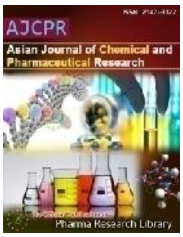
Asian Journal of Chemical and Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ajcpr



Research Article **Open Access**

Antihypertensive activity of the acetatic extract of *Morinda morindoides* on the arterial hypertension induced by adrenalin in rabbits

Bahi Calixte, Boga Gogo Lucien*, Kouangbé Mani Adrien, N'guessan Jean David, Coulibaly Adama

Department of Biosciences, Biochemical Pharmacodynamy Laboratory, University Félix Houphouët-Boigny, PO Box 582, Abidjan 22-Côte d'Ivoire, Africa.

A B S T R A C T

The aim of this work is to study the effect of the acetatic extract of *Morinda morindoides* on the arterial hypertension induced by adrenalin in rabbits. With this intention, we studied the effect of the EAC of *Morinda morindoides* on the blood pressure in healthy rabbits, and then the effects of the EAC *Morinda morindoides* of on the cardiovascular parameters in rabbits made hypertensive in comparison with those of tenordate, a reference antihypertensive drug. The acetatic extract is obtained after evaporation of the filtrate resulting from homogenization of the ethanolic extract in mixture of ethyl acetate and water. Doses of the acetatic extract of *Morinda morindoides* (1000 and 2000 mg/kg bw) and of tenordate (10 and 20 mg/kg bw) are admistrated by gavage to healthy rabbits and the blood pressure measured using a sphyngomanometer. For the study of the effect of acetatic extract of *Morinda morindoides* on arterial hypertension, doses of EAC of *Morinda morindoides* (1000 and 2000 mg/kg bw) and of tenordate (10 and 20 mg/kg bw) are administrated by gavage to rabbits made hypertensive with adrenalin at 1 mg/kg bw. The EAC of *M. morindoides* decreased systolic blood pressure, diastolic blood pressure and heart frequency. The hypertension induced by adrenaline (1 mg/kg bw) is completely inhibited by the EAC of *M. morindoides* at doses of 1000 and 2000 mg/kg bw and Tenordate at 10 and 20 mg/kg bw. The EAC of *M. morindoides* exerts antihypertensive and hypotensive effects on rabbits.

Keywords: *Morinda morindoides*, hypertension, antihypertensive, gavage.

A R T I C L E I N F O

CONTENTS

Article History: Received 18 January 2016, **Accepted** 27 February 2016, **Available Online** 12 April 2016

***Corresponding Author**
Boga Gogo Lucien
Department of Biosciences, Biochemical Pharmacodynamy Laboratory, University Félix Houphouët-Boigny, PO Box 582, Abidjan 22-Côte d'Ivoire, Africa.
Manuscript ID: AJCPR2876

PAPER-QR CODE

Citation: Boga Gogo Lucien, *et al*. Antihypertensive activity of the acetatic extract of *Morinda morindoides* on the arterial hypertension induced by adrenalin in rabbits. *A. J. Chem. Pharm, Res.*, 2016, 4(1): 55-60.

1. Introduction

Cardiovascular diseases including high blood pressure are causing 48% of deaths due to noncommunicable diseases worldwide (1). High blood pressure is the first chronic disease worldwide. She is responsible of 7 to 8 million deaths worldwide (2) and 7% of disability (3). In the world, 40% of adults aged 25 and older had hypertension diagnosed in 2008. In the WHO African Region, 46% of adults aged 25 and over suffer from high blood pressure and this prevalence is from 33.4% in Côte d'Ivoire. This prevalence of hypertension is a major public health problem. The treatment of hypertension, which is based primarily on the use of antihypertensive drugs, reduces mortality and cardiovascular morbidity (4).

