DOI: https://doi.org/10.31351/vol34iss3pp249-256

Nephroprotective Effect of Turkesterone Against Daunorubicin-Induced Acute Kidney Injury in Rats

Alaa R. Khudhair[*,1], Mohammed Abdulameer Oleiwi[2] and Israa Radhi Khudhair[3]

[1] Department of Pharmacology and Toxicology, College of Pharmacy, University of Baghdad, Iraq.
[2] Department of Pharmaceutical Chemistry, College of Pharmacy, University of Baghdad, Iraq.
[3] Department of Biology, College of Education of Pure science (Ibn Al-Haitham), University of Baghdad, Iraq.

[*]**Corresponding author**
Received 2/6/2024, Accepted 12/11/2024, Published 20/9/2025

Abstract

Turkesterone, a phytoecdysteroid that possesses an 11-α-hydroxyl group, is an analogue of 20-hydroxyecdysone which is an insect steroid hormone. Phytoecdysteroids, a group of ecdysteroid hormones naturally in plant species *Ajuga turkestanica*, *Rhaponticum carthamoides* Willd. and *Cyanotis arachnoidea C.B.Clarke* that centuries used due to their tonifying, adaptogenic, and antioxidant and ability to enhance physical performance. ecdysterone and turkesterone have been associated with different biological effects, as neuroprotective, anabolic, antihyperlipidemic and antidiabetic. Several studies suggested that the mechanism of Daunorubicin-induced nephrotoxicity by the production of the reactive oxygen species by anthracycline–iron complexes redox cycling as well as of their aglycones that is the main mechanism that resulted in their cell damage. This study was designed in order to investigate the nephroprotective effect of Turkesterone, against the nephrotoxicity induced by Daunorubicin. Twenty-four (24) adult Sprague- Dawley female rats. The animals are divided into six rats in each group (four groups): Group I: given dimethyl sulfoxide (10%) (4 ml per kg/day) orally fifteen days. Group II: single oral dose of dimethyl sulfoxide (10%) for fifteen days, then subsequently given Daunorubicin 20 mg/kg in days 13, 14 and 15 (cumulative dose of 60 mg /kg) intraperitoneally. Group III: given Turkesterone (5mg/kg/day) orally for 15 consecutive days. Group IV: given Turkesterone (5mg/kg/day) orally for 15 days, then subsequently given Daunorubicin 20 mg/kg in days 13, 14 and 15 (cumulative dose of 60 mg/kg) intraperitoneally. Nephrotoxic rats, with daunorubicin, pretreated with Turkesterone (Group IV) both urea and creatinine levels were significantly reduced in serum; moreover, markers of oxidative stress by measuring the levels of Glutathione peroxidase 4 were reversed to their level in the control group. Also, markers of apoptosis, inflammation were decreased as shown through the measuring of the kidney tissues homogenate levels of cleaved caspase-3 and the interleukin 6 levels respectively, in. It was concluded that several hallmarks of the nephrotoxicity caused by daunorubicin were mitigated by the pretreatment with Turkesterone.

Keywords: Nephroprotective, Turkesterone, Daunorubicin, Cleaved caspase-3 and Glutathione peroxidase 4.

Introduction

One of the frequent complications of both the malignancies and their treatments are the kidney disease. The kidney disease spectrum in this setting may include acute renal failure (ARF), tubular disorders, and chronic renal failure [(1)]. Daunorubicin (DNR) is anti-tumor drug belong to the anthracycline antibiotics, is an effective chemotherapy for the myeloblastic and acute lymphoblastic leukemias [(2)]. However, due to its production of free radical that induced toxicity, the use of DNR is limited in addition to the limitation of its doses and efficacies. The most important side effects of DNR that limited its optimal uses are cardiotoxicity and nephrotoxicity [(2, 3)].

Several studies suggested that the mechanism of DNR-induced cardiotoxicity and nephrotoxicity by the formation of the reactive oxygen species (ROS) through their anthracycline–iron complexes redox cycling as well as of their aglycones that is the principal mechanism that induces their cellular damage [(4)].

Topoisomerase poisons, like anthracyclines, stabilize the intermediate and the catalytic enzyme reaction blocked leading to DNA strand broken and covalently bonded to the enzyme. As the DNA has been damaged, the intermediate reaction named as DNA -Top2 cleavage complex (Top2cc) [(5)], this

complex trigger cell death. Moreover, Top2a overexpression in the tumor cells was noticed, Top2b which expressed in cardiomyocytes targeted by the anthracyclines [6].

Turkesterone, a phytoecdysteroid that possesses an 11-α-hydroxyl group, that is an analogue of 20-hydroxyecdysone which is a steroid hormone in insect [7]. Phytoecdysteroids, a group of ecdysteroid hormones naturally in plant species *Ajuga turkestanica*, *Rhaponticum carthamoides* Willd. and *Cyanotis arachnoidea C.B.Clarke* that centuries used due to their tonifying, adaptogenic, and antioxidant and ability to enhance physical performance [8]. Different biological effects have been associated with ecdysterone and turkesterone, as neuroprotective, anabolic, antihyperlipidemic and antidiabetic [9-12]. β-estrogen receptors activation mediates the pharmacological properties of Ecdysteroids that are determined by their ability in enhancing the physical performance by Ecdysteroids beneficial changes both the composition of the body and the anabolic effects [13]. This study designed in order to investigate the possible nephroprotective effects of Turkesterone, A muscle Building Supplement against the nephrotoxicity induced by Daunorubicin through the measurement of serum urea and creatinine; Glutathione peroxidase 4 levels in rat, rat IL6 (interleukin 6) levels in addition to levels of cleaved caspase-3 in kidney tissues of rats.

