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Anti oxidative activities of aqueous and ethanolic extracts of stem barks from trichilia emetica in albinos rats

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A B S T R A C T

Introduction: In chronic diseases in general and in diabetes mellitus and hypertension in particular, there is an important imbalance between antioxidant defenses and the production of free radicals due to reactive oxygen species, thus leading to an increase in oxidant stress markers. Therefore, this study was designed to evaluate the antioxydative and protective effects of aqueous and ethanolic extracts of trichilia emetica stem bark in albinos rats with alloxan-induced diabetes or adrenaline-induced hypertensive.
Methodology: Two different batches of albinos rats were used distinctly and including a control one of 3 rats for each batch so a test group of 21 rats. Diabetes was induced by injecting Alloxane® intraperitoneally for 7 days. Hypertension was induced by injecting Adrenaline® intraperitoneally for eight days and we used visitech BP 2000 tools to measure arterial pressure. The aqueous and ethanolic extracts of Trichilia emetica were prepared and the obtained mixture was homogenized using a magnetic stirrer for 24 hours. Rats received the above-mentioned extracts orally at doses of 100 and 200 mg/kg bw for 6 days.
Results: Aorta and heart activities of catalase were significantly increased. This same trend was observed with superoxide dismutase activity together with increasing AChE catalytic activity in vessels. Treatment of rats for seven days with extracts of Trichilia emetic and nifedipine^{6}produced a significant decrease of antioxidative markers activities of catalase and SOD for aqueous and ethanolic extracts as well. This action was slightly above nifedipine^{6}one administrated at 10 and 20 mg/kg bw. For rats treated with Trichilia emetica or with diastabol^{6}we registered a significant decrease of MDA and GSH concentration.
Conclusion: Our results showed that the extracts have the potential to reduce the rate of reactive oxygen species and free radicals in rats with alloxane-induced diabetes or adrenaline-induced hypertensive. However, further large studies are needed to investigate the specific action and particularity of Trichilia emetica that could justify these activities.

1. Introduction

The notion of oxidative stress in biological systems dates back to the 1970s following research on the activation of molecular oxygen and its potential toxicity in mammalian organs. In biological systems, oxidative stress is therefore the consequence of an imbalance between the production of free radicals and their destruction by antioxidant defense systems.[1] In chronic diseases in general and in diabetes mellitus and hypertension in particular, both a decrease in antioxidant defenses and an increase in the production of free radicals have been observed, leading to an increase in oxidant stress markers. The decrease in antioxidants could be explained, among other things, by the glycation of enzymes, which would lead to their

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inactivation.[2] Pancreatic beta cells are poor in Cu/Zn, superoxide dismutase, catalase, glutathione peroxidase and reduced glutathione.[3] The increase in oxidative stress during the course of these pathologies has therefore been mainly demonstrated by an increase in the damage caused by free radicals on proteins and lipids.[4]

However, modern medicines are very often limited due to the issues of this disease which appear certainly regardless the treatment. Thus, the introduction of alternative and complementary medicine is hugely recommended owing to the properties of herbal and their richness in anti-oxidative activity. There is therefore an increasing need to develop new drugs and prevention strategies with fewer side effects, such as phytotherapy.[5,6] Over the years, the use of plants in traditional medicine to treat various diseases has become popular and widely accepted throughout the world. The World Health Organization (WHO) estimates that about 80% of medications in developing countries depend mainly on traditional medicine, which involves the use of plant extracts.[7,8] This because plants generally contain a variety of chemical compounds with important biological functions. In recent years, many researchers have demonstrated that natural products are a potential source of new drug candidates for many diseases in general and metabolic diseases in particular. Medicinal plants are used for diabetics control in many countries. Indeed, studies have hypothesized and demonstrated the hypoglycemic and hypotensive activities of several plants.[9–12]

Trichilia emetica is a plant widely used in several traditional medicines to cure various diseases. Several pharmacological properties of this plant have been demonstrated by literature. Thus, immunomodular, antibacterial and cardioprotective activities were investigated to name a few.[13–15] Studies related diabetes have mostly been carried out on flavonoid-rich fractions from the leaves of this plant but not on stem bark extracts. However, the phytochemical study of aqueous and ethanolic extracts of this part of the plant revealed the presence of several groups of secondary metabolites. Moreover this study was carried out to assess the potential antioxidative activities of aqueous and ethanolic extracts of stem barks from Trichilia emetica in albinos rats made diabetic or hypertensive.

