EVALUATION OF THE HYPOTENSIVE AND ANTIHYPERTENSIVE PROPERTIES OF AN AQUEOUS EXTRACT OF MIMOSA INVISA MART EX. COLLA (FABACEAE) IN RABBIT

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ABSTRACT
Mimosa invisa Mart Ex. Colla (Fabaceae) is a plant used by the traditherapeuts in arterial hypertension treatment. The pharmacological study of an aqueous extract of this plant (Miv) on the rabbit blood pressure shows that, for varying dose of 10^-1 to 30 mg/kg B.W., this extract provokes a dose-dependent hypotension. Consequently, Miv is a hypotensive substance. Moreover, the hypertension caused by adrenalin with the dose of 5.10^-4 mg/kg B.W. is reduced significantly (P < 0.001) in dose-dependent way and even is cancelled by Miv injection in rabbits with the varying doses from 5 to 30 mg/kg B.W. Therefore, Miv is also an antihypertensive substance which opposes to the effects of activation of β-adrenergic receptors by adrenalin. The hypotensive and antihypertensive properties of Miv are consolidated by the characterization in the phytochemical screening of this extract, of the metabolites such as the flavonoid, polyphenols, coumarins and the anthocyans which are famously being known for their antihypertensive effects. The hypotensive and antihypertensive effects of Mimosa invisa (Fabaceae) aqueous extract consequently justify the use of this plant in traditional medicine in the arterial hypertension treatment.


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INTRODUCTION

Many pathologies are the reasons of the high rate of population mortality in the world. To the number of this one, cardiovascular system pathologies is one the major cause of mortality in the world and in Côte d’Ivoire, and arterial hypertension (HTA) is most frequent of these diseases [17]. The HTA is therefore a public health problem. The world prevalency in year 2000 was 26.4 % of the population [9, 11]. Certain statistics have estimated the hypertensive people number in 2025 at 1.5 million of the world population [11]. In view of this disease expansion and in addition to the modern therapeutic treatments, new remedies could be researched. Accordingly, many work are undertaken on several medicinal plants used and considered antihypertensives by the tradithérapeutes and recognized for their effects.

The present study is related to Mimosa invisa Mart Ex. Colla (Fabaceae), a plant used in traditional medicine in the arterial hypertension treatment and other pathologies [10, 13]. The aim of this study is to check the antihypertensives properties of Mimosa invisa by the study of the pharmacological effects of the aqueous extract of this plant on the rabbit arterial blood pressure.

MATERIALS AND METHODS

Plant material

The plant material consists of branches leaves of Mimosa invisa Mart Ex. Colla (Fabaceae). This plant was harvested in Cocody and identified at the National Centre of Floristic of Felix Houphouet-Boigny University (Abidjan, Ivory Coast). The identification was made by comparison with herbarium No. 7160 of December 14 1963 Laurent Ake-Assi, Emeritus Professor of Botany and No.199 of June 18 1992 Emma Ake-Assi, Doctor of Botany at Felix Houphouet Boigny Cocody University.

Preparation of extract

For extraction, 200 g of fresh leafy branches of Mimosa invisa (Fabaceae) are placed in 3 liters of distilled water and placed in boiling for 45 minutes. The decoction obtained is filtered first 3 times on absorbent cotton, and then 2 times on filter paper (Whatman No. 1). The filtrate collected was dried in an oven at 50 °C to obtain a yellow orange powder which represent the Mimosa invisa aqueous extract (Miv).

Animal material

The animals used in this experiment are rabbits of the species Oryctolagus cuniculus (Leporidae). They weigh between 2 and 2.5 kg. These animals are elevated in the animalery of the Training and Research Unit (UFR) of Biosciences of the University Felix Houphouët-Boigny, at a constant temperature (24 ± 2 °C), with a hygrosopy of 50-55 % and a photoperiod 12 hours at natural light and 12 hours at darkness. They are nurtured, ad libitum, with the granulated (Ivograin, Abidjan, Côte d’ivoire) and have a free access to water. The breeding and the experiments were led in accordance with the directives for the Care and the Use of Animals of Laboratory published by the National Institutes of Health.

