Original Article

Assessment of the Histological Changes of the Heart and Kidneys Induced by Berberine in Adult Albino Wistar Rats

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Abstract

Background: Berberine is a natural compound found to have numerous pharmacological activities such as anti-inflammatory and antioxidant effects. It has been the subject of intensive scientific research; however, there have been scanty information on its subacute effect on the heart and kidney. **Aims:** This work was done to investigate the hepatocellular changes induced by berberine in adult Wistar rats. **Materials and Methods:** Twenty adult apparently healthy rats were used for this study. The rats were divided into four groups of five per group and fed with pellets and water *ad libitum*. Group A served as the control, Group B were fed with 2 mg/kg of berberine, Group C with 20 mg/kg, while Group D were fed with 200 mg/kg body weight. Doses were administered once daily using oral gavage for 28 days. Prior to the time of sacrificing the animals, blood samples were collected into plain test tubes and the animals anesthetized before sacrifice. Necropsy was performed, and the tissues (heart and kidneys) processed and stained using hematoxylin and eosin-staining techniques. Serum electrolyte (sodium and potassium), urea, creatinine, creatine kinase, and lactate dehydrogenase were analyzed. **Statistical Analysis Used:** Data obtained from the study were statistically analyzed using SPSS software (version 21). **Results:** There were significant increases in urea and creatinine (40.05 ± 14.32, $P = 0.031$ and 1.93 ± 0.80, $P = 0.044$) as well as potassium (7.45 ± 1.81, $P = 0.026$) in the 200 mg/kg-treated animals when compared with the control (14.59 ± 8.03, 0.40 ± 0.03, and 3.60 ± 1.01). The histological architecture of the kidneys showed glomerular atrophy in the 200 mg/kg-treated rats. There was no noticeable histological alteration in the heart. **Conclusions:** The result showed that berberine was toxic to the kidney at concentrations high as 200 mg/kg.

Keywords: Berberine, heart, kidney, oxidative stress, rats

Introduction

Berberine is an isoquinoline alkaloid, with a characteristic intense yellow color found in several plants, including *Coptidis rhizoma* (Huanglian), *Coptis chinensis* (Chinese goldthread), *Coptis trifolia* (American goldthread), *Mahonia aquifolium* (Oregon grape), *Berberis aristata* (tree turmeric), *Berberis vulgaris* (common barberry), and *Hydrastis canadensis* (goldenseal).[1,2] Berberine has been studied extensively, and Gan[3] as well as Kumar *et al.*[4] described its anticancer, antimicrobial, uterotonic, immunostimulatory, sedative, anticonvulsant, hypotensive, choleretic, and antihelminthic properties.

This study was carried out to investigate the histological changes of the heart and kidneys induced by berberine in adult Wistar rats.

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DOI: 10.4103/MTSM.MTSM_4_20

Materials and Methods

Twenty apparently healthy adult Wistar rats which were between 10 and 13 weeks of age having a weight range between 200 and 240 g were used for this study. The rats were divided into four groups of five rats in each group and were allowed 2 weeks to acclimatize and fed with standard Pfizer-branded rodent feed obtained from Livestock Feed, Nigeria Ltd., *ad libitum* and water was available to the rats in water bottles of the downspout type (drinking nozzle facing downward). The acute

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How to cite this article: Uwaifo F, Favour JO. Assessment of the histological changes of the heart and kidneys induced by berberine in adult albino wistar rats. Matrix Sci Med 2020;4:70-3.

Received: 21-03-2020, **Accepted:** 28-04-2020, **Published:** 14-07-2020

toxicity test of berberine showed that no deaths were recorded in rats up to 2000 mg/kg body weight. Different doses of berberine were administered to the rats, Group A: served as the control and were fed with feed and water only, Group B: 2 mg/kg, Group C: 20 mg/kg, and Group D: 200 mg/kg (which represented one-thousandth, one-hundredth, and one-tenth of the toxic dose, respectively). The doses were administered once daily using oral gavage for 28 days, at the end of which the animals were anesthetized with chloroform, while blood samples were collected through the cardiac puncture into plain bottles using 21G needles mounted on a 5 ml syringe. Necropsy was done and the heart and kidney were excised and fixed in 10% formal saline for histological evaluation.

Data obtained from the study were statistically analyzed using SPSS software (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp). Statistical significance between the groups was analyzed by means of two-way analysis of variance. The results were presented as mean ± standard deviation. The values of $P < 0.05$ were considered statistically significant.

After blood samples were taken and vital organs (heart and kidney) eviscerated, the carcass was taken far away from human habitation and buried.

