Egypt. J. Vet. Sci. **Vol. 56,** No. 2, pp. 299-310 (2025)

Egyptian Journal of Veterinary Sciences
https://ejvs.journals.ekb.eg/

Effects of Quercetin on Codeine-Induced Reproductive Hormone Disorder

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THE CURRENT research studies quercetin's potential to attenuate its effects on adult male rats' codeine-induced reproductive disorders. Twenty-four male adult rats were separated into four sets, consisting of six male adult rats in every set, and a 56-day treatment was obtained. General, the first set is control, and the second set (Q1) obtained quercetin using a gavage needle administered at a specific dosage (300 mg/kg/day). In contrast, the third set (Q2) obtained codeine(50mg/kg/day) using a gavage needle, and the fourth group (Q3) obtained quercetin and codeine until 56 days. As a result of exposure to codeine, the rats› blood concentrations of luteinizing hormone (L.H.) and testosterone (T.) decreased. Nevertheless, the administration of quercetin caused an elevation in the levels of (L.H.) plus (T.) hormones in the set (Q3) compared with the set (Q2). In group (Q2), there were changes in the testicle›s structure and tissue, mainly in the Sertoli cells. In addition, there was amyloid accumulation inside the seminiferous tubules; these cells were disarrangements and lacked germ cells. Meanwhile, rats given quercetin (Q1) showed improvement in testicular histopathological abnormalities. The present study›s findings, taking quercetin with codeine (Q3), demonstrated that quercetin consumption can attenuate the harmful influences of exposure to codeine on male reproductive function. In conclusion, this study investigated quercetin›s capability to protect rat testis from the histological damage that codeine causes by oxidative stress.

Keywords: Quercetin, codeine, luteinizing hormone, testosterone, testis, adult male rats.

Introduction

Quercetin, one of the most essential flavonoid compounds, influences the diet and affects various biological functions of the body [1]. The utilization of quercetin as a dietary supplement is restricted due to its inadequate solubility and restricted bioavailability [2]. Hence, dimethylsulfoxide (DMSO) functions as a solvent for the quercetin semiquinone radical [3]. Quercetin is an endogenous compound that functions as an antioxidant. Quercetin is a superior antioxidant compared to curcumin and flavonol glycosides [4,5]. Furthermore, it can be observed in most biological activities, so it is considered an anti-inflammatory and anti-radical substance [6]. Additionally, quercetin enhances the ability to resist oxidative stress and improves glycogen storage, which enhances muscle performance and acts as a powerful anti-fatigue and stress drug [7]. Quercetin is recognized for its ability to defend against oxidative stress in many circumstances. Incorporating 50 μM of quercetin into the freezing buffer decreased oxidative damage and improved sperm quality while through the dissolution process, hence assisting in the preservation of frozen canine sperm [8]. Moreover, empirical studies have shown that quercetin protects against oxidative stress (O.S.), namely in the testes of rats. Multiple studies suggest that long-term exposure to harmful compounds, including cadmium, rotenone, and acrylamide, can lead to oxidative harm in the testes. Codeine can cause a decrease

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(Received 03/02/2024, accepted 16/04/2024)
DOI: 10.21608/EJVS.2024.267562.1821

