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# EFFECT OF CLIMATIC VARIABILITY ON THE ANTIHYPERTENSIVE ACTIVITY OF THE HYDROETHANOLIC EXTRACTS OF *BLIGHIASAPIDA* (*SAPINDACEAE*) FROM THREE REGIONS WITH DISTINCT PEDOCLIMATIC CHARACTERISTICS

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***ABSTRACT***

*This study aimed to evaluate the impact of climate variability on the antihypertensive effect of hydroethanolic extracts of Blighiasapida from three Ivorian regions in rats rendered hypertensive by a fructose diet. In fact, the rats were divided into eleven batches of four rats each of which lot 1 was considered as a control and batches 2 to 11 were fed on the fructose diet for 30 days. These hypertensive rats were treated with hydroethanolic extracts of Blighiasapida from three regions. At the end of the treatment, the cardiovascular parameters were measured and the oxidative stress markers were assayed. The results showed a regulation of cardiovascular parameters and an improvement of fructose oxidative stress markers in rats. This regulation of the different parameters was better observed at a dose of 400 mg/kg bw of the hydroethanolic extract from the region of Adzopé. The hydroethanolic extracts of Blighiasapida showed better antihypertensive activity by regulating cardiovascular parameters and markers of oxidative stress. This antihypertensive effect of Blighiasapida varied according to region and climate. This would explain its use in traditional medicine and could then be used for the formulation of an improved traditional medicine for the treatment of high blood pressure.*

***KEYWORDS:****Hypertension, Blighiasapida, antioxidant, pedoclimatic.*

## INTRODUCTION

Hypertension (HTA) also called silent killer, is one of the most important causes of cardiovascular diseases [1; 2]. This disease is responsible for 49% of ischemic heart complications, 62% of strokes, 76% of cardiac failure and kidney disease events, and approximately 30% of worldwide deaths per year 80% come from low-income countries [3; 4].HTA has been a major public health hazard in recent years as it is increasingly prevalent in both developed and developing countries[5; 6]. It is due to behavioral and lifestyle factors such as smoking, unhealthy eating and excessive salt intake, harmful alcohol use, sedentary lifestyle, overweight and obesity[7].In addition, it is the leading cause of morbidity and mortality in the world and intensifies the urgency to combat it [8]. The treatment of hypertension uses various synthetic molecules to reduce morbidity and cardiovascular mortality. However, according to the [5], the high cost of conventional medicines and synthetic products means that in disadvantaged countries, access to health care is problematic and a major cause of high mortality[9; 10].Also, the effectiveness of these drugs is only 40% to 60% and it is necessary mainly to associate two or more antihypertensive drugs belonging to different categories to obtain optimal results, but the side effects of these drugs are an important concern[11]. This is causing populations in developing countries to increasingly switch to traditional pharmacopoeia [12].In addition, the 80% of

 

the African population using traditional medicine to heal themselves have made plant therapies more popular in recent years because of the decrease in the purchasing power of populations[13; 9]. Traditional healers often use this same strategy in the treatment of hypertension [14].Also, the multifactorial nature of hypertension makes that a good antihypertensive remedy should not stop at a mere drop in blood pressure values, but it must be based primarily on the effectiveness in treating all factors of onset of hypertension disease. Among the plants used, *Blighiasapida*, a *sapindaceae* from the African pharmacopoeia recognized for its therapeutic virtues[15; 16; 17; 18]and many represented in Ivory Coast has been selected.

Unfortunately, this plant is threatened by repeated droughts, insufficient rainfall, change and climatic changes in Ivory Coast. These scourges cause several consequences such as the decline of soil fertility, soil erosion, depletion of vegetation, reduction of wildlife products, animal and plant species [19]. Moreover, with this degradation of biodiversity, the supply of this resource used by traditional medicine is likely to decline.This will affect poor and rural populations who rely heavily on nature's products for both medicine and income and food security [20]. In addition, it could also affect the chemical composition of plants such as *Blighiasapida* which is sufficiently represented in Ivory Coast and thus influence its therapeutic activity. Thus, the objective of this work was to show the impact of climate variability on the antihypertensive activity of *Blighiasapida*.