Materials and Methods

Reagents

ELISA KITs (SUNLONG BIOTECH CO., China): Rat (GPX4), Rat cleaved caspase-3 and the Rat (IL-6). Drugs: the pure powder of Turkesterone was obtained from HONG KONG ZELONG BIO CO., LTD. Hong Kong; vials of 10mg/5ml Daunorubicin from India (Fresenius Kabi).

Animals and experimental design

Twenty-four Sprague- Dawley adult female rats, weighing 160- 210gm was provided by the Animals house in College Pharmacy- Baghdad University, in the controlled, convent conditions of the lab. Rats cage housed, in temperature of (25°C), normal relative humidity and light/dark cycle. Standard chow and water of the lab rodent was in *ad libitum* provided. Adapted rats prior to the experiment for seven days. The rats were distributed into (4) groups each group of (6) rats:

- **GroupI (Control):** (4 ml/kg) of dimethyl sulfoxide (10%) given orally for fifteen days.
- **GroupII (Daunorubicin-treated):** single oral dose of dimethyl sulfoxide (10%) for fifteen days, then subsequently given Daunorubicin 20 mg/kg for the last three days [14] (60mg/kg cumulative dose) intraperitoneally.
- **GroupIII (5mg Turkesterone /kg/day)** [15]**:** given oral dose of Turkesterone (5mg/kg, in dimethyl sulfoxide10%) daily by oral gavage for fifteen consecutive days.
- **GroupIV (5mg Turkesterone /kg** [15] **+ Daunorubicin):** received Turkesterone (5mg/kg in dimethyl sulfoxide10%) daily by oral gavage for fifteen days, intraperitoneal 20mg/kg of Daunorubicin given in the last three days subsequently [14] (60mg/kg cumulative dose).

After ending the treatment (about twenty - four hours) euthanization of the rats by using the diethyl ether and blood samples withdrawn from the neck carotid artery and collected using the gel tubes which then leaved 20 min for clotting at the room temperature to get the serum, that was separated by centrifuging blood samples after clotting at 3000 rpm for about 20 min, that is used for the measurement of the serum urea and creatinine, rats' kidney tissues were quickly excised and after that placed in (pH 7.4) phosphate buffer solution (PBS) that was chilled at 4^0C, to prepare the kidney tissue homogenates (10%) through using blotted and weighed filter paper by adding 1gm of kidney tissue to (9ml) phosphate buffer solution (pH 7.4) and homogenized the tissue for about 1 minute at temperature of 4 ^{0}C by using the tissue homogenizer. These tissues homogenate that freshly prepared kept in the frozen state if did not work immediately for the measuring of rat (GPX4), (IL-6) in addition to the cleaved caspase-3 in the homogenization of the kidney tissue [16].

Statistical analysis

Expression and analysis of the data values was done using the Statistical Package Social Sciences (SPSS) version 23 and the mean ± standard deviation (mean± SD). Among different groups statistically significant determined using the one-way analysis of variance. For statistically significant the P value was determined to be less than 0.05 (P<0.05).

Results and Discussions

Nephrotoxicity caused by the treatment with daunorubicin (Group II), associated with significant (P<0.05) elevation in the serum urea and serum of creatinine levels (Figure. 1 and 2, respectively), in addition to significant (P<0.05) raising in the levels of the cleaved caspase-3 and significant (P<0.05) raising in the levels of interleukin 6 in the tissues of the kidney (Figure. 3 and 5, respectively) also associated by significant (P<0.05) decreasing in kidney tissues levels of the GSH peroxidase 4 (Figure. 4), each comparing their levels in the rats of the control group.

Administration of Turkesterone (5mg/kg) with daunorubicin (Groups IV) showed significant (P<0.05) reduction in the serum urea and serum creatinine (Figure. 1 and 2, respectively), moreover there was significant (P<0.05) decreasing in kidney tissues levels of the interleukin 6, and the kidney tissues levels of cleaved caspase-3 (Figure. 3, 5

respectively); also, resulted in significant (P<0.05) increasing in the kidney tissues levels of the GSH peroxidase 4 (Figure. 4) each compared to Group II rats. The cytotoxicity of chemotherapeutic drugs depends on their capability to induce apoptosis (programmed cell death). Both of the carcinogenesis and chemotherapeutic drug resistance linked to cancer cells is a common characteristic of evading apoptosis [17], in the fast-proliferating tumor daunorubicin results in the intercalation of DNA in addition to the inhibition of topoisomerase II thereby act as topoisomerase II poisons by blocking enzyme catalyzing reaction, also an intermediate stabilization that lead to formation of broken DNA, eventually may causing cell apoptosis as the irreversible cuts in the DNA occur [18].

In addition, the releasing of cytochrome c of the mitochondria which may act in the cascade of apoptosis reactions activation and results in cell death eventually through activation of the caspases [19, 20]. This study revealed that as shown through the significant (P<0.05) increasing the kidney tissue homogenates levels of the cleaved caspase-3 (Figure. 5). Nephrotic syndrome caused by daunorubicin and doxorubicin anthracyclines drugs, with focal segmental glomerular sclerosis and significant renal lesions in which the cumulative dose of daunorubicin reported in numerous cases are related to the occurrence of hemolytic uremic syndrome which leads to a slowly progressive renal failure [21]. The current study confirms the nephrotoxicity caused by daunorubicin as showed by serum urea and creatinine significant (P<0.05) elevation (Figure.1 and 2, respectively).