in body weight, disruption of hormone levels, and increased lipid peroxidation [9,10,11]. However, the administration of quercetin counteracts these effects by improving the function of antioxidant enzymes, alleviating symptoms of oxidative stress (O.S.), and enhancing the quality of sperm [12,13]. Quercetin shields the testes of rats against oxidative damage. Reference [11] reports that rats exposed to vanadium pentoxide (V.P.) industrial pollutants exhibited elevated levels of testosterone (T.) and luteinizing hormone (L.H.) in their plasma. Moreover, using quercetin by injection alleviates the harmful effects that may be observed on acrylamide (ACR), which causes oxidative stress (O.S.) and (DNA) damage in various organs of mice, such as the brain, liver, kidneys, and testicles [13]. Some manuscripts have also shown that giving diabetic rats treated with streptozotocin (STZ) quercetin supplements has a positive effect because it reduces levels of oxidative stress (O.S.) and increases testosterone levels in the testes. Moreover, research has proven that intravenous administration of quercetin effectively protects testicular tissue in diabetic rats that showed symptoms of oxidative stress (O.S.) and caused cell apoptosis [14]. Codeine is a chemical substance that has a hypnotic and hallucinogenic effect and is produced mainly from the papaver somniferum poppy plant. It possesses several medical applications, such as pain-relieving, cough-suppressing, and diarrhea-controlling characteristics. For increased pain relief, codeine is frequently coupled with other medications such as paracetamol, acetylsalicylic acid, and nonsteroidal anti-inflammatory drugs [15]. Codeine, treating mild to severe pain, is still often utilized. Hence, deglucuronidation is the primary process of its metabolism, followed by other secondary pathways, including O-demethylation to morphine and N-demethylation to norcodeine [16]. Codeine is the most consumed opioid globally [17]. Therefore, codeine is converted into morphine by being metabolized in the hepatic, which is considered a prodrug that has an analgesic effect on the body. Additionally, individual differences in reactivity to codeine result from significant genetic variation in hepatic enzyme activity responsible for metabolism [18]. Reproductive hormone abnormalities have been connected to codeine treatment in adult male rats. Codeine treatment caused significant alterations in hematological and biochemical parameters in research by Owoade et al., including decreased red blood cell count (RBCs), the count number of platelets, and white blood cell count (WBCs), besides increased mean corpuscular volume and mean corpuscular hemoglobin [19,20]. Furthermore, daily consumption of codeine decreased total protein and increased amounts of alkaline phosphatase, creatinine, aspartate aminotransferase, and urea. Additionally, it resulted in increased amounts of thiobarbituric acid-reactive compounds and decreased antioxidant enzymes. These changes were responsible for increased oxidative stress (OS) levels, hepatotoxicity, and nephrotoxicity [19]. Several research studies have shown that the administration of codeine causes oxidative stress. In the same way that Archibong et al. found, treating animals with codeine led to a significant drop in enzymes like superoxide dismutase, catalase (CAT), and a rise in malondialdehyde levels, which is a sign of oxidative stress [21]. Similar results were found in another study by Ajayi and Akhigbe, which showed that exposure to chronic levels of codeine caused oxidative damage and increased caspase 3 activation in sperm cells, indicating oxidative stress-induced death [22].

Material and Methods

Sampling

The research experiment was applied to 24 adults male Wistar albino rats; their weights ranged from 210 to 250 grams at the age of 3 months. They obtained adoptions from the Al-Noor University College's animal shelter. The rats remained in well-ventilated plastic enclosures for the duration of the experiment, fed a regular pellet diet, and given unlimited water. Throughout the day cycle of the experiment, the room temperature was 23°C.

Experiment Design

The manuscript designed the experiment by randomly taking twenty-four adult male rats from the animal house and dividing the rats into four sets, each containing an equal number (6 rats per set). They received daily treatment for 56 days. Control set: The control set(Con) consisted of adult male rats given standard tap water and dimethyl sulfoxide (DMSO 1%) orally by gavage needle and set(Q1) was intubated with quercetin at a dosage of (300mg/kg B.W.) only dissolved in 1% DMSO, set(Q2): codeine was given to rats in the laboratory daily at 50 mg/kg [23,24,19]. Furthermore, set(Q3) was intubated daily with quercetin (300 mg/kg body weight) in addition to receiving daily intubation with codeine (50mg/kg body weight).

Serum Biochemical Parameters

The blood specimens were collected on day zero until the completion of the experiment on day 56. Blood was drawn using (the retro-orbital sinus (technique [25,26] from anesthetized adult male rats via intramuscular injection of xylazine (5mg/kg B.W.) and ketamine (100mg/kg B.W.) using microcapillary tubes [27, 28]. Centrifugation was used to separate serums for (15 minutes at 3000 rpm) and stored in containers with tight-fitting stoppers at (-20 °C) for subsequent chemical analysis [29,30]. The levels of testosterone hormone (T.) and luteinizing hormone (L.H.) were measured using an enzyme-linked immunosorbent assay reagent provided.

