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EFFECT OF THE EXTRACT OF A MEDICINAL RECIPE ON ALCOHOL AND TOBACCO INDUCED HYPERTENSION

Etou Ossibi A. W.[1]*, Ngolo E.[1], Elion Itou R. D. G.[1], Mboungou Bouesse B.[1], Ouamba J. M.[2] and Abena A. A.[1]

[1]Laboratoire de Biochimie et Pharmacologie, Faculté des Sciences de la Santé, Université Marien Ngouabi, Congo.

[2]Unité de Chimie du Végétal et de la Vie, Faculté des Sciences et Techniques, Université Marien Ngouabi, Congo.

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***Corresponding Author**
Dr. Etou Ossibi A.W.
Laboratoire de Biochimie et Pharmacologie, Faculté des Sciences de la Santé, Université Marien Ngouabi, Congo.

ABSTRACT

The objective of this study was to evaluate the effects of the aqueous extract of a recipe based on *Brillantaisia patula* T. Anderson and *Desmodium velutinum* (Willd) D.C leaves on alcohol (ethanol 30°) and tobacco (Fine brand cigarette) induced high blood pressure (hypertension). Female rats were treated daily with ethanol 30° for eight weeks to induce hypertension; and then for four additional weeks in conjunction with the recipe (250 and 500 mg/kg/j, p.o). In another model, female rats were pretreated every day for three days with the aqueous extract of the recipe (250 and 500 mg/kg/j, p.o). On the fourth day, they were exposed to smoke of 'Fine' cigarette for an hour. In the two models, the SBP (systolic blood pressure) and the HR (heart rate) were measured using the invasive method. In the ethanol model, serum biochemistry was measured using R Vesir II type machine (automaton). The results obtained showed SBP and HR values substancially low in treated rats to the recipe at both doses in comparison with those of rats treated with ethanol 30° + distilled water. That recipe tended to reduce the SBP and the HR in rats exposed to cigarette smoke. In addition, at doses of 250 and 500 mg/kg, it opposes considerably the increased levels ($p < 0.05$) of LDL-c (low density lipoprotein) and serum glucose; and triglycerides at 250 mg/kg. Those results suggested that the recipe had an antihypertensive effect that could justify its use in traditional medicine for high blood pressure.

KEYWORDS: Recipe, ethanol 30°, tobacco, hypertension (high blood pressure).

INTRODUCTION

Hypertension is a worldwide public health problem causing strokes. Researchers estimate that hypertension kills nine million people a year. Among the risk factors for hypertension, there are alcohol and tobacco (Primatesta, 2001). WHO in its objective " health for all in the 21st century" by using primary health care considered as a policy for the African region (OMS/AFRO, 2002), encourages African States to use traditional medicine (OMS/AFRO, 2001). In the Congo, many medicinal plants are used in traditional medicine to treat various pathologies including hypertension. Among these plants, there are Brillantaisia *patula* T. Anderson (*B. patula*) and *Desmodium velutinum* (Willd) D.C (*D. velutinum*) used as a recipe to treat the hypertension. A previous study, in the cardiovascular study, has showed the hypotensive effect of the aqueous extract of the recipe based on leaves from two different plants (Ngolo et al., 2018). Those data supported the hypothesis that our recipe had antihypertensive proprieties. The purpose of this study is thus to evaluate the effects of the aqueous extract of the recipe based on leaves from *B. patula* Anderson and *D. velutinum* (Willd) D.C on the models of ethanol 30° and tobacco induced hypertension in the Wistar rat.

MATERIAL AND METHODS

Plant material

The dried leaves of *B. patula*T. Anderson and *D. velutinum* (Willd) D.C were used. Those leaves were harvested at Makana, located about 56 km south of Brazzaville. Leaf samples of each plant were identified and compared to the respective reference samples, numbers 1384 and 636 of the National institute of Research in Exact sciences and Natural (IRSEN) herbarium. Leaves of both plants were dried at room temperature (28 ± 1 °C), out of the sun for two weeks and then pulverized using a wooden mortar.

Animal material

Female rats of Wistar strain aged 17-21 weeks, which weighed between 150 and 175 g were used. Those rats were provided by the pet shop of the Technology and Faculty of Science of the Marien Ngouabi University (Congo-Brazzaville). They were raised under standard temperature of the air conditions of approximately 28 ± 1°C on a 12 hours of day and 12 hours of night photoperiod cycle.

