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Evaluation of the cardioprotective potential of aqueous extract of *Datura metel* (Solanaceae) leaves on doxorubicin-induced acute myocardial infarction in Wistar rats

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Abstract

The present study aimed to evaluate the cardioprotective effect of the aqueous extract of *Datura metel* leaves (AELDM) on myocardial damage caused by doxorubicin in Wistar rats. This study required 30 Wistar rats, which were randomized and divided into 6 groups of 5 animals each. Rats from control groups (normal and negative) received orally 1 mL/200 g of distilled water daily for 6 days, those in the positive control group received 100 mg/kg of vitamin E, and those in the test groups received the plant extract at doses of 100, 200, and 300 mg/kg respectively. On the 7th day of treatment, animals from all groups except the normal control group received a single intraperitoneal injection of doxorubicin (15 mg/kg), followed by respective treatments until the 10th day of the experimental period. Variations in serum transaminase activities (AST/ALT), biochemical markers of oxidative stress (MDA, SOD, CAT, GSH), and lipid parameters (total cholesterol, triglycerides, HDL, and LDL) were evaluated. Heart tissue histological sections were performed, and the acute toxicity of the extract was assessed.

The findings revealed that aqueous extract of *Datura metel* leaves contains bioactive compounds that confer pharmacological properties to the plant. Indeed, AELDM treatment resulted in a significant decrease ($P < 0.001$) of MDA levels, triglycerides, LDL-cholesterol, AST/ALT activity, and a significant increase ($P < 0.001$) of HDL-cholesterol concentration and SOD, CAT, and GSH activity, compared to the negative control group. Furthermore, histological section observations revealed that the extract protected the heart against doxorubicin-induced damage and appears safe for health as the LD_{50} of the extract is greater than 2000 mg/kg. In conclusion, the aqueous extract of *Datura metel* leaves at a dose of 300 mg/kg body weight throughout the experimental period is well tolerated by the heart and would have a cardioprotective effect in rats.

Keywords: *Datura Metel*; Cardioprotection; Myocardial Infarction; Doxorubicin; Antioxidant

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1. Introduction

Traditional medicine occupies a prominent place in the treatment of various conditions in Cameroon as elsewhere in Africa. Indeed, plants contain phytochemical compounds that confer pharmacological properties upon them [1]. Thus, medicinal plants are used for the treatment of metabolic diseases such as diabetes, hypertension, and many others [2]. The survival and intensification of this practice today, despite the advancement and modernization of modern medicine, is explained by certain factors, notably economic constraints, sociocultural data, and especially the great availability and efficacy of plants that are an integral part of the immediate environment of populations [3]. However, despite this renewed interest in medicinal plants, it is important to identify through experimental studies the different plants that have pharmacological properties on specific pathologies, such as heart diseases, which are responsible for several deaths worldwide.

According to the World Health Organization (WHO), approximately 16.7 million people die each year from heart diseases, corresponding to one-third of annual global deaths [4]. These pathologies affect approximately 30% of the African population [5], causing several deaths in Cameroon [6] . Myocardial infarction (MI) is one of the most lethal manifestations of heart diseases, occurring when there is an imbalance between oxygen supply and demand, causing myocardial hypoxia [7]. It is the most common form of ischemic heart disease, generally accompanied by numerous pathophysiological and biochemical changes such as lipid peroxidation, hyperglycemia, and hyperlipidemia [8]. In developed countries and most developing countries, MI is the leading cause of mortality and morbidity. This pathology, commonly called as heart attack, generally occurs when blood circulation is interrupted in any part of the heart, leading to the death of cardiac tissues [9].

Studies on *Datura metel* show that it possesses hypolipidemic and anti-hyperglycemic properties, which could be beneficial in the treatment of cardiovascular diseases [10]. Recent work on the aqueous extract of seeds of this plant shows that it has cardiotonic and antioxidant potential [11, 12, 13] . The phytochemical study of this plant mentioned in the literature reveals that it's rich in alkaloids, tannins, and flavonoids [14, 15], which are bioactive compounds responsible of antioxidant properties [16, 17]. The various pharmacological properties listed, as well as previous work, raise real hopes in the management of cardiovascular conditions in general and heart diseases in particular.