## MATERIAL AND METHODS

### 2.1. Plant material

The plant material consisted of the bark of *Blighiasapida*. They were harvested in the north (Korhogo), in the center (Bouaké) and in the south (Adzopé) of Ivory Coast. This plant has been identified at the national floristic center of the Félix Houphouët-Boigny University of Ivory Coast. A specimen has been filed under the number: 12613.

### 2.2. Animal material

*Rattusnorvegicus* rats of *Wistar* strain weighing between 200 and 300 g were used for this study. They were provided by the animal physiology laboratory of the UFR Biosciences of Félix Houphouët-Boigny University (Abidjan, Ivory Coast). These animals were kept in plastic cages with stainless steel blankets and acclimated in the animal nursery of the EcoleNormaleSupérieure (ENS) (Abidjan, Ivory Coast).

### 2.3. Preparation of hydroethanolic extracts of *Blighiasapida*

The barks after drying, were crushed and reduced to a fine powder. The hydroethanolic extracts were prepared according to the method of [21 and 22]. Thus, 300 g of this plant powder was mixed with 3 L of 70% ethanol on a magnetic stirrer at room temperature. The macerate obtained was filtered successively on hydrophilic cotton and on Wattman paper. The volume of the filtrate was reduced under vacuum (at 50 °C) using a rotary evaporator. The dry evaporate was recovered in powder form which constitutes the hydroethanolic extract.

### 2.4. Phytochemical Cryblage

The secondary metabolites of *Blighiasapida* have been demonstrated according to the methods used by [23]. The spectrophotometric assays of the total polyphenols and total flavonoids were carried out according to the methods used by [24].

### 2.5. Animal treatment

The rats (44) were divided into eleven (11) batches of four rats each. Lot 1 constituted the control group and was fed single pellet and distilled water. Hypertension was induced in the other 10 batches of rats by a high fructose diet for 30 days. These hypertensive animals were treated during 07 days by the extracts of the different regions as follows:

Lot 2: Witness sick;
Lot 3: rats that received no treatment;
Lot 4: rats treated with the hydroethanolic extract of Adzopé (EHEA) at 200 mg / kg bw;
Lot 5 : rats treated with the hydroethanolic extract of Adzopé (EHEA)at400 mg/kg bw;
Lot 6 : rats treated with the hydroethanolic extract of Bouaké (EHEB)at200 mg/kg bw;
Lot 7 : rats treated with the hydroethanolic extract of Bouaké (EHEB) at 400 mg/kg bw;
Lot 8 : rats treated with the hydroethanolic extract of Korhogo (EHEK) at 200 mg/kgbw;
Lot 9 : rats treated with the hydroethanolic extract of Korhogo (EHEK)at 400 mg/kg bw;
Lot 10 : rats treated with nifedipine (reference molecule) at 5 mg/kg bw;
Lot 11 : rats treated with nifedipine (reference molecule) at10 mg/kg bw.
At the end of the treatment, the cardiovascular parameters (SBP, DBP and HR) were measured by the indirect method. Then, the blood from each rat was taken to measure the markers of oxidative stress (MDA, CAT and SOD).

**Statistical analysis**
The recorded data were processed using the Graphpad Version 5 software. For each variable, the mean (m) and the standard deviation of the mean (SD) were calculated. The results of the different groups were compared using Turkey's ANOVA. The level of statistical significance of the results was set at $p < 0.05$.

## RESULTS

### 3.1. Extraction yield

The results of the yield of the different hydroethanolic extractions were recorded in **Table I** below. Thus, the EHEK and EHEB extracts showed significantly higher yields (respectively 2.54% and 2.20%) ($p<0.05$) compared with the EHEA extract (0.88%).

**Table I: Yield of hydroethanolic extracts of *Blighiasapida* from different regions**

| Extraits | EHEA | EHEB | EHEK |
|---|---|---|---|
| Yield(%) | 0,88 | 2,20 | 2,54 |

EHEA: hydroethanolic extract of Adzopé, EHEB: hydroethanolic extract of Bouaké and EHEK: hydroethanolic extract of Korhogo

### 3.2. Phytochemical Screening

Phytochemical screening showed no significant difference in the chemical composition of extracts from different regions (**Table II**). Sterols, polyterpenes, polyphenols, flavonoids, catechic tannins, quinone substances and alkaloids were present. In addition, the absence of gallic tannins and saponosides was noted in each of the three extracts.

