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Effect of *Ximenia americana* (Olacaceae) leaves on ovalbumin induced asthma in mice

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ABSTRACT

Ximenia americana commonly known as Sea Lemon is a plant of the Olacaceae family with anti-inflammatory, antioxidant and antiviral properties. *Ximenia americana* is used in traditional medicine for the treatment of diseases such as cancer, diabetes, asthma, etc. In this work, six groups of five mice were formed. The prevalence of clinical asthma is estimated at around 4.3% of the world's population, which is a real public health problem. Hence the aim of this work, which was to evaluate the effects of the aqueous extract of the leaves of *X. americana* on ovalbumin-induced asthma (OVA) in mice. The test animals received aqueous extract from *Ximenia americana* at doses 75 mg / kg, 150 mg / kg and 300 mg / kg. In order to measure the intensity of bronchial inflammation, the inflammatory cell rate has been evaluated. The results obtained after analysis of the different biochemical parameters show a significant decrease ($p < 0.05$) of the white blood cells in the positive lots, tests at 75 mg / kg, 150mg / kg, 300mg / kg compared to the negative light. In addition, a significant decrease in the average globular volume (MCV), blood platelets were recorded in these same animals ($p < 0.01$); ($p < 0.001$) respectively with respect to the negative group. The results also show that this allergen causes intense lipid peroxidation, as well as a significant reduction in the activity of different antioxidant systems (GSH, SOD and CAT). However, the pretreatment of *Ximenia americana* aqueous extract is effective, as to the significant reduction in the MDA rate ($p < 0.001$) and significant increase ($p < 0.05$) of the activity of CAT. The rebalance of the balance between oxidant and antioxidant during the plant administration, would probably be attributed to the antioxidant and anti-inflammatory capacity of the compounds contained in our extract.

Keywords: *Ximenia americana*, Asthma, Oxidative stress, Ovalbumin, Anti-inflammatory.

INTRODUCTION

Asthma is a chronic inflammatory disease of the airways [12]. It is caused by an interaction between an individual's genetic profile and their environment [1]. The main environmental factors favoring bronchial inflammation are viral infections, respiratory allergies and bronchial irritants [7].

MATERIEL AND METHOD

Preparation of plant

The preparation of the aqueous extract of the leaves of *Ximenia americana* was subjected to a decoction. For this, 300 g of this powder were taken and brought to the boil for 15 minutes in 02 L of distilled water. This preparation was filtered and the filtrate was dried in an oven at a temperature set at 50 ° C.

Chemicals

Awareness was carried out using small quantities of OVA (1 mg/ml) (Sigma-Aldrich, St. Louis, MO, USA) combined with an aluminum hydroxide (from Sigma-Aldrich) adjuvant dissolves at the rate of 1 mg/ml in a 9 ‰ saline solution**.** Control animal received orally distilled water and salbutamol (from Sigma-Aldrich) drugs used to reduce asthma.

Phytochemical analyses

Phytochemical analyses of the extract were tested using the following chemicals and reagents (Trease et al. 1983). Saponin (frothing test), tannins (FeCl3), flavonoid (NaCl and HCl), phenol (FeCl3 and K3Fe (CN)6) and lipids (filter paper).

Animal and experimental design

Animals BALB/c strain mice of both sexes weighing 25 ± 5g and aged 10 ± 2 weeks at the start of the experiment were used. The animals were kept in a room at room temperature in cages lined with litter before and during the period of the experiment. The mice were given free access to tap water and fed a standard diet.