Histopathological Findings

After the experiment concluded, the testicular tissues were extracted, washed, and instantly preserved in a solution of 10% formaldehyde. The solution was buffered and contained 54 mM NaH_2PO_4 and 28 mM NaH_2PO_4 at a pH of 7.4 [31]. The samples, which had been preserved using formaldehyde, were subsequently placed in paraffin, dissected to a thickness of (5–6 micrometers), and subjected to staining with a Eosin–hematoxylin stain following established histological protocols [32]. The data were analyzed using a simple experimental system (Microsoft Excel 365) and a completely randomized design. The coefficients were compared using Duncan's multiple range test under the probability level of($P<0.01$). Different coefficients are distinguished significantly by different alphabetical letters [33,34].

Statistical analysis

The data were analyzed using a simple experimental system (Microsoft Excel 365) and a completely randomized design. The coefficients were compared using Duncan›s multiple range test under the probability level of ($P<0.01$). Different coefficients are distinguished significantly by different alphabetical letters [33,34].

Results

The manuscript indicates that adult rats in group Q2 (0.81±0.58) revealed a significant decrease ($P < 0.01$) after 56 days in the concentration of the male hormone testosterone in blood serum after taking codeine via gavage needle compared to the other groups (control, Q1 plus Q3 sets), with mean values of (1.25±0.040, 1.51±0.19, and 1.14±0.049), sequentially. Conclusion of the study: Group Q1 recorded a significant increase($P<0.01$) in the level of testosterone (T.) compared to the values in the other groups (1.51±0.19) (Table 1). Therefore, the findings exhibited a statistically significant ($P<0.01$) increased blood serum concentration of testosterone in group (Q3) compared to the concentrations observed in the codeine-treated set(Q2) at the end of the research(Table 1), except for the value in the group (Q1), where the concentration of the hormone testosterone exhibited a significant increase ($P<0.01$), in the meantime, a significant decrease ($P<0.01$) was show in the Q2 and Q3 groups throughout the experiment compared to zero time, as illustrated in Table 1. Moreover, Table 2 showed that codeine (Q2) caused a significant ($P<0.01$) decrease in the luteinizing hormone (L.H.) in the serum in the set(Q2) during the experimental period of (1.34±0.03) compared to the observed values in the other sets. Additionally, the findings indicated that there were no statistically significant disparities ($P > 0.01$) between the control (C) set and the sets (Q1 and Q3) during the experimental period compared to the start of the study. The significances were (2.27 ± 0.031), (2.37 ± 0.17), and (1.95 ± 0.056) for the control (C) set, Q1, and Q3 over time. It is illustrated in Table 2. In the meantime, during the comparison with the control(C) set and the Q1 set, histological sections of the testes of rats in the Q2 set, administered codeine, showed a significant decrease ($P < 0.01$) in the height of epithelial cells and the diameter of the seminiferous tubules. However, the codeine plus quercetin treatment set (Q3) showed statistically nonsignificant ($P > 0.01$) but significant increases in tubule diameter and germ cell number compared to the Q2 set, as shown in Table 3. Furthermore, the Q3 value often standardizes the value of the control. Nevertheless, no statistically significant differences ($P>0.01$) were observed between sets Q1, and the control(C) set when comparing them. The histological examination results corroborated the findings above. The control group did not exhibit any histological alterations (Figure 1). Accordingly, it was observed that the testes of rats treated with codeine (Q2) alone showed signs such as severe testicular amyloidosis, which was characterized by the accumulation of eosinophilic, homogeneous, and amorphous substances in the interstitial space of the testicular lobules and within the seminiferous tubules. Additionally, as shown in Figure 3, there is a decrease in the amount and a rupture of the seminiferous tubules along with this accumulation. The histological investigation demonstrated significant degeneration and necrosis