**Table II: Result of the phytochemical screening of hydroethanolic extracts of *Blighiasapida* from different regions**

| Extracts / Secondary metabolites | | EHEA | EHEB | EHEK |
|---|---|---|---|---|
| Sterols et polyterpenes | | + | + | + |
| Polyphenols | | + | + | + |
| Flavonoids | | + | + | + |
| Tannins | Cat. | + | + | + |
| | Gal. | - | - | - |
| Quinones | | + | + | + |

| | | | | |
|---|---|---|---|---|
| Alkaloids | Bou. | + | + | + |
| | Drag. | + | + | + |
| Saponosides | | - | - | - |

EHEA: hydroethanolic extract of Adzopé, EHEB: hydroethanolic extract of Bouaké, EHEK: hydroethanolic extract of Korhogo, Cat: catechic, Gal: gallic, Bou: Bouchardat, Drag: Dragendorf, +: presence, -: absence.

### 3.3. Quantification of total polyphenols and flavonoids in extracts

The EHEA extract showed a total polyphenol content (68.88 mg EAG/g extract) and total flavonoids (26.4 mg EQ/g extract) significantly higher (at $p < 0.05$) compared to extracts from other regions (EHEB and EHEK) (**Figure 1** and **2**).

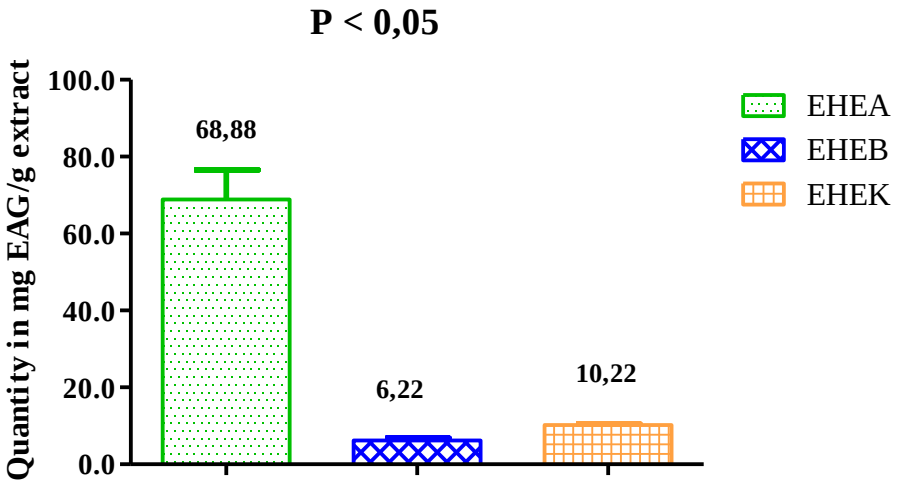


**Figure 1:** Quantity in total polyphenols of hydroethanolic extracts

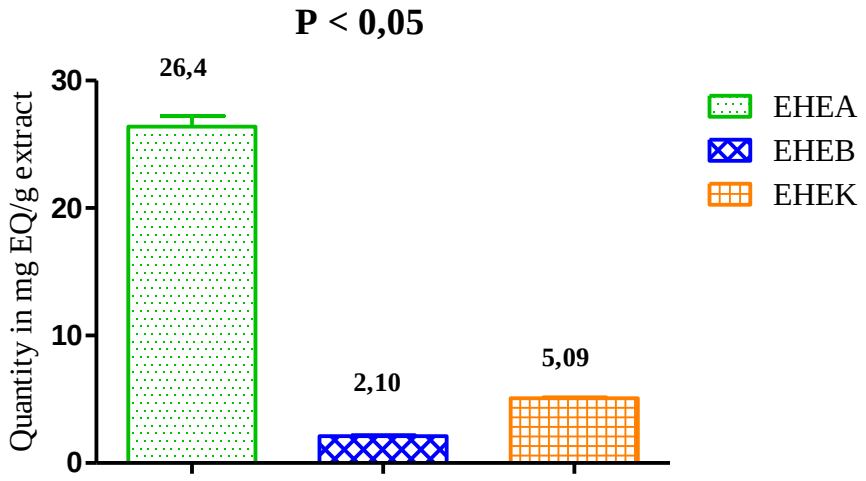


**Figure 2**: Quantity of total flavonoids in hydroethanolic extracts

EHEA : hydroethanolicextractof Adzopé, EHEB : hydroethanolicextract of Bouaké and EHEK : hydroethanolicextract of Korhogo.