Treatment and induction of ovalbumin asthma in mice

This protocol is carried out according to that described by Narimène CHEKCHAKI in 2017. The 30 mice were randomized and divided into 6 batches of 5 animals each, therefore: a normal control batch, a negative control batch, a positive control batch and 3 test batches. The normal, negative and positive control groups received distilled water (1 ml / 200 g) for the first two and salbutamol (25 mg / kg), respectively. The test groups, for their part, received the aqueous extract of the leaves of *Ximenia americana* at doses 75; 150 and 300 mg / kg. This treatment lasted fourteen (14) days. On the fifteenth day of the treatment considered as the first day of induction of asthma, the negative control batch, the positive control batch and the 03 test batches were sensitized to OVA adjuvanted with aluminum hydroxide (OVA / Alum). intraperitoneally (IP), on the first day (D0) and repeated 7 days later (D7). Normal control animals received intraperitoneal injections of similar volumes of 9 ‰ saline at the same times and under the same conditions. In order to induce the pathology in these mice, the negative, positive and control batches and the test batches were exposed, on days D14, D15 and D16 after the initial sensitization, to a nebulization of ovalbumin (10 µg) in a saline solution at 9 ‰. Each exposure lasted 30 minutes in a device made using the experimental basins. The normal control batch was also exposed, under the same conditions, to a 9 ‰ saline solution only.

Statistical analyzes

Results were expressed as the mean ± standard error of the mean (ESM) for each group. Number per group = 5. The one way analysis of variance test (Anova) was used followed by the Student Newman Kells post test to compare the values with each other. The results were considered to be significantly different for $p < 0.05$.

RESULTS

Table 1: Distribution of Animal

Groups	Treatment	Route
Normal	Eau distillée	Orale
Positif control	Salbutamol (25mg/kg)	Orale
Negative control	Eau distillée	Orale
Test 1	*X. americana* (75mg/kg)	Orale
Test 2	*X. americana* (150mg/kg)	Orale
Test 3	*X. americana* (300mg/kg)	Orale

Qualitative Phytochemistry

The phytochemical screening of the aqueous extract of *of Ximenia americana* revealed the presence of certain classes of bioactive compounds such as alkaloids, flavonoids, coumarins, terpenoids and tannins (Table 2).

Table 2: Result of the qualitative Phytochemistry of the aqueous extract of *Ximenia americana*

Class of compound	Observations
Alkaloids	+
Flavonoids	+
Tannins	+
Saponins	+
Terpenoids	+
Sugars	-
Quinones	+
Coumarins	+

-Absence ; + presence

Effect of *Ximenia americana* aqueous extract on body weight

The variation in the absolute weight of the mice, based on the mean values taken during the periods of pretreatment, intraperitoneal sensitization, exposure to the allergen by inhalation and at the end of the time of sacrifice, is shown in Figure 1.

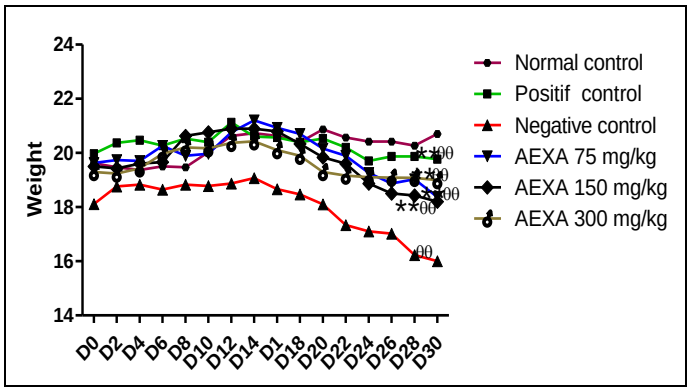

Figure 1: Change in absolute weight of control mice, mice treated with aqueous extract of *Ximenia americana* and mice sensitized to ovalbumin (OVA).

Each of these values is expressed as the mean ± SEM. Significant differences: * compared to the negative control ($p * \leq 0.05$; $p ** \leq 0.01$; $p *** \leq 0.001$). θ compared to the normal control ($p \theta \leq 0.05$; $p \theta\theta \leq 0.01$; $p \theta\theta\theta \leq 0.01$)

Effect of aqueous extract of *Ximenia americana* on haematological parameters

Table 3 shows the level of blood cells. Based on these results, we observed a significant decrease in white blood cells in the positive batches, test at 75 mg / kg, 150 mg / kg, 300 mg / kg ($p < 0.05$) compared to the negative control.