However, in developing countries such as Côte d'Ivoire, this treatment remains problematic because of the high cost of these antihypertensive drugs. People then turn to traditional medicine for healing. Several plants used in the treatment of hypertension in Côte d'Ivoire, have been identified (5). This work has focused on *Morinda morindoides*, a Rubiaceae, used by the Dida people (South-West of Côte d'Ivoire) in drug revenues against hypertension. This plant is used in Côte d'Ivoire and in Democratic Republic of Congo in the treatment of diarrhea (6), rheumatism (7), diabetes, malaria, skin rashes, pruritus and microbial infections (8). Boga *et al.* (9) showed that dichloromethane ethanol extract of M. morindoides (ETDE) has antihypertensive effects on Hypertension-induced in rabbits. It is in this work to study the effects of the acetatic extract of *Morinda morindoides* on cardiovascular parameters in rabbits made hypertensive with adrenaline.

2. Materials and Methods

Material

Rabbits of species *Oryctolagus cuniculus* aged eight to twelve weeks were used as animal material and leaves of *Morinda morindoides* were used as plant material. Leaves of *Morinda morindoides* (Baker) Milne-Redh (Rubiaceae) used, were collected from Daloa in the Central West of Côte d'Ivoire. The collection was made between July and August of 2012. The authentication was made by Professor Laurent AKE ASSI through the herbarium of the National Centre of Floristic (CNF), where a specimen was kept under number 10378 of 22-05-1980.

Methods

Preparation of the acetatic extract of *Morinda morindoides*

The acetatic extract of *M. morindoides* was prepared by dissolving 25 g of ethanolic extract (ETOH 70 %) of *M. morindoides* into 1000 mL of ethyl acetate and water mixture (50: 50, V/V) and homogenized during 24 hours at using a magnetic stirrer. After decantation, two phases were obtained, an acetatic upper phase and aqueous residue lower phase. The two layers were collected and evaporated using a Büchi rotary evaporator at 30 ° C. The acetatic upper phase gave a greenish paste and the aqueous lower phase a blackish powder. The acetatic extract obtained was used for experimentation.

Effects of substances on normal blood pressure rabbit

Twenty-five rabbits aged eight to twelve weeks, weighing between 1.5 and 2.5 kg were used for the study of normal blood pressure. After acclimatization for four weeks at the Laboratory of Animal Physiology, animals were divided into five batches of five rabbits each. The animals of group I or control group received throughout the experiment 1 ml of normal saline (NaCl 9 %). Animals of lots 2, 3, 4 and 5 were tests lots or experimental lots. Lots 2 and 3 received the acetatic extract (EAC) at different doses (1000 to 2000 mg / kg.bw) and the lots 4 and 5 of Tenordate at 10 and 20 mg/kg.bw. Before the administration of different substances to rabbits, measurement of normal blood pressure has been made, using sphygmomanometer, in all lots to determine the initial normal blood pressure to day 0. At day 2, day 4, day 6 and day 8, 1 mL of EAC of *Morinda morindoides* at 1000 and 2000 mg/kg.bw and the tenordate at 10 and 20 mg/kg.bw were administrated to the animals using intubation cannula. The blood pressure was properly taken every other day until the 10th day. The normal cardiovascular parameters (systolic blood pressure, diastolic blood pressure and mean arterial pressure and heart frequency) were determined.

Induction and treatment of experimental hypertension

For this experiment, thirty rabbits aged twelve to sixteen weeks, weighing between 1.5 and 2.5 kg were used. These rabbits were acclimatized for four weeks at the Laboratory of Animal Physiology, Faculty of Biosciences, and then divided into six lots of five rabbits each. Before induction of hypertension in animals, the blood pressure was noted in all lots. The animals of lot 1 or control lot received orally 1mL of saline (NaCl 9 ‰) using a cannula, for ten days. All test lots (2, 3, 4, 5 and 6) received by intravenous injection, every day for ten days, 1 mL of adrenaline (ADR) at 3.10^{-2} mg/kg.bw to cause sustained hypertension which stabilized after 10 days of treatment. These made hypertensive animals were treated by the EAC and the Tenordate at different doses. The animals of lot 1 (control lot) received 1 mL of physiological fluid during treatment. Lot 2 is the lot of untreated hypertensive animals (Lot MTN). Animals of this lot received 1 mL of ADR during the treatment period. Animals of Lots 3 and 4 were treated with the EAC to 1000 and 2000 mg/kg.bw; those lots 5 and 6 were given by oral way, 1 ml of Tenordate at 10 and 20 mg/kg.bw. The cardiovascular parameters of the animals were measured the days of treatment but before the treatment, during 7 days.