2. Materials and methods

2.1. Plant Material

2.1.1. Collection, Identification, and Aqueous Extract of Datura metel Leaves preparation

Fresh leaves of *Datura metel* were harvested in the city of Koza (11°03'15.22"N; 13°58'35.09"E; 405 m altitude), Mayo-Tsanaga Department, Far-North Region of Cameroon. Taxonomic identification of the plant was done by comparison with a specimen N° 6408/HEFG deposited at the Herbarium of the Garoua Fauna School. The harvested fresh leaves were washed, cut, and dried in the shade at ambient temperature for about two weeks. These dried leaves were ground using an electric mill (BINATONE, Model N°: BLG-450). The obtained powder was then sifted using a stainless steel sieve (16 cm; mesh 0.8 mm). Fine powder weighing 200 g was dissolved for 1 hour in 2 L of distilled water heated to 70°C. The obtained homogenate was filtered using Whatman GF/C paper (90 mm) until a filtrate was obtained, which was evaporated in an oven at 45±1°C for 48 hours. After this evaporation phase, we obtained 13 g of a greenish paste representing the crude aqueous extract of *Datura metel* leaves, which will be used during the experimental study. The extraction yield was therefore 9%.

2.1.2. Qualitative and Quantitative Phytochemical Screening of AELDM

Qualitative phytochemical screening was performed to determine the presence of different classes of bioactive compounds in the extract according to classical method [18]. Similarly, the quantity of total phenolic compounds in the extract was estimated by the Folin-Ciocalteu method [19], flavonoids by the aluminum trichloride method [20], and tannins by the method described by [21].

2.2. Animal Material

Strain of male adult Wistar rats of 12 weeks old (for the cardioprotective evaluation) ; weighing between 180 and 200 g and non-pregnant female rats weighing between 140 and 150 g, aged 8 to 10 weeks (for acute toxicity evaluation) were obtained from the Animal Physiology Laboratory at the University of Ngaoundéré. These rats were acclimatized for two weeks at the Animal Facility of the Laboratory of Biological Sciences at the University of Maroua, which was

well-ventilated and naturally lit (12 hours out of 24 hours) before the start of the various experiments. These animals were kept in plastic cages containing wood shavings renewed every two days. Standard feed for laboratory rodents composed of corn flour (50%), soy flour (20%), fish powder (15%), calcined bone powder (4%), palm oil (0.1%), complex vitamins (0.1%), cotton seed powder (10%), table salt (0.8%), as well as drinking water, were provided *ad libitum* to the rats throughout the experimental period. The experiments on rats in this study were carried out in accordance with the European Convention for Protection of Vertebrate Animals used for Experimental and other Purposes.

2.3. Experimental Protocol

2.3.1. Induction and Treatment of Acute Myocardial Infarction

Male rats were divided into 6 groups of 5 animals each. Animals in groups I and II, considered as normal control and negative control respectively, received orally 1 mL/200 g of distilled water daily for 6 days. Those in group III (positive control) received 100 mg/kg of vitamin E, while animals in groups IV, V, and VI (test) received AELDM at doses of 100, 200, and 300 mg/kg respectively. All animals, except those in group I (normal control), received on the 7th day of treatment a single intraperitoneal injection of 15 mg/kg doxorubicin [22]. From the 8th day of the experimental period, animals in the positive control group and those treated with different doses of AELDM received their respective treatments until the 10th day of the experimental period [23].

2.3.2. Animal Sacrifice and Sample Collection

All animals were fasted for 12 hours on the 10th day of the different treatments. They were sacrificed by cervical dislocation the following day, and blood was immediately collected in dry tubes after rupture of the jugular vein. This blood was centrifuged at 3000 rpm for 15 minutes using a centrifuge (UNIVERSAL 320 R HETTICH). The serum was separated and collected for biochemical parameter analysis. The heart of each rat was removed and divided into two parts. One part (0.5 g) of each heart was ground in a glass mortar and homogenized in 2.8 mL of phosphate buffer. The homogenates were centrifuged at 3000 rpm for 10 min at 4°C, and the supernatant was collected for analysis of various biochemical parameters. The second part of each heart was rinsed in saline solution (0.9%), then fixed in 10% formalin for histological section preparation.

2.3.3. Serum Transaminase Activity (AST/ALT) Assay

The assay of transaminases such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) in serum was performed following the protocol described by Murray in 1984 using the CHRONOLAB kit. This assay was done using a semi-automatic spectrophotometer brand "MINDRAY BC-2800". The device was programmed and calibrated for reading according to the instructions on each reagent's package insert.