Table 3: Effect of aqueous extract of *Ximenia americana* on the blood cell count

	Expérimental lots					
Parameters	**Normal control**	**Negative control**	**Positive control**	**AEXA 75mg/kg**	**AEXA 150mg/kg**	**AEXA 300mg/kg**
WBC	3.34±0.17	4.73±0.55	3.66±0.55*	2.10±0.17**	3.55±0.34*	3.70±0.21*
RDW	7.16±0.41	6.24±1.29	7.90±0.49*****	7.10±0.25*****	6.92±0.25*****	7.04±0.25*****
HCT	37.40±0.32	34.50±3.37	48.73±0.77	37.63±1.15	38.06±1.59	39.88±0.99
HGB	110.33±2.84	95.33±12.71	113.33±3.84*	106.00±1.52*	116.00±3.21*	104.00±2.08*
PLT	347.00±31.6	511.00±9.81	281.67±10.08***	380.00±28.05***	316.67±10.17***	279.67±9.52***
VGM	50.86±1.45	56.70±2.69	50.33±2.57	41.56±2.88**	49.26±1.18*	43.70±2.60**
VMP	7.20±0.32	8.33±0.66$^{\theta\theta}$	6.73±0.37	7.13±0.63	7.83±0.37	6.79±0.49

Each of these values is expressed as the mean ± SEM. The significant differences: * compared to the negative control (p * ≤ 0.05; p ** ≤ 0.01; p *** ≤ 0.001). θ compared to the normal control (p θ ≤ 0.05; p θθ ≤ 0.01; p θθθ ≤ 0.01)*

Effect of aqueous extract of *Ximenia americana* on changes in oxidative stress parameters

Effect of the aqueous extract of the leaves of *Ximenia americana* on the concentrations of Malondialdehyde (MDA) in the lungs of asthmatic mice

According to the results obtained, a significant increase in the level of the liver (p < 0.01) in the level of MDA is observed in the negative and positive control mice and the test group at a dose of 75 mg / kg in comparison with the control normal. On the other hand, we do not note any significant difference between them (positive groups, test at 75 mg / kg and the negative control). However, administration of the aqueous extract of *Ximenia americana* at doses of 150 mg / kg and 300 mg / kg resulted in a significant reduction in lipid peroxidation (Figure 2).

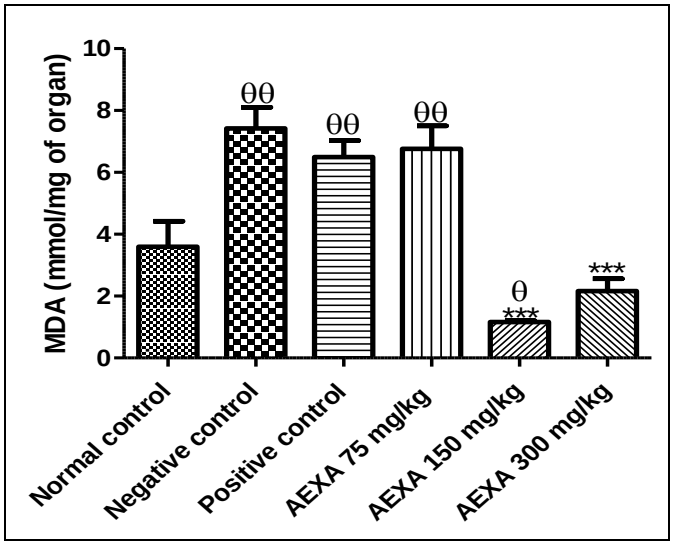

Figure 2: Variations in Malondialdéhyde (MDA) enzymatic activities in the livers of control, sensitized and treated mice.

Each of these values is expressed as the mean ± SEM. The significant differences: * compared to the negative control (p * ≤ 0.05; p ** ≤ 0.01; p *** ≤ 0.001). θ compared to the normal control (p θ ≤ 0.05; p θθ ≤ 0.01; p θθθ ≤ 0.01).