of germ cells in group Q2 (Figure 3) compared to the seminiferous tubules of group Q1 and the control groups. The tests conducted on groups of rats, one treated with quercetin and codeine (Q3) and the other treated with codeine (Q2), revealed that the Q3 group exhibited enhanced histological structure and an organized arrangement of germinal cells. In contrast, the Q2 group displayed typical cytoarchitecture of spermatogenesis, with only a few sections showing slight micro vacuolation of germ cells (Figure 4). Furthermore, the sections exhibited a modest presence of peritubular amyloidosis, as depicted in Figure 4. It demonstrates the efficacy of quercetin in mitigating the harmful impacts of codeine on tissue caused by codeine. Quercetin (Q1) provided excellent protection in the histological findings, as seen in Figure 2.

TABLE 1. The Ameliorative Potential of Quercetin on Codeine-Induced Reproductive (Testosterone) Hormone Disorder.

Testosterone (T.) Hormone Concentration (ng/mL) (ppb)				
(Q3)	**(Q2)**	**Groups (Q1)**	**(C)**	**Time**
1.33±0.051 ^{A}	1.34±0.09 ^{A}	1.30±0.015^{A}	1.29±0.015^{A}	Zero
1.14±0.049^{AB}	0.81±0.58 ^{B}	1.51±0.19^{A}	1.25±0.040^{A}	56 days

*Average ± standard error for three replicates.

Different letters are positioned vertically before the numbers, signifying a significant difference at the probability level (P≤ 0.01) according to the Duncan test.

TABLE 2. The Ameliorative Potential of Quercetin on Codeine-Induced Reproductive (Luteinizing) Hormone Disorder.

Luteinizing Hormone Concentration (ml U /ml)				
(Q3)	**(Q2)**	**Groups (Q1)**	**(C)**	**Time**
2.26±0.094 ^{A}	2.38±0.14 ^{A}	2.42±0.042 ^{A}	2.39±0.23 ^{A}	Zero
1.95±0.056 ^{B}	1.34±0.03 ^{C}	2.37±0.17 ^{A}	2.27±0.031 ^{A}	56 days

*Average ± standard error for three replicates.

Different letters are positioned vertically before the numbers, signifying a significant difference at the probability level

TABLE 3. Effects of Quercetin and Codeine on the Diameter of Seminiferous Tubules and High of Germinal Epithelial Cells of Tubules in Adult Male Rats.

(Q3)	**(Q2)**	**Groups (Q1)**	**(Con)**	**Parameters**
380.6± 70.96 ^{AB}	293.4±49.01 ^{B}	450±232.72 ^{A}	499.8±198.40 ^{A}	Diameter of seminiferous tubules diameter
111.4±25.69 ^{C}	53.4±24.83 ^{C}	96.6±9.29 ^{C}	136.4±55.48 ^{C}	High of germinal epithelial cells of tubules

*Average ± standard error for three replicates.

Different letters are positioned vertically before the numbers, signifying a significant difference at the probability level (P≤ 0.01) according to the Duncan test.