2.3.4. Some Oxidative Stress Parameters assay

Malondialdéhyde (MDA) concentration was evaluated using the method described by Wilbur *et al* [24]; superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) activity were measured according to the methods described respectively by Misra and Fridovich [25], Sinha [26], and Ellman [27] in the homogenates of the different hearts.

2.3.5. Lipid Parameters Assay

Total cholesterol and triglyceride levels were evaluated following a colorimetric enzymatic method described by Parekh *et al* [28] and Rice [29] respectively, using DIALAB and INMESCO kits. Lipoprotein levels (HDL and LDL) were evaluated following the method described by Burstein and Scholnick [30].

2.3.6. Histology of Rat Hearts

After fixation, the hearts were treated respectively with alcohol and xylene at different concentrations, impregnated in paraffin, then sectioned at 4 µm for the preparation of white slides, which were subsequently stained respectively with hematoxylin and eosin for reading under a light microscope (Olympus BX51) and capture of micrographs (40X, 100X, 200X).

2.3.7. Study of Acute Toxicity of AELDM

This study was conducted in accordance with OECD Guideline N^{o} 423 dedicated to chemical testing [31]. Indeed, three batches of three female rats each were randomly formed to evaluate the toxicity of our extract. Before the start of the

actual test, all female rats were first fasted for 12 hours. On the first day of the experiment, female rats in the normal control group received distilled water (10 mL/kg) via gastric gavage. Those in the first test group received a single oral dose of 2000 mg/kg of the aqueous extract of *Datura. metel* leaves. These animals from the first test group were observed for 48 hours, and signs of toxicity were noted starting from the 4th hour after administration. After observing the signs presented by the animals of the first test group, three other female rats considered as the second test group (confirmation group) were also fasted for 12 hours and then received the same single dose of 2000 mg/kg of the aqueous extract of *Datura metel* leaves orally. The animals were observed individually half an hour after extract administration, one hour after, the following four hours, then daily. The explored toxicity signs essentially concerned mortality rate, body weight, and certain clinical signs observable on the animals' biological systems.

2.4. Statistical Analysis

Statistical analysis of results was performed using GraphPad Prism 5.00 software. Results are presented as mean ± Standard Error of the Mean (SEM), for a sample size of n = 5 rats per group. After one-way analysis of variance (ANOVA), intergroup means were compared using Tukey's non-parametric test. Significant differences were considered at a probability threshold of 0.05.

3. Results

3.1. Qualitative and Quantitative Phytochemical Screening of AELDM

Qualitative phytochemical analysis of aqueous extracts of *Datura metel* leaves and seeds revealed the presence of several secondary metabolites belonging to different families of chemical compounds (Table 1).

Table 1 Qualitative phytochemical analysis of aqueous extracts of *Datura metel* leaves

Compounds	**Assay**	**Aqueous extracts of *Datura metel* leaves**
Glycosids	Borntrager	-
Tannins	Ferric chloride	+
Saponins	Froth	+
Flavonoids	Shinoda	+
Alkaloids	Dragendorff	+
Steroids	Liebermann burchard	-
Terpenoids	Liebermann burchard	+
polyphenols	Ferric chloride	+

+ = Present - = Absent

Quantitative phytochemical screening evaluated for some groups of chemical compounds exhibited variable levels of flavonoids (4.31 Eq g quercetin/100 g of extract), tannins (1 Eq g catechin/100 g of extract), saponins (94 Eq mmol galactose/100 g extract), and total phenolic compounds estimated at approximately 16.87 Eq g gallic acid/100 g extract.

3.2. Effect of the Extract on Transaminase Activity

Table 2 shows that rats in group II (negative control) presented a significant increase ($p < 0.001$) in AST and ALT activity of the order of 62.63% and 82.34% respectively compared to group I (normal control). This increase ranged from 82.31 to 127.29 for AST activity and from 42.25 to 118.12 for ALT activity in these animals. Animals in groups IV, V, and VI (AELDM 100, 200, and 300 mg/kg) presented respectively a significant decrease ($p < 0.001$) in the activity of these transaminases compared to the negative control. This decrease was below the value presented by the normal control.

