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Effects of Aqueous and Ethanolic Extracts of *Entandrophragma angolense*, *Cola nitida* and *Gomphrena celosioides* against Doxorubicin-induced Cardiotoxicity in Rats

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Authors' contributions

This work was carried out in collaboration among all authors. The author BA designed the study, wrote the protocol, performed the statistical analyzes and drafted the first version of the manuscript. Author FYH supervised and corrected all versions of the manuscript. Authors BGA and DBN managed biochemical analyzes of the study. Author DAP performed the documentary research. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: The present study was undertaken with an aim of evaluating the capacity of the aqueous and ethanolic extracts *of Entandrophragma angolense, Cola nitida* and *Gomphrena celosioides* to protect the heart of rats.
Study Design: Cardioprotective properties of plant extracts *in vivo*.

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Place and Duration of Study: Laboratory of Biochemical-Pharmacodynamics, UFR Biosciences, Felix Houphouet Boigny University of Cocody-Abidjan, vivarium of Higher Normal School and the Institut Pasteur in Abidjan between November 2015 and January 2016.
Methodology: The extractions were carried out by maceration, using a magnetic stirrer for 24 hours, of 100 g of dry plant powder in 2 liters of distilled water for the aqueous extraction or in 2 liters of water / ethanol mixture (30/70 v / v) for ethanol extraction. Cardioprotective properties of the extracts (200 and 500 mg/kg) were assessed relative to that of resveratrol (25 mg / kg) against doxorubicin-induced intoxication of 8mg/kg body weight.
Results: The results showed that the aqueous and ethanolic extracts of *Entandrophragma angolense Cola nitida* and *Gomphrena celosioides* significantly attenuate ($p < 0.05$) the effect of doxorubicin on biochemical parameters. Indeed, extracts significantly reduce ($p < 0.05$) serum level of alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), lactate dehydrogenase (LDH), creatinine kinase (CK-MB), cholesterols, triglycerides and significantly increase ($p < 0.05$) serum level of HDL cholesterol. The extracts also dampen the weight loss caused by doxorubicin. The relative weight of the heart remained statistically the same ($p > 0.05$) regardless of the treatment compared to the control rat.
Conclusion: This study suggests that the studied extracts all have cardioprotective properties. This protective property would be higher at a dose of 500 mg/kg. However ethanolic extract of *Entandrophragma angolense* would have a cardioprotective activity more interesting at 500 mg/kg, comparable to that of resveratrol.

Keywords: Cardiotoxicity; resveratrol; Entandrophragma angolense; Cola nitida; Gomphrena celosioides.

1. INTRODUCTION

Medicinal plants are widely used for the prevention and treatment of various diseases in Africa and in developing countries [1], because they are believed to be very effective, available at low cost, less or no side effects and used as an alternative to allopathic drugs [2]. *Cola nitida*, *Gomphrena celosiodes* and *Entandrophragma angolense* are three plants used by traditional Ivorian medicine for the treatment of various diseases such as malaria, jaundice, fever, stomachaches, gastric ulcers, earaches, the kidney pain, coughing, the fontanel and adjuvant for several drugs [3-5]. The phytochemical study of these plants has revealed the presence of bioactive compounds such as saponins, tannins, flavonoids, terpenes and phenols which are known for their antioxidant properties [6-8]. On the other side, doxorubicin is a cytotoxic antibiotic. It is mainly administered intravenously for the treatment of lymphomas, leukemias and cancer [9]. It has been reported that high doses of doxorubicin has a serious adverse effect on the heart. Therefore, higher cumulative doses may cause [10] cardiomyopathy, which actually leads to heart muscle disorders. Overall, 41% of cancer patients suffer from cardiotoxicity by the administration of anticancer drugs [11]. However, Heart failure is a serious disease and a major cause of death and disability in children and adults [12]. Cardiovascular disease is a leading cause of death worldwide, a 60% rate of these diseases is registered in developing countries where the drug, diagnosis and basic living standards are not provided [13].

Natural antioxidants, which are capable of protecting cells from oxidative damages, should be included in the potential antioxidant therapy. Therefore, there is a need for identifying alternative, natural and safer sources of antioxidants [14]. For these reasons there is an urgent need for the development of new methods of prevention, detection and treatment of these diseases.

This study aimed to evaluate the effects of *Cola nitida*, *Gomphrena celosiodes,* and *Entandrophragma angolense* against doxorubicin-induced cardiotoxicity in rats.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Plant material

The plant material consists of *Gomphrena celosioides* (stems, leaves, flowers) of the family Amaranthaceae, fruits of *Cola nitida* (Sterculiaceae) and bark of *Entandrophragma angolense* (Meliaceae). A sample of each plant was authenticated by the Laboratory of Botany

and Plant Biology of the Biosciences UFR (Training and Research Unit) Felix Houphouet Boigny University of Cocody-Abidjan.