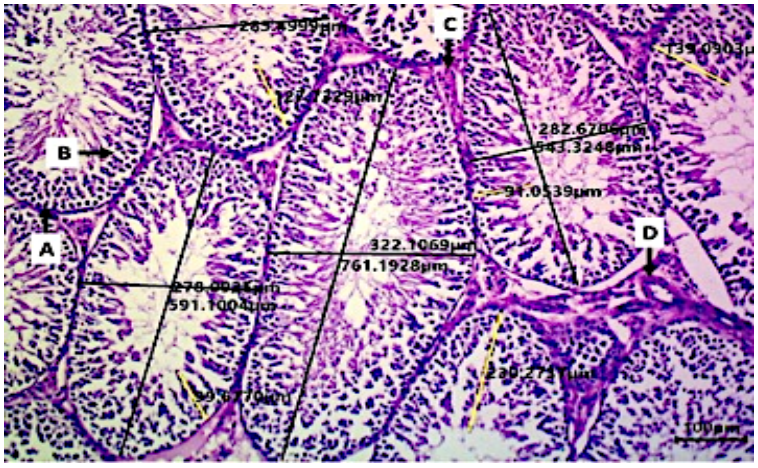

Fig. 1. Displays a photomicrograph of a rat's testis from the control (Con) group. The image reveals seminiferous tubules (A) containing spermatogenesis cells (B), interstitial tissue (C), and blood vessels (D). Additionally, the measurements of the seminiferous tubules' width and the height of the germinal epithelial cells within the tubules are shown. Hematoxylin and eosin stain, 100X.

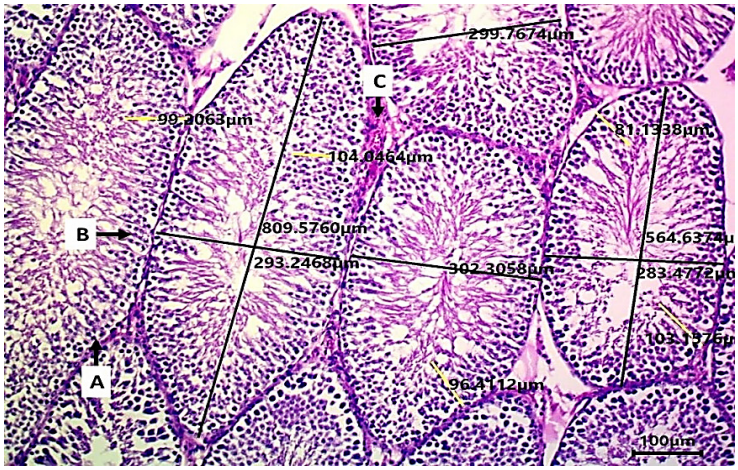

Fig.2. Displays a photomicrograph of a rat's testis from the quercetin (Q1)-treated group. The image shows seminiferous tubules (A) containing spermatogenesis cells (B), as well as interstitial tissue (C). The measurements provided include the width of the seminiferous tubules and the height of the germinal epithelial cells within the tubules. Hematoxylin and eosin stain, 100X.

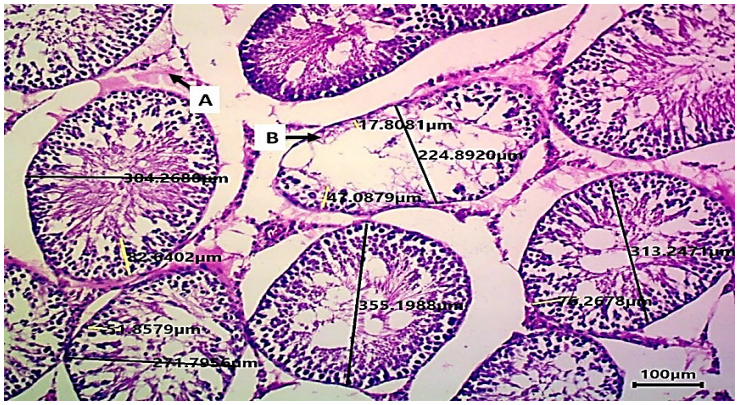

Fig. 3. Display a microscopic image of a rat testicle from the codeine-treated group (Q2). The image shows edema between the seminiferous tubules (A) containing degeneration and necrosis of spermatogenic cells (B), as well as measurements of the intratubular germ cells and height epithelial cells and the diameter of the seminiferous tubules. Hematoxylin and eosin stain were used under 100X microscopic magnification.

