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Amphibian & Reptile Conservation
19(1): 106–117 (e346).

Curcumin as a Potential Natural Therapeutic for Mitigating Drug-Induced Metabolic Disturbances: Insights from a Rodent Model with Relevance to Amphibian and Reptile Conservation Medicine

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Abstract.*—Most of the species of amphibians and reptiles are facing a decline because of drug-induced metabolic disturbances and exposure to environmental contaminants. Consequently, focus is being directed to identifying various natural products with an aim of alleviating drug-induced metabolic disequilibrium. The testicular damage is due to different metabolic disturbances that are observed such as oxidative stress, liver damage, and glucose level disturbances. The given research aims to evaluate the effectiveness of curcumin in the context of preventing the testicular damage caused by the influence of ketoconazole through the utilization of a rodent organism. The results of the present research are also a prospect of amphibian and reptile conservation (ARC) medicine. To accomplish this, a sample of 36 male rodents was chosen, and they were separated into 6 groups (Group A: control, Group B: ketoconazole, Group C: Ketoconazole and low dose of curcumin, Group D: Ketoconazole and high dose of curcumin, Group E: low dose of curcumin, and Group F: high dose of curcumin). Statistical analysis was done on blood tests and serum concentrations and weight of the body. The findings indicate that in Group B, the levels of serum testosterone and SOD were reduced to 2.0 ng/ mL and 6.0 U/ mg respectively. On the contrary, MDA and glucose levels rose by 3.1 nmol/ mg and 119.9 mg/ dL, respectively, in Group B. This demonstrates that ketoconazole affects the male reproductive system to a great extent. Conversely, group D, E, and F were statistically equal, with significant results (a). The article has a clinical impact in highlighting the use of curcumin in addressing drug-induced disruption of metabolism by inhibiting oxidative stress and enzymatic action. Thus, the current study has future implications on analyzing the role of curcumin in offsetting various drug-induced metabolic disturbances in different species of amphibians and reptiles by enhancing the veterinary protocols in that matter.

Keywords. Curcumin antioxidant, amphibian and reptile conservation medicine, drug-induced metabolic disturbances, veterinary toxicology

Citation: Aydin M, Eğilmez Ü, Onmaz DE, Ünlü A. 2025. Curcumin as a Potential Natural Therapeutic for Mitigating Drug-Induced Metabolic Disturbances: Insights from a Rodent Model with Relevance to Amphibian and Reptile Conservation Medicine. *Amphibian & Reptile Conservation* 19(1): 106–117 (e346).

Accepted: 10 February 2025; **Published:** 30 November 2025

Introduction

The spread of fungal diseases contributes to the decline of different exotic animals. For instance, *Nannizziopsis* spp. results in fatal dermatomycoses in captive reptiles, making it an emerging infectious disease of herpetofauna (Visvanathan et al., 2023). Different fungal diseases and changes in the anthropogenic environment have also led to the global decline of amphibians (Nkwonta et al., 2025). According to the "International Union for the Conservation of Nature (IUCN)", 30% of different amphibian spp. are at the verge of extinction, whereas 484 of these species are considered to be endangered. Chytridiomycosis, which is caused by "amphibian chytrid fungi," has become one of the main reasons for the decline of the amphibian population

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(Pessier & Mendelson, 2017). It is mainly caused by *Batrachochytrium dendrobatidis (Bd),* which targets the amphibian skin's keratinized parts as well as the tadpole's mouth. This disrupts the respiration and exchange of ions across the epidermal layer, leading to cardiac arrest. Different conditions for the growth of *Bd* include a higher rate of humidity and temperature ranging from 17-23 °C (Soto-Pozos et al., 2025). As a result, focus is being given on various ex situ and in situ efforts in the context of amphibian and reptile conservation (ARC) medicine.

The current development of climate change has rendered most habitats inhabited by amphibians less habitable and this has accentuated the mitigation of chytridiomycosis. A previous research study conducted by Berger et al. (2024) has demonstrated that itraconazole has a great effect in treating this fungus in amphibians. Nevertheless, it also brings about metabolic distress and subsequent side effects of reduced growth rate, lethargy, depigmentation and death. Moreover, such conditions can also be treated with the help of other antifungal drugs like ketaconazole, and they lead to various metabolic disturbances. Obesity, diabetes, hyperthyroidism, and metabolic syndrome are the most prevalent metabolic diseases caused by drugs (Qiu et al., 2023). Other past studies have also indicated that ketoconazole has the ability to induce testicular toxicity. To a large extent, it is caused by depletion of germ cells, oxidative stress, and histopathologic changes (Onoja et al., 2024b). Thus, it is also showing interest in exploring various natural compounds as pertaining to ARC medicine. In this scenario, Curcumin has become a useful natural medicine. It is a natural polyphenolic compound (figure 1) which is extracted out of the rhizomes of Curcuma (Zhai et al., 2020). It is also employed currently in various clinical trials in the treatment of metabolic diseases in case of adverse events of various medications. An examination by Tarlan et al. (2025) indicated that curcumin possesses proactive nature that is vital in safeguarding the reproductive health of male subjects against drug induced problems. It also inhibits inflammatory and oxidative stress. These traits aid in maintaining male fertility. Due to this, the use of a more practical and clinical approach has been placed on so that the prominence of curcumin in the medicine of ARC is guaranteed.