2.1.2 Animal material

The animal material consists exclusively of albino rats (*Rattus norvegicus*) of Wistar strain. They were provided by the Laboratory of Animal Physiology of the Félix Houphouet Boigny University. Altogether 96 rats of both sexes and of average weight 165.13 g have been used for the assessment of cardioprotective properties. They were put in cages and acclimated for two weeks at the pet store of ENS (Higher Normal School) Abidjan Cocody. In these premises, the photoperiod was 12 hours and the animals were housed in environmental conditions and standards, fed with a standard rodent diet, water ad libitum, with the care and treatment conditions, consistent with the guidelines of the Organisation for Economic Cooperation and Development [15]. All the animals experimental procedures were conducted after the approval of the Ethical Guidelines of University (Côte d'Ivoire) Committee on Animal Resources. They were in strict accordance with the guidelines for Care and Use of Laboratory Animals [16] and the statements of the European Union regarding the handling of experimental animals (86/609/EEC) [17].

2.2 Methods

2.2.1 Preparation of aqueous and ethanolic extracts

The aqueous extraction was conducted using the method described by Guede-Guina [18]. Hundred (100) grams of plant dry powder were soaked in 2 liters of distilled water using a magnetic stirrer for 24 hours. The obtained homogenate is sieved, filtered 3 times on cotton wool and once on Whatman N°1 filter paper. The filtrate is thereafter brought to evaporation in vacuo at 50°C in an oven. A dry powder is thus obtained which constitutes the aqueous extract.

Ethanol extract was prepared according to the same principle by macerating 100 g of powder of the plant in 2 liters of water / ethanol mixture (30/70 V / V) with a magnetic stirrer.

2.2.2 Treatment of animals

The method used by Momin [19] is that we have used with some modifications to assess the cardioprotective properties of our plant extracts. The principle of this method is to treat animals for several days and then to induce cardiac toxicity to evaluate the protective activity of the treatment. This is a preventive treatment that highlights the cardioprotective properties of extracts compared to those of the resveratrol, cardioprotective reference [20] against doxorubicin induced intoxication. Intoxications are conducted with doses that induce significant cardiotoxicity in animals without causing their death during the experiment. Treatments are performed every day at the same time for fourteen days and solutions were prepared immediately before treatment. The animals were deprived of food for 12 hours and water only one hour before manipulations. They were fed one hour after the manipulations and weighed every other day during the experimental period. Distilled water, Resveratrol (25 mg/kg) and the different extracts (200 and 500 mg/kg) were orally administered to rats for 14 consecutive days. The single dose of doxorubicin (8 mg/kg) was only administered on 13th day by intra-peritoneal route. The experiment was performed according to the following:

Batch (C) Control: distilled water 1 ml / 100 g. Batch (RC) Reference Control: 1 ml / 100 g of resveratrol at 25 mg/kg.

Batch (NC) Negative control: Distilled water 1 ml /100 g for 14 days and then 0.5 ml of doxorubicin at 8 mg/kg on the 13th day.

Batch (PC) Positive Control: 1ml / 100g of resveratrol to 25 mg/kg for 14 days and then 0.5 ml of doxorubicin at 8 mg/kg.

Batch EEG1: 200 mg/kg of ethanolic extract of *Gomphrena celosioides* and 0.5 ml of doxorubicin at 8 mg /kg.

Batch EEG2: 500 mg/kg of ethanolic extract of *Gomphrena celosioides* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EAG1: 200 mg/kg of aqueous extract of *Gomphrena celosioides* and 0.5 ml of doxorubicin to 8 mg/kg.

BatchEAG2: 500 mg/kg of aqueous extract of *Gomphrena celosioides* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EEE1: 200 mg/kg of ethanolic extract of *Cola nitida* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EEE2: 500 mg/kg of ethanolic extract of *Cola nitida* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EAE1: 200 mg/kg of aqueous extract of *Cola nitida* and 0.5 ml of doxorubicin, 8mg/kg.

Batch EAE2: 500 mg/kg aqueous extract of *Cola nitida* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EEY1: 200 mg/kg of ethanolic extract of *Entandrophragma angolense* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EEY2: 500 mg/kg of ethanolic extract of *Entandrophragma angolense* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EAY1: 200 mg/kg of aqueous extract of *Entandrophragma angolense* and 0.5 ml of doxorubicin at 8 mg/kg.

Batch EAY2: 500 mg/kg of aqueous extract of *Entandrophragma angolense* and 0.5 ml of doxorubicin at 8 mg/kg.

2.2.3 Samples

The samples were taken 24 hours after the last treatment. The animals were anesthetized and the sampling by puncturing the retro-orbital sinus was performed using a heparinized Pasteur pipette. The pipette tip was slowly introduced in the medial or lateral angle of the eye. Progression through the tissues has been facilitated by printing a slight rotation in the pipette. The vessel wall is very fragile and as soon as we reached the venous plexus, blood gushed into the periorbital area and rose by capillary action into the pipette need to maintain horizontal while she was filling. You could easily collect between 0.5 and 2 ml of blood, according to the weight and age of the animals [21]. Blood was collected in tubes without anticoagulant for determining biochemical parameters. After blood collection, all test animals were euthanized. Their heart is removed, examined, flushed with normal saline, weighed and fixed in bouin.

2.2.4 Biochemical study

Blood samples collected in the tubes without anticoagulant were centrifuged at 3000 revolutions / min for 15 minutes. The collected sera were used to assay the following biochemical parameters: alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT), lactate deshydrogenase (LDH), creatine kinase (CK-MB), total cholesterol, triglycerides, HDL-c with an Automate type of Cobas C311 HITACHI, ROCHE (France).