**3.4. Effect of hydroethanolic extracts on hypertension**

3.4.1. Effectof *Blighiasapida*extracts oncardiovascularsparameters

The results of the treatment of hypertensive rats with the different doses of the hydroethanolic extracts of *Blighiasapida* from different regions are shown in Figures **3, 4** and **5** below. Cardiovascular parameters (SBP, DBP, and HR) were significantly elevated after consumption of the fructose diet ($p < 0.05$) (Figs **3, 4,** and **5**) compared with healthy controls.This increase in arterial pressure and fructose-induced heart rate was controlled in hypertensive rats receiving hydroethanolic extracts of *Blighiasapida* or nifedipine compared to untreated sick rats. This dose-dependent effect is better seen with the hydroethanolic extract from the Adzopé region (EHEA) compared to extracts from the other two regions (Bouaké and Korhogo). The effect of this extract is similar to that of nifedipine, a reference antihypertensive molecule used during this study.

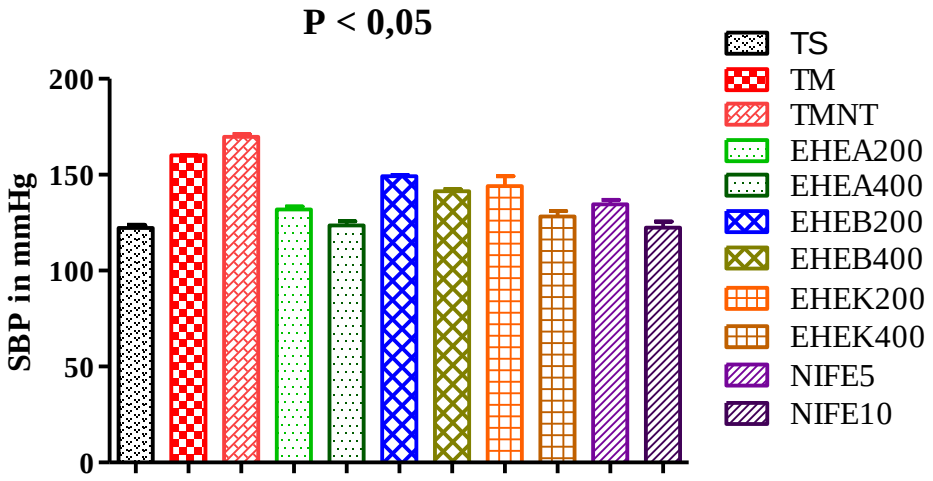


**Figure 3:** Effect of hydroethanolic extracts on systolic arterial pressure

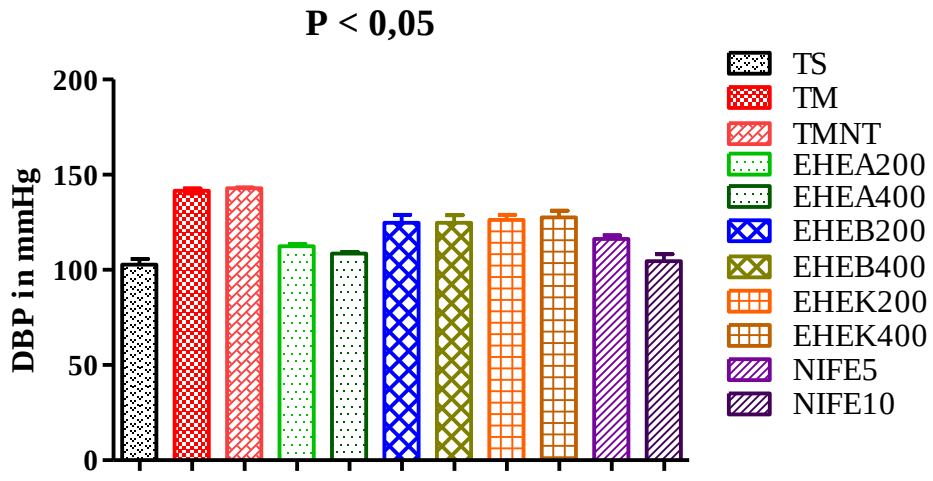


**Figure 4:** Effect of hydroethanolic extracts on diastolic arterial pressure

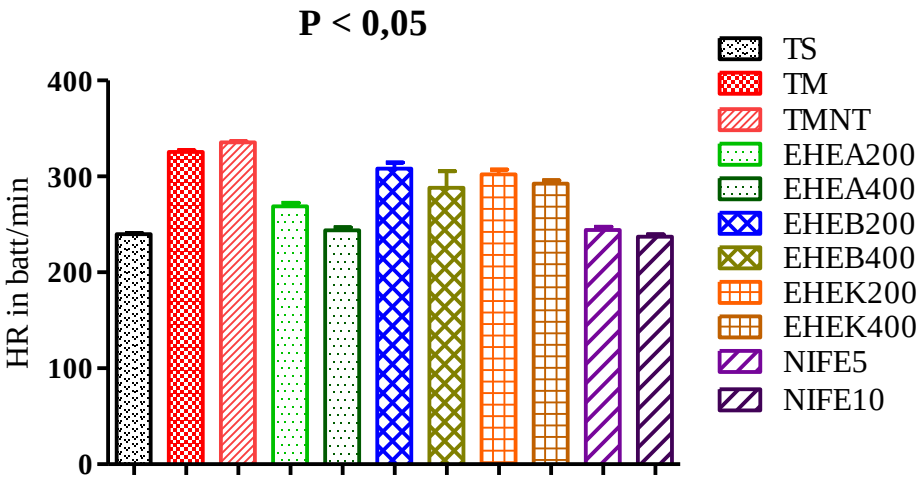


