EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Coden USA: EJBPBO
Volume: 13
Issue: 6
Year: 2026

CARDIOPROTECTIVE EFFECT OF VITELLARIA PARADOXA LEAVES ON BENZENE INDUCED WISTAR RATS

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DOI: https://doi.org/10.5281/zenodo.20441723

How to cite this Article: [*1]Olubunmi Olusoga Ezomoh, [1]Jeremiah Oyinbarakemi, [2]Peter P. Erigbali, [1]Sule Jimoh Olayiwola. (2026). Cardioprotective Effect of Vitellaria Paradoxa Leaves on Benzene Induced Wistar Rats. European Journal of Biomedical and Pharmaceutical Sciences, 13(6), 167–171.

Article Received on 28/03/2026 **Article Revised on 18/04/2026** **Article Published on 01/05/2026**

ABSTRACT
This study evaluated the protective effects of N-Hexane extract of Vitellaria paradoxa (shea butter) leaves against benzene-induced toxicity in Wistar rats, focusing on body weight changes, cardiotoxicity, and oxidative stress markers. thirty (30) rodents were grouped in 6 having 5 each and treated as follows for 21 days: Group1 (Normal control) were given normal saline, group 2 (Positive control) were given 0.2 ml/kg of benzene 48 hourly, group 3,4 and 5 (Test groups 1, test group 2 and standard control) were given 0.2 ml/kg of benzene 48 hourly followed by daily administration of 200 mg/kg b.wt, 400 mg/kg b.wt of the extract and 200 mg/kg b.wt of vitamin E respectively. Benzene exposure (0.2 ml/kg mg/kg) significantly reduced weight gain (9.03%) relative to normal control animals (35.7%) Co-treatment with Vitellaria paradoxa (200 and 400 mg/kg) dose-dependently restored weight gain (21.53% and 30.2%, respectively), with 400 mg/kg matching vitamin E (31.97%), suggesting its role in mitigating metabolic impairment. Benzene also induced cardiotoxicity, significantly ($p<0.05$) elevating markers of stress, cardiac injury and dyslipidemia markers (including triglycerides and LDL while reducing HDL. Vitellaria paradoxa (200 mg/kg b.wt and 400 mg/kg b.wt) reversed these parameters to near-normal similar to vitamin E, likely due to antioxidant and lipid-modulating bioactive compounds (triterpenes, flavonoids). Oxidative stress assays revealed benzene-mediated depletion of SOD, catalase, and GSH, alongside increased MDA, all counteracted by Vitellaria paradoxa in a dose-dependent manner. The 400 mg/kg dose restored antioxidant enzymes and reduced MDA to levels akin to vitamin E. These findings underscore Vitellaria paradoxa's protection against benzene-induced toxicity, with 400 mg/kg exhibiting efficacy rivaling synthetic antioxidants. Further research should elucidate molecular mechanisms and long-term effects to validate its therapeutic potential.

INTRODUCTION
Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide, often associated with exposure to environmental pollutants like benzene. Benzene, a volatile organic compound, is widely used in industrial processes and known for its toxic effects on multiple organs, including the heart (Rajan *et al.*, 2020). Chronic benzene exposure can induce oxidative stress, inflammation, and cardiotoxicity, leading to structural and functional cardiac impairments (Qiao *et al.*, 2022). Therefore, the search for natural compounds with cardioprotective effects has gained attention in mitigating benzene-induced cardiac damage. Benzene is a ubiquitous environmental pollutant abundant in household products, petrochemicals, and cigarette smoke. Benzene is a well-known carcinogen in humans and experimental animals; however, little is known about the cardiovascular toxicity of benzene. Recent population-based studies indicate that benzene exposure is associated with an increased risk for heart failure. Nonetheless, it is unclear whether benzene exposure is sufficient to induce and/or exacerbate heart failure (Zelko *et al.*, 2021).