Table 2 Effect of AELDM on transaminase activity (AST/ALT**)**

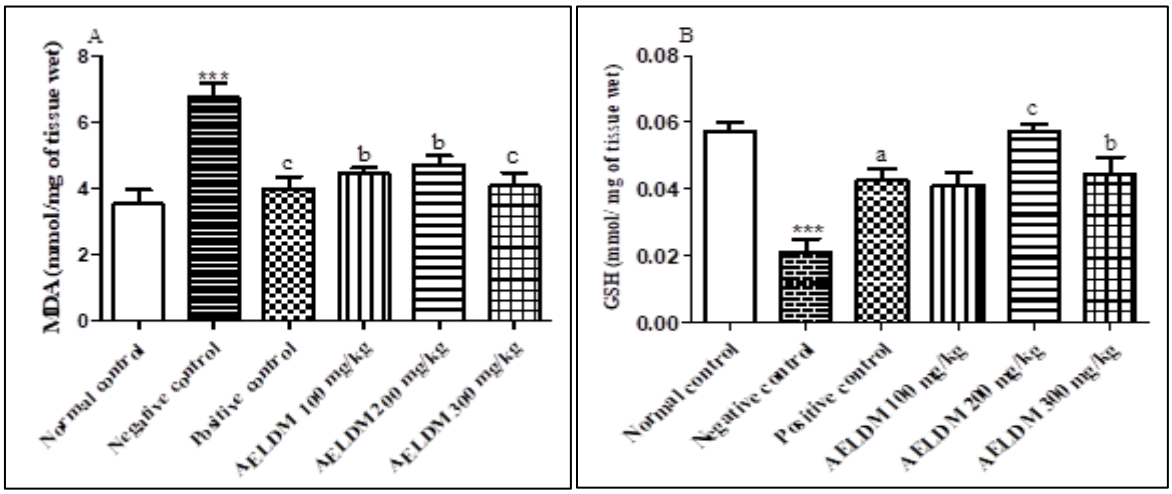
GROUPS	ASAT (UI/L)	ALAT (UI/L)
Group I (distilled H_2O , 10 mL/kg)	82.31 ± 0.45	42.25 ± 0.54
Group II (distilled H_2O, 10 mL/kg)	127.29 ± 0.35***	118.12 ± 0.22 ***
Group III (Vit-E, 100 mg/kg)	82.16 ± 1.62^c	52.55 ± 0.55^c
Group IV (AELDM 100 mg/kg)	86.92 ± 0.84^c	53.34 ± 0.46^c
Group V (AELDM 200 mg/kg)	72.56 ± 0.91^c	39.09 ± 0.41^c
Group VI (AELDM 300 mg/kg)	63.25 ± 0.96^c	36.84 ± 2.57^c

Each value represents mean ± SEM, n=5. ***p < 0.001: statistically significant difference compared to normal control group. ^{c}p < 0.001: significantly different compared to negative control group. Vit-E = vitamin E; AELDM = aqueous extract of *Datura metel* leaves.

3.3. Effect of AELDM on Some Oxidative Stress Parameters

3.3.1. Effect of AELDM on Malondialdehyde (MDA) and Glutathione (GSH) Concentration

Figure 1A reveals that malondialdehyde (MDA) concentration increased significantly (P < 0.001) while glutathione (GSH) concentration decreased significantly (P < 0.001) (Figure 1B) in rats subjected to doxorubicin injection without prior treatment, compared to the normal control. However, a significant reduction (P < 0.001) in MDA concentration correlated with a significant increase (P < 0.001) in GSH was observed in the hearts of rats subjected to AELDM treatment compared to the negative control (distilled H_2O, 10 mL/kg).