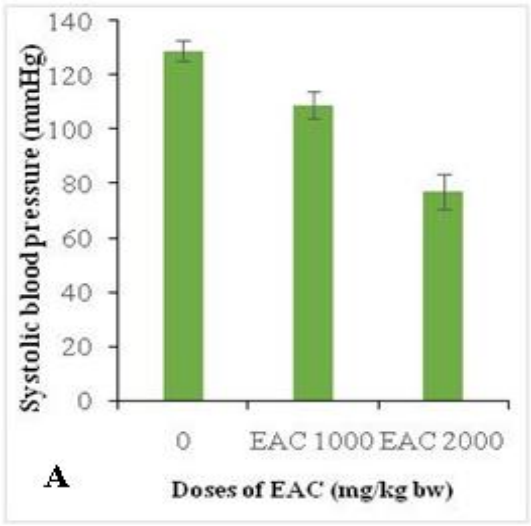
3. Results and discussion

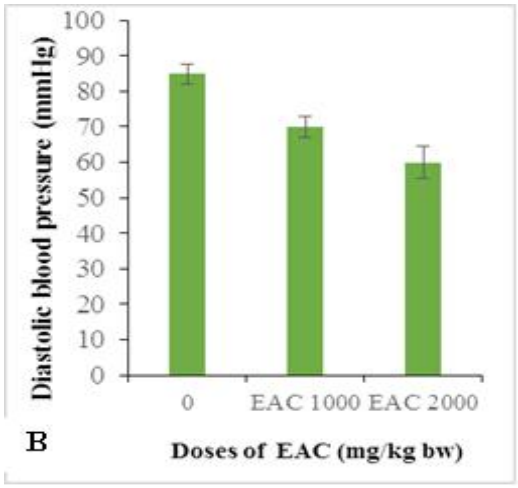
In-vivo dose-response effect of the acetatic extract of *Morinda morindoides* and Tenordate on blood pressure and heart frequency

The histograms of figure1: A, B, C and. Figure 2: D, E, F respectively show typical results of the dose-response

effects of acetatic extract (EAC) of *M. morindoides* and Tenordate (a reference antihypertensive) on the variation of systolic blood pressure, diastolic blood pressure and heart frequency of rabbits. The normal value of the systolic blood pressure determined in the experimental conditions is 129 ± 4 mmHg, the diastolic blood pressure is 85 ± 2,8 mmHg; the value of the heart frequency in the same experimental conditions is 401 ± 5 beats per minute. Administrated by oral way, the doses of 1000 and 2000 mg/kg.bw of EAC of *M. morindoides* then 10 and 20 mg/kg.bw of Tenordate, respectively involved in rabbits, a progressive reduction and proportions dependent on the systolic blood pressure and diastolic or hypotension. The value of the normal systolic blood pressure unregistered dropped by 129 ± 4 mmHg with 109 ± 5 mmHg (15,50 %) for the EAC 1000, and 77 ± 6,2 mmHg for the EAC 2000 (40,31 %). As for the diastolic blood pressure, it fell of 85 ± 2,8 mmHg with 70 ± 3 mmHg (17,64 %) for the EAC 1000 and with 60 ± 4,5 mmHg (29,41 %) for the EAC 2000.

The normal values of the heart frequency also underwent a reduction. They evolved/moved of 356 ± 5 beats / min with 345 ± 4 beats/min (3,09%) for the EAC 1000 and with 338 ± 6 beats/min (5,05 %) for the EAC 2000 (**Figures 1: A, B,** C). The similar values were obtained with Tenordate.