Shea leaf (Vitellaria paradoxa), widely known for its medicinal properties in traditional African medicine, has emerged as a promising candidate for cardioprotection. Rich in phytochemicals such as flavonoids, phenolic compounds, and triterpenes, vitellaria paradoxa exhibits potent antioxidant, anti-inflammatory, and cytoprotective

property (Desam & Al- Rajab, 2021). These bioactive compounds have been shown to decrease tissue stress and enhance cardiac function in preclinical studies (Abdulazeez *et al.*, 2023). Several studies have investigated the therapeutic potential of shea leaf in models of oxidative stress and inflammation. However, its cardioprotective effects against benzene-induced toxicity remain underexplored. The mechanism by which shea leaf protects the heart likely involves the attenuation of oxidative stress markers, inhibition of pro-inflammatory cytokines, and enhancement of endogenous antioxidant defenses (Adebayo *et al.*, 2021).

The use of Wistar rats as a model for studying benzene-induced cardiotoxicity provides a controlled platform for understanding the cardioprotective efficacy of shea leaf. By evaluating cardiac biomarkers, and oxidative stress parameters, this study aims to elucidate the potential of shea leaf as a cardioprotective agent.

This research not only advances the understanding of natural antioxidants in cardiotoxicity management but also highlights the potential therapeutic applications of shea leaf in mitigating the adverse effects of environmental toxins like benzene.

METHODOLOGY

Fresh leaves of Vitellaria paradoxa were collected from Agoare Atisbo in Oyo State, Nigeria. The plant leaves were collected in large quantity after identification by Professor Kola Ajibesin and left under shade at room temperature for two weeks to dry. Afterwards, they were ground into a coarse powder. 500g of the powder was soaked in 2 litres of N-Hexane and allowed to stand for 48 hours with intermittent stirring. The extract was filtered with cheese cloth paper and the filtrate was evaporated using a rotary evaporator at 40 0c. The dry residue was reconstituted with 10% tween 80 accordingly.

Thirty (30) apparently disease-free animals between one hundred and fifty to two hundred grams were acclimatized over fourteen-day period with appropriate laboratory exposure. They were grouped in 6 having 5 each and treated as follows for 21 days;

Group I: Normal control: distilled water (for 21 days).
Group II: Positive control: distilled water (daily) and 0.2 ml/kg benzene (48 hourly for 21 days)
Group III: Treatment group 1: Extract (200 mg/kg b.wt of extract daily and 0.2 ml/kg benzene (48 hourly for 21days)
Group IV: Treatment group 2: Extract (400 mg/kg b.wt of extract daily and 0.2 ml/kg benzene (48 hourly for all 48 days)
Group V: Standard Control: Vitamin E (200 mg/kg b.wt for daily and 0.2 ml/kg benzene (once 48 hourly for 21 days)

RESULT

The results of the present study are presented shows the mean body weight of benzene induced wistar rats before and after pretreatment with *vitellaria paradoxa*. Table 3.2 shows the mean serum concentrations of LDL, creatinine kinase, total cholesterol, triglyceride, LDH and HDL shows the mean heart concentration of SOD, catalase, GSH, and MDA in wistar rats pretreated with *Vitellaria paradoxa* for 21 days and induced with benzene for 21 days.

Effect of benzene and *Vitellaria paradoxa* on the mean body weight (g) of wistar rats.

GROUPS	Mean weight before treatment (g)	Mean weight after treatment	% mean weight change (g)
Group 1 normal control	159.83±2.79 [a]	195.5±3.45 [a]	35.7 [a]
Group 2 positive control with benzene (0.2ml/kg b.wt)	161.17±2.48 [a]	170.2±2.86 [b]	9.03 [b]
Group 3 with benzene (0.2ml/kg b.wt) and *Vitellaria paradoxa* (200mg/kg b.wt)	160.67±3.08 [a]	182.2±5.60 [c]	21.53 [c]
Group 4 with benzene (0.2ml/kg) and *Vitellaria paradoxa* (400mg/kg b.wt)	162.00±2.97 [a]	192.2±4.67 [a]	30.2 [a]
Group 5 standard control with vitamin E (200mg/kg b.wt) and benzene (0.2ml/kg b.wt)	162.83±1.83 [a]	194.8±2.13 [a]	31.97 [a]

Data are expressed as the mean ± SD (n = 5). Means within the same column carrying the same superscript are not significantly different ($p < 0.05$) different.