Table 1: Effect of berberine on the renal oxidative status of treated animals

	Oxidative stress biomarkers			
	MDA (nmol/g)	GSH (ug/ml)	SOD (ug/ml)	CAT (ug/ml)
Control	0.73±0.02	4.96±0.03	3.17±0.02	0.44±0.004
2 mg/kg	0.71±0.01	5.00±0.05	3.17±0.02	0.49±0.005
20 mg/kg	0.77±0.01	4.95±0.03	3.20±0.02[b]	0.40±0.008
200 mg/kg	1.24±0.01[a]	4.40±0.07[b]	2.71±0.02[b]	0.21±0.003[b]

Result expressed as mean±SD. [a]Significant increase; [b]Significant decrease (P<0.05) compared with control; n=5 per group. SD: Standard deviation, MDA: Malondialdehyde, GSH: Glutathione, SOD: Superoxide dismutase, CAT: Catalase

Table 2: Effect of berberine on the cardiac oxidative status of treated animals

	Oxidative stress biomarkers			
	MDA (nmol/g)	GSH (ug/ml)	SOD (ug/ml)	CAT (ug/ml)
Control	0.81±0.02	5.17±0.02	3.10±0.02	0.53±0.006
2 mg/kg	0.84±0.01	5.15±0.02	3.13±0.01	0.51±0.007
20 mg/kg	0.80±0.01	5.10±0.04	3.08±0.01	0.51±0.004
200 mg/kg	0.82±0.01	5.10±0.01	3.08±0.02	0.49±0.003

Result expressed as mean±SD; n=5 per group. SD: Standard deviation, MDA: Malondialdehyde, GSH: Glutathione, SOD: Superoxide dismutase, CAT: Catalase

Results

The values present in Table 1 show significant ($P < 0.05$) increases in the level of malondialdehyde (MDA) detected at 200 mg/kg of the treated rats when compared with the control. However, there were significant ($P < 0.05$) decreases of superoxide dismutase (SOD), glutathione (GSH), and catalase (CAT) activities at 200 mg/kg of the treated rats when compared with the control. There was, however, no significant ($P > 0.05$) difference in SOD, GSH, and CAT activities and MDA level of the eviscerated heart when compared with the control [Table 2].

Discussion

There were significant increases in urea and creatinine (40.05 ± 14.32, $P = 0.031$ and 1.93 ± 0.80, $P = 0.044$) as well as potassium (7.45 ± 1.81, $P = 0.026$) in the 200 mg/kg-treated animals when compared with the control (14.59 ± 8.03, 0.40 ± 0.03, and 3.60 ± 1.01).

The values from the findings present in Table 3 show that there were statistically significant increases in urea and creatinine (40.05 ± 14.32, $P = 0.031$ and 1.93 ± 0.80, $P = 0.044$) as well as potassium (7.45 ± 1.81, $P = 0.026$) in the 200 mg/kg-treated animals when compared with the control (14.59 ± 8.03, 0.40 ± 0.03 and 3.60 ± 1.01).

These findings agree with a study conducted by Ajibade *et al*.[5] who noted an increase in serum urea and potassium in berberine-treated rats.

The heart photomicrograph [Figure 1] shows no distinct cytoarchitectural alteration and as a result no significant difference from that of the control [Figure 2], this finding does not agree with the reports of Verma *et al*.,[6] as well as Sreelatha and Padma, (2009).[7] This study agrees with the report of Bharali *et al*.,[8] whose findings showed that berberine

Table 3: Effect of extract on cardiac and renal biochemical parameters

Parameters	n	Mean±SD				
		Control	20 mg/kg	P	200 mg/kg	P
CK	5	43.28±16.02[#]	50.75±22.94	0.208	55.53±26.94	0.253
LDH	5	138.44±29.42[#]	151.42±21.05	0.104	154.27±29.44	0.128
Sodium	5	16.07±5.96[#]	16.41±7.15	0.170	16.63±5.71	0.240
Potassium	5	3.60±1.01[#]	3.98±1.26	0.144	7.45±1.81	0.026*
Urea	5	14.59±8.03[#]	19.17±8.91	0.114	40.05±14.32	0.031*
Creatinine	5	0.40±0.03[#]	0.66±0.04	0.307	1.93±0.80	0.044

Result expressed as mean±SD. [#]Dependent variable, *Significance compared to control at P<0.05. n: Number of rats, CK: Creatine kinase, LDH: Lactate dehydrogenase, SD: Standard deviation

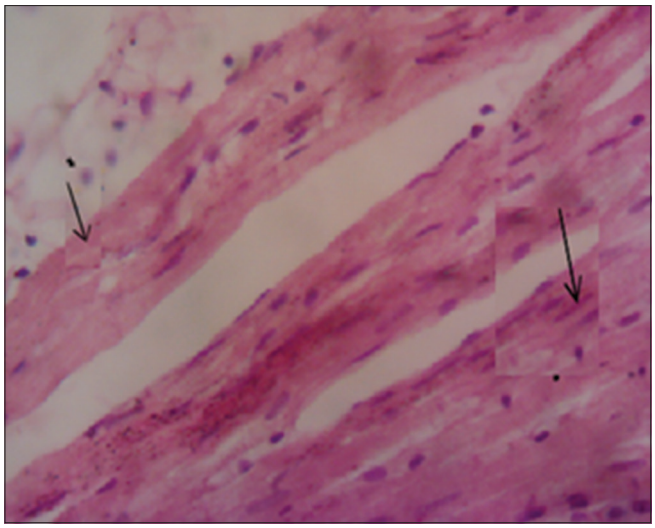

Figure 1: Photomicrograph of 200 mg/kg-treated heart tissue showing normal cytoarchitecture with intact nuclei (black arrows) (H and E, ×100)