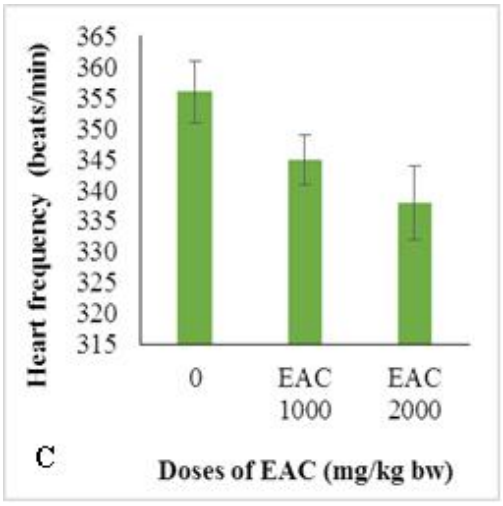
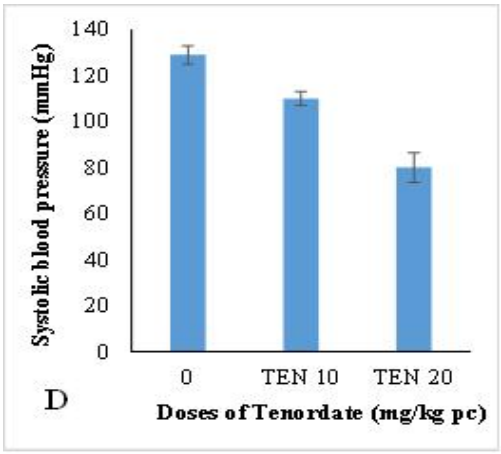
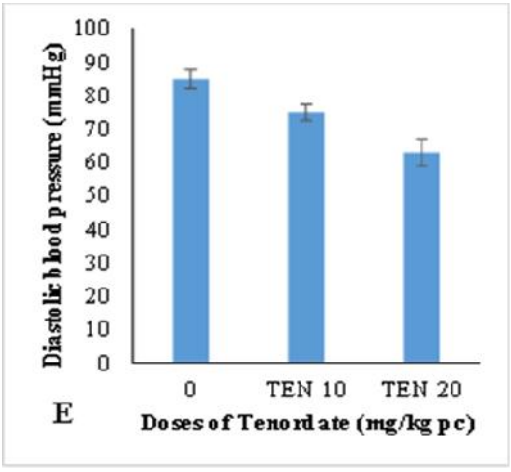


Figure 1: Effects of the acetatic extract of Morinda morindoides on normal arterial pressure of rabbits

A: Effect on the Systolic blood pressure (SBP) in mmHg;
B: Effect on the diastolic blood pressure (DBP) in mmHg;
C: Effect on the heart rate (beats/ min)

The various doses of the EAC of M. morindoides (1000 and 2000 mg/kg bw) cause a fall of these various cardiovascular parameters or hypotension compared to the control lot. The EAC of M. morindoides decreases considerably the contractile activity of the heart of rabbit. Its effects on the heart are comparable to those of β-blocking





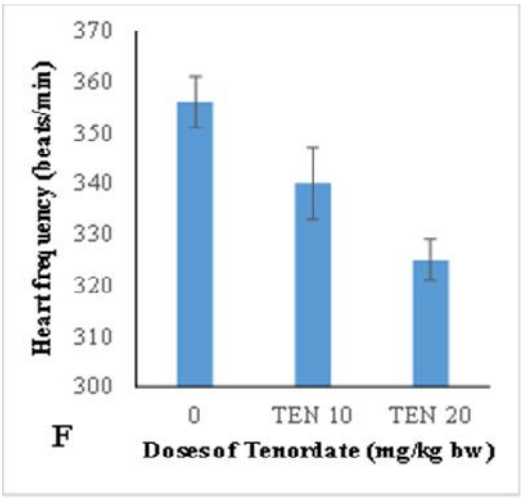


Figure 2: Effects of Tenordate (TEN) on the normal blood pressure

D: Effect on the systolic blood pressure (SBP) in mmHg
E: Effect on the diastolic blood pressure (DBP) in mmHg;
F: Effect on the heart frequency (beats / min)

The various doses of TEN (10 and 20 mg/kg bw) cause a reduction of these cardiovascular parameters or a hypotension compared to the control lot.