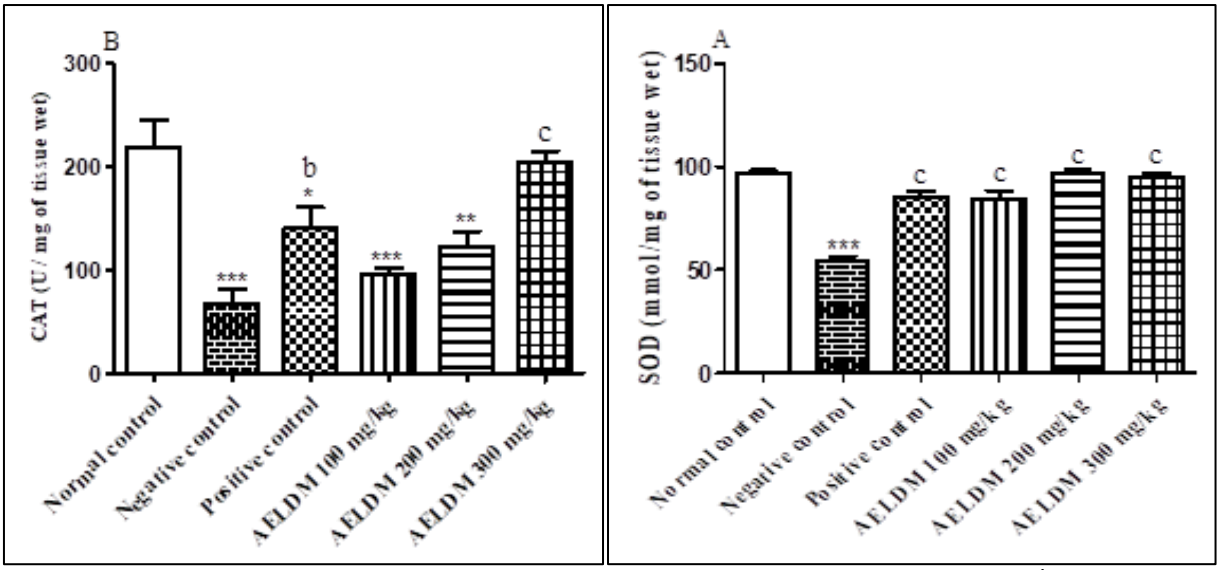


Each value represents the mean ± SEM, n=5. ***p < 0.001: significantly different compared to the normal control group. ^{b}p < 0.01 and ^{c}p < 0.001: significantly different compared to the negative control group (distilled H_2O, 10 mL/kg). Vit-E = Vitamin E; AELDM = Aqueous Extract of *Datura metel* Leaves.

Figure 1 Effect of AELDM on MDA (A) and GSH (B) concentrations in rat cardiac tissue

3.3.2. Effect of AELDM on Superoxide Dismutase (SOD) and Catalase (CAT) Activity

Figure 2 illustrates the variation of superoxide dismutase (SOD) and catalase (CAT) activity in the hearts of rats from different experimental groups. It appears from this figure that SOD activity (Figure 2A) and catalase activity (Figure 2B) significantly decreased (P < 0.001) in the hearts of rats that received only an intraperitoneal injection of doxorubicin without prior pretreatment, compared to the normal control. Similarly, it was observed that the activity of these antioxidant enzymes increased significantly (P < 0.001) in the hearts of rats subjected to AELDM treatment at a dose of 300 mg/kg, compared to the negative control (distilled H_2O, 10 mL/kg).



Each value represents the mean ± SEM, n=5. ***p < 0.001: significantly different compared to the normal control group. [b]p < 0.01 and [c]p < 0.001: significantly different compared to the negative control group (distilled H_2O, 10 mL/kg). Vit-E = Vitamin E; AELDM = Aqueous Extract of *Datura metel* Leaves.

Figure 2 Effect of AELDM on SOD (A) and CAT (B) concentrations in rat cardiac tissue

3.4. Effect of AELDM on Lipid Parameters

Table 3 presents the effect of AELDM on lipid parameters (Total Cholesterol, HDL-Cholesterol, LDL-Cholesterol, Triglycerides). According to this table, a significant decrease (P<0.001) in serum HDL-cholesterol content is noted, while triglyceride and LDL-cholesterol levels increased in rats that received doxorubicin injection without prior pretreatment, compared to the normal control. Furthermore, a significant increase (P<0.01) in serum HDL-cholesterol level and a significant decrease in LDL-cholesterol level (P<0.001) and triglycerides (P<0.05) were observed in rats treated with doses of 200 and 300 mg/kg of AELDM, compared to negative control (distilled H_2O, 10 mL/kg).