Result shows the pretreatment with *Vitellaria paradoxa* (200 mg/kg body weight and 40 mg/kg body weight) caused a significant ($p < 0.05$) increase in the rate of weight gain (21.53 and 30.2) when compared with normal (35.7 %) and positive (9.03%)

GROUPS	CREATINE KINASE (u/l)	LDH	TOTAL CHOLESTOROL	TRIGLYCERIDE (mg)	HDL (mg)	LDL
Group 1 normal control	9.80±0.78 [a]	12.23±1.44 [a]	74.53±1.59 [a]	5.57±0.18 [a]	58.98±2.61 [a]	43.44±2.62 [a]

Group 2 positive control with benzene	35.94±1.24 [b]	43.37 ±2.19 [b]	124.61±1.94 [b]	18.75 ± 3.09 [b]	29.56±2.21 [b]	112.58±3.73 [b]
Group 3 with benzene(0.2ml/kg) and *Vitellaria paradoxa* (200mg/kg)	24.39±1.12 [c]	27.56±3.89 [c]	98.83±2.00 [c]	9.09±0.18 [c]	46.46±2.80 [c]	79.12±2.09 [c]
Group 4 with benzene (0.2ml/kg) and *Vitellaria paradoxa* (400mg/kg b.wt)	24.39±1.12 [d]	20.08±5.16 [d]	89.04±6.29 [d]	5.96±0.22 [a]	37.79±1.96 [d]	59.87±1.81 [d]
Group 5 standard control with vitamin E (200mg/kg) and Benzene (0.2ml/kg)	11.85±1.12 [d]	19.28±3.05 [d]	83.03±2.36 [d]	5.95±0.25 [a]	53.99±1.57 [a]	53.51±2.11 [d]

The biochemical role of *Vitellaria paradoxa on benzene induced cardiac toxicity of wistar rats*

Data are expressed as the mean ± SD (n = 5). Means within the same column carrying the same superscript are not significantly different ($p < 0.05$) different.

GROUPS	SOD(u/mg)	CATALASE(u/mg)	GSH(u/mg)	MDA(u/mg)
Normal control	10.02±0.20 [a]	8.89±0.42 [a]	8.07±0.59 [a]	1.93±0.19 [a]
Positive control with benzene (0.2ml/kg b.wt)	2.05±0.12 [c]	2.13±0.06 [b]	1.99±0.08 [b]	8.27±0.49 [a]
Test group 1 with benzene (0.2ml/kg b.wt) and *Vitellaria paradoxa* (200mg)	4.32±0.14 [a]	4.28±0.09 [c]	4.23±0.12 [c]	5.87±0.2 [c]
Test group 2 with benzene (0.2ml/kg b.wt) and *Vitellaria paradoxa* (400mg)	5.90±0.24 [c]	5.55±0.28 [d]	5.54±0.19 [d]	3.90±0.12 [d]
Standard control 0.2ml/kg with vitamin E (200mg/kg b.wt)	7.24±0.49 [c]	6.45±0.29 [e]	5.68±0.29 [d]	2.12±0.06 [a]

The result shows that benzene administration caused a significant increase in the concentration of creatine kinase (35.94±1.24), LDH (43.37 ±2.19), total cholesterol (124.61±1.94), triglyceride (18.75 ± 3.09), HDL (29.56±2.21) and LDH (112.58±3.73) and a significant decrease in concentration of LDL (112.58±3.73) and HDL (29.56±2.21) positive control relative to normal rats. However, treatment with *Vitellaria paradoxa* doses of 200 mg/kg and 400 mg/kg b.wt showed a significant ($p < 0.05$) dependent decrease in serum concentration of LDL of total cholesterol (98.83±2.00 and 89.04±6.29), triglyceride (9.09±0.18 and 5.96±0.22), LDH (27.56±3.89 and 20.08±5.16), creatine kinase (24.39±1.12 and 24.39±1.12) and a significant ($p < 0.05$) dose dependent increase in serum concentration of LDL (79.12±2.09 and 59.87±1.81) and HDL (46.46±2.80 and 37.79±1.96) respectively, relative to benzene treated group.

Antioxidant role of *Vitellaria paradoxa on benzene induced wistar rats*

Data are expressed as the mean ± SD (n = 5). Means within the same column carrying same superscript are not significantly different ($p < 0.05$) different.