**Figure 5**: Effect of hydroethanolic extracts on heart rate

TS: healthy control; TM: sick control; TMNT: untreated patient control; EHEA 200: hydroethanolic extract of Adzopé at 200 mg/kg bw; EHEA 400: hydroethanolic extract of Adzopé 400 mg/kg bw; EHEB 200: hydroethanolic extract of Bouaké at 200 mg/kgbw; EHEB 400: hydroethanolic extract of Bouaké at 400 mg/kg bw; EHEK 200: hydroethanolic extract of Korhogo at 200 mg/kg bw; EHEK 400: hydroethanolic extract of Korhogo at 400 mg/Kg bw; NIFE 5: nifedipine 5 mg/Kg bw; NIFE 10: nifedipine 10 mg/kg bw.

### 3.4.2. **Effect of hydroethanolicextracts on oxidative stress parameters**

Figures **6, 7, 8** and **9** show the effect of *Blighiasapida* extracts on some markers of oxidative stress. Fructose-induced hypertension caused disruption of oxidative stress parameters in hypertensive animals. Thus, there was a significant reduction in cardiac catalase (CAT) and superoxide dismutase (SOD) levels and an increase in cardiac malondialdehyde (MDA) compared to healthy controls.The administration of plant extracts at doses of 200 and 400 mg/kg bw resulted in a significant increase in the level of cardiac catalase and SOD, and a significant reduction in cardiac MDA compared to untreated sick controls.The hydroethanolic extract from the Adzopé region showed a more significant dose-dependent effect on these parameters compared to extracts from the other regions (Bouaké and Korhogo).