***In-vivo* antihypertensive effects of the acetatic extract of *Morinda morindoides* and Tenordate on the blood pressure and the heart frequency of hypertensive rabbits**

Histograms of figure 3: **G, H, I** and **J** show the *in vivo* antihypertensive activities of the acetatic extract (EAC) of *M. morindoides* and of Tenordate on the variation of the systolic blood pressure, the diastolic blood pressure, the average blood pressure and the heart frequency of rabbits

The pilot values of the systolic blood pressure, the diastolic blood pressure, the average blood pressure and the heart frequency are respectively: 123,5 ± 6 mmHg; 107,15 ± 4mmHg, 112,6 mmHg and 413 ± 6,8 beats/min. The values of the systolic blood pressure, the diastolic blood pressure, the average pressure and the heart frequency of the hypertensive sick animals untreated (Lot MNT) are: 180 ± 8 mmHg; 160 ± 6 mmHg; 166 mmHg and 508 ± 9 beats/min.

The treatment of the hypertensive animals by the acetatic extract of *M. morindoides* at doses of 1000 and 2000 mg/kg.bw and by Tenordate at doses of 10 and 20mg/kg.bw, cause a progressive diminution of the values of the systolic blood pressure, the diastolic blood pressure, the average blood pressure and the heart frequency until the standardization of those. The systolic pressure passes from 180 ± 6 mmHg to 125,76 ± 4 mmHg; the diastolic pressure evolves of 160 ± 7 mmHg with 107,12 ± 9 mmHg; the average pressure of 166 mmHg with 113,58 mmHg and the heart frequency varies from 508 ± 9 beats/min to 413 ± 7 beats/min. The respective percentages of reduction are 69, 44 % for the systolic blood pressure, 66,874 % for the diastolic blood pressure, 68 % for the average pressure and 81, 30 % for the heart frequency.