The mechanism of nephrotoxicity caused by anthracycline drugs including daunorubicin is not fully understood but their metabolisms may induce toxicity to the mitochondria through the disruption of mitochondrial membrane, lipid peroxidation, induction of free radical, impairment of calcium homeostasis, and the release of cytochrome C which led to glomerular and tubular cells apoptosis or necrosis [22].

The reactive oxygen species production by many of the anticancer drug's results in significant toxicity in the organs as associated with elevated oxidative stress in addition to apoptosis such as cardiotoxicity, nephrotoxicity and hepatotoxicity [16, 23]. Free radicals' production by daunorubicin from the quinone group reduction by the cytochrome P450 reductase enzyme through the addition of one electron that produce a superoxide anion by quickly binds with oxygen then produces H2O2, this increase in the free radical's formation causes damage to the components of the cells, causing death of the cell [24]. That was confirmed by the current study as shown by the kidney tissue homogenate levels of the GPX-4 significant (P<0.05) reduction (Figure. 4).

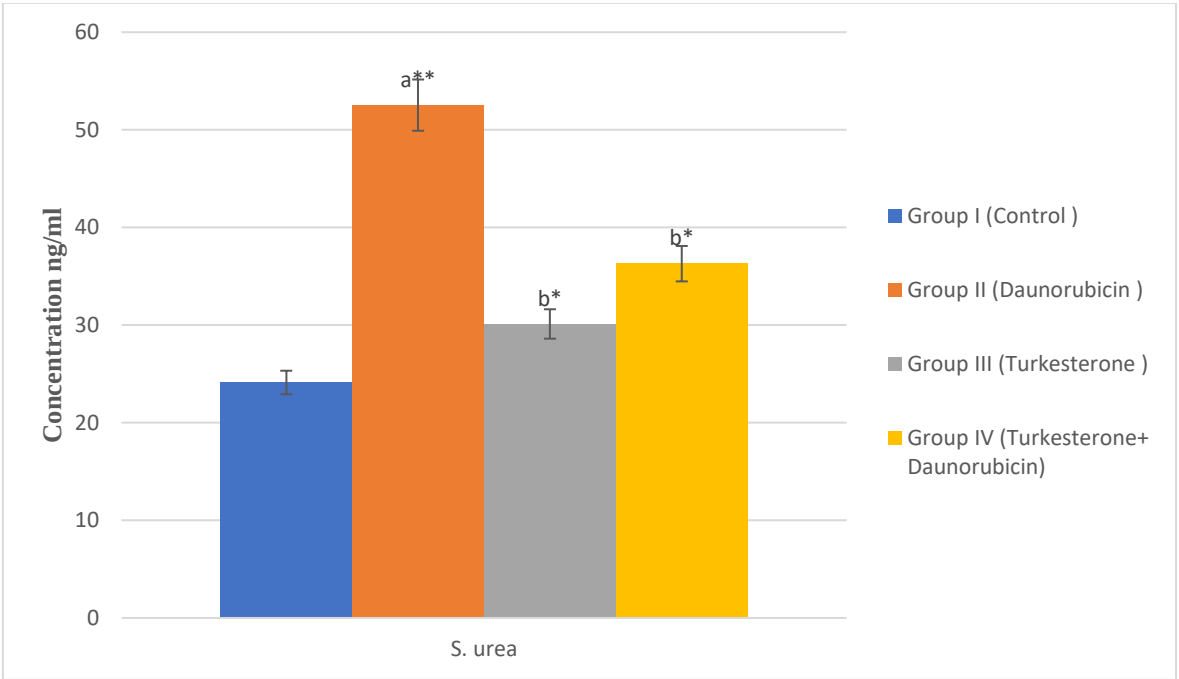

Figure 1. Effect of Turkesterone (5mg/kg) on Serum urea level in rats with nephrotoxicity induced by daunorubicin. Expressed data as Mean±SD, n =6. Small letters symbols (a) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to control. Small letters symbols (b) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to daunorubicin group.