Table 3 Effect of AELDM on Lipid Parameters

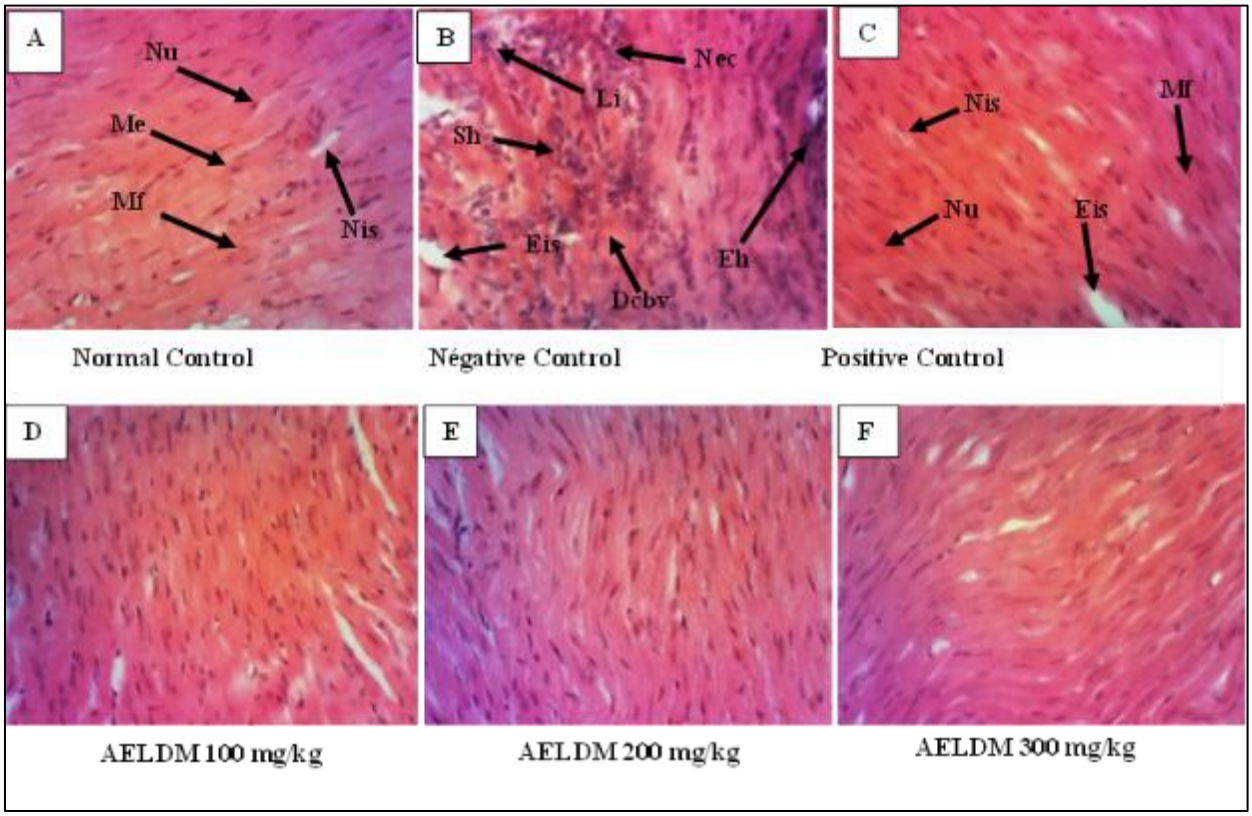
GROUPS	Total Cholestérol (mg /dL)	HDL-Cholestérol (mg /dL)	LDL-Cholestérol (mg /dL)	Triglycerides (mg /dL)
Normal control	167.71 ± 5.60	135.71 ± 5.64	18.09 ± 1.07	79.48 ± 5.06
Negative control	175.30 ± 2.21	91.69 ± 2.71***	37.74 ± 1.98 **	179.29 ± 3.77***
Positive control	139.56 ± 3.83 **[b]	112.89 ± 3.82 *[a]	15.01 ± 0.83 [b]	58.28 ± 4.05 [c]
AELDM 100 mg/kg	151.24 ± 2.43	113.19 ± 4.48	17.36 ± 2.34	103.43 ± 3.14
AELDM 200 mg/kg	146.67 ± 1.50	124.02 ± 3.14	12.95 ± 1.26	98.47 ± 4.63
AELDM 300 mg/kg	138.72 ± 3.52	132.52 ± 1.43	8.92 ± 1.61	75.64 ± 2.81

Each value represents mean ± SEM, n=5. * p < 0,05 ; **p < 0,01 ; *** p < 0,001: significantly different compared to normal control group. [a]p < 0,05 ; [b]p < 0,01 ; [c]p < 0,001 significantly different compared to negative control group. Vit-E = vitamin E; AELDM = aqueous extract of *Datura metel* leaves.