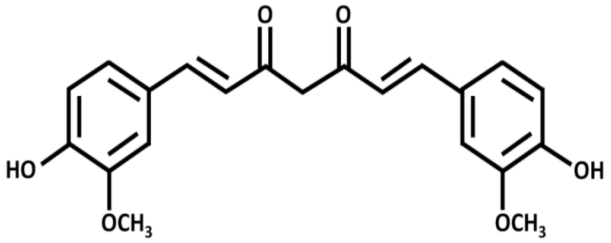

Fig. 1. Structure of curcumin.
Source: (Zhai et al., 2020)

Moreover, curcumin is also being used to reduce other drug-induced metabolic disturbances. Zobeydi et al. (2025) have also utilized the synergist effect of curcumin and "aerobic interval training" (AIT) to decrease "endoplasmic reticulum (ER) stress-mediated apoptosis." Additionally, the role of curcumin in preventing chemoresistance is also inevitable (Soni et al., 2021). It allows curcumin to manage liver cancer effectively. Over the years, the clinical significance of curcumin has increased due to its multifaceted pharmacological characteristics such as anti-inflammation, cytoprotective, and antioxidant properties (Kaur et al., 2024). In addition, curcumin also modulates signaling pathways providing essential responses against cellular stress. A past research by Boarescu et al. (2019) has also highlighted the cardio-protective and antidiabetic effects of curcumin to improve its nutritional interventions in herpetological medicine. Its hepatoprotective and antioxidant effects also increase its effectiveness in reducing oxidative stress among reptiles that are being treated with antifungal drugs (Chen et al., 2018). It is also being used for preventing metabolic distress which is faced by amphibians due to environmental pollutants and exposure to heavy metals (Rutschmann et al., 2023). Curcumin also preserves mitochondrial functions (Hu et al., 2023) along with its cytoprotective effects (Fouda et al., 2023). Besides the vast literature on curcumin, its role in mitigating drug-induced metabolic disturbances remains undervalued. This allows the current research to address this gap by determining the therapeutic efficacy of curcumin in decreasing anti-fungal-induced metabolic disturbances such as oxidative liver damage, increased glucose level and reduced testosterone level. These findings are also beneficial in relevance to ARC medicine.

This study seeks to determine curcumin's efficacy in reducing "ketoconazole-induced testicular damage" by using a rodent model. For this purpose, an experimental study was conducted to determine the underlying mechanisms of curcumin's protective effects within the context of drug-induced metabolic disturbances. Although a well-established rodent model has been used for investigating the efficacy of curcumin, the findings of this study also provide a translational potential for ARC medicine. Amphibians and reptiles are largely exposed to heavy metals and other environmental contaminants. This exposure results in different metabolic disturbances, emphasizing the integration of a natural antioxidative compound to manage oxidative stress. Additionally, the captive reptiles and amphibians are also given different antifungal drugs, resulting in drug-induced metabolic disturbances and oxidative stress. The identification of an effective and safe natural product such as curcumin is considered to be highly relevant to the veterinary protocols of different amphibians and reptile species. The overall goal of this research is to provide important information for future researchers to evaluate other drug-induced metabolic disturbances that can be mitigated by curcumin (Boarescu et al., 2019) in the context of herpetofauna.

Materials and methods

For this study, an experimental study was conducted. For this purpose, a rodent model was used, incorporating about 36 male rodents. The average weight of these rats was 116.5 g. These rodents were obtained from Acıbadem University, Turkey. For this purpose, important ethical guidelines were considered. These rodents were kept in plastic cages, which were covered with metal. These rodents were categorized into six groups. Each group included 6 rodents. An electronic weighing machine was analyzed during acclimatization as well as when the experiment ended. Their weight was also determined pre- and post-administration of curcumin extract.

Justification for the rodent model

In this study, the rodents are selected as mammalian analogs for determining the antioxidant characteristics of curcumin. Past research has also used a mouse/ rodent model for assessing antioxidative and metabolic effects of curcumin (Cox et al., 2022; Guariglia et al., 2023). This supports the integration of the rodent model for the present research. This model also supports different metabolic disturbances that are faced by amphibians and reptiles due to the administration of different drugs during captivity. The findings of this study will provide a base for future trials on amphibians or reptiles, focusing on the utilization of curcumin to reduce oxidative and metabolic stress due to environmental changes.

Experimental drug procurement

For this experiment, the ketoconazole tablets were obtained from a local pharmacy. These tablets were later fed to selected rodents from different groups.

Curcumin extraction and curcuminoid isolation

The turmeric collected for this study was cleaned with distilled water. It was later divided into ten various rhizomes. Slices of the washed rhizomes were done. These slices were then dried for at least seven days. 0.1 g of the dried sample was obtained, and it was added to ethanol (30 ml). It was later mixed for 2 hours and 20 minutes. The produced sample was then filtered, and the volume of the prepared solution was maintained at 100 ml. From this solution, 20 ml of the extract was taken and further diluted to 250 ml.

Sample preparation

The produced extract included oleoresins and curcuminoids. Three solvents were used for extracting curcuminoids from these oleoresins. These solvents included acetone, chloroform, and hexane.

Experimental design

A rodent model comprising of 36 male rodents was used. These rodents were categorized into 6 groups (each group included 6 male rodents) as stated below:

- Group A (control group) includes rodents that were administered 5 ml/ kg of distilled water for about 4 weeks.
- Group B (ketoconazole group) includes rodents that were administered 100 mg/ kg of ketoconazole for 2 weeks.
- Group C includes the rodents that were administered 100 mg/ kg of ketoconazole and 10 mg/ kg of curcumin (low dose) for 2 weeks.
- Group D includes the rodents that were administered 100 mg/ kg of ketoconazole and 20 mg/ kg of curcumin (high dose) for 2 weeks.
- Group E includes the rodents that were administered 10 mg/ kg of curcumin (low dose) for 2 weeks.
- Group F includes the rodents that were administered 20 mg/ kg of curcumin (high dose) for 2 weeks.

