Research Article

Assessment of Therapeutics Effects of Morinda morindoides on Organ Function and Metabolic Alterations in Adrenaline-Induced Hypertension in Wistar Rats

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ABSTRACT

Hypertension remains a public health problem in developing countries. Often called a "silent killer," it causes a disruption of the body's metabolism, characterized by damage to vital organs. This study aimed to evaluate the protective properties of *Morinda morindoides* extract for the heart, liver, and kidneys, as well as its lipid profile and blood glucose level, during experimental hypertension. The methodology consisted of treating hypertensive rats with adrenaline using dichloromethane extract of *Morinda morindoides* at doses of 500 and 1500 mg/kg bw and with Tenordate at doses of 10 and 20 mg/kg bw for 7 days. At the end of the experiment, blood samples were collected and specific markers of the lipid profile and vital organs were perofrmed. Tests were repeated three times and statistical analysis was carried out on the data obtained. Adrenalinee-induced hypertension significantly ($p < 0.05$) increased electrolyte levels (K^+, Na^+, and Ca^{2+}), urea, creatinine, total cholesterol, LDL cholesterol, triglycerides, glucose, transaminase activity, and LDH, and significantly reduced ($p < 0.05$) HDL cholesterol levels compared to the control. Both of extract at dose of 1500 mg/kg bw of and Tenordate® at dose of 20 mg/kg bw normalized all parameters at the end of treatment. These results demonstrated the therapeutic effect of *Morinda morindoides* for vital organs in hypertension and justify its use in traditional medicine.

Keywords: *Morinda morindoides*, biochemical markers, normalization, metabolic dysfunction, Wistar rats.

1. INTRODUCTION

World Health Organization indicated that globally, nearly 1.4 billion people were living with hypertension by 2024[1]. The disease is a leading cause of myocardial infarction and stroke[2] and contributes significantly to mortality and morbidity rates[3]. Millions of people die from it, particularly in low- and middle-income countries where treatment costs could account for approximately 2% of their GDP[1].

At its 7th congress in 2025, the Ivorian Society of Cardiology stated that in Côte d'Ivoire, hypertension remains a public health problem with a prevalence ranging from 30% to 40%. Given the severity of the condition, the increasing prevalence rate, and the still difficult access to healthcare, impoverished populations are increasingly turning to medicinal plants or products made from plant extracts[4] This traditional approach is not new. Indeed, Kouamé et al. (2019)[5] reported that more than 30% of respondents in their study used plants to treat hypertension. Several plants have also been mentioned for their antihypertensive potential, including *Annona muricata*[6], *Lippia multiflora*[7] and *Gmelina arborea*[8] etc. Although their effects are proven in lowering blood pressure, their effects on blood parameters and other biochemical markers of vital organs such as the heart, liver, kidneys, or lungs are not always taken into account during treatment. The purpose of this study was to evaluate the effects of *Morinda morindoides*, a plant with antihypertensive properties, on blood electrolytes and biochemical markers of vital organs during experimental adrenalinee-induced hypertension in rats.

2. MATERIALS AND METHODS

2.1 Materials

Plant material

The plant material consisted of fresh leaves of *Morinda morindoides* (Baker) Milne-Redhead (Rubiaceae) harvested in March 2025 in the commune of Lakota, a town in the Southwest of Côte d'Ivoire located about 225 km from Abidjan. The leaves were dried for two weeks in the shade. Then, they were finely chopped and ground using an IKAMAG-RCT grinder. The resulting powder was used to prepare the plant extract.

Animal material

White Wistar albino rats of both sexes aged 60 to 90 days and weighing between 140 and 180 g were used for this study. They were acclimated for two weeks at room temperature (22±2°C) in the animal facility of the École Normale Supérieure (ENS) in Abidjan. The animals were fed regularly with standard rat pellets and received tap water as drinking water.

2.2 Methods

Sample extract preparation

The preparation method described by Zihiri et al. (2003)[9] and modified by Boga et al. (2015)[10] was used. A 150 g of

Morinda morindoides powder was dissolved in 800 mL of a dichloromethane-ethanol solvent mixture (1/3V/V). The mixture was homogenized for 24 hours at room temperature (22-25 °C) using an IKAMAG-RCT magnetic stirrer. The resulting homogenate was filtered twice through absorbent cotton and once through Whatman filter paper 3 mm. The collected filtrate was evaporated using a BÜCHI rotary evaporator. This dried extract named total dichloromethane/ethanol extract (ExT), were stored in tightly stoppered bottles and kept in a refrigerator at 4°C.