3.5. Effect of AELDM on Histological Parameters

Microscopic observation of hematoxylin-eosin stained heart sections from the normal control group showed intact cardiac parenchyma without damage, with well-distinct cardiomyocyte nuclei and muscle fibers (Figure 3A). Administration of doxorubicin to animals of negative control group caused the formation of leukocytic infiltration zones in the myocardium, widening of muscle bundles, and cellular necrosis (Figure 3B). Treatment with vitamin E in positive control animals and the aqueous extract of *Datura metel* leaves corrected these myocardial histopathological

alterations. Indeed, the hearts of animals treated with AELDM, like vitamin E, have a normal structure closer to that of the normal control group (Figures 3C, 3D, 3E, and 3F).



A = Normal control; B = Negative control (distilled H_2O, 10 mL/kg); C = Positive control (Vit-E, 100 mg/kg); D, E, F = Aqueous extract of *D. metel* leaves at respective doses of 100, 200, and 300 mg/kg. *Abbreviations:* Sh: Slight haemorrhage; Nis: Narrow intracellular space; Me: Mild edema; Nec: Necrosis; Co: Congestion; Eis: Expanded intracellular space; Dcbv: Dilated and congested blood vessel; Eh: Expanded haemorrhage; Nu: Nucleus; Mf: Muscle fiber; Li: Leukocytic infiltration

Figure 3 Micrographs of rat hearts (Hematoxylin-Eosin x 200).

3.6. Effect of AELDM on Toxicity Signs

The aqueous extract of *Datura metel* leaves administered at a single dose of 2000 mg/kg orally caused a decrease in sensitivity to pain induced by tail pinching and reaction to external stimuli (cage tapping) compared to control rats (distilled water 10 mL/kg, per os). A modification in the appearance of rat feces was observed, as well as certain aggressiveness when approaching an object in test animals. At the end of this experimental period, it was noted that the relative body weight of animals did not vary significantly in female rats that received the single dose of 2000 mg/kg of the aqueous extract of *Datura metel* leaves, compared to the control group. Similarly, no mortality cases were observed during the 14-day of experimental period, and the median lethal dose (LD_{50}) was therefore estimated to be greater than 2000 mg/kg.

4. Discussion

The present study aimed to evaluate the cardioprotective potential of the aqueous extract of *Datura metel* leaves (AELDM) on doxorubicin-induced cardiotoxicity (Dox) in rats. The results obtained from this work highlighted the richness of the extract in phytochemical compounds, prevention of doxorubicin-induced toxicity, as well as apparent safety of the extract at a single dose of 2000 mg/kg.

Qualitative and quantitative phytochemical analysis of AELDM revealed the presence of several secondary metabolites, notably flavonoids, tannins, saponins, alkaloids, and total phenolic compounds. These results are similar with those of several authors who also reported a diversity of bioactive compounds in extracts of *Datura metel* [14, 15, 32]. Flavonoids, alkaloids, and phenolic compounds, known for their antioxidant properties, could be responsible of the protective effects observe [17, 33, 34].

Administration of doxorubicin to the different animals led to an elevation of cardiac transaminase activity (AST/ALT), thus indicating cardiac damage [35, 36]. This increase is a classic indicator of cellular toxicity induced by reactive oxygen species generated by doxorubicin [37]. Indeed, doxorubicin is a drug used in the treatment of a variety of solid and hematological malignant tumors [38, 39]. However, its clinical use is limited by the development of cardiomyopathies and congestive heart failures that it may cause [40]. The reactive oxygen species (ROS) generated during DOX metabolism are responsible for lipid peroxidation, which plays an essential role in the onset of cardiomyopathies [41, 42, 43]. The heart is an organ particularly sensitive to free radicals, compared to other organs such as the liver and kidneys, due to the deficit of antioxidant defense systems at this level [44, 45].

Treatment of animals with AELDM significantly reduced the activity of these enzymes, notably at doses of 200 and 300 mg/kg, thus suggesting membrane protection and cardiomyocyte stabilization. This result reveals that AELDM inhibits lipid peroxidation, due to flavonoids and polyphenols present in this extract. Several previous studies have shown the cardioprotective effect of plant extracts against cardiac toxicity characterized by a significant decrease in AST/ALT transaminase activity [46, 47].