Animal sacrifice and data collection

The rodents were weighed before the sacrifice. For this purpose, they were anesthetized with the help of chloroform. The blood samples were withdrawn from all groups of the rodents. An abdominal incision was made in the midline of each rodent to observe the reproductive organs. The testes of each rodent were extracted and weighed using an electronic weighing balance. The testosterone concentrations within the plasma were analyzed by using the strategy of Onoja et al. (2024a). It was also considered for evaluating the levels of glucose, cholesterol, Malondialdehyde (MDA), and Superoxide dismutase (SOD).

Statistical analysis

For this experimental study, statistical analysis was performed. Initially, descriptive statistics were performed for each group. For this purpose, focus was given on the levels of glucose, testosterone, cholesterol, MDA, and SOD. "Duncan's multiple range tests" were also performed. Finally, "a one-way analysis of variance (ANOVA)" was performed. This test was found to be beneficial for comparing the control and other intervention groups. The level of significance was kept at a threshold of $p \leq 0.05$.

Results

Descriptive statistics

Table 1 presents the descriptive statistics for this study. The control group presents the baseline and healthy state of the rodents (represented by "a"). The level of serum testosterone decreased from ~4.49 ng/ mL (in the control group) to 2.01 ng/ mL (in the ketoconazole group), presenting endocrine disruption. At the same time, the level of SOD decreased to 6.00 U/ mg, and the level of MDA increased by 3.12 nmol/ mg in the ketoconazole group, leading to an increase in oxidative stress. In

Table 1: Descriptive statistics (mean ± SEM) with post-hoc letters.

Group	BodyWeight_ Gain	Serum_ Glucose	Serum_ Cholesterol	Serum_ Testosterone	Liver_SOD	Liver_MDA	BodyWeight_ Gain (Letter)	Serum_ Glucose_ (Letter)	Serum_ Cholesterol (Letter)	Serum_ Testosterone_ (Letter)	Liver_SOD (Letter)	Liver_MDA (Letter)
Control	7.79 ± 0.53	94.63 ± 1.86	121.63 ± 3.25	4.67 ± 0.18	12.34 ± 0.43	1.50 ± 0.10	a	a	a	a	a	a
Ketoconazole	5.99 ± 0.59	119.93 ± 2.28	143.03 ± 2.02	2.01 ± 0.26	6.00 ± 0.49	3.12 ± 0.13	a	b	a	b	b	b
Ket+Curcumin_Low	5.71 ± 0.51	105.87 ± 1.70	130.88 ± 2.20	3.35 ± 0.21	9.54 ± 0.46	2.17 ± 0.15	a	a	a	c	c	c
Ket+Curcumin_High	7.46 ± 0.76	101.58 ± 1.63	126.28 ± 3.92	5.04 ± 0.25	12.19 ± 0.66	1.46 ± 0.09	a	a	a	a	a	a
Curcumin_Low	9.82 ± 0.28	92.55 ± 2.22	112.17 ± 3.03	5.28 ± 0.23	13.52 ± 0.29	1.19 ± 0.16	a	a	a	a	a	a
Curcumin_High	9.30 ± 0.52	88.68 ± 1.89	115.88 ± 2.93	5.79 ± 0.22	14.27 ± 0.66	1.02 ± 0.08	a	a	a	a	a	a

Table 2: One-way ANOVA summary.

Variable	F-value	p-value	eta^2
BodyWeight_Gain_g	9.230	$2.111e^{-05}$	0.606
Serum_Glucose_mg_dL	34.063	$1.679e^{-11}$	0.850
Serum_Cholesterol_mg_dL	14.146	$3.88e^{-07}$	0.702
Serum_Testosterone_ng_mL	39.098	$2.922e^{-12}$	0.867
Liver_SOD_U_mg_protein	35.313	$1.067e^{-11}$	0.855
Liver_MDA_nmol_mg_protein	41.753	$1.253e^{-12}$	0.874

Table 3: Post-hoc group letters (Tukey HSD).

Group	BodyWeight_Gain_g (Letter)	Serum_Glucose_mg_dL (Letter)	Serum_Cholesterol_mg_ dL (Letter)	Serum_Testosterone_ng_ mL (Letter)	Liver_SOD_U_mg_ protein (Letter)	Liver_MDA_nmol_mg_ protein (Letter)
Control	a	a	a	a	a	a
Ketoconazole	a	b	a	b	b	b
Ket+Curcumin_Low	a	a	a	c	c	c
Ket+Curcumin_High	a	a	a	a	a	a
Curcumin_Low	a	a	a	a	a	a
Curcumin_High	a	a	a	a	a	a

addition, serum glucose is also found to be increased by 119.93 mg/ dL in the ketoconazole group, highlighting its role in increasing metabolic disturbances. Similarly, the amphibians or reptiles that are given itraconazole or other antifungal drugs in captivity also show such metabolic distress and dysfunction (Cabral et al., 2023).

However, the group with ketoconazole and low dosage of curcumin showed an improved level of serum testosterone (3.35 ng/ mL) as compared to the ketoconazole group. The levels of SOD (9.54 U/ mg) and MDA (2.17 nmol/ mg) were also found to be improved in this group. In contrast, the group with ketoconazole and high dosage of curcumin showed the protective effects of curcumin as the values of serum testosterone, SOD, and MDA were found to be identical to the control group ("a"). Similarly, the groups with low and high dosages of curcumin were also found to be statistically identical to the control group ("a"). Therefore, the antioxidant characteristics of curcumin also support its application in different amphibians/ reptiles which are exposed to metabolic dysfunction and oxidative stress due to heavy metals and environmental changes.