Experimental design

Thirty (30) rats were used. Rats were divided into two groups : a normotensive control group (group T) of 5 rats and a hypertensive trial group of 25 rats divided into 5 groups of 5 rats each. The normotensive control group received distilled water orally for the 14 days of the experiment.

To induce hypertension, the rats in the trial group received 1 mL of ADR by intraperitoneal injection at a dose of 3.6 x 10^{-1} mg/kg bw for 7 days[10]. Once hypertensive, they were divided into five groups of five rats each and treated for 7 days as follows:

- lot Tm (untreated hypertensive animals) received distilled water orally;

- lot ExT 500 received the extract orally at a dose of 500 mg/kg bw;

- lot ExT 1500 received the extract orally at a dose of 1500 mg/kg bw;

- lot Ten 10 received Tenordate® orally at a dose of 10 mg/kg bw;

- lot Ten 20 received Tenordate® orally at a dose of 20 mg/kg bw.

The day after the treatment period, the animals were euthanized under ether anesthesia, and blood samples were collected in ETDA tubes and non-ETDA tubes[11]. The measurement of the different parameters was carried out with the veterinary automated analyzers BH-HA310VET (China) for hematological markers and BA-SA-100V (France) for biochemical markers.

The experiment was conducted in accordance with the ethical policy of the Pasteur Institute of Côte d'Ivoire regarding the rights of laboratory animals (Pasteur Institute Ethics Charter, February 2022 version).

2.3 Statistical analysis

The statistical software GraphPad Prism 5.0 was used for statistical tests and graphing. The results are presented as the mean ± standard error of the mean. Comparisons were performed using one-way ANOVA followed by Tukey's multiple comparison test at the 5% significance level.

3. RESULTS

3.1 Effects of extract and Tenordate on renal profile of hypertensive rats

Effect on serum electrolyte levels

Potassium (K^+), sodium (Na^+) and calcium (Ca^{2+}) were assessed in hypertensive rats (Figure 1 a, b and c).

Adrenaline-induced hypertension increased K^+ level from 9.3 ± 0.07 mmol/L (control value) to 10.90 ± 0.05 mmol/L in hypertensive rats, Na^+ level from 158 ± 1.83 mmol/L (control value) to 176 ± 2.77 mmol/L, and Ca^{2+} level from 10.80 ± 0.36 mmol/L (control value) to 12.02 ± 0.40 mmol/L. This corresponded to percentage increases of 17.20%, 11.39%, and 11.29%, respectively. Extract at a dose of 500 mg/kg body weight reduced serum levels of K^+ by 13.76%, Na^+ by 7.39%, and Ca^{2+} by 12.48%.

At a dose of 1500 mg/kg bw, the extract completely normalized serum levels of K+, Na+ which respectively went from 10.90 ± 0.05 to 9.280 ± 0.06 mmol/L and from 176.0 ± 2.77 to 160.0 ± 2.19 mmol/L, then reduced Ca^{2+} level below its normal value (from 12.02 ± 0.40 to 10.21 ± 0.35 mmol/L).

Tenordate® also reduced electrolyte levels similarly to the extract. Thus, K^+, Na^+, and Ca^{2+} levels decreased, respectively, from 10.90 ± 0.05, 176.0 ± 2.77, and 12.02 ± 0.40 mmol/L in hypertensive rats to 9.340 ± 0.08, 159.0 ± 2.50, and 10.01 ± 0.31 mmol/L in hypertensive rats treated with Tenordate® at a dose of 20 mg/kg bw.

Effect on urea and creatinine levels

Figure 2 (a and b) illustrate the change in serum urea and creatinine levels in rats at the end of the 7-day treatment period.

Hypertension significantly increased ($p < 0.05$) urea levels from 0.68 ± 0.05 g/L (control value) to 1.70 ± 0.06 g/L and creatinine levels from 50.30 ± 0.67 g/L to 83.06 ± 0.78 g/L, representing respective increases of 150% and 65.01%.