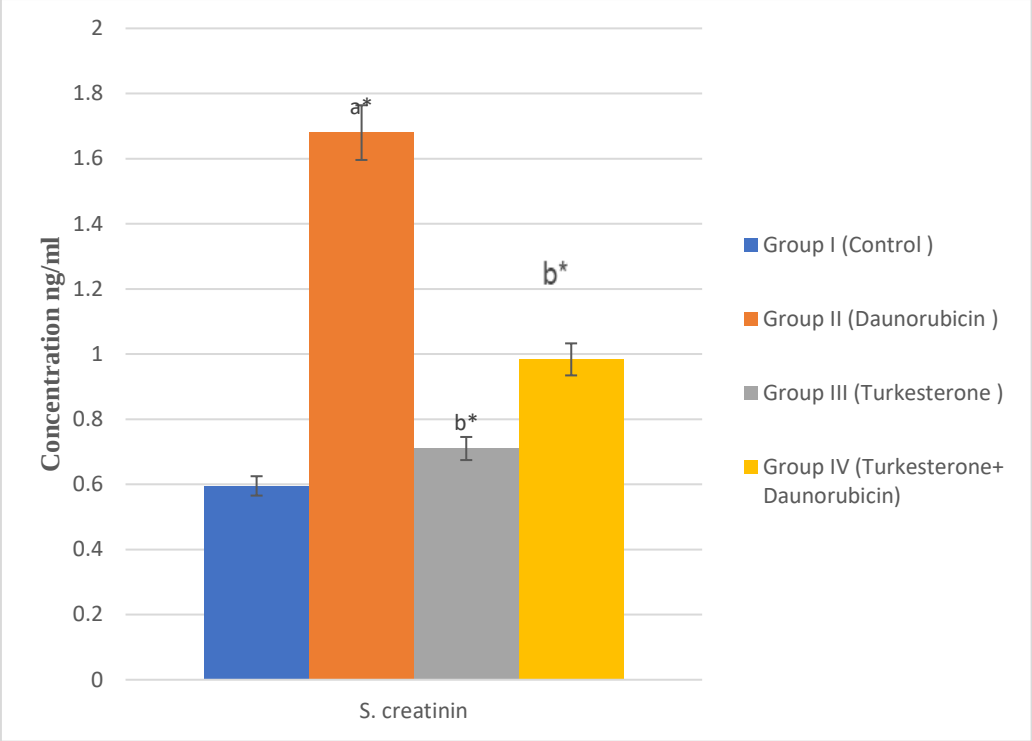

Figure 2. Effect of Turkesterone (5mg/kg) on Serum creatinine level in rats with nephrotoxicity induced by daunorubicin. Expressed data as Mean±SD, n =6. Small letters symbols (a) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to control. Small letters symbols (b) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to daunorubicin group.

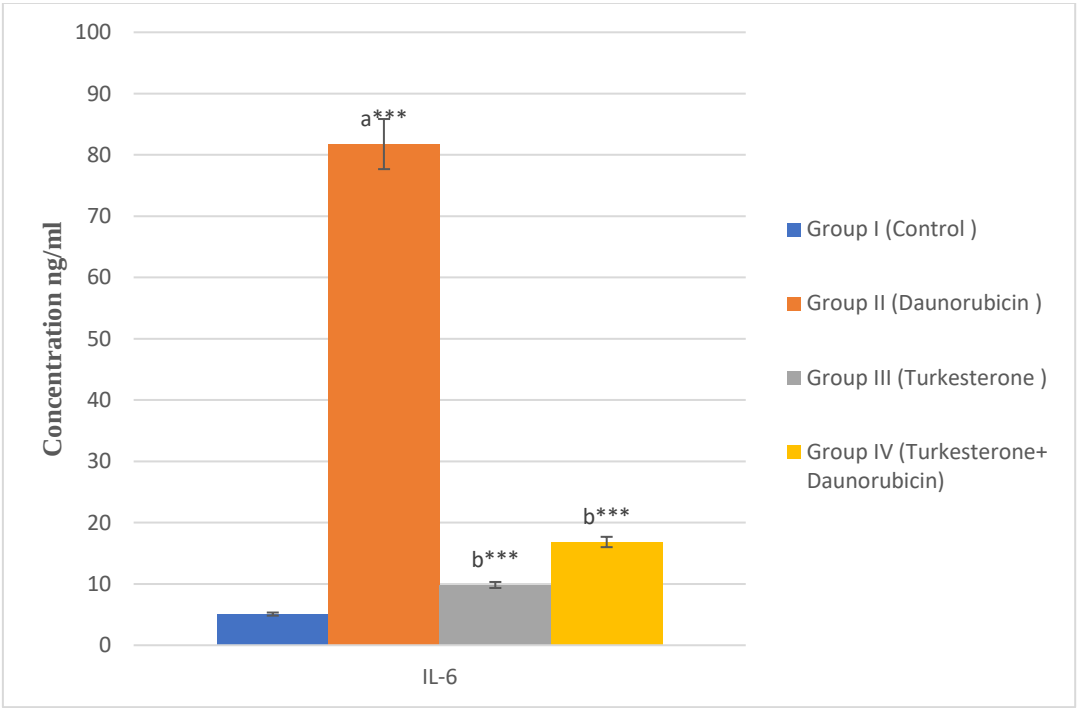

Figure 3. Effect of Turkesterone (5mg/kg) on IL-6 levels in rats with nephrotoxicity induced by daunorubicin. Expressed data as Mean±SD, n =6. Small letters symbols (a) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to control. Small letters symbols (b) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to daunorubicin group.