2.2.5 Processing and analysis of data

Data entry is performed using Excel 2010 software.

The relative weight (RW) of the heart was determined relatively to Body Weight with the following formula:

$$RW = \frac{\text{heart weight}}{\text{Body Weight (BW)}} \times 100 \quad [1].$$

The results were expressed as mean ± SD. The graphical representation of the data was carried from the Graph Pad Prism 5.0 software (Microsoft USA). The statistical analysis was performed using analysis of variance (ANOVA ONE WAY). The differences between averages were determined according to the multiple comparison test of Tukey. These differences are considered significant when p was less than 0.05 ($p< 0.05$).

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Effect of different treatments on serum concentration of ALAT

The assay results of alanine aminotransferase show that doxorubicin increases ($p < 0.001$) serum concentration of ALAT in the batch NC (155.5 ± 3.2 IU/L) compared to that of C (102.1 ± 3 2 IU/L), RC and PC (108.57 ± 4.7 IU/L). Control C, RC and PC are identical ($p > 0.05$) between them (Fig. 1). The administration of the extract and Resveratrol has resulted in a decrease ($p <0.001$ and $p <0.05$) of serum concentration of ALAT in the corresponding batch, compared to NC. The results also show that the batch EEY2 gives identical results ($p > 0.05$) to those of controls C, PC and RC.

3.1.2 Effect of different treatments on serum concentration of ASAT

The results in Fig. 2 indicate that the extracts favoured decreases ($p < 0.05$; $p < 0.01$; $p <$

0.001) in ASAT concentration compared with those of animals batch NC (236.9 ± 4,4IU/L). These results also show that the concentration of ASAT batch NC is greater ($p < 0.001$) than that of C (172.6 ± 4.4 IU / L), RC (174.7 ± 4.4 IU / L), and PC (184 ± 4.7 IU/L) .The batch EEY2 has a concentration of ASAT (191.9 ± 4.4 IU/L) identical ($p > 0.05$) to that of C, PC and RC.

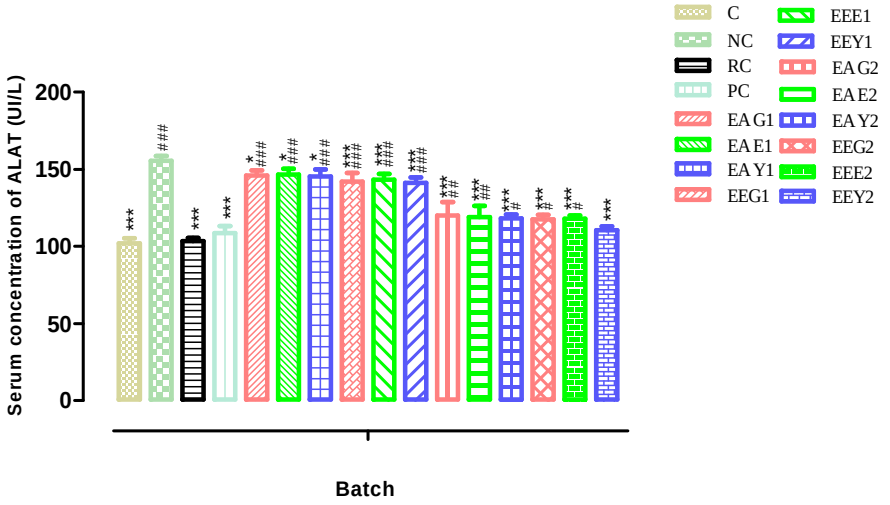

Fig. 1. Effect of extracts and resveratrol on serum concentration of ALAT

*Values are mean ± SD with n = 6. * P <0.05; ** P <0.01; *** P <0.001: significantly different from the batch NC. # P <0.05; ## P <0.01; ### P <0.001: significantly different from the batch PC*

C: distilled water, NC: distilled water + Doxorubicin, RC: distilled water + Resveratrol, PC: Resveratrol + Doxorubicin, EAG1: 200 mg/kg of aqueous Extract G celosioides + Doxorubicin, EAE1: 200 mg/kg of aqueous Extract C. nitida + Doxorubicin, EAY1: 200 mg/kg of aqueous Extract E. angolense + Doxorubicin, EEG1: 200 mg/kg of Ethanolic extract G. celosioides + Doxorubicin, EEE1: 200 mg/kg of Ethanolic extract C. nitida + Doxorubicin, EEY1: 200 mg/kg of Ethanolic extract E. angolense + Doxorubicin, EAG2: 500 mg/kg of aqueous Extract G. celosioides + Doxorubicin, EAE2: 500 mg/kg of aqueous extract C. nitida + Doxorubicin, EAY2: 500 mg/kg of aqueous extract E. angolense + Doxorubicin, EEG2: 500 mg/kg of Ethanolic extract G. celosioides + Doxorubicin, EEE2: 500 mg/kg of Ethanolic extract C. nitida + Doxorubicin, EEY2: 500 mg/kg of Ethanolic extract E. angolense + Doxorubicin