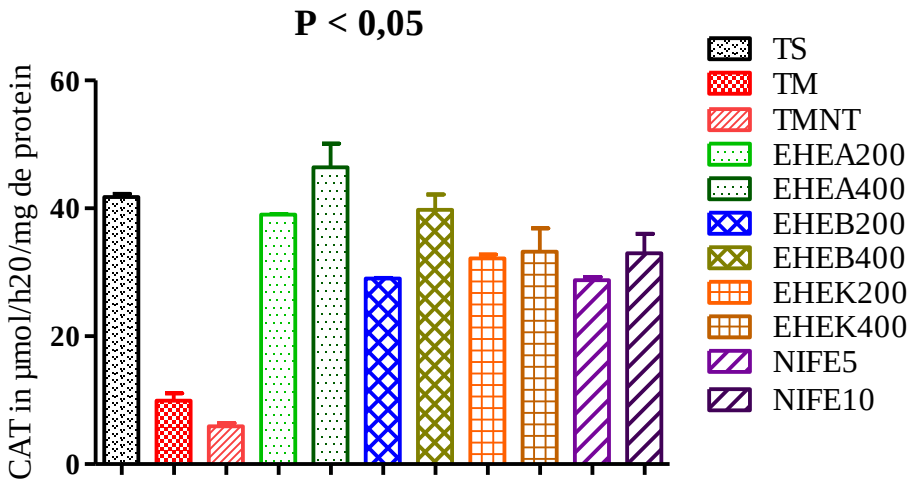


**Figure 6**: Effect of hydroethanolic on catalase

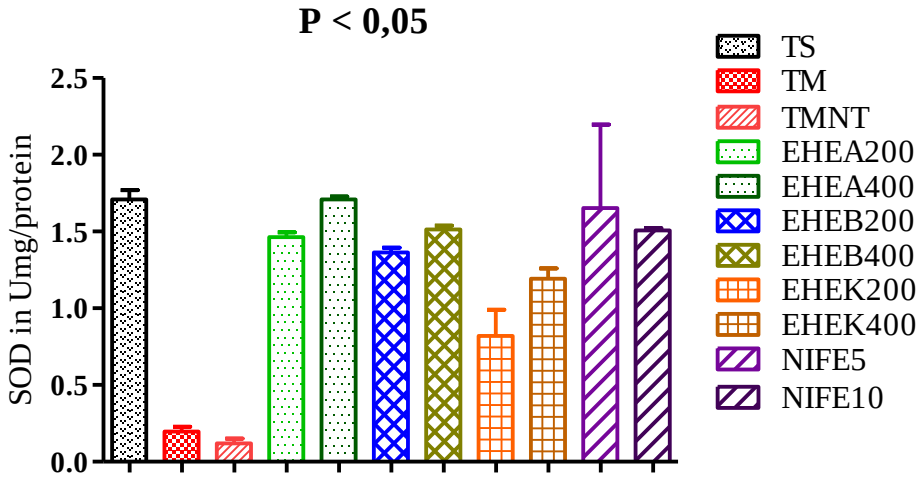


**Figure 7**: Effect of hydroethanolic extracts on superoxyde dimutase

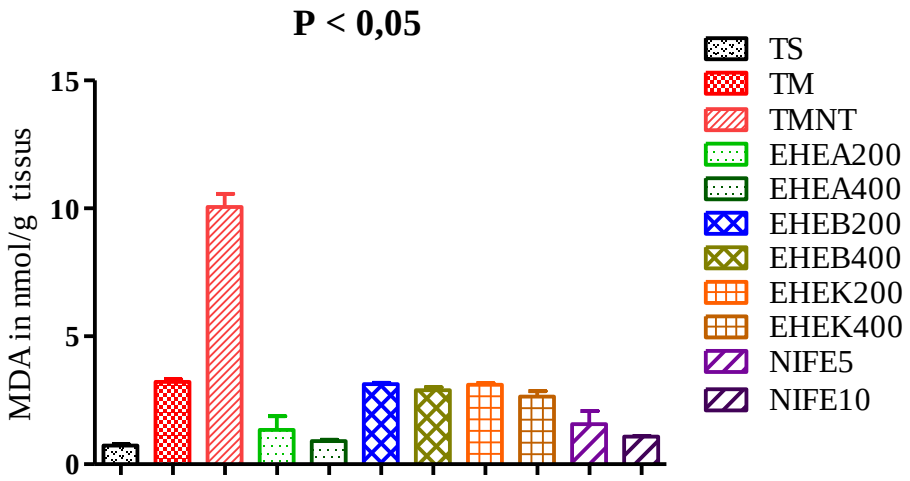


**Figure 8**: Effect of hydroethanolic extracts on malondialdehyde

## DISCUSSION

The objective of this work was to show the impact of climate variability on the antihypertensive activity of the hydroethanolic extracts of *Blighiasapida* from three regions of Ivory Coast in rats rendered hypertensive by fructose. The bark of *Blighiasapida* comes from three regions of Ivory Coast with different pedoclimatic characteristics. In addition, phytochemical screening, effects on oxidative stress indicators were studied.