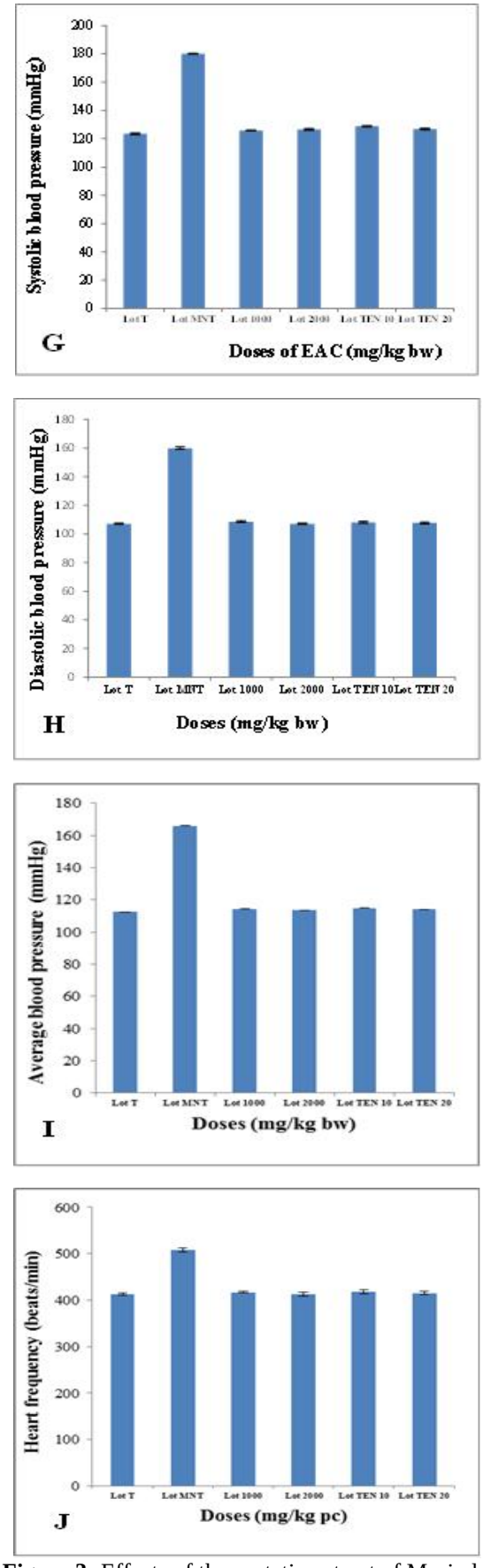


Figure 3: Effects of the acetatic extract of Morinda morindoides and Tenordate on the variation of cardiovascular parameters of hypertensive rabbits

G: Effect on the Systolic blood pressure (SBP) in mmHg;
H: Effect on the diastolic blood pressure (DBP) in mmHg;
I: Effect on the average blood pressure (ABP) in mmHg
J: Effect on the heart frequency (HF) in bbm

The data are expressed by average ± SEM., (n=5).Control lot = lot T, Lot MNT = lot of the untreated sick animals; EAC 1000 = lot of the hypertensive animals treated with the EAC at 1000 Mg/kg bw, EAC 2000 = lot of the hypertensive animals treated with the EAC at 2000 mg/kg bw, TEN 10 = lot of the hypertensive animals treated with the tenordate at 10 Mg/kg bw and TEN 20 = lot of the hypertensive animals treated with tenordate at 20 mg/kg bw

Discussion

The study of the influence of acetatic extract of *M. morindoides* on blood pressure of rabbits in comparison with that of Tenordate, the results showed that the acetatic extract of *M. morindoides* induced in rabbits, a dose-dependent hypotension. The EAC *M. morindoides* decreased systolic blood pressure, diastolic blood pressure and heart frequency that suggested that this extract contains hypotensive compounds. These results are comparable to those obtained with dichloromethane-ethanol extract of *Morinda morindoides* (9). Moreover, these results also showed that adrenalin (ADR) at 1mg/kg bw induced hypertension in rabbits. ADR exerts its hypertensive effect through the intermediary of two receptor subtypes: vascular alpha adrenergic receptor and cardiac receptor beta1 adrenergic (10). On blood vessels, epinephrine stimulates alpha-adrenergic receptors and induces vasoconstriction responsible for the observed hypertension (11,12). On the heart, the stimulation receptor beta1 adrenergic causing inotropic and chronotropic positive effects (12) that would result in an increased blood volume and hence blood pressure. The hypertension induced by adrenaline (1 mg/kg bw) is completely inhibited by EAC of *M.* morindoides at doses of 1000 and 2000 mg/kg bw and Tenordate at 10 and 20 mg/kg bw. This suggests that EAC of *M. morindoides* contain compounds that have anti-hypertensive effects. The antihypertensive effects resemble those of extracts of *Hibiscus sabdariffa* on rats (13) and of aqueous extract of *M. morindoides* (14) on rabbits. These authors showed that treatments of hypertensive rats and rabbits by aqueous extracts of *Hibiscus sabdariffa* and of *Morinda morindoides* normalize their cardiovascular parameters. The treatment of hypertensive rats by EAC of *M. morindoides* and ténordate® significantly reduced and normalized cardiovascular parameters. These results agree with those obtained with dichloromethane-ethanol extract of *M. morindoides* (9).

The EAC *M. morindoides* as the Tenordate (a reference antihypertensive), exerts antihypertensive and hypotensive, this could push for the use of the EAC in the treatment of hypertension.