ANOVA

Table 2 shows that F-values are found to be higher for serum testosterone (39.1) and MDA (41.75). This shows significant group effects. The values of *p* were also found to be below 0.05, showing significant outcomes. Eta^2 values were found to be higher for body weight gain (0.606), serum glucose (0.850), serum cholesterol (0.702), serum testosterone (0.867), SOD (0.855), and MDA (0.874). These values present the significant impact of therapeutic and nutritional interventions of curcumin for amphibians/ reptiles.

Post-hoc group letters

Table 3 presents the post-hoc group letters. It has been clearly observed that the body weight gain, serum glucose level, serum cholesterol level, serum testosterone level, liver SOD, and liver MDP are statistically identical for groups with ketoconazole and high dosage of curcumin, low dosage of curcumin, and high dosage of curcumin

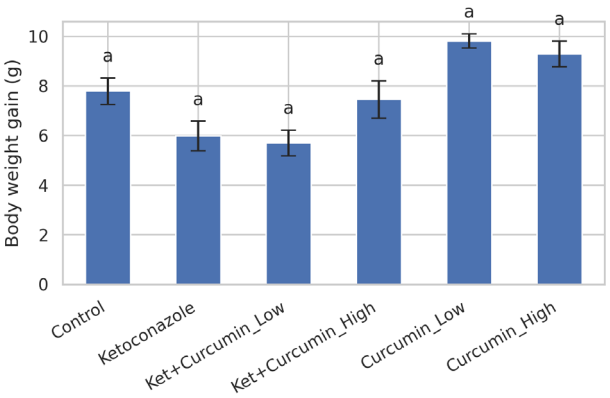

Fig. 2. Body weight gain (mean ± SEM) with Tukey letters.

("a") in association with the control group ("a"). In contrast, the value of serum glucose level, serum testosterone level, liver SOD, and liver MDP varied between the ketoconazole group and the control group. In addition, the value of serum testosterone level, liver SOD, and liver MDP varied between the ketoconazole and low dosage curcumin group and the control group. This shows that curcumin has significant therapeutic effects in protecting male reproductive health against the adverse effects of ketoconazole. These findings also support the integration of curcumin in veterinary protocols within the context of ARC medicine.

Metabolic disturbances and curcumin

Figure 2 shows that weight gain was decreased in the ketoconazole group, showing an insignificant impact. However, "a" for all groups showed a significant decrease in the testosterone level, which was later maintained by the high dosage of curcumin.

Figure 3 clearly shows an increase in glucose level in the ketoconazole group ("b") as compared to groups that were administered with curcumin. This shows that a high level of glucose in the ketoconazole group often leads to testicular damage. As a result, the male reproductive health is damaged ineffectively. However, the cholesterol level was found to be higher in ketoconazole, but it remained statistically identical to other groups ("a").

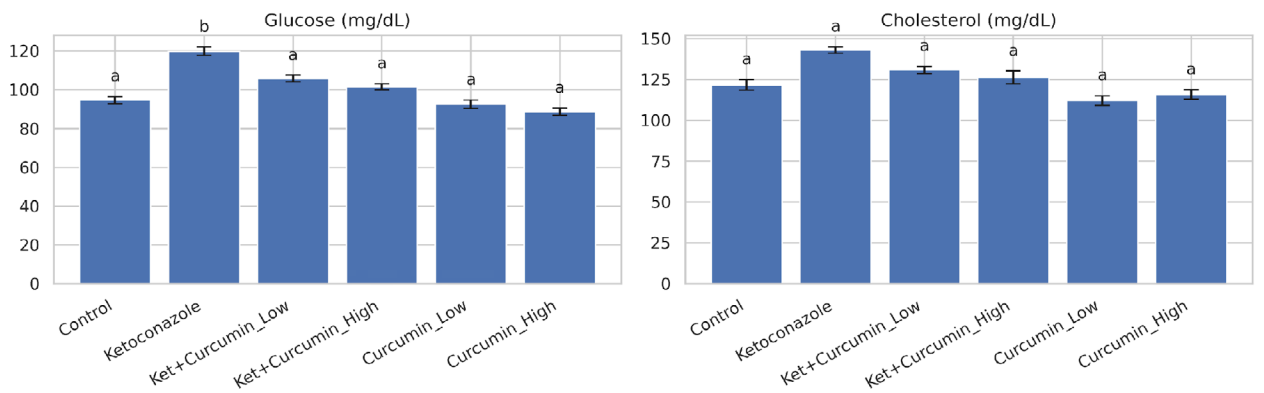

Fig. 3. Metabolic markers: Serum glucose & cholesterol (mean ± SEM).

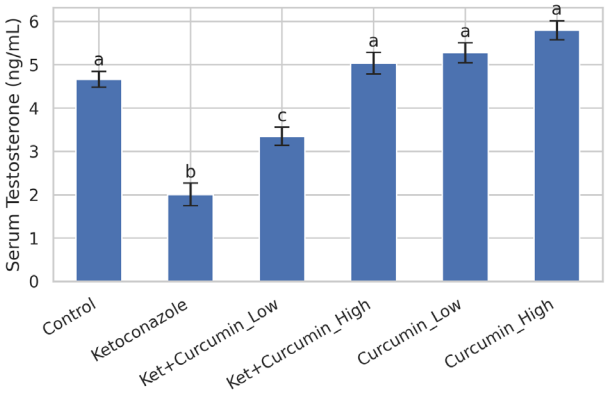

Fig. 4. Serum testosterone (mean ± SEM).

Figure 4 shows that ketoconazole has an insignificant impact on the serum levels of testosterone. As a result, the level of serum testosterone decreased on ketoconazole. It was also found to be statistically insignificant ("b") as compared to the control group and other groups ("a"). At the same time, the level of serum testosterone was found to be higher but not insignificant in the group with ketoconazole and low dosage of curcumin ("c"). Contrarily, the level of serum testosterone was found to be significant in the control group, the group with ketoconazole and high dosage of curcumin, and groups with low and high dosages of curcumin ("a").