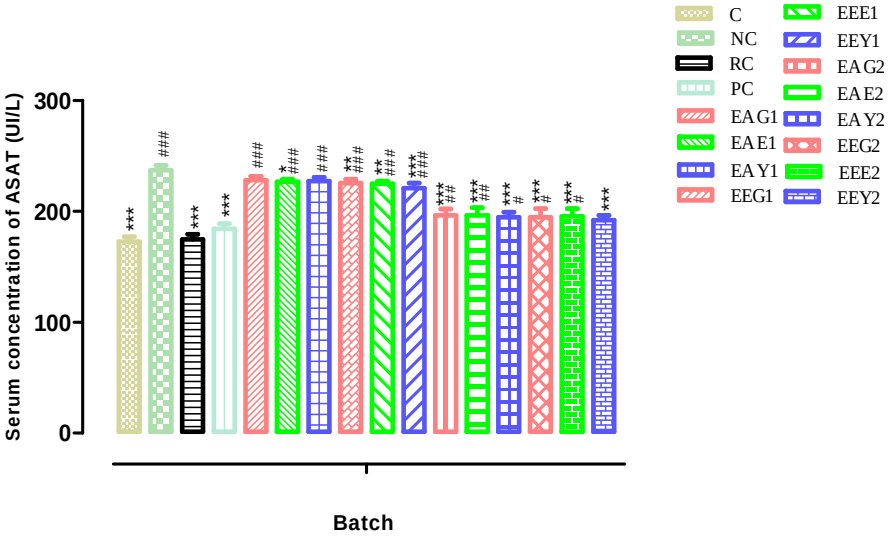

Fig. 2. Effect of extracts and resveratrol on serum concentration of ASAT

3.1.3 Effect of different treatments on serum concentration of LDH

According to Fig. 3 serum LDH of batch NC (2789.3 ± 44 IU/L) is greater ($p < 0.001$) than the ones of batches C (2286.1 ± 49 IU/L), RC (2294.5 ± 28 IU/L) and PC (2319.1 ± 32.7 IU/L) and also higher ($p < 0.001$) in all the batches treated with plant extracts. Note also that the batch EEY2 showed identical LDH levels ($p > 0.05$) to those of C, PC and RC. We also note that the batches EAE1, EAG1, EAY1, EEA1, EEG1, EEY1 have higher serum concentrations of LDH ($p > 0.05$) than EAE2, EAG2, EAY2, EEA2, EEG2 and EEY2.

3.1.4 Effect of different treatments on serum concentration of CK-MB

These results suggest that treatment with the extracts and resveratrol led to a decrease ($p < 0.001$) in the serum concentration of CK-MB in the corresponding batches in comparison with batch NC. Intoxication with doxorubicin increases ($p < 0.001$) serum concentration of CK-MB in the batch NC (1759.22 ± 41.13 IU/L) compared to that of batch C (1346.01 ± 66, 22 IU/L), RC (1351.62 ± 25.18 IU/L) and PC (1411.19 ± 24.59 IU/L). The results also show that the batch EEY2 (1425.5 ± 31.9 IU/L) has a serum concentration of CK-MB identical ($p > 0.05$) to C, PC and RC (Fig. 4).

3.1.5 Effect of different treatments on the serum concentration of cholesterol

The results of the cholesterol assay (Fig. 5) shows that the batch EEY2 yielded identical results ($p > 0.05$) to those of C, PC and RC. The serum concentration of cholesterol of the batch NC (1.07 ± 0.03 IU/L) showed an increase ($p < 0.001$) compared to that of C (0.59 ± 0.02 IU/L), RC (0.59 ± 0.02 IU/L) and PC (0.62 ± 0.02 g / L). It is also noted that treatment with each of the extracts studied for two doses promotes significant decrease ($p < 0.05$; $p < 0.01$; $p < 0.001$) in cholesterolemia compared with the NC rats.

3.1.6 Effect of different treatments on serum concentration of triglycerides

The results in Fig. 6 show that the concentration of triglycerides of batch NC (0.98 ± 0.03 IU/L) experienced an increase ($p < 0.001$) compared to the ones of C (0.49 ± 0.01 IU/L), RC (0.49 ± 0.02 IU/L) and PC (0.52 ± 0.02 IU/L). This figure also indicates that EEY2 has the same serum concentration ($p > 0.05$) to that of C, PC and RC. We also note that batches treated with extracts at a dose of 200 mg/kg of Bw have higher serum concentration of triglycerides ($p < 0.05$) to those batches treated with the extracts at a dose of 500 mg/kg Bw.