4. Conclusion

The study of the effect of the EAC *Morinda morindoides* on blood pressure of healthy rabbits showed that this extract exerts a dose-dependent hypotension on blood pressure of these animals. At doses of 1000 and 2500 mg/kg bw, EAC *Morinda morindoides* like the Tenordate at a dose of 20 mg/kg bw, restore cardiovascular parameters (SBP, DBP, MAP) increased by high blood pressure. These results reflect the antihypertensive effect of the EAC *Morinda morindoides* that could, by this fact, be of great interest in the treatment of high blood pressure

5. References

[1] WHO, 2012. - World health statistics 2012. 176p.
[2] Blacher J., Halimi JM, Hanon O, Mourad JJ, Pathak A, Schnebert B, Girerd X. Prise en charge de l'hypertension artérielle de l'adulte. Recommandations 2013 de la société française d'HTA. *Presse Med* , 2013, 25 (5): 297-305
[3] Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Barker-Collo S. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, 2012, 380(9859): 2095-2128.
[4] Elsik M, Krum H. Hypertension: how to go? *Austr. Presc.* 2007, 30: 6.
[5] Tra bi FH, Irié MG, N'gaman CCK, Mohou HBC. Etudes de quelques plantes thérapeutiques utilisées dans le traitement de l'hypertension artérielle et du diabète : deux maladies émergentes en Côte d'Ivoire. *Sci. Nat.*, 2008, 5(1): 39-48.
[6] Bahi C, N'Guessan JD, Guédé-Guina F. Mise en évidence d'une action myorelaxante et cholinolytique de BITTER GG (BGG), un antidiarrhéique de source végétale. *Afrique Biomedicale*, 2000, 3: 25-36.
[7] Cimanga K, Hermans N, Sandra A, Van M. S., Hilde VDH., Magda C, Luc P, VLietinck AJ. Complement inhibiting Iridoids from*Morinda morindoides*. *J. Nat Prod.*, 2003, 66: 97-102
[8] Mankele K, Ouamba JM, Abena AA, Yala F. Etudes des effets de *Morinda morindoïdes* (Baker) sur le système immunitaire de l'homme. *Phytothérapie*, 2006, 4: 68-73.
[9] Boga GL, Trebissou ND, Bahi C, Kouangbé MA, Zirihi GN. Effect of dichloromethane-ethanol extract of *Morinda morindoides* (Baker) Milne-redhead (Rubiaceae) (ETDE) on rabbit carotid blood pressure. *IJABPT*, 2013, 4: 158-165.
[10] Ahlquiest R.P. Adrenoreceptors from figment to fact In: Trends in autonomic Pharmacology. Kalsner 2. Baltimore-Munich, *Urban and Scharzenberg***,** 1982, pp3-13.
[11] Cohen MW, Jacobson C, Yurchenco PD., Morris GE, Carbonetto S. Laminin-induced clustering of distroglycan on embryonic muscle cells: comparison with agrin-induced clustering. *Journal of Cell Biology*, 1997, 136: 1047-1058.

[12] Almange C. 1998. "Introduction à la thérapeutique cardiologique." from www. Med.univ.rennes1.fr :cardio /therapeutique.htm. .

[13] Mojiminiyi F. B. O., Dikko M., Muhammad B. Y., Ojobor P. D., Ajagbonna O. P., Okolo R. U., Igbokwe U. V., Mojiminiyi U. E., Fagbemi M. A., Bello S. O, Anga T. J. Antihypertensive effect of an aqueous extract of the calyx of *Hibiscus sabdariffa*. *Fitoterapia*, 2007, 78: 292-297.

[14] N'Guessan JD, Trebissou ND, Bahi C, Zirihi GN, Guede-Guina F. Effet de BGG, F5 (fraction chromatographique de *Morinda morindoïdes*) sur la pression artérielle carotidienne de lapin. *Rev Med Pharm Afr*, 2004, 18: 1-10.