Figure 5 shows that the levels of liver SOD and MDA were irregular in the ketoconazole group ("b") and the group with ketoconazole and a lower dosage of curcumin ("c"). However, the levels of liver SOD and MDA were found to be statistically significant in the control group, the group with ketoconazole and high dosage of curcumin, and the groups with low and high dosages of curcumin ("a").

Metabolic effect of drug and curcumin treatment

Table 4 shows metabolic disturbances caused by ketoconazole, such as a decrease in body weight and increased levels of cholesterol and glucose ($p < 0.0001$), whereas the curcumin groups with low and high doses showed a significant decrease in these metabolic disturbances (Fig. 6A-6C), supporting its therapeutic role in ARC medicine.

Antioxidant and hepatoprotective effects of curcumin

Ketoconazole causes severe liver damage and oxidative stress by decreasing SOD level and increasing MDA level ($p < 0.0001$) (Table 5). The antioxidant and

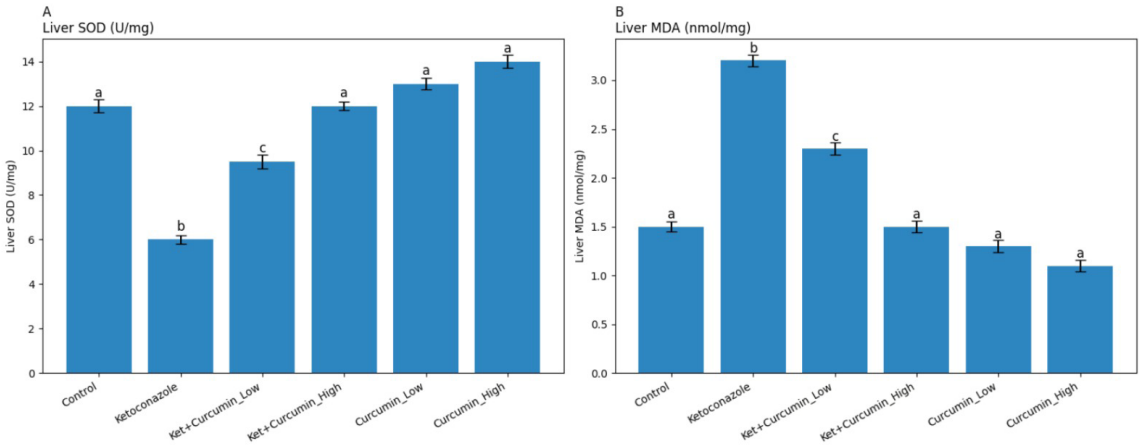

Fig. 5. Liver oxidative stress markers: SOD & MDA (mean ± SEM). **(A)** Impact of ketoconazole and curcumin on SOD level. **(B)** Impact of ketoconazole and curcumin on MDA level.

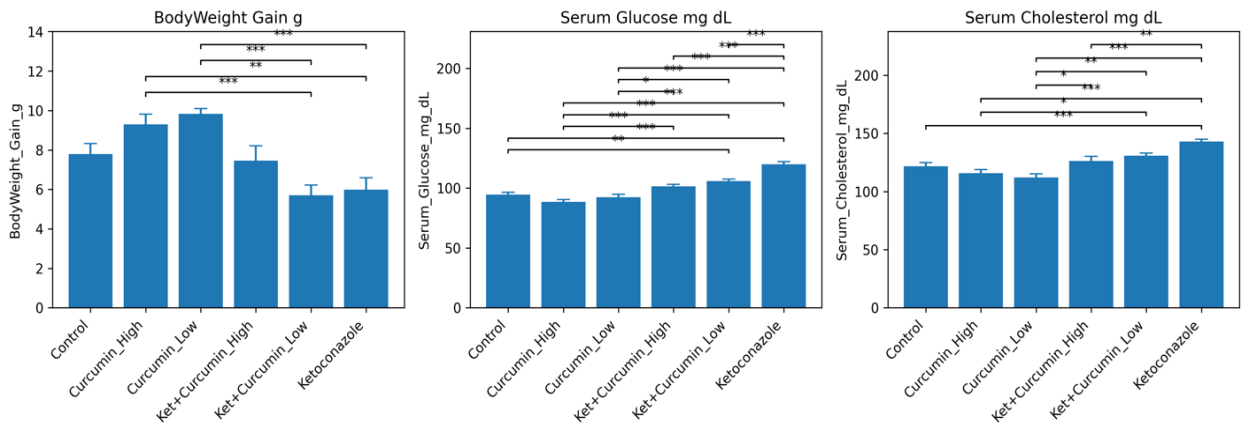

Fig. 6. Metabolic effect of drug and curcumin treatment. **(A)** Impact of ketoconazole and curcumin on body weight. **(B)** Impact of ketoconazole on glucose level. **(C)** Impact of ketoconazole and curcumin on cholesterol level.

Table 4: Metabolic effect of drug and curcumin treatment.