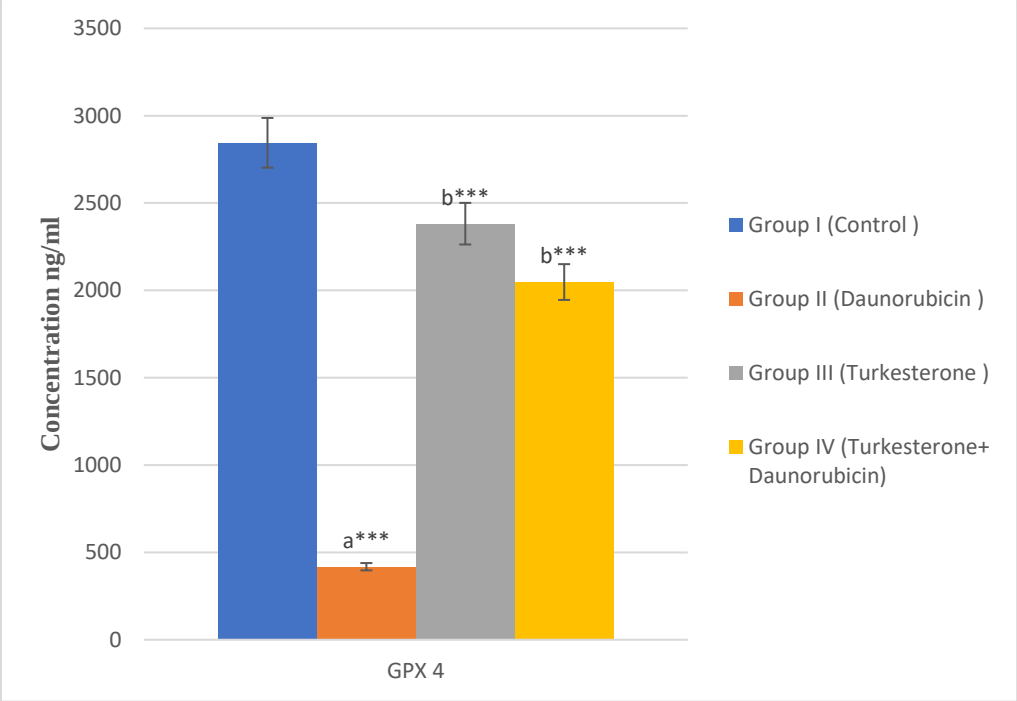

Figure 4. Effect of Turkesterone (5mg/kg) on levels of GPX4 in rats with nephrotoxicity caused by daunorubicin. Expressed data as Mean±SD, n =6. Small letters symbols (a) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to control. Small letters symbols (b) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to daunorubicin group.

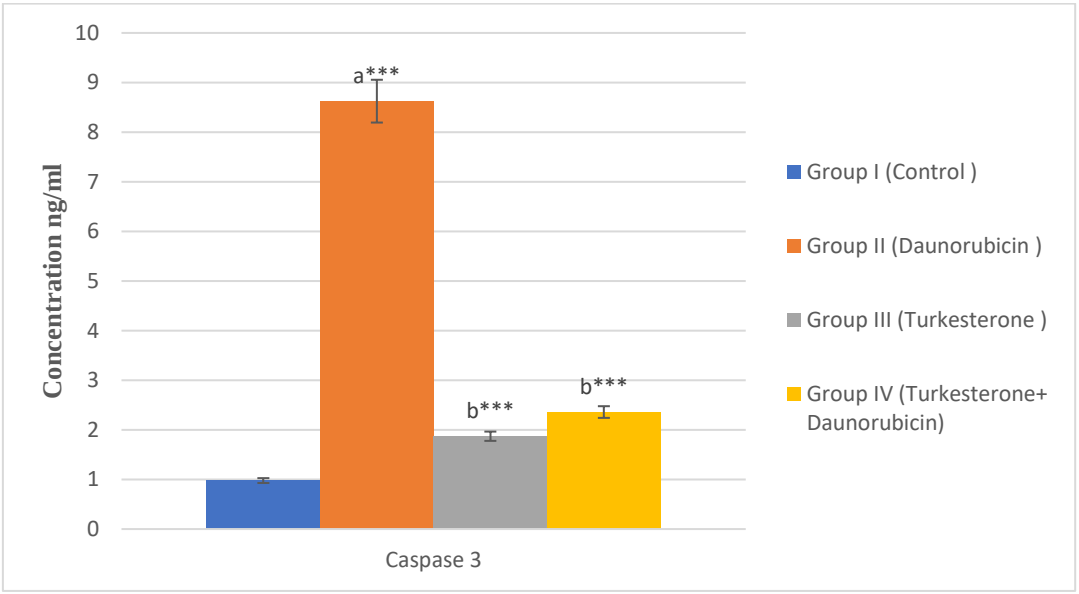

Figure 5. Effect of Turkesterone (5mg/kg) on levels of the Caspase 3 in rats with nephrotoxicity caused by daunorubicin. Expressed data as Mean±SD, n =6. Small letters symbols (a) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to control. Small letters symbols (b) are significant (* $p \leq 0.05$, ** $p \leq 0.01$, ***$p \leq 0.001$) comparing to daunorubicin group.

Anthracyclines cytostatic effects confirmed by many previous studies that can resulted in the cells apoptosis and the immunogenic deaths among other types of death program [5]. The induction of inflammation contributes to the anthracycline anticancer activity in addition to IFN responses and to the immune system stimulation [25]. The present study emphasize that as shown with significant ($P<0.05$) kidney tissue homogenate increasing in the interleukin 6 (Figure. 3).

Turkesterone is a Phytoecdysteroids, which are a class of plants produced bioactive molecules that act as a defense versus the herbivorous insect [26]. Turkesterone structure contains 27 carbon atoms and seven OH-groups; at the C-20 and C-11 OH groups are responsible for the Turkesterone effects

[27]. Wound-healing effects associated with Turkesterone extracted from *Ajuga turkestanica* [26]. as antimicrobial, anti-stress and immune-stimulating, antioxidant effects and antiproliferative [28].