Preparation of the aqueous extract of the recipe

The recipe was prepared by maceration at 10%. Thus, 100 g of powdered leaves (50 g of *B. patula* and 50 g of *D. velutinum*) were left in maceration in 1000 mL of distilled water for sixty-two hours. The macerated obtained was triple filtered using hydrophilic cotton and then, the filtrate obtained was evaporated to dryness in a rotary evaporator of RII Buchi brand. The powder obtained was used as the aqueous extract of the recipe for the antihypertensive tests.

Evaluation of the antihypertensive effect by the ethanol model

Preparation of the ethanol 30°

The ethanol at 30°C was prepared by diluting 100 mL at 90° in 206.22 mL of distilled water according to Gay Lussac table, (2009).

Induction of the hypertension by the ethanol and treatment of rats using the aqueuos extract of the recipe

The protocol described by Miniand Rajamohan, (2013) amended and based on the one described by Etou Ossibi, (2012) on the induction of the hypertension by the DOCA-salt was used. For that purpose, twenty-five (25) rats were used. Five (5) rats (group 1) received distilled water (1 mL/100g/j, p.o) for twelve (12) weeks. Twenty (20) other rats received ethanol 30° at the rate of 2 mL/100g/j, p.o for eight (8) weeks. At the end of eight (8) weeks, the twenty (20) rats were divided into four (4) lots of five (5) rats each and treated for four (4) additional weeks as follows:

- Group 2 received ethanol 30˚ (2 mL/100g/j, p.o) + distilled water (1 mL/100g/j, p.o);
- Groups 3 and 4 received ethanol 30˚ (2 mL/100g/j, p.o) + the aqueous extract of the recipe at doses of 250 and 500 mg/kg/j. p.o respectively;
- Group 5 received ethanol 30˚ (2 mL/100g/j, p.o) + furosemide (40 mg/kg/j, p.o).

The weight, the animals water and food consumption were noted at the end of every week for the twelve (12) weeks of study. At the end of the treatment, the SBP and the HR were measured by the invasive method using MP36-type Biopac student and then the animals were sacrificed by decapitation (Etou Ossibi, 2010).

The arteriovenous blood was collected into dry tubes for the determination of risk biochemical parameters of the hypertension using conventional methods of biochemistry with the aid of an automaton.

Evaluation of the antihypertensive effect by the tobacco model

The method described by Yeo et al., (2008) was used. Fifteen (15) rats divided into three (3) lots of five (5) rats each were pretreated in the following way:

- The control group 1 received distilled water (1 mL/100 g/j, p.o)
- Groups 2 and 3 received the aqueous extract of the recipe at respective doses of 250 and 500 mg /kg.

After three days of pretreatment, the rats were placed individually in cages exposed to cigarette smoke ("Fine" cigarette produced by SIAT Company in Congo) for an hour. After an hour, the effects of the aqueous extract of the recipe on the SBP and the HR were measured by the invasive method (Etou Ossibi, 2010).

Statistical analysis

The results are expressed as average affected by standard error (M±ESM). The comparison of the averages of the measures between lots was made by the Student t test. The significance level was set at $p < 0.05$.

RESULTS

Antihypertensive effect by the ethanol 30° model

Effects of the aqueous extract of the recipe on the weight situation

Figure 1 shows that the administration of the ethanol 30° caused a gradual decline in body weight in rats at 94.31 ± 13.41 % ($p < 0.001$) in the 12th week compared with rats that only received distilled water (168.12 ± 24.17 %). However, in rats that received ethanol 30° plus the aqueous extract of the recipe at doses of 250 and 500 mg/kg or with the furosemide 20 mg/kg. There was a weight gain at 113.76 ± 10.08 ($p < 0.001$), 139.38 ± 6.71% ($p < 0.001$) et 120.80 ± 4.61 % ($p < 0.001$) respectively compared with rats treated with ethanol 30° plus distilled water (94.31 ± 13.41 %).

Effect of the aqueous extract of the recipe on food and fluid intake

Figure 2 shows that the aqueous extract of the recipe caused a decrease in food consumption in rats given ethanol 30° plus distilled water compared to control rats (distilled water) for the first eight (8) weeks. The administration of the aqueous extract of the recipe (250 and 500 mg/kg) caused from the 9th week a significant increase in food consumption of rats treated with chronic ethanol 30° administration. Concerning water intake, a decrease was noted (except at the 3th and 7th week) in rats treated with ethanol 30° compared with control rats

that received distilled water (Figure 3). However, the administration of the extract at 250 mg/kg and furosemide at 20 mg/kg caused an increase in water consumption in rats treated with ethanol 30° (Figure 39).