Group	BodyWeight_Gain_g (MeanÂ±SEM)	BodyWeight_ Gain_g (N)	Serum_Glucose_mg_ dL (MeanÂ±SEM)	Serum_ Glucose_mg_ dL (N)	Serum_ Cholesterol_mg_ dL (MeanÂ±SEM)	Serum_ Cholesterol_ mg_dL (N)
Control	7.79 Â± 0.53	6	94.63 Â± 1.86	6	121.63 Â± 3.25	6
Curcumin_High	9.3 Â± 0.52	6	88.68 Â± 1.89	6	115.88 Â± 2.93	6
Curcumin_Low	9.82 Â± 0.28	6	92.55 Â± 2.22	6	112.17 Â± 3.03	6
Ket+Curcumin_ High	7.46 Â± 0.76	6	101.58 Â± 1.63	6	126.28 Â± 3.92	6
Ket+Curcumin_ Low	5.71 Â± 0.51	6	105.87 Â± 1.7	6	130.88 Â± 2.2	6
Ketoconazole	5.99 Â± 0.59	6	119.93 Â± 2.28	6	143.03 Â± 2.02	6
p-value (group test)	<0.0001		<0.0001		<0.0001	
Test method	one-way ANOVA		one-way ANOVA		one-way ANOVA	

Table 5: Antioxidant and hepatoprotective effects of curcumin.

Group	Liver_SOD_U_mg_protein (MeanÂ±SEM)	Liver_SOD_U_mg_ protein (N)	Liver_MDA_nmol_mg_ protein (MeanÂ±SEM)	Liver_MDA_nmol_ mg_protein (N)
Control	12.34 Â± 0.43	6	1.5 Â± 0.1	6
Curcumin_High	14.27 Â± 0.66	6	1.02 Â± 0.08	6
Curcumin_Low	13.52 Â± 0.29	6	1.19 Â± 0.16	6
Ket+Curcumin_High	12.19 Â± 0.66	6	1.46 Â± 0.09	6
Ket+Curcumin_Low	9.54 Â± 0.46	6	2.17 Â± 0.15	6
Ketoconazole	6.0 Â± 0.49	6	3.12 Â± 0.13	6
p-value (group test)	<0.0001		<0.0001	
Test method	one-way ANOVA		one-way ANOVA	

hepatoprotective properties of curcumin help in decreasing the oxidative stress by increasing SOD level and decreasing MDA level (Fig. 7A-7B).

Endocrine modulation under curcumin supplementation

Ketoconazole also has a negative endocrine impact, resulting in decreased testosterone level (4.67 to 2.01 ng/ mL) (Table 6). However, curcumin has a significant endocrine impact, improving the overall release of testosterone ($p < 0.0001$) (Fig. 8).

Correlation matrix

An insignificant association was observed between glucose/ MDA levels and testosterone levels (Fig. 9). This presents the oxidative damage and hormonal disruption which is caused by ketoconazole. However, the relationship between liver SOD and testosterone levels was found to be significant, supporting the therapeutic impact of curcumin.

This study emphasizes the therapeutic value of curcumin within ARC medicine to manage oxidative stress and metabolic dysfunction in different species of amphibians/ reptiles. This can help in preventing the decline of reptile and amphibian populations worldwide. Curcumin can also be used as a nutraceutical supplement for reptiles/ amphibians due to its hepatoprotective and antioxidant characteristics.

Discussion

A rodent model is used in this study to determine the antioxidant and hepatoprotective effects of curcumin in relevance to ARC physiology. The administration of antifungals or antiparasitic also cause metabolic disturbances among amphibians and reptiles. For instance, itraconazole is likely to cause hepatotoxicity among the amphibians and reptiles, suggesting the integration of curcumin to decrease ALT and AST levels. Furthermore, the antioxidative characteristics of curcumin also encourage its nutraceutical application within the diets of different species of amphibians.

Drug-induced metabolic disturbances

The findings of this study showed significant effects for the control group, while the ketoconazole group showed decreased body weight and reduced levels of testosterone due to different metabolic disturbances. This contributes to increased testicular damage. A past study by Onoja et al. (2024a) has also emphasized the negative impact of ketoconazole on the male reproductive environment. This drug largely impacts the heart condition of an individual, lowering its overall activity. Similarly,

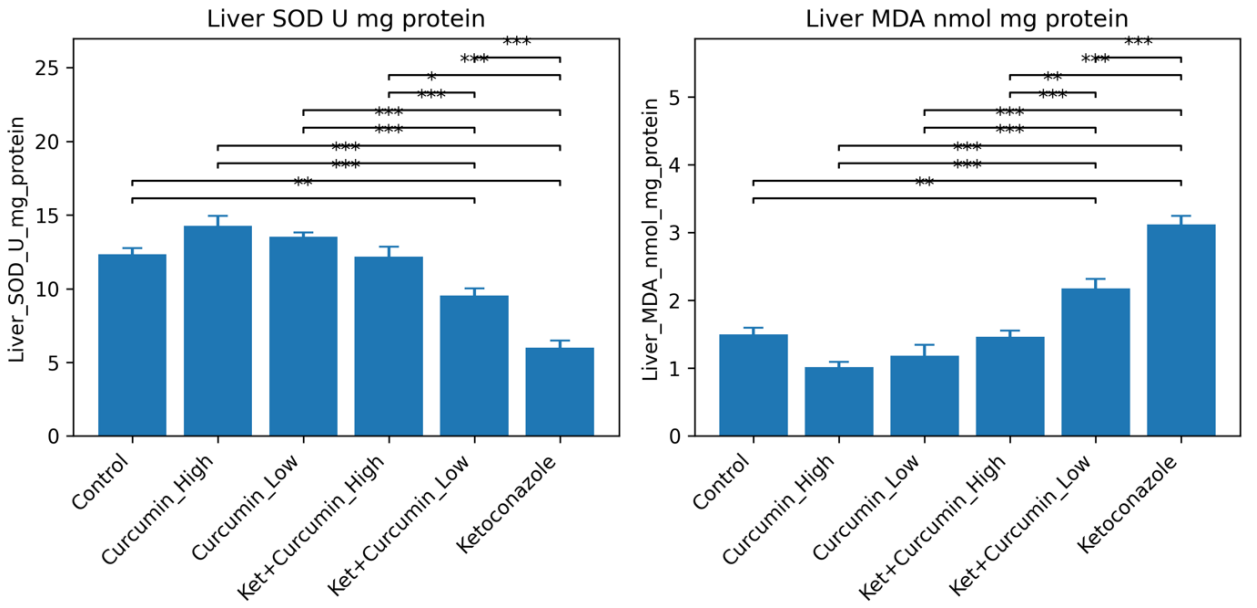

Fig. 7. Antioxidant and hepatoprotective effects of curcumin. **(A)** Impact of ketoconazole and curcumin on liver SOD. **(B)** Impact of ketoconazole and curcumin on liver MDA.