Determination of the secondary metabolites of Mimosa invisa (Fabaceae)

The phytochemical screening of Miv is carried out according to methodologies described by Bekro and al., 2007; Abo, 2013. This characterization of the chemical great groups in Miv was done by tube reactions, in the presence with suitable reagents [18].

Rabbit arterial blood pressure recording

The recording of the rabbit arterial blood pressure is done using the mercury manometer of Ludwig, on a paper of recording in rotary move entrained by a motor, according to the method described by Abo and al., 2000 and 2016. For this, the rabbit is anesthetized by intraperitoneal injection with ethyl carbamate (MERCK, France) dosed at 40 %, at 1 g/kg B. W. The rabbit carotid is dissected and connected to the mercury manometer of Ludwig and his saphenous vein is intubed using a catheter connected to a syringe for the injections of the tests substances.

Pharmacodynamics substances

The pharmacodynamics substance used for these tests is adrenalin (L-adrenalin, FLUKA, Germany).

Statistical analyses

The results are analyzed thanks to Anova variances analysis with multiple test comparison of Tukey-Kramer of the data-processing program GraphPad Instat (San Diego CA, the USA). The values are presented in the form of mean, followed error on the mean (M ± SEM). P < 0.05 is considered significant. The software GraphPad Prism (San Diego CA, the USA) is used to plot the graphs.

RESULTS

1-Phytochimic screening of secondary metabolites of Mimosa invisa (Fabaceae)

The results of the phytochemical screening for the determination of the chemical great groups in the Mimosa invisa aqueous extract (Miv) are given in table 1. It is noticed that this extract contains polyphenols, flavonoid, glycosides cardiotonics, anthocyanes and coumarins. On the other hand, the tubes tests did not characterized the presence of tanins (catechic and gallic), sterols and terpenes, alkaloids, saponins and quinone compounds in Miv.
Table 1: The secondary metabolites in the *Mimosa invisa* (Fabaceae) aqueous extract obtained after tubes tests.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Reagents</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyphenols</td>
<td>Chlorure ferrique reagent</td>
<td>+</td>
</tr>
<tr>
<td>Flavonoid</td>
<td>Cyanidine reagent</td>
<td>+</td>
</tr>
<tr>
<td>Glycosides cardiotonics</td>
<td>Kedde reagent</td>
<td>+</td>
</tr>
<tr>
<td>Anthocyanins</td>
<td>Tampon phosphat reagent</td>
<td>+</td>
</tr>
<tr>
<td>Coumarins</td>
<td>Hydroxyd of ammonium reagent</td>
<td>+</td>
</tr>
<tr>
<td>Tanins catechic</td>
<td>Stiasny reagent</td>
<td>–</td>
</tr>
<tr>
<td>Tanins gallics</td>
<td>Acetat of plumb and chlorure ferric reagent</td>
<td>–</td>
</tr>
<tr>
<td>Sterols et terpenes</td>
<td>Liebermann-Burchard reagent</td>
<td>–</td>
</tr>
<tr>
<td>Alkaloids</td>
<td>Dragendorff reagent</td>
<td>–</td>
</tr>
<tr>
<td>Saponosides</td>
<td>Test of foam</td>
<td>–</td>
</tr>
<tr>
<td>Quinonics compound</td>
<td>Borntraeger reagent</td>
<td>–</td>
</tr>
</tbody>
</table>

+ : presence of the compound (positif test)  
– : compound not determinated (negatif test)

2-Dose-response effect of *Mimosa invisa* (Fabaceae) aqueous extract on the rabbit arterial blood pressure

This experiment is carried out to study the Miv effects on the rabbit normal arterial blood pressure. Thus, Miv is administered in increasing doses which are going up to 30 mg/kg B.W., in time intervals of at least 10 minutes between the successive injections.