2. Methodology

2.1. Plant

Trichilia emetica (Meliaceae) stem bark were selected from the African pharmacopoeia. The plant was identified at the National Center of the Floristry of the Félix Houphouët Boigny University in Abidjan, Cocody. The collection of fresh stem barks was done during ethno-pharmacological investigations in February 2014 in the north of Côte d'Ivoire.

2.2. Animal

Albinos Wistar healthy rats obtained from an Animal House are used for this study. The animals were kept in plastic cages in the environmental conditions. They had free access to standard food pellets and were allowed to drink water ad libitum. Animal care and handle were in line with the international guidelines.

2.3. Protocol of extraction

The barks of Trichilia emetica were harvested, dried under room temperature for two weeks and made into fine powder by grinding with a IKAMAG type mill. The aqueous and 70% ethanolic extracts were prepared according to the method of Kra and Zihiri.[16] Into 100 g of this powder was added 1 liter of distilled water or the hydroalcoholic solvent (70/30, v / v). The obtained mixture was homogenized using a magnetic stirrer for 24 hours. The solution was subjected to successive filtration twice over cotton wool and then once over the Whatman paper. The collected filtrate was concentrated in oven at 50°C to dryness. This was used for pharmacological activities.

3. Experimental Design

Diabetes induction was performed using alloxan experimentation.[17] A total of 24 rats of similar weight were divided into 2 groups, including a control one of 3 rats and a test group of 21 rats. Diabetes was induced by injecting Alloxane® intraperitoneally (125 mg/kg bw) in solution in 0.1 M pH 4.5 citrate buffer for 7 days. Thereafter, the diabetic test batch is divided into 6 batches of 3 rats:

1. NC: Normal Control rats received normal saline,
2. DC: Diabetic control was constituted of untreated diabetic rats and was used as a control for the batches made diabetic and treated.
3. DD10: Diabetic animals treated by gavage with Diastabol® at 10 mg/kg bw for 6 days after the onset of diabetes,
4. DD20: Diabetic animals treated by gavage with Diastabol® at a 20 mg/kg bw for 6 days after the onset of diabetes,
5. DTEE100: Diabetic animals treated with ethanolic extract by gavage at 100 mg/kg bw for 6 days after the onset of diabetes,
6. DTEE200: Diabetic animals treated with ethanolic extract by gavage at 200 mg/kg bw for 6 days after the onset of diabetes,
7. DTEA100: Diabetic animals treated with aqueous extract by gavage at 100 mg/kg bw for 6 days after the onset of diabetes,
8. DTEA200: Diabetic animals treated with aqueous extract by gavage at 200 mg/kg bw for 6 days after the onset of diabetes.

Another bacth of 24 rats, aged from 2 to 3 months, with similar weight were divided into 2 groups, including a control one of 3 rats and a test group of 21 rats. Hypertension was induced by injecting Adrenaline® intraperitoneally (1.46. 10^{-3}mg/kg bw) for eight days and we used visitech BP 2000 tools to measure arterial pressure. Thereafter, the hypertensive group was divided into 7 batches of 3 rats following the next scheme:

1. HNT (rats induced hypertensive naïve of treatment/ positive control batch)
2. NIF 1: batch treats by gavage, after eight days of hypertension with Nifédipine® at 10mg/Kg bw for six days;
3. NIF 2: batch treats by gavage, after eight days of hypertension with Nifédipine® at 20mg/Kg bw for six days;
4. E 100: batch treats by gavage with ethanolic extracts at 100 mg/kg bw for six days after hypertension induction;
5. E200: batch treats by gavage with ethanolic extracts at 200 mg/kg bw for six days after hypertension induction;
6. A100: batch treats by gavage with aqueous extracts at 100 mg/kg bw for six days after hypertension induction;
7. A200: batch treats by gavage with aqueous extracts at 200 mg/kg bw for six days after hypertension induction;

After 28 days of experimentation, rats are sacrificed and their blood have been collected for the determination of some biochemical parameters and oxidative indicators.