Effects on systolic blood pressure and heart rate

Figure 4 shows that the administration of ethanol 30° for 12 weeks to normotensive rats resulted in an increase in SBP from 119.79 ± 5.28 to 159.61 ± 3.70 mmHg ($p < 0.001$) in rats that only received ethanol 30°. However, the administration of ethanol 30° plus the aqueous extract of the recipe at doses of 250 and 500 mg/kg reduced the SBP at 110.05 ± 11.06 ($p < 0.001$) and 128.73 ± 22.45 ($p < 0.01$), respectively versus 159.61 ± 3.70 mmHg in rats given ethanol 30° only. The percentages of decrease were 31.05 and 19.34%, respectively. Furosemide at 20 mg/kg also significantly reduced ($p < 0.001$) the SBP. With respect to HR, Figure 5 shows no significant variation in HR in rats treated with ethanol 30° plus distilled water compared to control rats (water distilled). However, there was a significant decrease in HR in rats treated with ethanol 30° plus aqueous extract of the recipe at 250 mg/kg (227.27 ± 19.09 BPM; $p < 0.001$) or plus the furosemide at 20 mg/kg (256.41 ± 32.00 BPM; $p < 0.001$) relative to ethanol 30° (314.13 ± 68.01 BPM) hypertensive rats, that is the percentages of decrease of 27.65 and 18.37 %, respectively.

Effects of the aqueous extract of the recipe on biochemical parameters in rats

Table I shows the effects of the aqueous extract of the recipe on the biochemical parameters in rats treated with ethanol 30°. It was noted that the administration of ethanol 30° caused a significant increase in serum of the ALT and the AST and a decrease in total cholesterol level. These levels increased from 3.92 ± 1.31 to 60.36 ± 30.33 IU/L ($p < 0.001$); from 8.20 ± 3.14 to 234.83 ± 88.25 IU/l ($p < 0.001$) and from 745.38 ± 0.50 to 549.28 ± 0.50 IU/l ($p < 0.001$), respectively. In rats given ethanol 30° plus the aqueous extract of the recipe at 250 and 500 mg/kg, serum ALT levels were reduced to 52.66 ± 0.5 mg/kg 1.60 ($p < 0.01$) and 36.84 ± 0.44 IU/l ($p < 0.001$) and AST at 102.71 ± 14.69 ($p < 0.001$) and 115.92 ± 27.38 IU/l ($P < 0.001$), respectively compared to rats treated with ethanol 30° plus distilled water. Concerning the total cholesterol level, a decrease at 441.28 ± 38.29 IU/l was noted ($p < 0.01$) in rats treated with ethanol 30° plus distilled water compared to control rats. The aqueous extract of the recipe (250 and 500 mg/kg) was opposed, but not significantly, to this cholesterol lowering caused by ethanol. At both doses, this recipe caused insignificant changes in serum TG, creatinine and glucose levels.

Antihypertensive effect by the tobacco model (Fine brand)

Figure 6 shows that the SBP increased from 119.79 ± 21.23 mmHg (in control rats) to 146.41 ± 22.32 mmHg in rats given distilled water (1 mL/100 g) and then exposed to the tobacco smoke. However, in rats exposed to tobacco smoke and pre-treated with the recipe (250 and 500 mg/kg) there is a reduction in SBP at 126.37 ± 33.33 ($p < 0.001$) and 139.40 ± 17.88 ($p < 0.01$) respectively; that is the percentage decreases of 13.68, and 4.78 %, respectively. With respect to HR, Figure 7 shows no significant variation in HR in rats who were given distilled water and then exposed to tobacco smoke compared to the control rats (water distilled). However, there was a significant decrease in HR in rats exposed to the tobacco smoke and pre-treated with the recipe (250 and 500 mg/kg) at 275.04 ± 66.67 ($p < 0.05$) and 288.57 ± 21.89 beats/min ($p < 0.05$) respectively compared to hypertensive rats by exposure to tobacco smoke (301.97 ± 56.67 beats/min); that is percentages of inhibition of 8.91% and 4.43% respectively.