Effect of the aqueous extract of the leaves of *Ximenia americana* on the concentrations of Superoxide dismutase (SOD) in the liver of asthmatic mice

Figure 3 illustrates the effect of aqueous extract of *Ximenia americana* on liver tissue SOD concentration in mice. It emerges from this analysis that the aqueous extract of *Ximenia americana* induced a significant increase (p < 0.05; p < 0.01 and p < 0.01) respectively at doses 75 mg / kg, 150 mg / kg and 300 mg / kg, of the activity of this enzyme compared to the negative control. Likewise, we note this significant increase in SOD at (p < 0.01; p < 0.001 and p < 0.01) respectively at doses 75 mg / kg, 150 mg / kg and 300 mg / kg compared to the normal witness. Therefore, it should be noted that the 150 mg / kg dose produces more effects. However, a significant difference was not observed between the control groups.

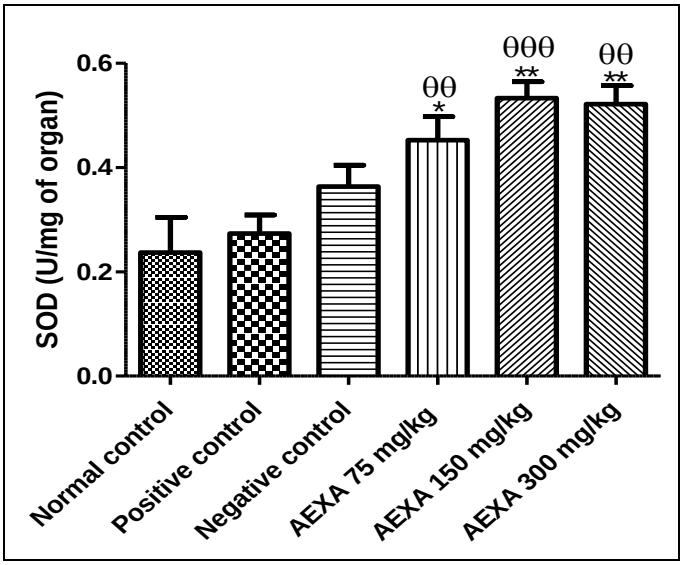

Figure 3: Changes in superoxide dismutase (SOD) enzyme activities in the livers of control, sensitized and treated mice.

Each of these values is expressed as the mean ± SEM. The significant differences: * compared to the negative control (p * ≤ 0.05; p ** ≤ 0.01; p *** ≤ 0.001). θ compared to the normal control (p θ ≤ 0.05; p θθ ≤ 0.01; p θθθ ≤ 0.01).

Effect of the aqueous extract of the leaves of *Ximenia americana* on the concentrations of Catalase (CAT) in the livers of asthmatic mice

It emerges from these results that the concentration of hepatic tissue in catalase (CAT) increased in a dose-dependent manner in the test groups compared to the negative and normal controls (figure 4). The 150 mg / kg and 300 mg / kg doses acted significantly (P < 0.05 and p < 0.001) compared to the normal control. Furthermore, the aqueous

extract only at a dose of 300 mg / kg resulted in a significant increase ($p < 0.001$) compared to the negative control.

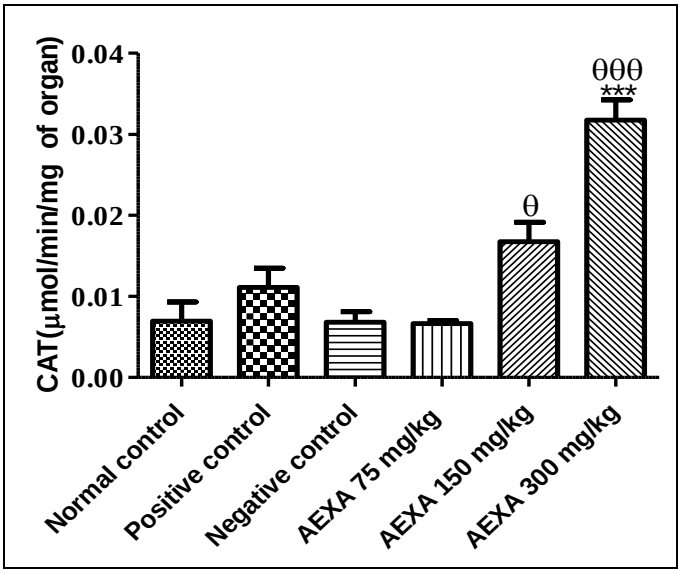

Figure 4: Changes in catalase (CAT) enzyme activities in the livers of control, sensitized and treated mice.