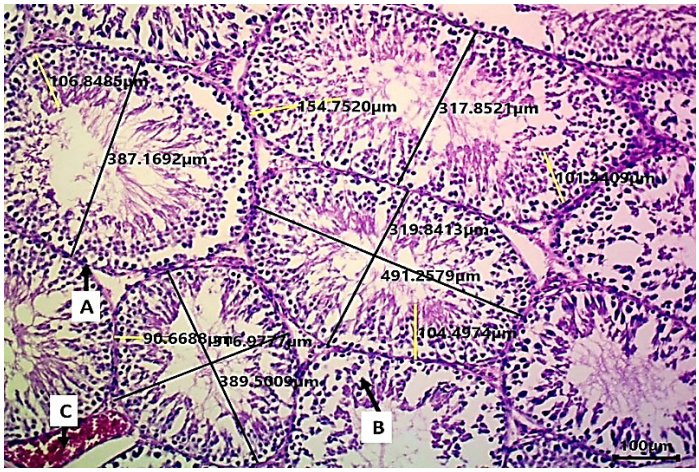

Fig. 4. Displays a micrograph of a rat's testis from the group treated with quercetin and codeine (Q3). The image reveals intact seminiferous tubules (A), mild degeneration of spermatogenesis cells (B), and congestion of blood vessels (C). The measurements provided include the diameter of the seminiferous tubules and the height of the germinal epithelial cells within the tubules. Hematoxylin and eosin stain, 100X.

Discussion

Evidently, in male rats with testicular dysfunction, this experiment assessed the adverse effects of codeine and how quercetin improved them. The findings demonstrated that rats administered a dosage of 50 mg/kg BW of codeine (group Q1) exhibited a notable decrease in testosterone (T.) and L.H. levels compared to the other groups. The testicular tissue exhibits a high level of testosterone, FSH, and LH production and secretion, along with other biochemical processes associated with sperm production and steroid synthesis [35]. While codeine lowers testosterone levels by decreasing the amount of zinc in the testicles, this reduction in zinc impairs the activity of the angiotensin-converting enzyme (ACE), inhibiting spermatogenesis. Furthermore, codeine inhibits androgen receptor mRNA in Sertoli cells in the testicle, which leads to a decrease in the levels of androgen receptors, which affect testosterone [36,37]. Therefore, codeine significantly decreases epidermal growth factor (EGF) and its receptor (EGFR) in Leydig cells, spermatocytes, and spermatogonia. Consequently, exerting a crucial influence on the male reproductive activities of rats [38,39]. Luteinizing hormone, or LH, is essential for the production and control of testosterone release by Leydig cells [40]. Codeine influences the activity of enzymes and works to inhibit metabolic processes such as glycolysis and protein synthesis and antioxidant pathways. Additionally, these modifications reduced body weight to decrease food consumption, leading to a decline in testis weights [41,42]. Fluctuations in androgen levels can lead to modifications in the weight of reproductive organs. Investigations have demonstrated that the removal of androgens, either through castration or the use of antiandrogens, has an impact on many organs, including the abdominal prostate, thymus gland, seminal vesicle, and epididymis. Intervention has been found to result in weight loss [43]. Besides, codeine usage can impact the pituitary gland and induce a decline in the levels of GnRH, FSH, and LH, which in turn inhibits or reduces the production of steroids [42]. Long-term consumption of codeine has been demonstrated to result in testicular degeneration and inhibition of testosterone production [37]. Nitric oxide and oxidative stress are believed to trigger caspase-dependent apoptotic testicular cell death, which has an impact on the reproductive system [44]. The current study observed a reduction in testosterone levels in the group treated with codeine (Q2), linked to changes in the testis›s histology. These changes included the absence of sperm production, vacuoles, and the disruption of germ cells and Leydig›s cells [36]. Reactive oxygen species (ROS) through the steroidogenic pathway have a role in spermatozoa and fertilization capacity [45]. However, increased oxidative stress eventually affects the structure and function of phospholipids and proteins, leading to increased production of reactive oxygen species [46]. ROS regulates spermatogenesis, sperm development, and fertilization ability [47]. Moreover, ROS acts as a chemical compound that has a signal transduction role in the pathways that control male reproductive activities (48). Instead,