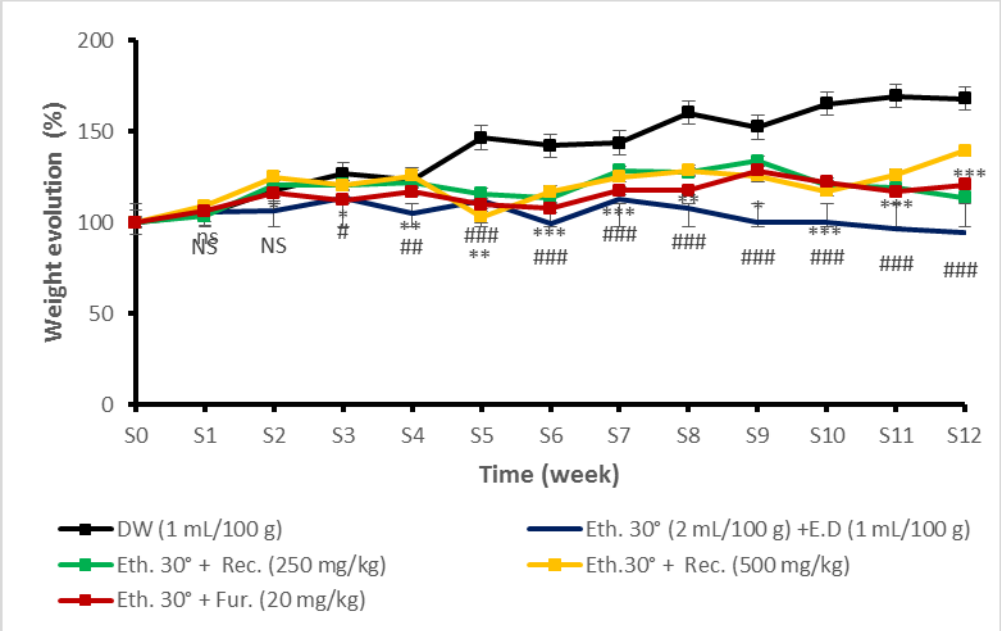

Figure 1: Evolution of rat weight as a function of time. Each value is an average ± SEM, with n = 5; $^{\#}$ $p < 0.05$, $^{\#\#}$ $p < 0.01$, $^{\#\#\#}$ $p < 0.001$, significant difference from control (distilled water);*$p < 0.05$, **$p < 0.01$, *** $p < 0.001$ significant difference from control (ethanol + distilled water); NS non-significant difference from control (distilled water) ns: non-significant difference from control (ethanol + distilled water). DW: Distilled water; Eth.: Ethanol; Rec: Recipe; Fur: Furosemide.

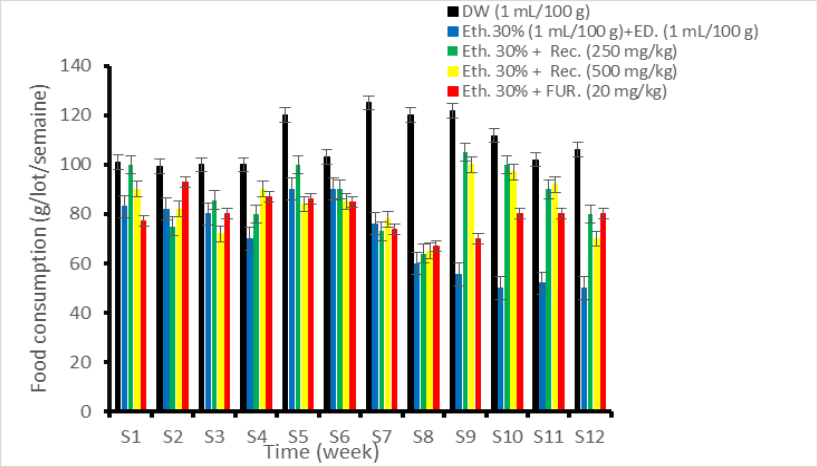

Figure 2: Effect of wood intake in rats as a function of time. DW: Distilled water; Eth.: Ethanol; Rec: Recipe; Qui: Quinapril; Syl: Sylimarin.