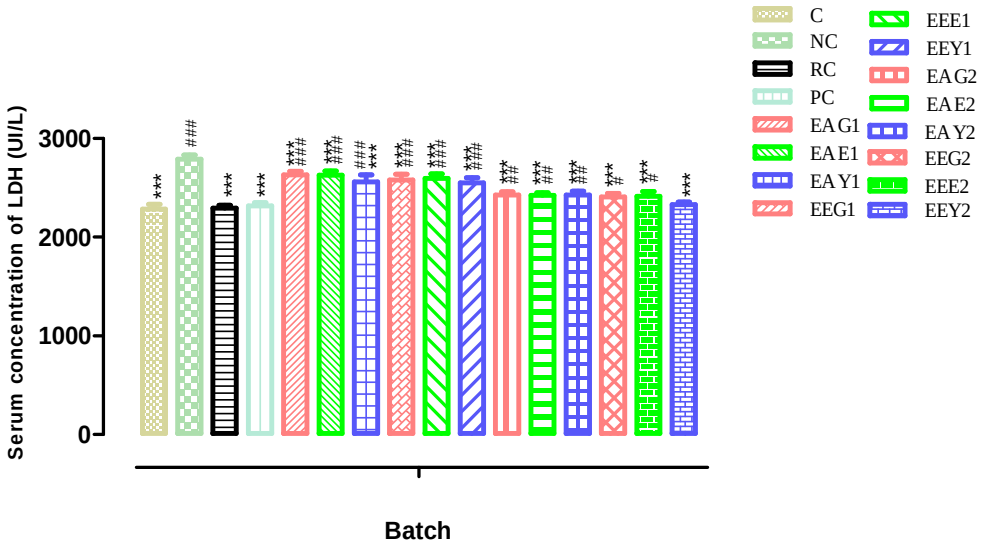

Fig. 3. Effect of extracts and resveratrol on serum concentration of LDH

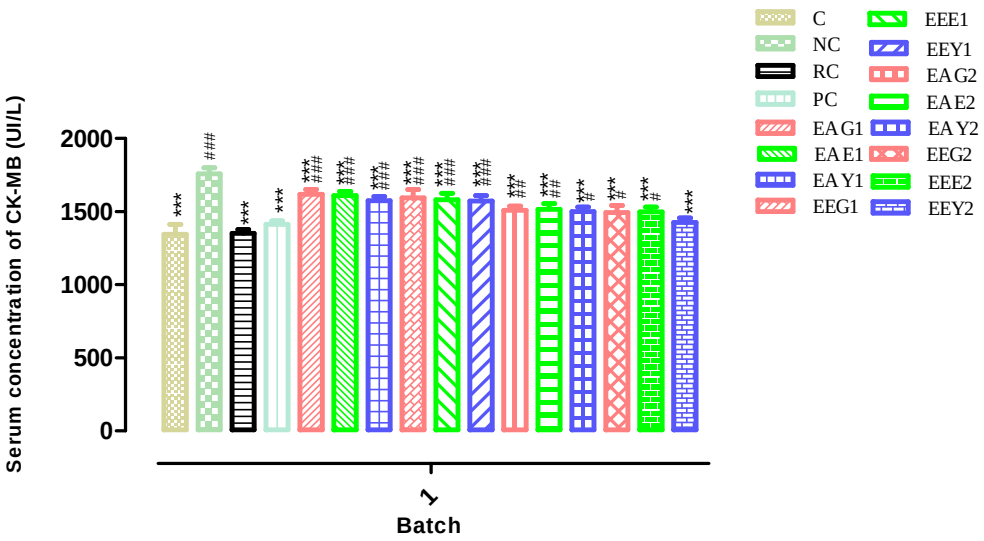

Fig. 4. Effect of extracts and resveratrol on serum concentration of CK-MB

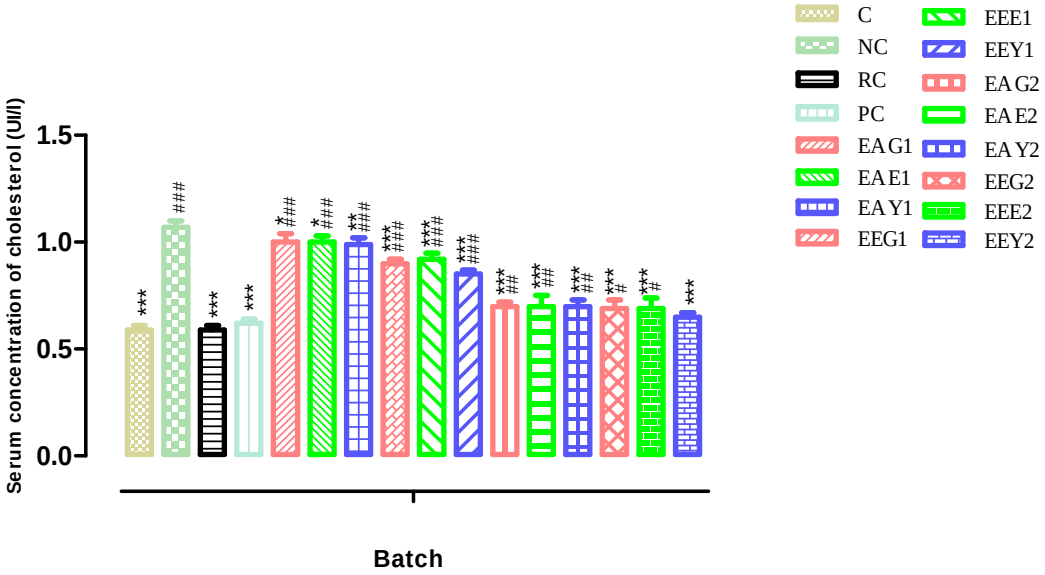

Fig. 5. Effect of the extracts of and resveratrol on the serum concentration of cholesterol

3.1.7 Effect of different treatments on the serum concentration of HDL-cholesterol

The assay results of the concentration of HDL-c (Fig. 7) indicate that treatment with the extracts promoted an increase ($p < 0.01$ and $p < 0.001$) in the concentration of HDL-C compared to those of animals of batch NC (0.11 ± 0.03 IU/L). The concentration of HDL-c of batch NC is less than ($p < 0.001$) than that of C (0.44 ± 0.01 IU/L), RC (0.43 ± 0.02 IU/L) and PC (0.43 ± 0.02 IU/L). The results also show that Batch EEY2 has a concentration of HDL-c (0.41 ± 0.02 IU/L) identical ($p > 0.05$) to that of C, PC and NC.