Lipid accumulation decreased in the adipocytes with the use of Turkesterone [29]. In a mouse model with stress-induced, the stress-related consequences are prevented by ecdysterone and turkesterone in addition to restoring the immunological activity [26]. In the alloxan-induced diabetes in rats model associated with improvement of the endocrine and exocrine function with the use of turkesterone [30]. PEs from *Ajuga turkestanica* showed beneficial effects in models of hyperglycemia and diabetes, that shows hypoglycemic activity [26]. Compared to the conventional anabolic steroids, Turkesterone represents to be safer in vivo animal studies, that result in the anabolic effects without the androgenic side effects [26], also muscle maintenance and regeneration enhanced by *Ajuga turkestanica* [31]. This study showed the ameliorative effect of Turkesterone (5mg/kg/day) in daunorubicin nephrotoxicity as shown by the production of significantly ($P<0.05$) decreased serum urea in addition to serum creatinine levels (Figure. 1, 2 respectively) and the production of significantly ($P<0.05$) decreasing the kidney tissues homogenates levels of interleukin 6, and the levels of cleaved caspase-3 (Figure. 3, 5 respectively); moreover, resulting in significantly ($P<0.05$) increasing kidney tissues homogenates levels of GSH peroxidase 4 (Figure. 4).

Conclusion

Several hallmarks of daunorubicin nephrotoxicity were mitigated through pretreatment with Turkesterone as markers of kidney function (serum urea and creatinine), inflammatory (IL6), markers of the oxidative stress (Glutathione peroxidase 4), and markers of the apoptosis (cleaved caspase-3). Further studies of the biological activities and the protective effects of Turkesterone on other organs may be needed.

Acknowledgment

We are grateful for the facilities provided by the Pharmacology and Toxicology Department of the College of Pharmacy/ University of Baghdad/ Iraq.

Conflicts of Interest

No conflict of interest was present in the publication of our manuscript.

Funding

There was no financial support receive from any Institutions

Ethics Statements

The Research Ethical Committee at scientific research by ethical approval of Department of Pharmacology and Toxicology in the College of Pharmacy, University of Baghdad, Iraq.

Author Contribution

The contribution of the present paper was as follow: design and study conception: Alaa R. Khudhair; collection of the data: Mohammed Abdulameer Oleiwi; the analysis of the results: Alaa R. Khudhair; preparation of the draft manuscript: Alaa R. Khudhair and Israa Radhi Khudhair. The manuscript final version reviewed and approved by all authors.

References

1. Safa Mustafa Najim, Mohammad Abdul Amir Ulaiwy, Intesar T. Numan, Maha N.Hamad, Alaa Radhi Khudhair. Nephroprotective Effects of Artichoke Extract against 5-Fluorouracil Induced Nephrotoxicity in Wister Rats: A comparative Study with Telmisartan. Int. J. Pharm. Sci. Rev. Res. 2018; 48(1): 70-74.
2. Wawaimuli Arozala, Kenichi Watanabea, Punniyakoti. Veeraveedu, Meilei Maa, Rajarajan. Thandavarayan, Vijayakumar Sukumaran, Kenji Suzuki, Makoto Kodama, Yoshifusa Aizawa. Protective effect of carvedilol on daunorubicin-induced cardiotoxicity and nephrotoxicity in rats. Toxicology. 2010; 274: 18–26
3. Wawaimuli Arozal, Kenichi Watanabe, Punniyakoti T. Veeraveedu, Meilei Ma, Rajarajan A. Thandavarayan, Vijayakumar Sukumaran, Kenji Suzuki, Makoto Kodama, Yoshifusa Aizawa, Telmisartan prevents the progression of renal injury in daunorubicin rats with the alteration of angiotensin II and endothelin-1 receptor expression associated with its PPAR-γ agonist actions, Toxicology. 2011; 279: 91-99,
4. Simunek T, Sterba M, Popelova O, Adamcova M, Hrdina R, Gersl V. Anthracycline-induced cardiotoxicity: overview of studies examining the roles of oxidative stress and free cellular iron. Pharmacol Rep PR 2009; 61:154–71.
5. Jessica Marinello, Maria Delcuratolo and Giovanni Capranico. Anthracyclines as Topoisomerase II Poisons: From Early Studies to New Perspectives. Int. J. Mol. Sci. 2018; 19: 3480.
6. Jasna Srankova, Gabriel Doka, Lenka Pivackova, Lucia Mesarosova, Jan Kyselovic, Jan Klimas and Peter Krenek. Daunorubicin Down-Regulates the Expression of Stem Cell Markers and Factors Involved in Stem Cell Migration and Homing in Rat Heart in Subchronic but not Acute Cardiomyopathy. Basic & Clinical Pharmacology & Toxicology. 2016; 119: 443–452
7. Laurence Dinan, Pauline Bourne, Pensri Whiting, Ada Tsitsekli, Ziyadilla Saatov, Tarlochan S. Dhadialla, Robert E. Hormann, René Lafont and Josep Coll. Synthesis and

biological activities of turkesterone 11α-acyl derivatives. Journal of Insect Science 2003; 3 (6):11pp.

8. Velislava Todorova, Kalin Ivanov, Diana Karcheva-Bahchevanska and Stanislava Ivanova. Development and Validation of High-Performance Liquid Chromatography for Identification and Quantification of Phytoecdysteroids Ecdysterone and Turkesterone in Dietary Supplements. Processes 2023; 11: 1786.

9. Isenmann, E.; Ambrosio, G.; Joseph, J.F.; Mazzarino, M.; de la Torre, X.; Zimmer, P.; Kazlauskas, R.; Goebel, C.; Botrè, F.; Diel, P.; et al. Ecdysteroids as Non-Conventional Anabolic Agent: Performance Enhancement by Ecdysterone Supplementation in Humans. Arch. Toxicol. 2019; 93: 1807–1816.