The present work has shown that the EHEK extract has the highest yield and that the EHEA extract has the lowest yield. This difference in yield may be due to the difference in soil composition. Because, the work of [25] identified soils of petroplinthic types on granite or remolded soils and ferrisols of PlinthicFerralsols Ferric types [26]in the Bouaké region.In addition, the results of the work of [27; 28] showed the presence of colluvio-alluvial lowland soils occupied by sablolimonous hydromorphic soils and the frequency of shallow armor and surface-insulated cuirass blocks at Bouaké[29; 30].While in the Korhogo region, it is the dominant Ferrisols type soils and the leached tropical ferruginous soils with concretions that have been identified. Soils of cambrisol or browned type have been identified in almost 80% of the area of the Adzopé region. The work of [31] and [32] has shown that cambrisols are soils with climatic evolution developing in temperate regions under forest climates.

Phytochemical screening revealed the presence of phytocompounds such as polyterpenes, sterols, polyphenols, flavonoids, catechic tannins, quinones and alkaloids but also the absence of saponosides and gallic tannins. These results are contrary to the results of [33] who showed that the 70% ethanolic extract of the roots of *Blighiasapida* contained only polysterols, saponins, polyamides and reducing sugars.Our results correlate with those of [16] and [34] who showed the presence of alkaloids, tannins and flavonoids. Our results are also similar to those of [35]which revealed the presence of these chemical compounds in the methanolic extract of *Blighiasapida*K. Kong.

The highest chemical content was observed in the EHEA extract and the lowest in the EHEB extract. The difference in the amount of secondary metabolites may be due to the distinct soil characteristics of each of the three regions. The difference in temperature and rainfall during the collection period may be responsible for this difference in quantity of chemical compounds.In fact, the temperature varied between 29 °C and 37 °C in Korhogo, between 27 °C and 34 °C in Bouaké and between 28 °C and 30 °C in Adzopé while the precipitation was 146 mm in Adzopé, 101 mm in Bouaké and 37 mm

in Korhogo. Our results corroborate those of [36], who pointed out that the distribution of secondary metabolites may be related to harsh climatic conditions (high temperature, sun exposure, drought and salinity) that stimulate the biosynthesis of these chemical compounds.According to [37], the polyphenol content varies qualitatively and quantitatively from one plant to another and may be due to several climatic and environmental factors such as geographical area, drought, soil, aggressions and diseases[38].Genetic heritage, harvest period, and stage of plant development may be partly responsible for the difference in polyphenol content [39]. This difference in concentrations of polyphenols and total flavonoids could also be explained by the distinction between the vegetation of Korhogo (savannah), Bouaké (wooded savannah) and Adzopé (dense forest).Weather, climate and environmental conditions would therefore be responsible for the difference in concentration of secondary metabolites between the three regions [37; 36]. The works of [24] also showed that external factors such as geographical factors, climatic factors, the degree of maturation of the plant and the duration of storage would have a strong influence on the content of secondary metabolites[40; 41].
In this study, high consumption of fructose resulted in a very significant increase in systolic blood pressure, diastolic blood pressure and heart rate. The different treatments with the hydroethanolic extracts significantly reduced the systolic and diastolic blood pressure, as well as the heart rate in the rats rendered hypertensive by the fructose. At the highest dose of hydroethanolic extracts, SBP, DBP and HR were significantly reduced compared to untreated sick controls.Hydroethanolic extracts produce dose-dependent antihypertensive effects. This effect can be attributed to the presence of alkaloids and total polyphenols in *Blighiasapida* extracts. This finding is consistent with the work done by [2] with 70% ethanol extract of leaves of *Moringastenopetala* (Barker f.) Cufod. But, the EHEA extract showed a highly dose-dependent effect on these hemodynamic parameters compared to other EHEB and EHEK extracts.This remark could be due to the high concentration of polyphenolic compounds of this extract compared to the EHEB and EHEK extracts. Because the biosynthesis of these compound would be favored by beneficial climatic conditions [37]. The climatic and environmental conditions and the geographical location of the plant affect the polyphenol contents [42]of the hydroethanolic extracts of *Blighiasapida*, which would be responsible for its antihypertensive activity.In addition, the antihypertensive activity of EHEA was significantly elevated for the EHEK extract compared with the EHEB. These findings could be its high content of polyphenols and total flavonoids compared with the other two extracts (**Figs 1** and **2**) because the antihypertensive effect of the extracts is inversely proportional to their content in total polyphenols and flavonoids.This claim was supported by the results of studies conducted by [43]. The antihypertensive activity of the hydroethanolic extracts of *Blighiasapida* is different from one region to another and also from one climate to another. The climate change of a plant can affect its antihypertensive effect.