Table 6: Endocrine modulation under curcumin supplementation.

Group	Serum_Testosterone_ng_mL (MeanÂ±SEM)	Serum_Testosterone_ng_mL (N)
Control	4.67 Â± 0.18	6
Curcumin_High	5.79 Â± 0.22	6
Curcumin_Low	5.28 Â± 0.23	6
Ket+Curcumin_High	5.04 Â± 0.25	6
Ket+Curcumin_Low	3.35 Â± 0.21	6
Ketoconazole	2.01 Â± 0.26	6
p-value (group test)	<0.0001	
Test method	one-way ANOVA	

other antifungals (such as itraconazole) administered to amphibians or reptiles in captivity also result in oxidative stress and metabolic dysfunction (Mastrostefano et al., 2024). This shows an association regarding the impact of antifungal drugs on rodents and amphibians/ reptiles. Additionally, the findings of this study also show that the levels of glucose, cholesterol, and MDA have increased rapidly after the administration of ketoconazole, leading to different metabolic disturbances.

Therapeutic effects of curcumin

Group C, with a low dose of curcumin and ketoconazole also showed insignificant levels of testosterone, SOD, and MDA. This is due to the reduced therapeutic effects of curcumin due to low dose. Previous research has also shown that curcumin has a significant impact on SOD levels, glutathione peroxide levels, and lipid peroxidation (Tsao et al., 2022). This helps in improving the quality of semen and decreasing levels of testosterone. In this regard, the intervention of a low-carbon diet is also considered to be vital for decreasing oxidative stress. As a result, emphasis has been given on high dosage of curcumin to deal with the metabolic disturbances due to ketoconazole. This also supports the therapeutic effect of higher doses of curcumin in mitigating metabolic

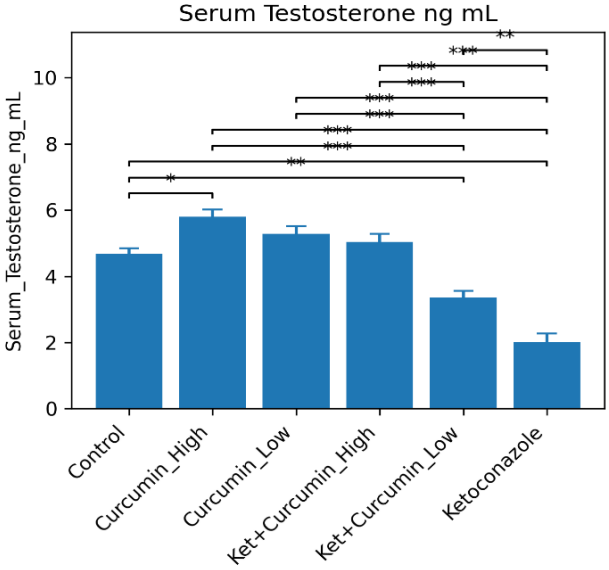

Fig. 8. Endocrine modulation under curcumin supplementation.