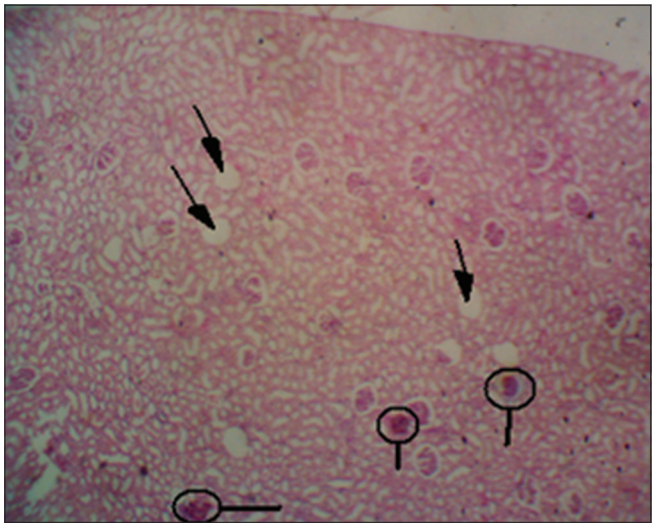

Figure 3: Photomicrograph of 200 mg/kg-treated kidney tissue showing glomerular atrophy (black arrows) (H and E, ×100)

did not prevent histopathological damage and ultrastructure perturbation caused due to isoproterenol-induced myocardial infarction.

The kidney photomicrograph [Figure 3] shows changes indicative of glomerular atrophy. These changes were, however, not seen in the control section [Figure 4] having a normal cytoarchetecture. Nanji *et al.*[9] and Lieber[10] described similar patterns in their research reports. However, other studies such as that described by Othman *et al.*[11] showed that berberine is able to prevent mercury-induced impairment in rats by inhibiting oxidative damage, inflammation, and apoptosis. The results of this study are not consistent with these researches.

Conclusions

In the present study, it was demonstrated that berberine

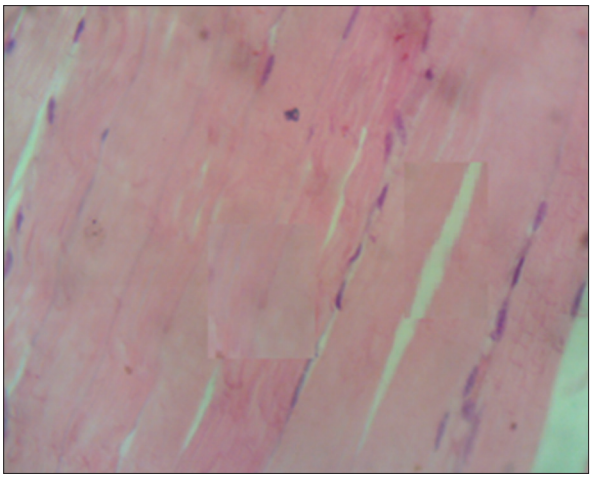

Figure 2: Photomicrograph of control heart tissue showing normal cytoarchitecture (H and E, ×100)

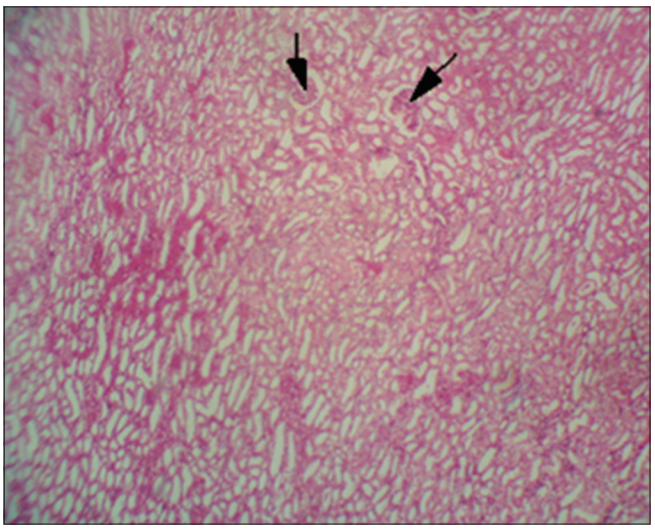

Figure 4: Photomicrograph of control kidney tissue showing normal cytoarchitecture with visible glomeruli (black arrows) (H and E, ×100)

significantly reduced GSH, SOD, and CAT levels in the kidneys and also significantly increased MDA levels. It was also found to cause a significant increase in urea, creatinine, and potassium levels. The renal histology showed alterations. The result showed that berberine is toxic to the kidneys at doses as high as 200 mg/kg.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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