The extract at a dose of 1500 mg/kg bw significantly reduced ($p < 0.05$) urea levels to 0.63 ± 0.05 g/L and creatinine levels to 50.40 ± 0.72 g/L in hypertensive rats. Tenordate® at a dose of 20 mg/kg bw also significantly reduced ($p < 0.05$) urea levels from 1.70 ± 0.05 to 0.61 ± 0.04 g/L and creatinine levels from 83.00 ± 0.78 to 50.30 ± 0.67 g/L in hypertensive rats.

3.2 Effects of extract and tenordate® on cardiac profile

Cardiac lactate dehydrogenase (LDH) activity was assessed (**Figure 3**). Hypertension caused a significant increase ($p < 0.05$) in lactate dehydrogenase (LDH) activity, rising from 248 ± 5.54 to 281 ± 4.7 IU/L, representing a 13.31% increase. The extract at a dose of 1500 mg/kg bw reduced this LDH activity to 246 IU/L, representing 0.8% decrease. Tenordate® at a dose of 20 mg/kg body weight also reduced LDH activity from 281.0 ± 4.7 to 240.0 ± 4.93 IU/L, representing a 14.59% reduction.

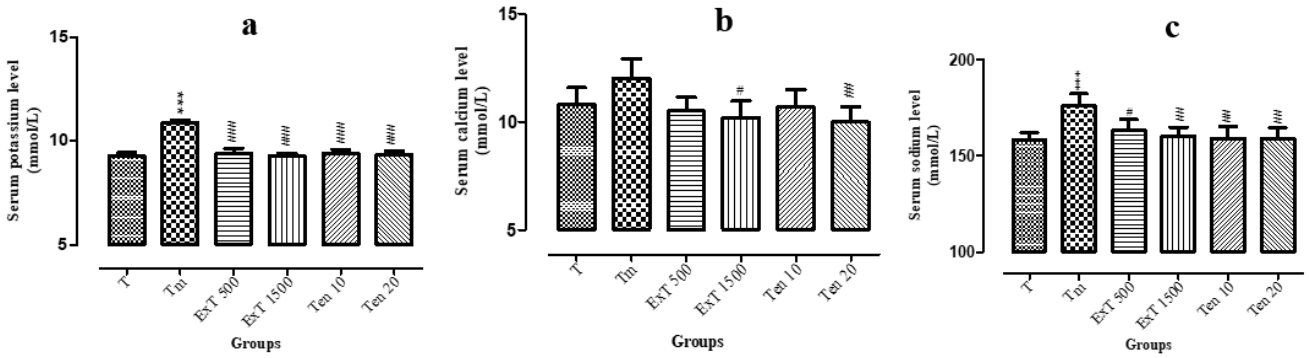

Figure 1: Effects of the extract and Tenordate® on serum electrolytes levels

a. Effects on serum potassium levels

b. Effects on serum calcium levels

c. Effects on serum sodium levels

*Each bar represents mean ± SEM, n = 5. ***P < 0.001 : significant difference compared to the control lot. ### P < 0.001 : significant difference compared to Tm lot. T = control lot, Tm = hypertensive and untreated lot (positive control) ; ExT 500 = hypertensive lot treated with extract at a dose of 500 mg/kg bw, ExT 1500 = hypertensive lot treated with extract at a dose of 1500 mg/kg bw, Ten 10 = hypertensive lot treated with tenordate® at a dose of 10 mg/kg bw, and Ten 20 = hypertensive lot treated with tenordate® at a dose of 20 mg/kg bw*