Each of these values is expressed as the mean ± SEM. The significant differences: * compared to the negative control ($p * \leq 0.05$; $p ** \leq 0.01$; $p *** \leq 0.001$). θ compared to the normal control ($p \theta \leq 0.05$; $p \theta\theta \leq 0.01$; $p \theta\theta\theta \leq 0.01$).

Effect of the aqueous extract of the leaves of *Ximenia americana* on the concentrations of Glutathion (GSH) in the livers of asthmatic mice

The results show that the administration of the aqueous extract at 75 mg / kg caused a significant increase ($p < 0.05$) in the level of GSH compared to the negative control group in the liver. However, at doses 150 mg / kg and 300 mg / kg, no significant difference was observed compared to the controls. (Figure 5).

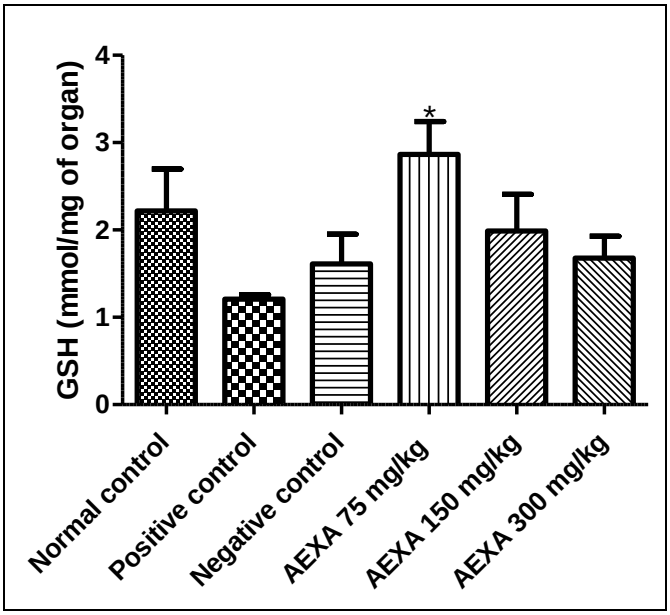

Figure 5: Changes in glutathione (GSH) enzyme activities in the livers of control sensitized and treated mice.

Each of these values is expressed as the mean ± SEM. The significant differences: * compared to the negative control ($p * \leq 0.05$; $p ** \leq 0.01$; $p *** \leq 0.001$).

Effects of the aqueous extract of the leaves of *Ximenia americana* on the histology of the lungs

Histological analysis of the lung tissue revealed in the normal control normal wall architecture indicating that the interalveolar area is very thin due to the absence of numerous inflammatory cells. In the negative control group, pathological changes were observed showing significant inflammatory infiltration in the lungs with an interalveolar area filled with exudates. The batches treated with the extract at different doses and with the reference substance showed a restructuring of the bronchial wall close to that of the normal control group.

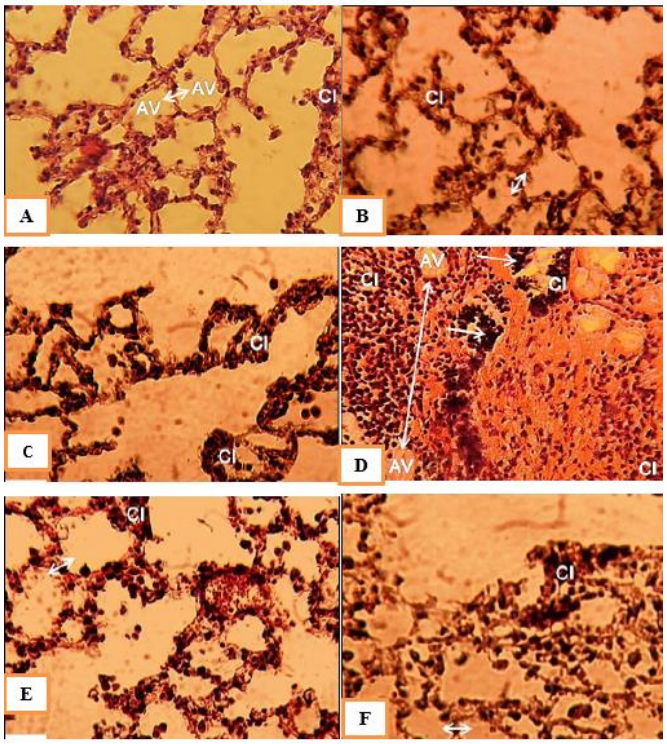

Figure 6: Histological sections of mouse lungs from the six experimental batches (x40). (Hematoxiline-eosin staining**)**