3.1.8 Effect of different treatments on weight gains of animals

The changes in body weight of the animals by treatment (Fig. 8) shows that the batches C (10.86 ± 0.2%), RC (10.68 ± 0.17%) and PC (10.36 ± 0, 21%) had higher

weight gains ($p < 0.05$; $p < 0.01$; $p < 0.001$) than those of all other batches. It is also noted that the batch NC (3.84 ± 0 24%) has a lower weight gain ($p < 0.001$) than those of all other batches. Also the effect of the extracts on weight gain is more interesting for Batches EEY2 (8.24 ± 0.22%), EEA2 (8.22 ± 0.31%) and EEG2 (8.22 ± 0.22%).

3.1.9 Effect of different treatments on the relative weight of the hearts

The change in the relative weight of animals per treatment is summarized in Fig. 9. The statistical analysis of relative weights reveals that all animals studied suffered no variation ($p > 0.05$) of the relative weight of the heart dependent on treatments made.

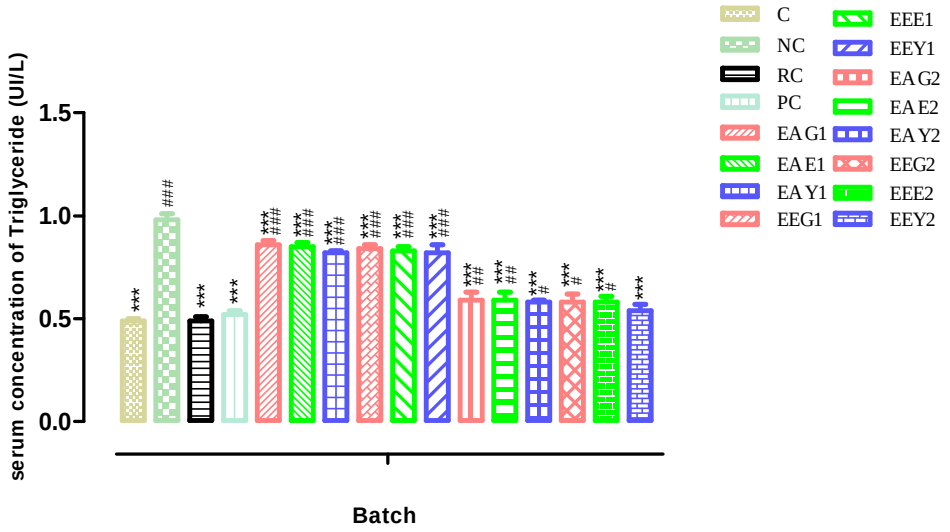

Fig. 6. Effect of extracts and resveratrol on serum concentration of triglycerides