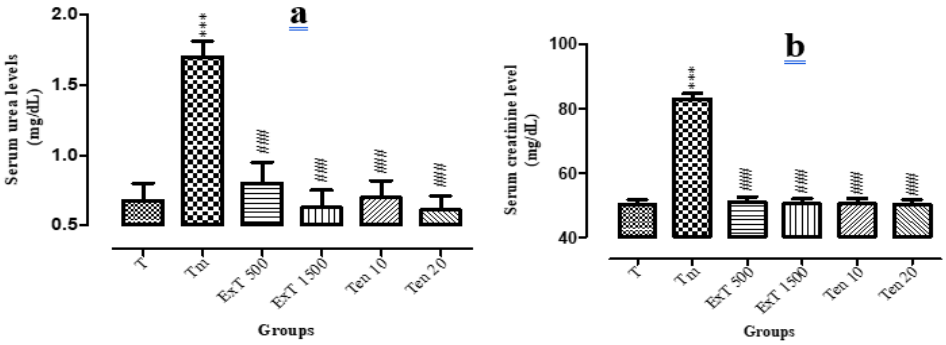

Figure 2: Effects of extract and Tenordate® on serum urea and creatinine levels

a. Effect of the extract and Tenordate® on serum urea level

b. Effect of the extract and Tenordate® on serum creatinine level

*Each bar represents mean ± SEM, n = 5. ***P < 0.001 : significant difference compared to the control lot. ### P < 0.001 : significant difference compared to Tm lot.*

T = control lot, Tm = hypertensive and untreated lot (positive control) ; ExT 500 = hypertensive lot treated with extract at a dose of 500 mg/kg bw, ExT 1500 = hypertensive lot treated with extract at a dose of 1500 mg/kg bw, Ten 10 = hypertensive lot treated with tenordate® at a dose of 10 mg/kg bw, and Ten 20 = hypertensive lot treated with tenordate® at a dose of 20 mg/kg bw.

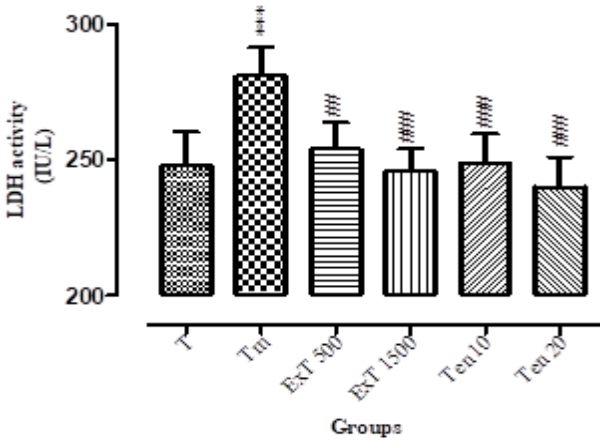

Figure 3: Effect of extract and Tenordate® on LDH activity

*Each bar represents mean ± SEM, n = 5. ***P < 0.001 : significant difference compared to the control lot. ### P < 0.001 : significant difference compared to Tm lot.*

T = control lot, Tm = hypertensive and untreated lot (positive control) ; ExT 500 = hypertensive lot treated with extract at a dose of 500 mg/kg bw, ExT 1500 = hypertensive lot treated with extract at a dose of 1500 mg/kg bw, Ten 10 = hypertensive lot treated with tenordate® at a dose of 10 mg/kg bw, and Ten 20 = hypertensive lot treated with tenordate® at a dose of 20 mg/kg bw.

3.3 Effects of extract and Tenordate® on lipid makers and blood glucose level

Lipid parameters

The effects of the extract and tenordate® on lipid parameters are shown in Figure 4 (a, b, c and d). Adrenaline-induced hypertension significantly increased ($p < 0.05$) total cholesterol (T-chol), LDL cholesterol (LDL-c), and triglyceride levels, and significantly reduced ($p < 0.05$) HDL cholesterol (HDL-c) levels. Thus, the levels increased from 2.15 ± 0.04 to 3.01 ± 0.04 mmol/L for T-chol, from 1.25 ± 0.04 to 1.88 ± 0.03 mmol/L for LDL-c, from 0.36 ± 0.04 to 0.92 ± 0.03 mmol/L for triglycerides and then from 0.87 ± 0.04 to 0.32 ±

0.04 mmol/L for HDL-c. This increase corresponds to percentage increases of 40% for T-chol, 50.4% for LDL-c, 155.55% for triglycerides, and a significant reduction ($p < 0.05$) of 136% in HDL-c levels compared to normotensive control rats.