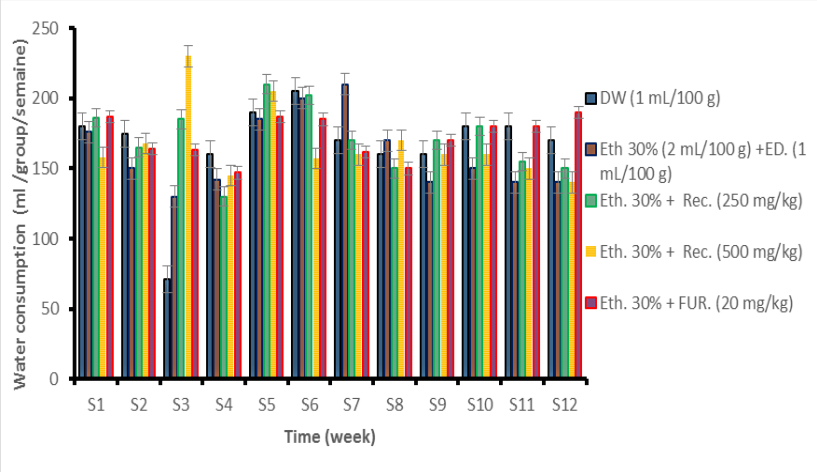

Figure 3: Effect of water intake in rats as a function of time. DW: Distilled water; Eth.: Ethanol; Rec: Recipe; Qui: Quinapril; Syl: Sylimarin.

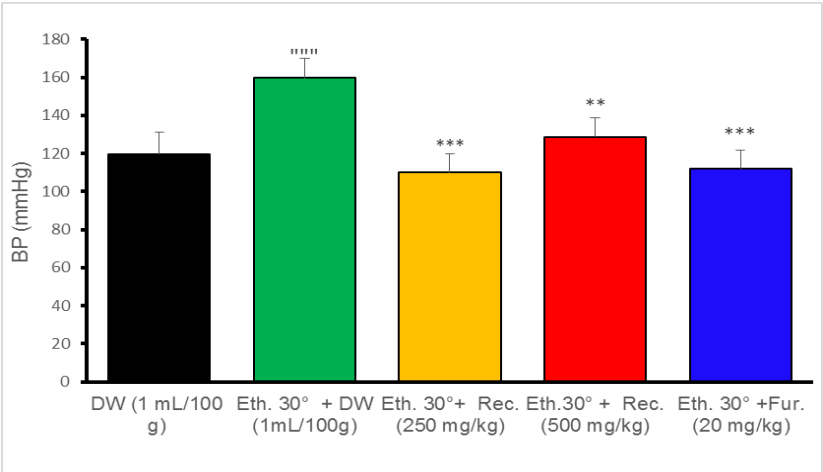

Figure 4: Effect of the aqueous extract of the recipe on blood pressure (BP) in rats treated with ethanol 30 °. Each value is a mean ± SEM, with n = 5; ###p <

0.001 significant difference from the control (distilled water); ** p < 0.01, *** p < 0.001 significant difference from the control (ethanol + distilled water); DW: Distilled water; Eth.: Ethanol; Rec.: Recipe; Fur: Furosemide.

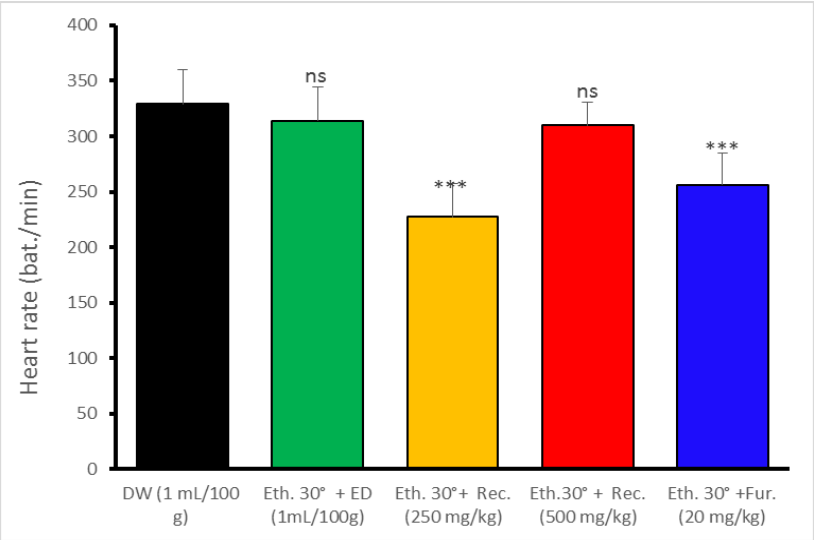

Figure 5: Effect of the aqueous extract of the recipe on heart rate in rats treated with ethanol 30 °. Each value is a mean ± SEM, with n = 5; ** p < 0.01, *** p < 0.001 significant difference from the control (ethanol + distilled water); NS: non-significant difference from the control (ethanol + distilled water); ED:distilled water; Eth.: Ethanol; Rec.: Recipe; Fur: Furosemide.