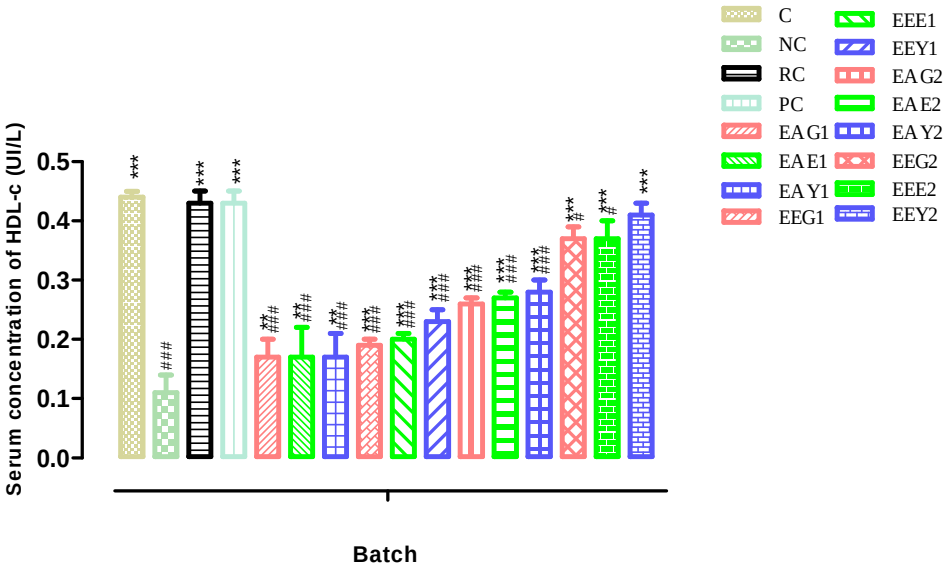

Fig. 7. Effect of extracts and resveratrol on serum concentration of HDL-c

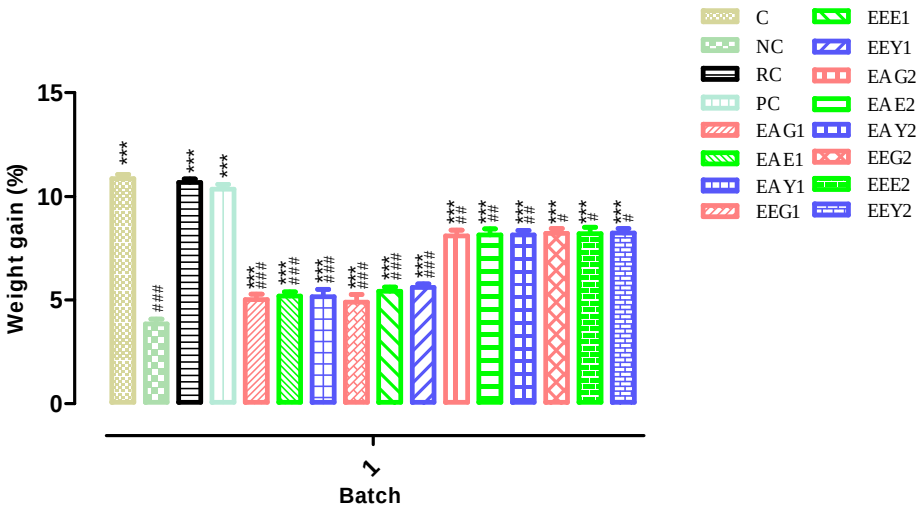

Fig. 8. Effect of extracts and resveratrol on the weight gain of the animals

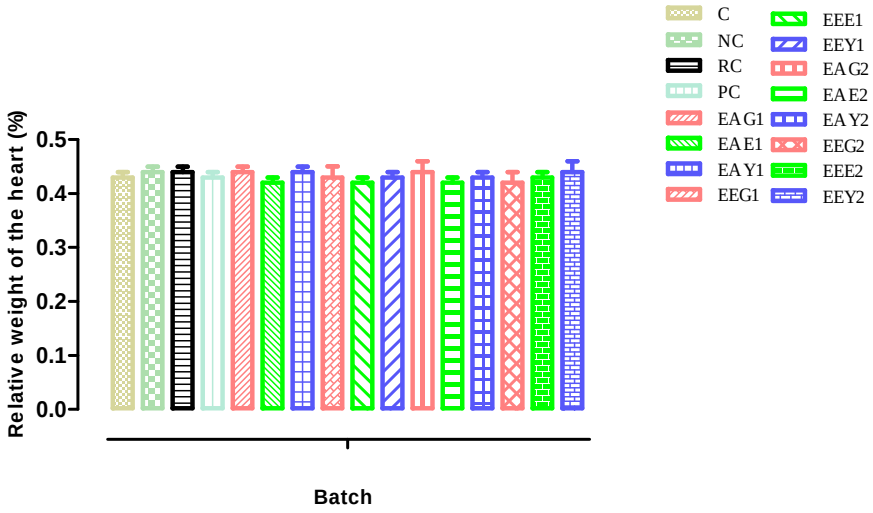

Fig. 9. Effect of extracts and resveratrol on the relative weight of the heart

3.2 Discussion

The entire world population is turning to natural medicine because of the widespread belief that "green medicines" are healthier and safer than synthetic [22]. Indeed, although modern drugs are effective in the prevention of cardiovascular disorders, their use is often limited because of their side effects [23]. Therefore, the acceptance of natural medicine by the public and the medical profession is growing due to significant progress in understanding the mechanism of action by which herbs can positively influence the health and quality of life [24]. Overall, myocardial infarction is one of the leading causes of death for men and women [25]. Heart failure is a serious disease and a major cause of death and disability in children and adults [12]. The present study was conducted to evaluate the cardioprotective properties of aqueous and ethanol extracts of *G. celosioides, C. nitida*, and *E. angolense* during adoxorubicin-induced cardiotoxicity compared to activity of resveratrol known for its cardioprotective properties. Doxorubicin is a cytotoxic antibiotic. It is mainly administered intravenously for the treatment of lymphomas, leukemias and cancer [9]. It has been reported that high doses of doxorubicin has a serious adverse effect on the heart. Therefore, higher cumulative doses can lead to cardiomyopathy [10], leading to cardiac muscle disorders. In clear, repeated administration of

doxorubicin beyond a certain overdose causes changes in cardiopathic patients [26] and in a variety of animal species [27]. On the other hand, resveratrol is a potent antiarrhythmic agent with cardioprotective properties in rats. The cardioprotective effects of resveratrol in rats can be correlated with the antioxidant activity and positive regulation of production of NO[20].

Our results suggest a slowdown in growth in animals of the batch treated only by the doxorubicin (NC). This slowdown results in a significantly lower weight gain in this batch in comparison with the batch of controls not intoxicated (C) and batch of intoxicated control and treated by resveratrol (PC). Treatment with aqueous and ethanol extracts of *G. celosioides, C. nitida*, and *E. angolense* favored a significant increase in weight gain in those Batches compared to NC batch. This significant increase in weight gain is more important for aqueous and ethanol extracts of *E. angolense*. On the other hand, the relative weight of the heart has not undergone any significant change dependent on different treatments made. The decrease in body weight in this study is consistent with that of a previous study [28]. This observation on the weight can be attributed to reduced food intake and the inhibition of protein synthesis due to the doxorubicin [19].