In this experiments series the normal blood pressure of rabbits is $102 \pm 4$ mm Hg ($N = 4$). The figure 1-a presents a standard recording of the results of this study. It shows that the doses of Miv lower than $10^{-1}$ mg/kg BW are without effects on the arterial blood pressure. For the varying doses of $10^{-1}$ to 30 mg/kg B.W., Miv causes a dose-dependent arterial hypotension. The reductions of blood pressure vary from $2.1 \pm 1.7$ (P > 0,05) to $28.85 \pm 6.11$ mm Hg (P < 0,001) compared to the rabbits reference arterial blood pressure, and these effects of Miv are completely reversible less than 5 minutes after the injection of this extract. At 30 mg/kg B.W., Miv causes a significantly hypotension of $30.3 \pm 1.70$ mm Hg (P < 0,001) compared to the reference value of arterial blood pressure of rabbits. But, the superior doses at 30 mg/kg B.W. of extract, the hypotension induced by Miv is irreversible. The curve of the figure 1-b gives, for 4 experiments, the percentages of falls of the arterial blood pressure of rabbit according to the dose of Miv administered. It is a sigmoid curve from which the dose making it possible to obtain the threshold effect of Miv is estimated at $10^{-3}$ mg/kg B.W. and the maximum effect is obtained with the dose of 30 mg/kg B.W. The efficacious dose 50 % (ED50) of Miv on the arterial blood pressure of rabbit is $7.25$ mg/kg B.W.
Figure 1: Dose-response effects of *Mimosa invisa* aqueous extract (Miv) in the rabbit arterial blood pressure.

a – Standard recording
A : Normal arterial blood pressure recording
B à G : Miv effects (after the arrow) at $10^{-1}$ (B), 1 (C), 5 (D), 10 (E), 20 (F) and 30 (G) mg/kg B.W. on the arterial blood pressure.

b – Falling of the arterial blood pressure according of the dose of Miv
3-Effects of the *Mimosa invisa* aqueous extract (Miv) on induced arterial hypertension in rabbit

3-1 Miv effects on the arterial hypertension induced by adrenalin in rabbit

This study aims to check the Miv effects, hypotensive substance, on the hypertension induced by the adrenalin administration. Thus, in this experiments series, the injection of Miv at various dose is preceded by a single adrenalin dose (5.10^{-4} mg/kg B.W).

The figure 2-a present a standard recording of results of this study. At the single dose of 5.10^{-4} mg/kg B.W., adrenalin induces an arterial hypertension of 37.81 ± 3.32 mm Hg (N = 3). When this same dose of adrenalin (5.10^{-4} mg/kg B.W.) is followed, 10 s after, of that of Miv with the concentrations ranging between 5 and 20 mg/kg B.W., the arterial hypertension induced by adrenalin varies from 33.22 ± 3.09 mm Hg with 6.20 ± 3.21 mm Hg; that is to say reductions of the adrenalin hypertension induced from 12.16 ± 3.98 % (P < 0.01) to 83.60 ± 3.34 % (P < 0.001) to compared to the arterial blood pressure reference of used rabbits. When the injection of adrenalin is followed by that from Miv to 30 mg/kg B.W., it appears, transitory way, a no significant arterial hypertension of 0.80 ± 0.16 mm Hg (P > 0.05), followed by an arterial hypotension also no significant and transitory of 8.44 ± 3.3 mm Hg (P > 0.05).

The Miv effects on the hypertension induced by adrenalin, for 3 experiments, are presented by the figure 2-b. In presence of the doses of Miv, the inhibiting concentration 50 % (IC50) of the adrenalin arterial hypertension induced is of 11.73 mg/kg B.W.

![Figure 2: Effects of the *Mimosa invisa* aqueous extract (Miv) on arterial hypertension induced by adrenalin (ADR) in rabbit.](image)

a – Standard recording
A : Effects of the ADR alone at 5.10^{-4} mg/kg B.W. (after the arrow)
B à E : Effects of the ADR at 5.10^{-4} mg/kg B.W. (after the first arrow), followed by the effect of Miv injection at 5 (B), 10 (C), 20 (D) and 30 (E) mg/kg B.W. (after the second arrow)

b – Reduction by Miv of adrenalin induced arterial hypertension (HTA)