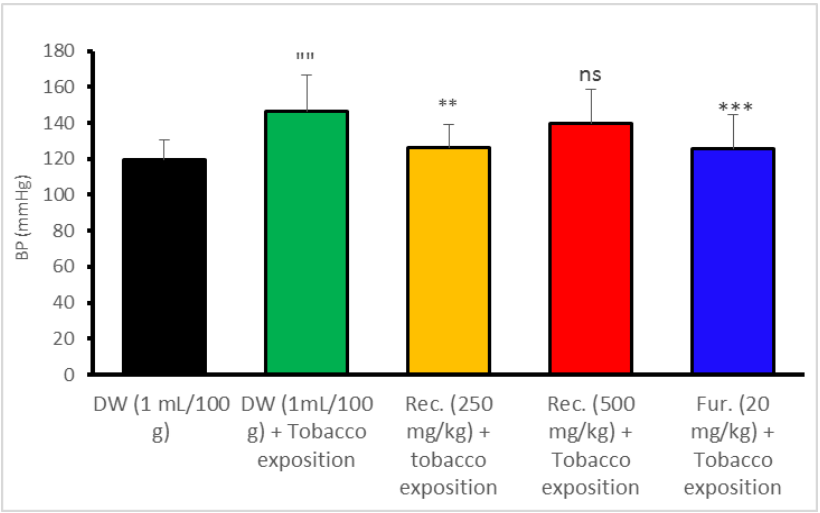

Figure 6: Effects of the aqueous extract of the recipe on blood pressure (BP) in rats exposed to tobacco smoke. Each value is a mean ± SEM, with n = 5; ## p < 0.05 significant difference from the control (distilled water); * p < 0.05; significant difference from the control (distilled water + tobacco); DW: Distilled water; Rec.: Recipe.

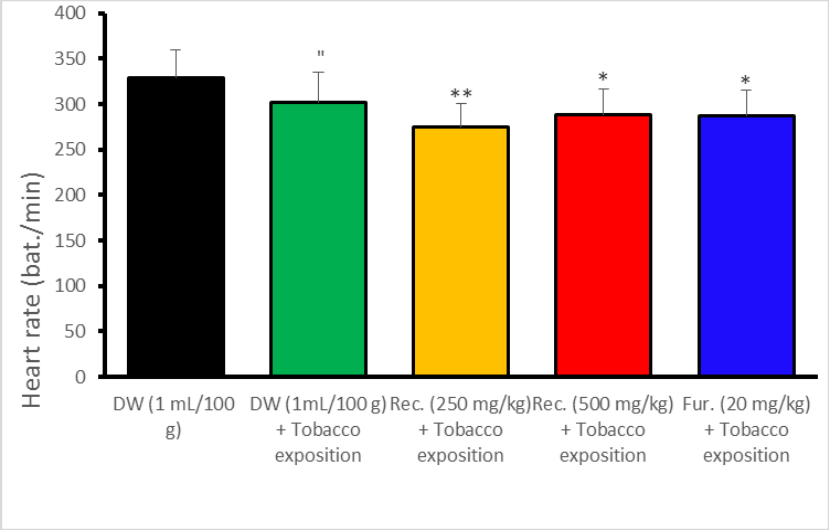

Figure 7: Effects of the aqueous extract of the recipe on the heart rate in rats exposed to tobacco smoke. Each value is a mean ± ESM, with n = 5; # p < 0.05 significant difference from the control (distilled water); * p < 0.05; significant difference from the control (distilled water + tobacco); DW: Distilled water; Rec.: Recipe.

Table I: Effect of the aqueous extract of the recipe on biochemical parameters in the rat.

Biochemical parameters	Treatments				
	DW 1mL/100g	Eth.30%+ED (1 mL/100g)	Eth.30%+Rec. (250 mg/kg)	Eth.30%+Rec. (500 mg/kg)	Eth.30%+Fur. (20 mg/kg)
ALT (UI/l)	3.92 ± 1.31	60.36 ± 30.33 ###	52.66 ± 1.60 **	36.84 ± 0.44 ***	8.84 ± 1.69 ***
AST (UI/l)	8.20 ± 3.14	234.83 ± 88.25 ###	102.71 ± 14.69 ***	115.92 ± 27.38 ***	147.40 ± 17.95 ns
TG (g/l)	2.15 ± 0.24	1.78 ± 0.03 NS	1.74 ± 0.18 ns	2.08 ± 0.11 ns	1.60 ± 0.44 ns
T. Chol (UI/l)	745.38 ± 0.50	441.28 ± 38.29 ###	482.42 ± 28.29 ns	476.56 ± 50.50 ns	730.36 ± 119.67 **
Creat. (g/l)	8.94 ± 1.79	2.52 ± 0.88 NS	5.48 ± 9.70 ns	4.16 ± 0.07 ns	6.72 ± 2.29 ns
GLY (g/l)	1.06 ± 0.33	0.52 ± 0.19 NS	0.47 ± 0.03 ns	0.47 ± 0.03 ns	1.70 ± 0.74 ns