Extract at a dose of 1500 mg/kg bw, significantly reduced ($p < 0.05$) T-chol, LDL-C, and triglyceride levels from 3.01 ± 0.04 to 2.18 ± 0.04 mmol/L; 1.88 ± 0.03 to 1.32 ± 0.04 mmol/L, and from 0.92 ± 0.03 to 0.38 ± 0.01 mmol/L respectively in hypertensive rats, representing respective percentage reductions of 38.07%, 42.42%, and 142.1%. At this same dose, the extract significantly increased ($p < 0.05$) HDL-c levels in hypertensive rats from 0.32 ± 0.04 to 0.89 ± 0.07 mmol/L (200% increase).

Tenordate® at a dose of 20 mg/kg body weight had the same effect as extract at a dose of 1500 mg/kg body weight. Thus, at this dose, tenordate® reduced T-chol levels from 3.010 ± 0.04 to 2.20 ± 0.04, triglycerides from 0.92 ± 0.03 to 0.37 ± 0.01, and LDL-c from 1.88 ± 0.03 to 1.27 ± 0.04 mmol/L, but it increased HDL-c levels from 0.32 ± 0.04 to 0.88 ± 0.03 mmol/L in hypertensive rats.

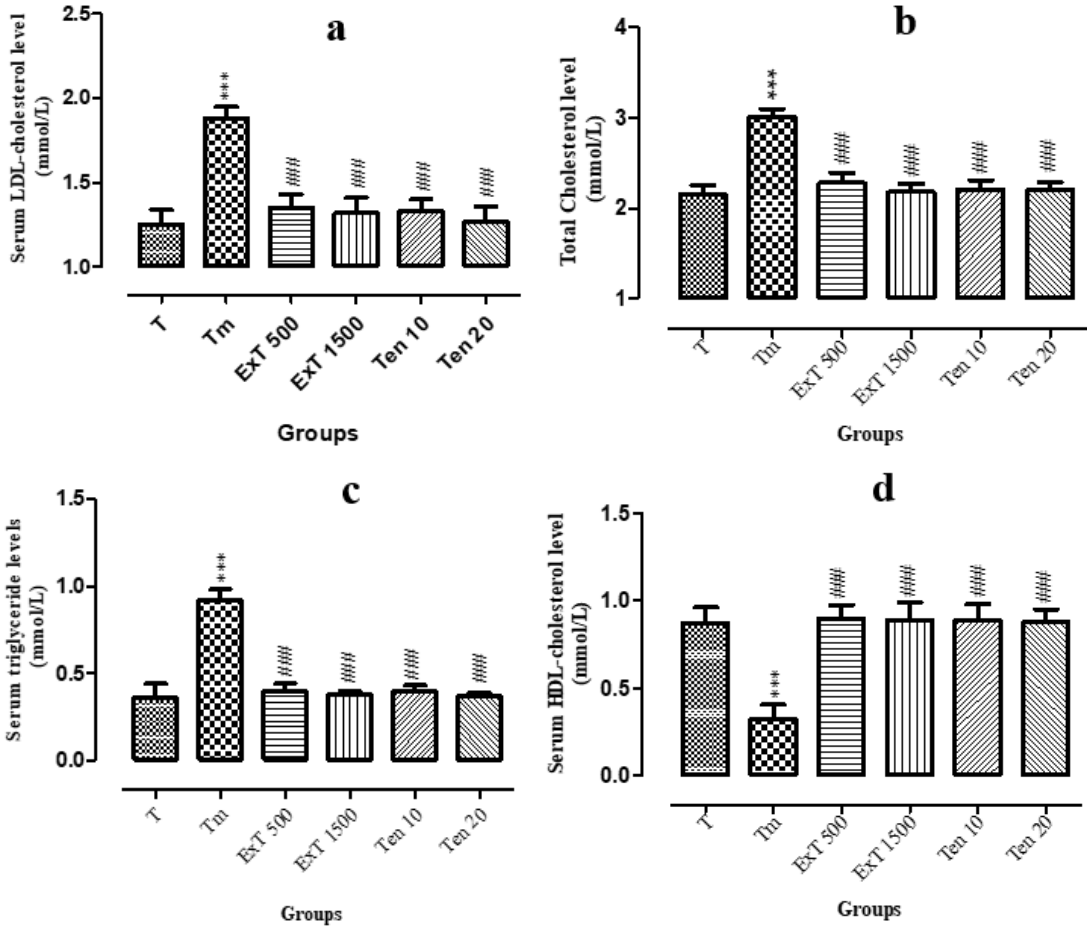

Figure 4: Effect of extract and Tenordate® on on lipid makers

a. Effects of extract and tenordate® on serum LDL-cholesterol levels
b. Effects of extract and tenordate® on serum total-cholesterol levels
c. Effects of extract and tenordate® on triglyceride levels
d. Effects of extract and tenordate® on HDL-cholesterol level