10. Tóth, N.; Szabó, A.; Kacsala, P.; Héger, J.; Zádor, E. 20-Hydroxyecdysone Increases Fiber Size in a Muscle-Specific Fashion in Rat. Phytomedicine 2008; 15: 691–698.

11. Bathori, M.; Toth, N.; Hunyadi, A.; Marki, A.; Zador, E. Phytoecdysteroids and Anabolic-Androgenic Steroids—Structure and Effects on Humans. Curr. Med. Chem. 2008; 15: 75–91.

12. Shuvalov, O.; Kirdeeva, Y.; Fefilova, E.; Netsvetay, S.; Zorin, M.; Vlasova, Y.; Fedorova, O.; Daks, A.; Parfenyev, S.; Barlev, N. 20-Hydroxyecdysone Confers Antioxidant and Antineoplastic Properties in Human Non-Small Cell Lung Cancer Cells. Metabolites 2023; 13: 656.

13. Maria Kristina Parr, Piwen Zhao, Oliver Haupt, *et al*. Estrogen receptor beta is involved in skeletal muscle hypertrophy induced by the phytoecdysteroid ecdysterone. Molecular Nutrition & Food Research. 2014; 58(9):1861-72.

14. Zorawar S and Harmanpreet K. Cardiotoxicity induced by antineoplastic drug Daunorubicin and its amelioration: A review of literature. Blood Heart Circ,. 2019; 3: 1-4.

15. Lafont R. and Dinan L. Practical uses for ecdysteroids in mammals including humans: and update. 30pp. Journal of Insect Science. 203; 3:7-37.

16. Alaa R. Khudhair and Nada N. Al-Shawi. Possible Protective Effects of high- versus low-dose of lutein in combination with irinotecan on Liver of Rats: Role of Oxidative Stress and Apoptosis. Indian Journal of Forensic Medicine & Toxicology. 2021; 15:2439-2445.

17. Mohammed Abdulameer Oleiwi, Munaf Hashim Zalzala, Alaa Radhi Khudhair, Mohammed Kamil Hadi, Zahraa Duraid Abdulazeez. Evaluation of the Wound-Healing Activity and Apoptotic Induction of New Quinazolinone Derivatives. Al-Rafidain J Med Sci. 2024; 6(2):32-36.

18. Austin, C.; Lee, K.; Swan, R.; Khazeem, M.; Manville, C.; Cridland, P.; Treumann, A.; Porter, A.; Morris, N.; Cowell, I. TOP2B: The First Thirty Years. Int. J. Mol. Sci. 2018; 19: 2765.

19. Alaa R. Khudhair and Nada N. Al-Shawi. Possible Protective Effects of Lutein against Ciprofloxacin Induced Bone Marrow Toxicity in Rats. Iraqi J Pharm Sci. 2021; 30(1): 233-239.

20. Alaa Radhi Khudhair, Nada N. Al-Shawi, Ali Faris Hassan. Impact of Omega 3 on the Genotoxicity of Irinotecan on Bone Marrow and Spleen of Rats: in-vivo Study. Iraqi J Pharm Sci, 2023; 32 (1): 53-58.

21. Santos MLC, Brito BB, da Silva FAF, Botelho ACDS, Melo FF. Nephrotoxicity in cancer treatment: An overview. World J Clin Oncol. 2020; 11(4): 190-204.

22. Zohaib Razaa, and Zainab Naureen. Melatonin ameliorates the drug induced nephrotoxicity: Molecular insights. Nefrologia. 2020; 40: 1-114.

23. Alaa Radhi Khudhair and Intesar T. Numan. Possible Cardio-Protective Effects of Telmisartan against 5-Fluorouracil-Induced Cardiotoxicity in Wister Rats. Int J Pharm Pharm Sci 2014; 6 (6): 397-400.

24. Arwanih E Y, Louisa M, Rinaldi I, et al. Resistance Mechanism of Acute Myeloid Leukemia Cells Against Daunorubicin and Cytarabine: A Literature Review. Cureus. 2022; 14(12): e33165.

25. Bracci, L.; Schiavoni, G.; Sistigu, A.; Belardelli, F. Immune-based mechanisms of cytotoxic chemotherapy: Implications for the design of novel and rationale-based combined treatments against cancer. Cell Death Differ. 2014; 21: 15–25.

26. Velislava Todorova, Stanislava Ivanova, Dzhevdet Chakarov, Krasimir Kraev and Kalin Ivanov. Ecdysterone and Turkesterone—Compounds with Prominent Potential in Sport and Healthy Nutrition. Nutrients. 2024; 16(9): 1382.

27. Todorova, V.; Ivanov, K.; Karcheva-Bahchevanska, D.; Ivanova, S. Development and Validation of High-Performance Liquid Chromatography for Identification and Quantification of Phytoecdysteroids Ecdysterone and Turkesterone in Dietary Supplements. Processes. 2023; 11: 1786.

28. Savchenko, R.G.; Veskina, N.A.; Odinokov, V.N.; Benkovskaya, G.V.; Parfenova, L.V. Ecdysteroids: Isolation, Chemical Transformations, and Biological Activity. Phytochem. Rev. 2022; 21: 1445–1486.

29. Todorova, V.; Savova, M.S.; Ivanova, S.; Ivanov, K.; Georgiev, M.I. Anti-Adipogenic Activity of Rhaponticum carthamoides and Its Secondary Metabolites. Nutrients. 2023; 15: 3061.