The result shows that benzene administration caused a significant decrease ($p < 0.05$) in heart SOD (4.32±0.14) catalase (4.28±0.09) and GSH (4.23±0.12) activities (positive control and a significant increase ($p < 0.05$) in heart MDA concentration (5.87±0.2) relative to normal control rat. However, treatment with *Vitellaria paradoxa* at doses of 200 mg/kg b.wt and 400 mg/kg b.w caused a significant ($p < 0.05$), dose dependent elevation of heart activities of SOD (4.32±0.14 and 5.90±0.24), catalase (4.28±0.09 and 5.55±0.28) and GSH(4.23±0.12 and 5.54±0.19), and a significant decrease in the heart MDA(5.87±0.2 and 3.90±0.12), concentration relative to the benzene treated group.

DISCUSSION

The present study assessed the impact of Vitellaria paradoxa (shea butter) on body weight changes in Wistar rats exposed to benzene. Benzene is a well-documented hematotoxic and carcinogenic compound known to interfere with normal metabolic processes and induce oxidative stress (Cordiano *et al.*, 2022). This investigation shows a significant decline of weight gain in the group exposed to benzene alone (Group 2), which had only a 9.03% increase in body weight, compared to the normal control (Group 1), which gained 35.7%. These corroborates reports by Akinmoladun et al. (2021) that observed weight suppression and metabolic derangements in benzene-treated rats due to lipid peroxidation and altered energy metabolism. Co-

treatment with Vitellaria paradoxa led to a dose-dependent mitigation of the benzene-induced weight reduction. The group receiving 200 mg/kg of Vitellaria. Paradoxa (Group 3) showed a 21.53% increase in body weight, while the group treated with 400 mg/kg (Group 4) exhibited a 30.2% gain, which was not significantly different from the normal control or the standard antioxidant control (Vitamin E, Group 5, 31.97%). These findings indicate that Vitellaria paradoxa has a protective role, possibly due to its bioactive components such as triterpenes, phenolics, and tocopherols, which possess antioxidant and anti-inflammatory properties (Ojo *et al.*, 2021).

Recent studies by Olayemi *et al.*, (2021) reported that shea butter administration in acetaminophen-induced hepatotoxic rats significantly improved body weight and reduced markers of oxidative damage. Similarly, Olaniyan and Fakunle (2022) demonstrated the hepatoprotective and growth-promoting effects of Vitellaria paradoxa against carbon tetrachloride-induced toxicity, attributing these effects to the plant's antioxidant defense boosting ability.

The performance of Vitellaria paradoxa at 400 mg/kg in this study was comparable to that of vitamin E, a well-established antioxidant, suggesting potential of Vitellaria paradoxa as alternate synthetic antioxidant; as corroborated by Abu et al. (2023), who emphasized the efficacy of plant-derived antioxidants in restoring physiological functions compromised by xenobiotics.

Moreover, the improvement in body weight despite benzene exposure suggests a restoration of appetite, digestion, and nutrient assimilation, possibly through the stabilization of gastrointestinal and hepatic functions, which are commonly impaired by benzene toxicity (Cui *et al.*, 2020).

The present study also evaluated the cardioprotective effects of Vitellaria paradoxa against benzene-induced cardiotoxicity in Wistar rats by assessing key biochemical markers, including creatine kinase (CK), lactate dehydrogenase (LDH), total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL). The results demonstrate that benzene exposure significantly increased cardiotoxicity markers (including CK, LDH, and LDL) while reducing HDL levels, indicating myocardial damage and dyslipidemia. But Vitellaria paradoxa administration ameliorated these adverse effects, with the higher dose (400mg/kg) showing near-normalization of some parameters, comparable to the vitamin E-treated control group.

The significant elevation in CK and LDH levels in benzene-exposed rats (Group 2) aligns with previous findings that benzene metabolites induce oxidative stress, leading to cardiomyocyte damage and leakage of these enzymes into circulation (Zeko *et al.*, 2022). The observed increase in total cholesterol, triglycerides, and LDL, along with reduced HDL, is consistent with studies demonstrating benzene's role in disrupting lipid metabolism and promoting atherosclerosis (Yuan *et al.*, 2019).