*Each bar represents mean ± SEM, n = 5. ***P < 0.001 : significant difference compared to the control lot. ### P < 0.001 : significant difference compared to Tm lot.T = control lot, Tm = hypertensive and untreated lot (positive control) ; ExT 500 = hypertensive lot treated with extract at a dose of 500 mg/kg bw, ExT 1500 = hypertensive lot treated with extract at a dose of 1500 mg/kg bw, Ten 10 = hypertensive lot treated with tenordate® at a dose of 10 mg/kg bw, and Ten 20 = hypertensive lot treated with tenordate® at a dose of 20 mg/kg*

Blood sugar level

The effect of extract and tenordate® on blood glucose levels is shown in Figure 5. Adrenaline-induced hypertension significantly increased ($p < 0.05$) blood glucose levels in rats from 3.4 ± 0.05 to 4.05 ± 0.09 mmol/L (18.53% increase) compared to normotensive control rats.

Extract at a dose of 1500 mg/kg bw significantly reduced ($p < 0.05$) blood glucose levels from 4.05 ± 0.09 to 3.42 ± 0.04 mmol/L (15.56% reduction).

Like the extract, tenordate® at a dose of 20 mg/kg bw reduced glucose levels from 4.05 ± 0.09 mmol/L to 3.45 ± 0.05 mmol/L (14.81% decrease).

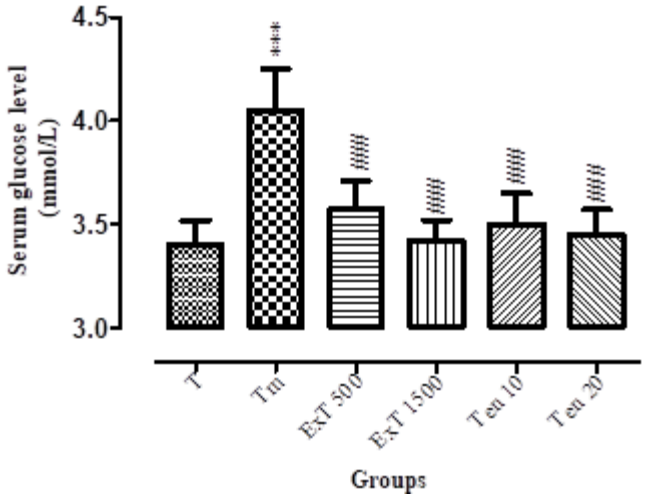

Figure 5: Effect of extract and Tenordate® on serum glucose levels

*Each bar represents mean ± SEM, n = 5. ***P < 0.001 : significant difference compared to the control lot. ### P < 0.001 : significant difference compared to Tm lot. T = control lot, Tm = hypertensive and untreated lot (positive control) ; ExT 500 = hypertensive lot treated with extract at a dose of 500 mg/kg bw, ExT 1500 = hypertensive lot treated with extract at a dose of 1500 mg/kg bw, Ten 10 = hypertensive lot treated with tenordate® at a dose of 10 mg/kg bw, and Ten 20 = hypertensive lot treated with tenordate® at a dose of 20 mg/kg bw*

3.4 Effects of extract and tenordate® on the liver profile in hypertensive rats

In liver, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity were evaluated and shown in Figure 6 (a and b). In hypertensive rats, there was a significant increase ($p < 0.05$) in transaminase activity compared to normotensive control group. Thus, ALT and AST activity increased from 66.00 ± 1.74 IU/L (control value) to 83.09 ± 2.33 IU/L and from 135.5 ± 1.52 (control value) to 147.63 ± 0.76 IU/L respectively, in the hypertensive group. Adrenalinee increased transaminase activity by 25.89% for ALAT and 9% for ASAT.