oxidative stress hurts the body, causes damage to the structure of sperm, and impairs their activity. Therefore, reactive oxygen species (ROS) are essential and act as antioxidants. Therefore, maintaining homeostasis in the redox state is vital for the excellent functioning of male reproductive processes (49). Codeine affects tissue abnormalities caused by oxidative stress and causes testicular dysfunction and infertility (50). Moreover, previous manuscripts have demonstrated that oxidative stress affects males and causes infertility (51,52). Reactive oxygen species (ROS) are generated from oxidative stress in the male reproductive system, which impacts changes in sperm morphology and physiology (53). Furthermore, excessive reactive oxygen species (ROS) and lipid peroxidation cause DNA breakage and apoptosis, decreasing fertility and poor sperm quality (37). Therefore, codeine induces oxidative stress that induces apoptosis in male cells, especially Sertoli cells, and this study also showed that vitamin C can mitigate the products of oxidative stress on these cells (54). The results of the investigation demonstrated a significant increase in the levels of testosterone(T.) and L.H. in the blood in the groups that received quercetin with codeine (Q3) or quercetin alone (Q1) compared to the group (Q2) that received codeine only. These results prove that quercetin acts as an antioxidant, which reduces the harmful effects of codeine on testicular function, can improve semen quality, reduce damage to the testicles in infertile men and rabbits exposed to cadmium as an antioxidant, reduces the generation of reactive oxygen species(R.O.S.), and resists the effects of cadmium. Lipid peroxidation (55). In addition, quercetin plays a role in the respiratory chain, producing ATP and an essential source of cellular energy (56). As a result, quercetin, an antioxidant that increases these hormones, caused higher blood levels of testosterone and luteinizing hormone in rabbits exposed to cadmium (57). In addition, the antioxidant properties of quercetin reduce oxidative stress-induced organ toxicity in mice (58). In the same way, quercetin can protect against osteoarthritis (OA) by stopping NLRP3-mediated alveolitis and reducing oxidative stress. It reduces chondrocyte loss and extracellular matrix (ECM) degradation (59). Also, quercetin lowers damage to the testicles and issues with testosterone production in male diabetic rats by stopping stress in the endoplasmic reticulum (ER) and increasing testosterone production through the miR-1306-5p/HSD17B7 pathway (60). Moreover, quercetin reduces the harmful effects on the liver by reducing oxidative stress and inflammatory damage while regulating fat metabolism, which causes acrylamide (61). Additionally, some manuscripts have shown that quercetin has an influential effect in rats with chronic unexpected mild stress (CUMS) because it acts as an antidepressant by modifying blood components, reducing oxidative stress, suppressing inflammation, and altering neurotransmitter systems (62). Quercetin has a potential role in sperm biochemistry and its effect on male infertility. Quercetin enhances male fertility and is linked to bioenergetic and antioxidant properties (63). In addition, oxidative stress in the diet can be reduced by using quercetin, which improves sperm motility and reduces sperm DNA fragmentation (64). Furthermore, quercetin also promotes embryonic growth and reduces apoptosis, thus improving the effectiveness of assisted reproductive techniques (65). In contrast, research has shown that quercetin reduces apoptosis in sperm cells when the body›s oxygen supply decreases, thus protecting against varicocele-related damage to sperm production (66). Quercetin›s function is as an antioxidant in the mitochondrial respiratory chain and, therefore, affects the treatment of infertility in men. Moreover, quercetin plays a role in improving testicular dysfunction in rats subjected to codeine treatment, which causes testicular dysfunction, and this role has an effect in alleviating the damage caused by codeine by enhancing the antioxidant defense mechanism and testicular function (67). Furthermore, quercetin protects the brain from damage caused by high-altitude conditions by targeting enzymes associated with oxidative stress and enhancing markers associated with oxidative stress (68). In addition, studies have shown that quercetin effectively attenuates the harmful effects of monosodium glutamate (MSG) on the testicles by reducing oxidative stress and enhancing anatomical, pathological, and biochemical factors (69). Quercetin improves sperm quality, reduces the adverse effects of oxidative stress, and controls abnormal cyanide-induced changes in testicular tissue. Therefore, quercetin can protect against oxidative damage and improve testicular function in various conditions (70).