Each value is a mean ± ESM, with n = 5; ###p < 0.001 significant difference from the control (distilled water); ** p < 0.01, *** p < 0.001 significant difference from the control (ethanol + distilled water); NS: non-significant difference from the control (distilled water); ns: non-significant difference from the control (ethanol + distilled water). DW: Distilled water; Eth.: Ethanol; Rec.: Recipe; Fur: Furosemide; ALT: Alanine aminotransferase; AST: Aspartate aminotransfrase; TG: Triglyceride; T. Chol: Total Cholestrol; Creat.: Creatinine; GLY: Glycemia

DISCUSSION

The antihypertensive effect of the aqueous extract of the *B. patula* T. Anderson and *D. velutinum* (Willd) D.C. leaves recipe was evaluated in two models of hypertension in the

female wistar rat. The results obtained showed that that recipe opposes the loss of weight caused by ethanol 30° in rats. It has been reported that chronic administration of ethanol 30° inhibits the appetite (Lieber, 2000); that would explain the low consumption of food and therefore the weight loss in rats treated with ethanol 30° + distilled water. The high food intake in rats treated with this recipe at both doses compared to the control rats (ethanol 30° + distilled water) could partly explain the weight gain in the rats of those lots.

The high water intake in ethanol-treated rats plus the aqueous extract of the recipe (250 and 500 mg/kg) compared to control rats (ethanol 30° plus distilled water) could be explained by the fact that ethanol developed a diuretic action which leads to an intense thirst after dehydration compared with the aqueous extract of the recipe based on the *B. patula* T. Anderson and *D. velutinum* (Willd) D.C leaves could stimulate. The present study shows that chronic administration of ethanol does indeed leads to a liver activity dysfunction resulting in elevated transaminase levels (ALT and AST) in accordance with the results of previous studies carried out on the same model (Nadejzda and al., 2007; Yun and al., 2007). The administration of the recipe (250 and 500 mg/kg) significantly reduced ($p < 0.001$) the serum transaminase levels compared to rats treated with ethanol 30° plus distilled water. This result suggests that this recipe would protect the liver from ethanol toxicity.

However, the aqueous extract from the recipe based on the leaves of *B. patula* T. Anderson and *D. velutinum* (Willd) D.C. has no significant effects on triglyceride, total cholesterol, creatinine and glucose levels.

Excessive alcohol consumption is a contributing factor in the elevation of blood pressure and is an important cause of secondary hypertension (Luther, 1985).

In this model of induction of hypertension by ethanol 30°, it was shown that the everyday administration of ethanol 30° resulted in a significant increase in systolic blood pressure for twelve (12) weeks and a significant decrease in heart rate in normotensive rats. This increase in systolic blood pressure is consistent with the work of Leonardo et al. (2006). For these authors, the installation of hypertension following chronic consumption of ethanol would be due to an increase in the secretion of hormones and neurotransmitters that stimulate the sympathetic nervous system, the myogenic mechanism involving the alteration of the contractile properties of the vascular smooth muscle and the alteration of baroreceptor activity in rats.

The administration of the recipe (250 and 500 mg/kg) reduced the systolic blood pressure to normal values. These results showed that the aqueous extract of the recipe has an antihypertensive effect. That effect could be explained by the negative chronotropic effect of that recipe. Indeed, the results of the present study shows that this recipe accentuates the decrease in heart rate, especially at the dose of 250 mg/kg. In addition, a previous study has showed that Intravenous administration of this recipe caused a decrease in heart rate in the normotensive rat (Ngolo et al., 2018).

In the second model of hypertension induction by tobacco, the obtained results showed that the aqueous extract of the recipe based on the leaves of *B. patula* T. Anderson and *D. velutinum* (Willd) D.C. (250 and 500 mg/kg) opposes the increase in SBP caused by tobacco. This recipe therefore has an antihypertensive effect.