Extract at doses of 500 and 1500 mg/kg bw reduced ALT activity by 7.5% and 17.60%, respectively. Similarly, the reduction rates of this enzyme were 18.76% and 24.78% for doses of 10 and 20 mg/kg bw of tenordate®, respectively. Regarding AST, the reduction rates were 4.18% and 7.04% for doses of 500 and 1500 mg/kg bw, respectively, and 8.25% and 9.60% for doses of 10 and 20 mg/kg bw of Tenordate®, respectively.

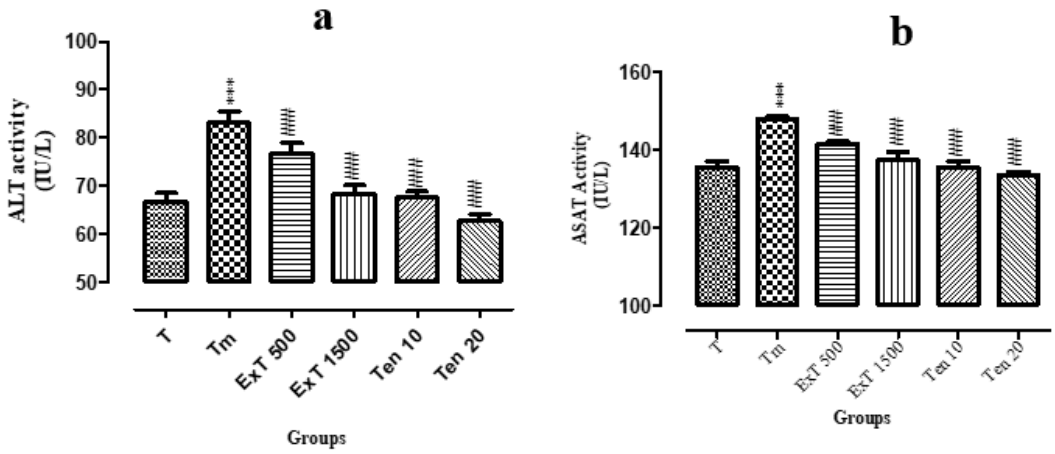

Figure 6: Effect of extract and Tenordate® on transaminases

a. Effects of extract and Tenordate® on alanine aminotransferase (ALT) activity

b. Effects of extract and Tenordate® on aspartate aminotransferase (AST) activity

*Each bar represents mean ± SEM, n = 5. ***P < 0.001 : significant difference compared to the control lot. ### P < 0.001 : significant difference compared to Tm lot. T = control lot, Tm = hypertensive and untreated lot (positive control) ; ExT 500 = hypertensive lot treated with extract at a dose of 500 mg/kg bw, ExT 1500 = hypertensive lot treated with extract at a dose of 1500 mg/kg bw, Ten 10 = hypertensive lot treated with tenordate® at a dose of 10 mg/kg bw, and Ten 20 = hypertensive lot treated with tenordate® at a dose of 20 mg/kg bw*

4. DISCUSSION

The present study investigated the protective effect of *Morinda morindoides* on vital organs that may be damaged during adrenaline-induced hypertensive in rats.

The results showed that, once established, hypertension caused various metabolic disorders, including abnormalities in LDH activity, lipid profile markers, creatinine, urea, and blood glucose levels.

With regard to kidney function, the observed disturbance manifested as a significant increase ($p < 0.05$) in blood levels of creatinine and urea, two routine biomarkers of kidney structure and function. This finding, also reported by Fagbohun et al. (2025)[12] suggests impairment of renal structure or function. The findings of Ukpe et al. (2023)[13] are supported this conclusion.

The total dichloromethane/ethanol extract (ExT) of *Morinda morindoides* administered to hypertensive rats significantly reduced ($p < 0.05$) and normalized serum levels of these renal biomarkers, suggesting that the extract corrects abnormalities resulting from hypertension. This result is consistent with those reported by Abou-Haleka et al.

(2023)[14] regarding renal parameters. The extract reduced these two parameters in a dose-dependent manner similarly to Tenordate® (reference compound).