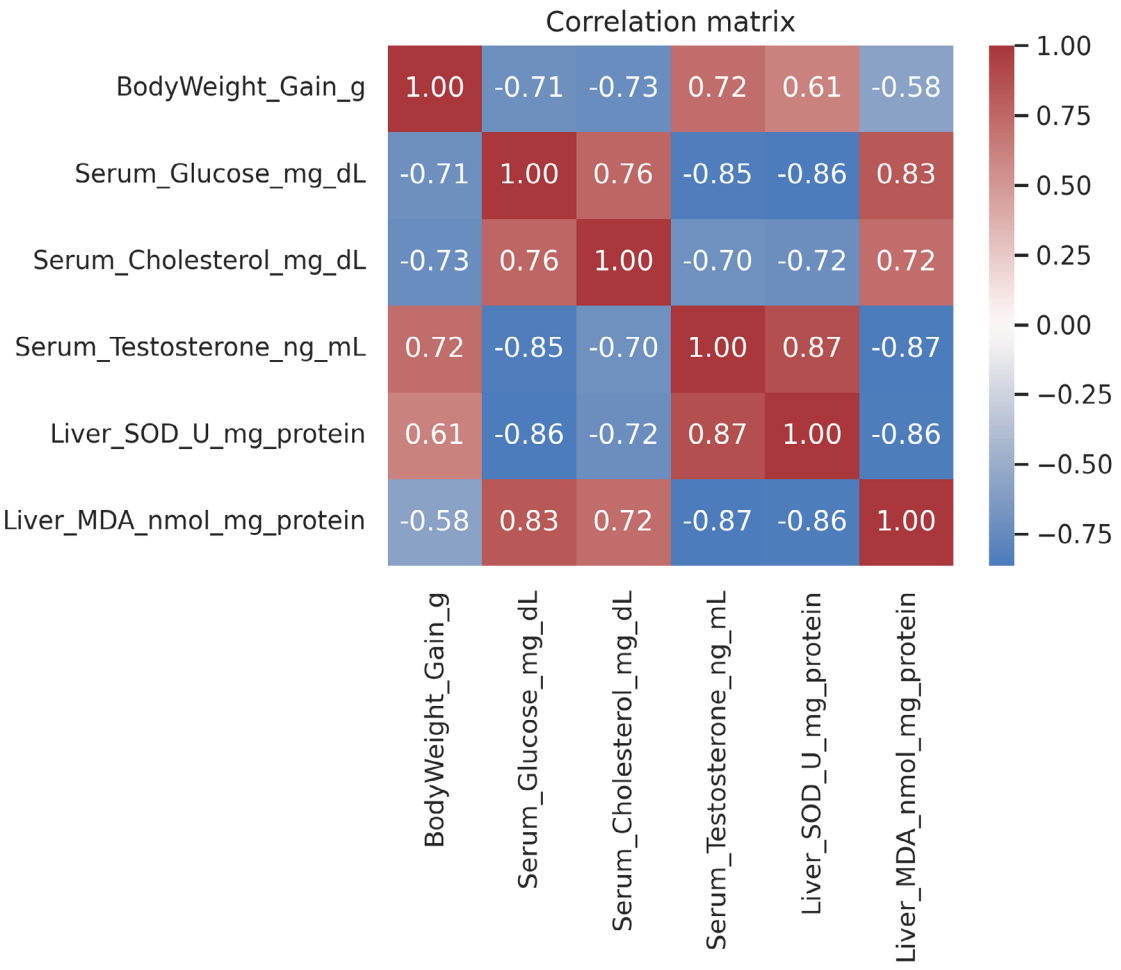

Fig. 9. Correlation matrix across outcome variables.

disturbances (which take place due to environmental changes or drug-induced issues) among the amphibians and reptiles

In contrast, rodents from Groups D, E, and F showed significant therapeutic effects of curcumin in mitigating the adverse events of ketoconazole. The low and high doses of curcumin were found to have significant therapeutic effects. Previous research has also highlighted the role of ketoconazole in causing hepatotoxicity (Similoluwa & Ebong, 2025). Therefore, the integration of curcumin is essential to decrease ketoconazole-induced oxidative stress. This helps in supporting the therapeutic effect of curcumin in reducing drug-induced metabolic disturbances. Sandhu et al. (2021) have also highlighted the role of curcumin in wound healing. Although past literature has focused on the therapeutic effects of curcumin in hepatoxicity and wound healing, limited focus has been given on its capability to mitigate drug-induced and environmental metabolic disturbances. The present study has been effective in filling this gap. It also improved the overall clinical knowledge and significance of curcumin within the context of ARC medicine.

This study has highlighted the role of curcumin in mitigating drug-induced metabolic disturbances. This provides an opportunity for future researchers to focus on the role of curcumin in managing different drug-induced metabolic disturbances among amphibians and reptiles in association with ARC medicine.

Relevance to ARC medicine

Climate change has largely impacted the habitats of reptiles and amphibians. As a result, they are largely exposed to different heavy metals and toxins resulting in oxidative stress among them (Westmoreland et al., 2016). The rodent model used in this study has supported the antioxidative and hepatoprotective effects of curcumin in context of ARC medicine. The effectiveness of curcumin in reducing liver damage by decreasing AST and ALT levels, has also been highlighted (Tuong et al., 2023). In addition, curcumin's efficacy has also been determined in reducing metabolic disturbances. These characteristics, makes it effective in managing drug-induced oxidative stress among the amphibians and reptiles. The antioxidant and hepatoprotective characteristics of this natural compound also support its nutritional interventions and veterinary protocols within ARC medicine.

This research also presents different academic and clinical implications. This study has addressed the therapeutic role of curcumin in mitigating drug-induced metabolic disturbances in association with ARC medicine. It has also emphasized curcumin's efficacy in mitigating different metabolic disturbances in relevance to ARC medicine (Damiano et al., 2021; Shrestha et al., 2025). The significance of curcumin in dealing with different drug-induced metabolic disturbances, such as high glucose, cholesterol, and MDA levels, has supported its antioxidant effects in context of ARC physiology (Kehinde et al., 2025). In addition, different policies can also be developed and implemented by wildlife rehabilitation centers to increase the utilization of curcumin due to its therapeutic effects.

Conclusion

Drug-induced metabolic disturbances have become common, leading to different adverse events. To avoid such events, the focus is shifted towards natural compounds such as curcumin. This study has also highlighted the metabolic distress caused by ketoconazole. Different identified metabolic disturbances include reduced body weight, increased levels of cholesterol, glucose, and MDA. At the same time, the levels of liver SOD were found to be decreased. These metabolic disturbances contribute to the reduced serum testosterone, influencing the male reproductive environment. In this regard, the integration of curcumin was found to be beneficial for reducing drug-induced metabolic disturbances. It possesses protective and antioxidative properties, which are essential to decrease drug-induced metabolic and oxidative stress among amphibians or reptiles.

In addition to the therapeutic value of this study, it also includes a few limitations. First, a sample of 36 rodents was taken for the experimental design. This limited the efficiency of this study. Second, this study only focused on ketoconazole-induced metabolic disturbances leading to testicular damage. Finally, the intervention of curcumin was observed in rodents, and no direct therapeutic effects were evaluated within the context of amphibians or reptiles. In future research, a larger sample of rodents or other animals can be considered. This will help in studying the impact of different doses of curcumin in mitigating drug-induced metabolic disturbances. For this purpose, other drugs which can induce metabolic disturbances (such as diuretics, corticosteroids, and beta blockers) can also be considered (D'Alessandro et al., 2022). Moreover, ethical guidelines and protocols are needed to be implemented to evaluate the therapeutic effects of curcumin in amphibians or reptiles.

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