon the reproductive parameters and 200 mg/kg of TOE had positive effects upon the biochemical parameters studied. When considering the effects on the reproductive and biochemical parameters, in case of the inflammation and pain, it was concluded that TOE could use as alternative of PRC and therefore can be avoided negative effects of PRC on biochemical and reproductive parameters. It is thought that the determination of the effects of obtained extract upon the reproductive parameters will contribute to the literature.

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