Conclusion

In conclusion of this research, the results showed that quercetin reduces and alleviates testicular damage caused by codeine in this

manuscript. Meanwhile, the administration of rat›s codeine, a substance that affects male hormones, resulted in testicular changes, such as variations in Sertoli cells, compared to the control set. According to previous research and studies, codeine causes gonadotoxicity, which indicates that oxidative stress (O.S.) has an essential role in the process of codeine-induced testicular toxicity. Thus, it has been shown that levels of testosterone (T.) and luteinizing hormone (L.H.) decrease in adult male rats after codeine administration. On the contrary, the administration of quercetin led to a significant increase in the levels of these hormones in the (Q3) set compared to the (Q2) set.

Acknowledgment

The authors express their gratitude to Al Noor University College for their invaluable help and provision of information, which significantly contributed to the completion of the research paper.

Conflict of interest

The authors of this research paper affirm that there are no conflicts of interest to disclose concerning its publication.

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أثار الكيرسيتين على اضطراب الهرمونات التناسلية الذي يحدثه الكودايين

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يدرس البحث الحالي قدرة الكيرسيتين على تخفيف آثار الفشل الإنجابي الناجم عن الكودايين لدى ذكور الجرذان البالغة. تم فصل أربعة وعشرين من الفئران الذكور البالغين إلى أربع مجموعات، تتكون من ستة فئران ذكور بالغين في كل مجموعة، وتم الحصول على علاج لمدة ٥٦ يومًا. بشكل عام، المجموعة الأولى هي السيطرة، أما المجموعة الثانية (Q1) فقد حصلت على الكيرسيتين بالتجريع عن طريق الفم بجرعة محددة (٣٠٠ ملغم/كغم/ يوم). في المقابل، حصلت المجموعة الثالثة (Q2) على الكودايين بالتجريع عن طريق الفم، وحصلت المجموعة الرابعة (Q3) على كيرسيتين (٣٠٠ ملغم / كغم / يوم) وكودايين (٥٠ ملغم / كغم / يوم) حتى ٥٦ يومًا. نتيجة للتعرض للكودايين، انخفض تركيز الهرمون اللوتيني (L.H.) والتستوستيرون (T.) في دم الفئران. من ناحية أخرى أدى إعطاء الكيرسيتين إلى ارتفاع مستوى هرموني (L.H.) و (T.) في المجموعة (Q3) مقارنة بالمجموعة (Q2). في المجموعة (Q2)، حدثت تغيرات في بنية الخصية وأنسجتها، خاصة في خلايا سيرتولي. بالإضافة إلى ذلك، كان هناك تراكم الأميلويد داخل الأنابيب المنوية؛ كانت هذه الخلايا غير مرتبة وتفتقر إلى الخلايا الجرثومية. وفي الوقت نفسه، أظهرت الفئران التي أعطيت كيرسيتين (Q1) تحسنا في التشوهات النسيجية المرضية في الخصية. أظهرت نتائج الدراسة الحالية، التي تناولت الكيرسيتين مع الكودايين (Q3)، أن استهلاك الكيرسيتين يمكن أن يخفف من التأثيرات الضارة للتعرض للكودايين على الوظيفة الإنجابية للذكور. في الختام، تهدف هذه الدراسة إلى التحقق من قدرة الكيرسيتين على حماية خصية الفئران من الأضرار النسيجية التي يسببها الكودايين بسبب الإجهاد التأكسدي.

الكلمات المفتاحية : كيرسيتين، الكودايين، الهرمون الملوتين، التستوستيرون، الخصية، ذكور الجرذان البالغة.