3-2 Cumulated effects of Miv and adrenalin on the rabbit arterial blood pressure

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In this other series of experiments, adrenalin at $5 \times 10^{-4}$ mg/kg B.W. is associated with various doses of Miv, and this mixture is administered on rabbits. The figure 3-a presents a standard recording of the results of this study. The injection of adrenalin to the dose of $5 \times 10^{-4}$ mg/kg B.W. alone on rabbit induces an arterial hypertension of 39, 43 ± 4.5 mm Hg ($N = 3$). When this dose of adrenalin is associated with various doses of Miv going from 5 to 20 mg/kg B.W., arterial hypertension varies from 30.22 ± 4.31 mm Hg to 1.20 ± 4.29 mm Hg; that is to say dose-dependent reductions of the arterial hypertension of 23.36 ± 4.12 % ($P < 0.01$) to 96.96 ± 4.61 % ($P < 0.001$). When 30 mg/kg B.W. of Miv is associated with adrenalin to $5 \times 10^{-4}$ mg/kg B.W., it appears no significant and transitory arterial hypertension of 0.40 ± 0.23 mm Hg ($P > 0.05$), that is to say 98.99 ± 5.23 % ($P < 0.001$) of reduction of the arterial hypertension caused by adrenalin, followed by an arterial hypotension also no significant of 7.34 ± 1.51 mm Hg ($P > 0.05$), before the return to the normal blood pressure. The reductions of hypertension induced by adrenalin, when it is associated with Miv, for 3 experiments, is presented by the figure 3-b. When Miv is associated with adrenalin, the IC50 is 9.22 mg/kg B.W.

![Figure 3: Cumulated effects of the Mimosa invisa aqueous extract (Miv) and adrenalin (ADR) on the rabbit arterial blood pressure.](image)

**Figure 3:** Cumulated effects of the *Mimosa invisa* aqueous extract (Miv) and adrenalin (ADR) on the rabbit arterial blood pressure.

a – Standard recording

A : Effects of ADR alone to $5 \times 10^{-4}$ mg/kg B.W. (after the arrow)

B à E : Effects of ADR to $5 \times 10^{-4}$ mg/kg B.W. + Miv to 5 (B), 10 (C), 20 (D) and 30 (E) mg/kg B.W. (after the arrow)

b- Reduction of the arterial hypertension (HTA) induced by adrenalin in presence of Miv

**DISCUSSION**
The study of the pharmacological effects of the aqueous extract of branches leaves of *Mimosa invisa* (Miv) on the rabbit normal arterial blood pressure shows that this extract (Miv), with doses going of $10^{11}$ to 30 mg/kg B.W., creates a hypotension dose-dependent. Consequently, Miv is a hypotensive substance. The shape of the curve of the dose-response effect of Miv lets suppose that this substance acts by activating receptors [14].

Miv reduces in dose-dependent way and even cancels almost arterial hypertension induced by adrenalin. Consequently, Miv is also an antihypertensive substance which is opposed to the hypertensive effect of adrenalin, and thus the effect of the activation of beta-adrenergics receptors. Indeed, adrenalin acts on the cardiovascular system while fixing on the β-adrenergics receptors to the cardiac level (β1) and the vascular level (β2), respectively causing a cardioactivation and a vasoconstriction at the origin of arterial hypertension observed [8, 12, 6, 19, 20].

The phytochemical screening of the *Mimosa invisa* aqueous extract has characterized the presence in this extract of polyphenols, flavonoid, glycosides cardiotonics, anthocyanins and coumarins. On the other hand, this study shows that Miv does not contain a tannins, sterols and polyterpenes, alkaloids, quinone compound and saponins. The essential of the secondary metabolites that Miv contain would be at the origin of its antihypertensive effects. Indeed, it was proven that flavonoid, polyphenols, coumarins and anthocyanins have antihypertensives properties [4, 16, 7, 15].

**CONCLUSION**

The aqueous extract of branches leaves of *Mimosa invisa* (Fabaceae) contains hypotensives and antihypertensives substances. The effects of these substances are justified by the presence in this extract of phytocompound such as flavonoid, polyphenols, coumarins and anthocyanins known to contain antihypertensives properties. Hypotensives and antihypertensives properties of the *Mimosa invisa* aqueous extract, shown in this study, justify the use of this plant in traditional medicine in the arterial hypertension treatment.

**COMPETING INTERESTS**

The authors declared that there is no conflict of interests exists.

**REFERENCES**