It is known that tobacco (through nicotine) can raise blood pressure by a chronic blocking effect of the cardiac baroreflex sensitivity (permanent sympathetic activation, activation of endocrine systems, increase in peripheral vascular resistance). Thus, in both models, the antihypertensive effect of this recipe could be explained by its interference with the sympathetic system via adrenaline. Indeed, a previous study has shown that prior intravenous administration of this recipe (20 mg/kg) prevents the adrenaline-induced increase in SBP at 50 µg/kg in normotensive rats (Ngolo and al., 2018).

CONCLUSION

The results of the present study show that the aqueous extract of the recipe based on *B. patula* T. Anderson and *D. velutinum* (Willd) D.C leaves protects the liver against the hepatotoxic effect of alcohol and has an antihypertensive effect on models of hypertension induction by ethanol 30° and tobacco. The effect of the two inducers of hypertension used in this study also involves the stimulation of vascular smooth muscle. Thus, a study of the effects of this recipe on aortic rings deserves to be carried out in order to further elucidate the mechanisms antihypertensive action of this recipe.

REFERENCES

1. Gay-Lussac. Table pour la dilution de l'alcool (table de Gay-Lussac), 2009.
2. Leonardo B.M.R., Tirapeli C.R., Lanchote V.L., Uyemura S.A., de Olivrira A.M., Corre F.M.A. Chronic ethanol consumption alters cardiovascular functions in conscious rats. Life Sciences, 2006; 78: 2179-2187.

3. Lieber C. Alcohol its metabolism and interaction with nutrients, Annu Rev Nutr., 2000; 20: 395-430.
4. Luther T. Alcoholic-induced hypertension: mechanisms, complications and clinical implications. Journal of the National medical association, 1985; 77: 385-389.
5. Nadejzda B., Letteron P., Fromenty B., Robin M., Effets hépatiques et métaboliques d'une administration chronique d'alcool chez des souris obèses. Cahiers IREB, 2007; 18: 93-99.
6. OMS/AFRO. Promotion du rôle de la médecine traditionnelle dans les systèmes de santé: Stratégie de la Région Africaine. Document AFR/RC50/9. Harare, Zimbabwe: OMS/AFRO, 2001; 20.
7. OMS/AFRO. Politique de la Sante pour tous dans la Région Africaine pour le 21e siècle: Agenda. Document AFR/RC50/8 Rev. 1. Harare, Zimbabwe: Organisation mondiale de la sante: Bureau régional de l'OMS pour l'Afrique., 2020; 25.
8. Yeo D., N'Guessan D., Sea T., Coulibaly Y.A., Djaman A.J., Tako A.J., Yavo J.C., Guede-Guina F. ´Evaluation de l'activité antiasthmatique et antitussive de *Combretum molle*, plante médicinale de la pharmacopée ivoirienne. Phytothérapie, 2008; 6(6): 348-351.
9. Yun J.W., Kim Y.K., Lee B.S., Kim C.W., Hyun J.S., Baik J.H., Kim J.J., Kim B.H. Effect of dietary epigallocatechin-3-gallate on cytochrome P450 2E1-Dependent alcoholic liver damage: Enhancement of fatty acid oxidation. Bioscience biotechnology biochemistry, 2007; 71: 2999-3006.
10. Primatesta P., Falaschetti E., Gupta S., Marmot M.G., Poulter N.R. Association between smoking and blood pressure: evidence from the health survey for England. Hypertension, 2001; 37(2): 187-93.
11. Ngolo E., Etou Ossibi A.W., Epa C., Loubanou C.A.C., Samba Ndossi A.S.F., Ouamba J.M., Abena A.A. Effet hypotenseur de l'extrait extrait aqueux de la recette à base de *Brillantaisia patula* T. Anderson (Acanthceae) et de *Desmodium velutinum* Willd. (DC) (Fabaceae) chez le rat. International Journal of Multidisciplinary and Current Research, 2018; 6: 1415-1423.
12. Etou Ossibi, A.W., Dimo, T., Elion Itou, R.D.G., Nsondé Ntandou, G.F., Nzonzi, J., Bilanda, D.C., Ouamba, J.M., Abena, A. A. Effets de l'extrait aqueux de *Lippia multiflora* Moldenke sur l'hypertension artérielle induite par le DOCA-sel chez le rat. Phytothérapie, 2012; 10(6): 363–368.

13. Etou Ossibi, A.W. Effets cardiovasculaires et antioxydants des extraits aqueux et hydroéthanolique de *Lippia multiflora* Moldenke (Verbenaceae). Thèse de Doctorat unique, Faculté des Sciences, Université Marien Ngouabi, Brazzaville, Congo, 2010; 198.