Furthermore, adrenaline-induced hypertension led to a significant increase in blood electrolyte levels (K^+, Ca^{2+}, and Na^+) in hypertensive rats compared to the normotensive control lot. This electrolyte imbalance has also been observed in hypertensive patients[15]. This disturbance reflects renal damage caused by hypertension. Indeed, these electrolytes are primarily eliminated by the kidneys, so their excess in the blood is a sign of impaired or failed renal function. Treatment of hypertensive animals with the extract reduced and normalized the levels of these blood electrolytes. This finding supports the conclusion that the extract restores normal kidney function.

Concerning cardiac function, administration of adrenaline to rats resulted in a significant increase ($p < 0.05$) in LDH activity, a marker of cardiac injury in acute conditions[16,17]. This increase in LDH activity in hypertensive animals is thought to be due to the onset of cardiac cell necrosis, which in turn is believed to result from an elevated heart rate or enzyme overactivity, as suggested by Romic et al. (2009)[18]**.** LDH activity was significantly ($p < 0.05$) reduced and normalized by the extract. Through this mechanism, the extract may protect the heart against damage or restore heart function and/or structure.

Furthermore, the results showed a significant increase ($p < 0.05$) in blood glucose levels in hypertensive rats. This finding was also reported by several authors, including Tiekpa et al. (2014)[19] and Semra et al. (2025)[20] in their respective studies. According to several authors, the increase in blood glucose levels caused by adrenaline depends on several factors, including obesity and inflammation[21]. This rise in blood glucose levels could be explained by the role adrenaline plays in regulating blood glucose levels. Specifically, it either inhibits glycogenesis or insulin production, or it limits glucose utilization by insulin-sensitive cells[22]. The significant decrease ($p < 0.05$) followed by normalization of blood glucose levels observed with the extract at a dose of 1500 mg/kg bw, suggests that secondary metabolites in the extract may antagonize or inhibit the metabolic effects induced by adrenaline.

Lipid profile biomarkers were also altered in untreated hypertensive rats, as evidenced by a significant increase ($p < 0.05$) in triglyceride, total cholesterol, and LDL-cholesterol levels, on one hand, and on other, a significant decrease in HDL-cholesterol levels. These findings are similar to those reported by Kabiru et al. (2016)[23]**.** These authors argue that such abnormalities in the lipid profile are prevalent among hypertensive humans. Furthermore, elevated LDL cholesterol levels are known to be a major risk factor for obesity, atherosclerosis, and other related diseases[24]. Furthermore, the increase in LDL cholesterol levels and the concomitant decrease in HDL cholesterol levels are considered excellent indicators of the onset of cardiovascular disease. The extract, like Ténordate®, corrected the metabolic disorders caused by adrenaline on the lipid profile. Through this beneficial effect, the extract is believed to have a protective effect against the onset of risk factors associated with hypertension.

In this study, the liver profile was assessed through transaminase activity. Adrenaline-induced hypertension led to a significant increase ($p < 0.05$) in transaminase activity (ALT and AST). These enzymes are known to be sensitive markers of hepatocellular damage in acute liver injury[25]. Their elevated activities following adrenaline-induced hypertension may explain the damage to liver structure. In fact, transaminase levels in the blood rise as a result of the rupture of the cytoplasmic membrane of liver cells[26]. The decrease and normalization of AST and ALT activity by *Morinda morindoides* extract in the treated groups suggest a normalization of liver integrity and function, as reported by Xiao et al. (2020)[27]. These results are similar to those obtained by Fagbohun et al. (2025)[12] using a combination of *Euphorbia hirta* and *Leptadenia hastata extracts*.

5. CONCLUSION

Experimental adrenaline-induced hypertension causes metabolic disturbances in the body, affecting lipid, hepatic, cardiac, and renal profiles, as well as blood glucose levels. The study results showed that the extract, like Tenordate®, corrects and normalizes the various parameters evaluated. Through this study, the results demonstrated that extract possesses beneficial cardioprotective, hepatoprotective, and renoprotective properties and would be beneficial in the management of hypertension, one of the main risk factors for cardiovascular disease. This study supports the traditional use of *Morinda morindoides* in the management of hypertension.

Acknowledgement

The authors express their gratitude to all the technicians who made this project possible.

Ethical considerations

The experimental procedures and the care of the animals in this study were conducted in accordance with the ethical and regulatory guidelines governing the rights of laboratory animals (Ethics Charter of Pasteur Institute, February 2022 version).

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