30. Kuchkarova, L.S.; Rokhimova, S.O.; Syrov, V.N. Effect of Turkesterone on the Pancreas Histology and Function in Diabetic Rats. Int. J. Curr. Res. Rev. 2020; 12: 2–5.

31. Arthur, S.T.; Zwetsloot, K.A.; Lawrence, M.M.; Nieman, D.C.; Lila, M.A.; Grace, M.H.; Howden, R.; Cooley, I.D.; Tkach, J.F.; Keith, M.D.; et al. Ajuga Turkestanica Increases Notch and Wnt Signaling in Aged Skeletal Muscle. Eur. Rev. Med. Pharmacol. Sci. 2014; 18: 2584–2592.

تأثير الحماية الكلوية للتركستيرون ضد إصابة الكلى الحاد الناجمة عن الداونوروبيسين في الجرذان

الاء راضي خضير [*،١]، محمد عبد الامير عليوي [٢] و اسراء راضي خضير [٣]

[١]فرع االادوية والسموم ، كلية الصيدلة ، جامعة بغداد، بغداد، العراق.

[٢]فرع الكيمياء الصيدلانية ، كلية الصيدلة ، جامعة بغداد، بغداد ،العراق.

[٣]فرع علوم الحياة ، كلية التربية للعلوم الصرفة ابن الهيثم ، جامعة بغداد، بغداد ،العراق.

الخلاصة

تركستيرون، وهو فيتوكديستيرويد يحتوي على مجموعة ١١-α-هيدروكسيل، هو نظير لـ٢٠-هيدروكسي إيكديسون وهو هرمون الستيرويد الحشري. Phytoecdysteroids، مجموعة من الهرمونات ecdysteroid موجودة بشكل طبيعي في الأنواع النباتية *Ajuga turkestanica*، *Rhaponticum carthamoides* Willd. و *Cyanotis arachnoidea C.B.Clarke* الذي تم استخدامه على مر القرون بسبب خصائصه المنشطة والتكيفية ومضادات الأكسدة وقدرته على تعزيز الأداء البدني. ارتبط الإكديستيرون والتركستيرون بتأثيرات بيولوجية مختلفة، مثل الحماية العصبية، والابتنائية، وخافضات للدهون ومضادات لارتفاع السكربالدم. اقترحت العديد من الدراسات أن آلية السمية القلبية والسمية الكلوية الناجمة عن الداونوروبيسين عن طريق تكوين أنواع الأكسجين التفاعلية من خلال مجمعات الأنثراسيكلين والحديد الخاصة بها وتدوير الأكسدة والاختزال وكذلك من الجليكونات هي الآلية الرئيسية التي تسبب التلف الخلوي. تم تصميم هذه الدراسة من أجل التحقق من إمكانية الحماية الكلوية للتركستيرون ضد السمية الكلوية الناجمة عن داونوروبيسين. أربعة وعشرون (٢٤) أنثى جرذان سبراغ داولي البالغة. تم تقسيم الحيوانات إلى أربع (٤) مجموعات مكونة من ستة (٦) فئران لكل منها: المجموعة I: تلقت جرعة يومية عن طريق الفم من ١٠٪ ثنائي ميثيل سلفوكسيد (٤ مل / كجم) لمدة ١٥ يومًا متتاليًا. المجموعة II: تلقت جرعة يومية واحدة عن طريق الفم بنسبة ١٠٪ ثنائي ميثيل سلفوكسيد لمدة ١٥ يومًا، ثم تلقت بعد ذلك داونوروبيسين ٢٠ ملغم/كغم خلال الأيام الثلاثة الأخيرة بجرعة تراكمية قدرها (٦٠ ملغم/كغم) عن طريق الحقن داخل الصفاق. المجموعة III: تناولت جرعة من تركستيرون عن طريق الفم (٥ ملجم/كجم/يوم) لمدة ١٥ يومًا متتاليًا. المجموعة IV: تلقت جرعة فموية من تركستيرون (٥ ملجم / كجم / يوم) لمدة ١٥ يومًا متتاليًا، ثم تلقت بعد ذلك داونوروبيسين ٢٠ ملجم / كجم خلال الأيام الثلاثة الأخيرة بجرعة تراكمية قدرها (٦٠ ملجم / كجم) عن طريق الحقن داخل الصفاق. أظهرت الفئران المستحثة بالسمية الكلوية، مع داونوروبيسين، والمعالجة بالتركستيرون (المجموعة IV) انخفاضًا ملحوظًا في مستوى كل من اليوريا والكرياتينين في مصل الدم، كما عكست علامات الإجهاد التأكسدي؛ للجرذان مستويات الجلوتاثيون بيروكسيديز ٤ ، إلى مستوى السيطرة. قمع علامات موت الخلايا المبرمج والالتهابات، عن طريق قياس مستويات إنترلوكين ٦ للجرذان ومستويات كاسباس ٣ المشقوقة على التوالي، في أنسجة الكلى. تم التوصل إلى أن العديد من السمات المميزة للسمية الكلوية الناجمة عن الداونوروبيسين تم تخفيفها عن طريق المعالجة المسبقة مع التركستيرون.

الكلمات المفتاحية: الحماية الكلوية، توركستيرون، داونوروبيسين، caspase-3 المشقوق والجلوتاثيون بيروكسيديز ٤.