The dose-dependent reduction in CK and LDH levels in Vitellaria paradoxa-treated groups (Groups 3 and 4) suggests myocardial membrane stabilization, possibly due to its antioxidant properties. Similar findings were reported by Ojo et al. (2021), where plant extracts rich in flavonoids and phenolic compounds attenuated doxorubicin-induced cardiotoxicity by scavenging free radicals.

The normalization in dyslipidemia with improved HDL) in Vitellaria paradoxa-treated rats supports its hypolipidemic potential. This effect is comparable to that of vitamin E (Group 5), a known antioxidant that prevents lipid peroxidation (Mbah *et al.*, 2022). The near-complete restoration of triglycerides and LDL at 400 mg/kg suggests that Vitellaria paradoxa may enhance hepatic lipid metabolism, similar to findings by Adesanwo et al. (2025) on its anti-hyperlipidemic activity.

The cardioprotection offered by Vitellaria paradoxa may be attributed to its bioactive constituents, such as saponins, tannins, and flavonoids, which exhibit antioxidant, anti-inflammatory, and lipid-lowering effects (Adebayo *et al.*, 2021). The results correlate with studies on other medicinal plants, such as Moringa oleifera and Garcinia kola, which mitigate cardiotoxicity via similar mechanisms (Ogunbolude *et al.*, 2019).

The present study also evaluated the antioxidant potential of Vitellaria paradoxa against benzene-induced oxidative stress in Wistar rats by assessing key biomarkers, including superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), and malondialdehyde (MDA). The results demonstrate that benzene exposure significantly depleted SOD, CAT, GSH and elevated lipid peroxidation (MDA), indicating severe oxidative stress. However, treatment with Vitellaria paradoxa (200 mg/kg and 400 mg/kg) significantly restored antioxidant defences and dose-dependently reduced oxidative damage, with the higher dose showing effects comparable to vitamin E, a well-known antioxidant.

The marked reduction in SOD, CAT, and GSH levels in benzene-exposed rats (positive control) aligns with previous studies demonstrating that benzene metabolites, such as hydroquinone and benzoquinone, generate reactive oxygen species (ROS), leading to depletion of endogenous antioxidants (Zhang *et al.*, 2021). The significant increase in MDA, a lipid peroxidation marker, further confirms oxidative damage to cell membranes, consistent with findings by Al-Attar (2020), who reported similar benzene-induced oxidative stress in hepatic and renal tissues.

The dose-dependent restoration of SOD, CAT, and GSH levels in Vitellaria paradoxa-treated groups suggests its potent free radical-scavenging activity. The observed effects at 400 mg/kg were particularly notable, approaching the efficacy of vitamin E (standard control). These findings corroborate studies by Adedara et al. (2019), who demonstrated that polyphenol-rich plant extracts enhance endogenous antioxidant enzymes by activating the Nrf2/ARE pathway, a key regulator of cellular antioxidant responses.

The significant reduction in MDA levels in Vitellaria paradoxa-treated rats indicates its ability to mitigate lipid peroxidation, similar to findings by Ojo et al. (2022) on the antioxidant properties of Garcinia kola and Moringa oleifera in toxin-induced oxidative stress models. The near-normalization of MDA at 400 mg/kg suggests that Vitellaria paradoxa may stabilize cell membranes by inhibiting ROS-mediated lipid degradation, a mechanism also observed with vitamin E.

The antioxidant effects of Vitellaria paradoxa can be attributed to its high content of bioactive compounds, including flavonoids, tannins, and phenolic acids, which have been shown to neutralize free radicals and enhance cellular antioxidant defenses (Ojo *et al.,* 2021). The results are consistent with previous reports on Vitellaria paradoxa's ability to chelate metal ions and inhibit xanthine oxidase, a key enzyme in ROS generation (Oyibo *et al.,* 2023).

CONCLUSION

The findings confirm that Vitellaria paradoxa exerts significant cardioprotective effects against benzene-induced toxicity, likely through antioxidant and lipid-modulating mechanisms. The 400 mg/kg dose demonstrated efficacy comparable to vitamin E, suggesting its potential as a natural therapeutic agent. Further studies should explore its long-term effects and molecular pathways to validate its clinical applicability.

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