Oxidative stress is the main mechanism of doxorubicin-induced cardiotoxicity induction [48, 49]. The production of free radicals by doxorubicin within myocardial cells has as a direct consequence on the evolution of the cell toward apoptosis [50]. By exploring biochemical markers of oxidative stress in cardiac tissue, it was revealed that doxorubicin induced an increase in malondialdehyde (MDA) levels, a marker of lipid peroxidation, and a decrease in reduced glutathione (GSH), reflecting the depletion of antioxidant defense [51, 52]. AELDM reversed these parameters in a dose-dependent manner, with a maximum effect at 300 mg/kg, suggesting that AELDM was able to protect the heart against oxidative stress and the cytotoxic action of DOX. This antioxidant action is probably linked to the ability of flavonoids to scavenge free radicals and regenerate GSH, a non-enzymatic antioxidant representing the first line of defense against free radicals [53, 54]. Moreover, the increased activity of antioxidant enzymes SOD and CAT in rats treated with AELDM confirms its potential to strengthen the endogenous defense system. These results are similar with those published by several authors, who observed a clear decrease in cardiac MDA levels, an increase in SOD and CAT activity after treatment with plant extracts [55, 56].

The lipid profile explored in this study shows that doxorubicin caused dyslipidemia characterized by a decrease in HDL-cholesterol and an increase in LDL-cholesterol and triglycerides. Administration of AELDM apparently improved these parameters, particularly at a dose of 300 mg/kg. This lipid modulation could be attributed in part to saponins and flavonoids, recognized for their hypolipidemic properties, beneficial in preventing risk factors for cardiovascular diseases, notably ischemic heart diseases [57].

Histological examination performed on cardiac tissues of tested animals confirmed the biochemical results obtained during our work. Indeed, the hearts of rats that received doxorubicin presented characteristic lesions, notably leukocytic infiltration, edema, congestion, and necrosis, as previously confirmed by several authors [12, 22, 23]. These alterations are typical of doxorubicin-induced cardiotoxicity [58]. Treatment with AELDM allowed restoration of a quasi-normal histological architecture, with a reduction in inflammatory infiltrates and signs of necrosis. These results are in line with previous work, whose induced effects were preferentially attributed to bioactive substances with antioxidant potential [12, 59].

Finally, the acute toxicity study showed that a single dose of 2000 mg/kg of AELDM did not cause any mortality or significant variation in body weight, although minor behavioral modifications were noted. The LD_{50} was estimated to be greater than 2000 mg/kg, indicating a wide safety margin for potential therapeutic use of this extract [31].

5. Conclusion

The results of the present study reveal that the aqueous extract of *Datura metel* leaves attenuates biochemical disturbances induced by doxorubicin, notably through restoration of serum transaminase activity, antioxidant enzymes, inhibition of lipid peroxidation, and improvement of the lipid profile. Histological observations confirmed these protective effects, with preservation of myocardial architecture and reduction of signs of inflammation, necrosis, and congestion in animals treated with the aqueous extract of *Datura metel* leaves, similar to vitamin-E. Furthermore, the acute toxicity study revealed relative safety of the extract at a dose of 2000 mg/kg, with an LD_{50} estimated to be greater than this value. This cardioprotective effect of the tested plant extract would be due to the antioxidant and hypolipidemic potential of this plant, attributable to a synergistic effect of certain classes of bioactive compounds (alkaloids, flavonoids, polyphenols). This plant could be a potential source of pharmacological substances of natural origin that could be used in the prevention of numerous heart conditions related to oxidative stress. However, complementary investigations are necessary to isolate the active molecules responsible for the observed effects,

elucidate the molecular mechanisms involved, and evaluate the efficacy and safety of the extract in more advanced preclinical models.

Compliance with ethical standards

Disclosure of conflict of interest

The authors declare that they have no competing interest.

Statement of ethical approval

Prior authorization for the use of animals in this study was obtained from the National Ethics Committee of Cameroon (Reg. N. FWA-IRB 00001954).

The experiments on rats in this study were carried out in accordance with the European Convention for Protection of Vertebrate Animals used for Experimental and other Purposes.

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