Regarding the relative weight of the heart, it should be noted that according to some studies, doxorubicin induces a significant decrease in this parameter. This is the case of the work of [29] which showed that doxorubicin in animals caused a scruffy fur and a significant decrease in body weight, heart weight, heart / body weight. This difference is justified by the duration of treatment, which is 14 days for us and 28 days for him.

Analysis of serum parameters indicates a significant increase in ALAT [30], ASAT [31] of LDH [32], the CK-MB [33], cholesterols, triglycerides and a decrease in HDL cholesterol serum levels for the batch NC compared to batches PC and C. Increase in levels of these parameters in serum indicates an increased leakage of these enzymes from mitochondria due to the toxicity induced by treatment with doxorubicin [34]. The administration of this antibiotic has led to damage of the myocardial cell membrane so that it becomes permeable. Which resulted in the leakage of ASAT, CK-MB and LDH in blood. This probably explains the increased level of these enzymatic markers in the serum [35]. The increase in the lipid profile (cholesterol triglycerides) and the decrease in HDL in NC group indicate that doxorubicin may interfere with the metabolism or lipid biosynthesis [34]. Also the free radicals generated by doxorubicin may alter the serum lipid profile with consecutive hyperglyceridemia, an increase in very low density lipoprotein (VLDL), and a reduction in the concentration of high density lipoprotein and low density lipoprotein (HDL, LDL) [36,37]. The mechanism of this induced cardiomyopathy has not yet been fully elucidated [12]. But we know that the heart is very sensitive to damage induced by free radicals, because it has relatively low levels of antioxidant enzymes such as catalase and superoxyde dismutase [36]. Recent studies have postulated the involvement of oxygen free radicals in the development of cardiomyopathy due to doxorubicin [36,37]. More precisely, it is believed that the formation of iron-anthracycline alloy complex generates free radicals, which in turn cause serious damage to the plasma membrane, and interfere with the cytoskeleton structure [38].

Treatment with aqueous and ethanol extracts of *G. celosioides*, *C. nitida*, and *E. angolense* mitigates the effect of doxorubicin on biochemical parameters, reducing serum ALAT, ASAT, LDH, CK-MB, cholesterol, triglycerides and increasing serum level of HDL cholesterol. The decrease in lipid profiles and increased HDL in treatment groups by extracts (EEY2, EEA2, EEG2, EAY2, EAE2, EAG2) may be due to the presence of certain bioactive compounds in plants. The hypolipidemic effect is due to inhibition of the biosynthesis of hepatic cholesterol, increased secretion of bile acid and stimulation of receptor mediated catabolism of LDL cholesterol and an increase in absorption of blood LDL cholesterol by the liver [34]. The mitigating effect of the extracts on the studied serum parameters is much more important at a dose of 500 mg/kg and for extracts *E. angolense*. These results are corroborated by those of [19,35,36]. Pretreatment with the extracts will likely lead to inhibiting ASAT, ALAT and LDH release in serum [39].

Previous phytochemical studies by some authors as [40-42] revealed the presence of sterols, terpenoids, saponins, fatty acids, flavonoids, phenolic compounds, alkaloids, tannins and carbohydrates in the extracts of these plants. These bioactive compounds may be responsible for the attenuation of oxidative stress induced by doxorubicin and also the restoration of the changes brought to normal physiology of the heart and other body tissues [19]. In other words,

these bioactive compounds scavenge free radicals produced and protect against heart damage. Increasingly, there is a growing interest in the use of natural antioxidants as a protection strategy against heart related problems such as ischemia and reperfusion [43]. Endogenous pharmacological increase in myocardial antioxidants has been identified as promising therapeutic approach in diseases associated with increased oxidative stress [44]. The extracts subjected to this study were found to possess many properties namely anti-inflammatory, antioxidant, anti-anemic, analgesic according to the work done by [8,7,6]. Yet antioxidants have been reported to have beneficial effects against cardiotoxicity induced by doxorubicin in mice and rats [45]. The overall protective effect of extracts is probably due to their ability to counteract free radicals by their antioxidant nature, so their ability to restore normalcy in the tissue submitted to oxidative stress. However, the precise molecular mechanism by which our extracts exert their protective effect against oxidative damage remains to be established [36].

4. CONCLUSION

Our study aimed to evaluate cardioprotective properties of *Gomphrena celosioides*, *Cola nitida*, *Entandrophragma angolanse*, three plants of the traditional medicine in Ivory Coast. The study evaluating the cardioprotection found that aqueous and ethanol extracts of *G. celosioides, C. nitida*, and *E. angolense* have the ability to counter the effects of the doxorubicin-induced cardiotoxicity. This protective activity of our extracts was demonstrated by a significant reduction in serum concentration of ALAT, ASAT, LDH, of CK-MB, cholesterol, triglycerides, and a significant increase in serum concentration of HDL-cholesterol. Also, these extracts have led to a significant increase in weight gain. Although the dose of 200 mg/kg of Bw led to suitable results, a dose of 500 mg/kg bw gives much more interesting results and the ethanolic extract of *Entandrophragma angolense* has the best cardio protection profile.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and Felix Houphouet Boigny University (ivory coast)

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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