A: normal control; B: positive control; D: negative control; C, E, F: Test batches treated with extract at different doses. AV: the alveoli; CI: inflammatory cells.

DISCUSSION

In this work, the aim was to evaluate the effects of the aqueous extract of *Ximenia americana* on the asthma experimentally induced by OVA in mice. Indeed, during our experiment, we observed a increase in the relative weight of the lungs of all our test groups. This weight change is probably due to the immunogenicity of ovalbumin [11]. These results are in the same direction as those of Mauser et al (2013) who suggested that provocation with the allergen induces increased plasma exudation and edemas, therefore swelling of the inflamed organ. In order to assess the variations in the inflammatory response triggered by treatment with ovalbumin and to study the therapeutic effect of the aqueous extract of *Ximenia americana*, we first examined a few haematological parameters. Our results allowed us to observe a significant increase ($p < 0.001$) in the platelet count in the negative

control mice compared to the normal group. They have FCƐRII receptors whose stimulation by IgE leads to platelet activation with release of superoxide anions [10]. Our results join those of the study by Vosooghi and his collaborators (2013) who also found an increase in the number of platelets in sensitized rats. This function is only effective if its activity is followed by the actions of CAT and GSH, since the hydrogen peroxide produced by SOD is subsequently cleaned by the latter [4]. This cooperation between antioxidant enzymes is disturbed by the high release of reactive oxygen and nitrogen species [6]. This explains the fact that we find, in our present study, significant increases in the enzymatic activities of GSH, SOD and CAT in the mice of the test groups, at the level of the tissues studied. In fact, SOD being a target for the nitration and oxidation of tyrosine, this could be at the origin of the loss of the function of this enzyme [2, 5]. Ovalbumin caused a significant decrease in MDA content. This decrease was correlated with increased levels of GSH and activities of CAT and SOD in the lung. In this way, this enzyme would manage to protect cells against damage generated by foreign agents such as egg albumin [3].

CONCLUSION

At the end of our work, the objective was to study the effects of aqueous extract of *Ximenia americana* on experimentally induced ovalbumin asthma in mice. This analysis shows that the extract has anti-inflammatory and antioxidant activity. The aqueous extract of *X. americana* improved the altered and obstructed condition of the lungs by significantly reducing the number of inflammatory cells and the mucus generated, and, as a result, a marked improvement in the inflammatory condition of asthma. Thus, the aqueous extract of *Ximenia americana* has anti-inflammatory and antioxidant activity and has definite pharmacological power.

Credit authorship contribution statement

Atsang à kiki gisele, Zramah Mathieu conceived and designed the experiments and carried out the major part of experiments. Egre finsia, Takvou Francisand Abouboubakar oumarou Bibi Farouck: Havested the plant and prepared the extract. Dzeufiet Djomeni Paul Désiré: Performed histopathological examination. Atsang à kiki gisele, Zramah Mathieu: Analyzed data and wrote the paper. Takvou Francis, Egre finsia, Zramah Mathieu, Aboubakar oumarou bibi Farouck, Dzeufiet Djomeni Paul Désiré: Made provision of reagent and proof read the paper. All authors read and approved the final manuscript.

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Conflict of interest statement

The authors declare that they have no conflict of interest to disclose.

Ethical considerations

The study was approved by ethic Committee of the Faculty of Sciences of the University of Maroua (Ref N°14/0261/Uma/D/FS/VD-RC), according to the guidelines of Cameroonian bioethics committee (Reg N.° FWA-IRB00001954).

Disclosure statement

The authors declare that they have no conflict of interest to disclose.

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