In this study, excessive consumption of fructose generated free radicals that inhibited the mechanism of synthesis of antioxidant enzymes. This inhibition led to the reduction of catalase and superoxide dismutase concentrations and the increase of the malondialdehyde level in the tissues. This damaged the antioxidant defense system, reflecting tissue sensitivity to lipid peroxidation [44].In hypertensive rats, a significant increase in catalase and SOD levels was observed while MDA was reduced during treatment with hydroethanolic extracts of *Blighiasapida* at doses of 200 mg/kg bw and 400 mg/kg bw. This increase in catalase and superoxide dismutase levels in the rats treated with the various extracts of *Blighiasapida* suggests that the extracts have direct scavenging properties of free radicals generated by fructose.The extracts thus allowed the regulation of antioxidant defense by strengthening the enzymatic defense system of the heart. This major antioxidant activity of the extracts can be explained by the rich polyphenolic compounds and flavonoids of the plant [17; 18]. Reduction of the content of plasma MDA lipid peroxidation marker means that the hydroethanolic extracts of *Blighiasapida* neutralized the reactive oxygen species by reducing the MDA level of the heart of fructose-induced hypertensive rats.These results confirm the antioxidant activity of the plant. They corroborate the results obtained by [44; 2 and 45]. The hydroethanolic extracts of *Blighiasapida*could therefore

stimulate the production of these enzymes by inhibiting their exhaustion in tissues due to the consumption of fructose.

Interestingly, it was found that the hydroethanolic extract of Adzopé showed an effect on the markers of oxidative stress induced by the high consumption of fructose at the highest dose of 400 mg/kg bw compared to the extracts of Bouaké and Korhogo. The EHEA extract exhibited the best antioxidant activity at the 400 mg/kg bw dose compared to EHEB and EHEK extracts. This could be explained by the fact that Adzopé extract has the highest levels of polyphenols and total flavonoids compared to the other two extracts of Bouaké and Korhogo.This is in line with the work of [46] who showed that phenolic compounds such as flavonoids, polyphenols, tannins and phenolic terpenes were associated with the remarkable antioxidant activity of the plant. This high concentration of secondary metabolites would be elucidated by the climate, the environment and the geographical area of the region favorable to the secretion of these chemical compounds which are mainly responsible for the therapeutic activity of plant extracts.

## CONCLUSION

This study has shown that the hydroethanolic extracts of *Blighiasapida* possess potential antihypertensive activity on fructose-induced hypertension. Indeed, these extracts played a vital role in regulating systolic and diastolic arterial pressures and heart rate by improving antioxidant status. This could validate the use of *Blighiasapida* in the treatment of hypertension and serve as a basis for the formulation of an improved traditional medicine. Also, weather, climate, environmental and geographical conditions could influence the concentrations of *Blighiasapida* chemical compound responsible for its therapeutic activities. The change in climate would therefore have an influence on the therapeutic activity of the hydroethanolic extracts of *Blighiasapida* by acting on the biologically active compound content.

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