3.1. Analyses

Blood sample was taken by incision of the tip of the tail during this study. Thus, after 28 days of treatment, on the rats anesthetized with ether, the blood is taken early in the morning at the level of the tip of the tail (5 mm from the end) previously disinfected with 96° ethanol. Blood or organ homogenate contained in the dry tubes were centrifuged using a centrifuge at 3000 rpm for five minutes. The serum obtained is collected and stored at -20°C for analysis of serum markers in the kidney, liver and heart using the COBAS INTEGRA® 400 Plus analyzer (France). The protocol of each assay has been pre-established and then incorporated into the device during assays according to the manufacturer's instruction manual (reagents kits).

AChE activity assay is based on the method of Worek et al.[18] The determination of nitric oxide (NO) was carried out using the GRIESS reagent, its preparation was done away from light. SOD activity was determined by the Nitro Blue Tetrazonium (NBT) test.[19] Catalase activity was measured in the organ homogenate using the spectrometric method used by Elia et al.[20] Finally, malonaldehyde (MDA) assay and GSH level assay were performed respectively by the method of Ohkawa et al.[21] and that of Ellman.[22]

3.2. Statistical analysis

Analysis of results based on the Tukey test, which was performed with Graph Pad Prism software 5.0 (Microsoft, USA). Results were expressed in means ± standard deviation. The level of significance of the tests used was set at a = 5%, difference was considered significant for P value < 0.05.

4. Results

Variation of oxidative markers between cases and controls: Effects of Trichilia emetic extracts and nifedipine^{ó}on catalase activity via aorta and heart were studied. Aorta and heart activities of catalase were significantly increased (P< 0,05). This same trend was observed with superoxide dismutase activity (P< 0,05) together with increasing acetylcholinesterase catalytic activity in vessels. In contrary, hypertension induced in rats lead to a significant reduction of nitric oxide proportion in hypertensive rats. Induction of diabetes also leads to augment lipoperoxidation markers such as malondialdehyde and GSH in diabetics rats in opposition to controls. Indeed alloxan significantly increases rate of MDA and GSH (Table 1). Effects of Trichilia emetic extracts versus nifedipine^{ó} on catalase and SOD activities: Treatment of rats for seven days with extracts of Trichilia emetica (Aqueous and ethamolic) and nifedipine^{ó} produced a significant decrease of antioxidative markers activities of catalase and SOD for aqueous and ethanolic extracts as well. This action was slightly above nifedipine^{ó} administrated at 10 and 20 mg/kg bw (Table 2). Compared effects of Trichilia emetica versus diastabol^{ó}on MDA and GSH for rats induced diabetics. For rats treated with Trichilia emetica (Aqueous and ethanolic) or with diastabol^{ó}we registered a significant decrease of MDA and GSH concentration (P< 0,05) (Table 3). Effects of Trichilia emetica on the percentage of acetylcholinesterase and nitric oxide in rats vessels versus nifedipine$^{ó:}$ Treatment of rats with different extracts or with nifedipine^{ó} showed a decrease of acetylcholinesterase activity in both categories. Thus, aqueous and ethanolic extracts inhibited catalytic activities of acetylcholinesterase. Otherwise, the same treatment lead to increase significantly the rate of nitric oxide. These effects were similar to those of nifedipine^{ó} (Table 4).

5. Discussion

Our results highlight an important rise of acetylcholinesterase activities in hypertensive-induced rats. Treatment of rats with trichilia emetica extracts aroused a significant reduction of these activities that suggested an inhibition of acetylcholinesterase (AChE) leading to an accumulation of neurotransmitter in synapses.

Table 1: Activities of oxidative stress markers in tissue among controls and test albinos rats

		Normotensive rats	Hypertensive rats
Catalase	Aorta	1.46±0.03	2.06±0.02
	Heart	2.34±0.01	3.25±0.02
Superoxyde dismutase (SOD)	Aorta	2.36±0.02	3.24±0.04
	Heart	2.34±0.01	3.25±0.02
Lipid peroxydation markers	MDA	0.53±0.02	0.96±0.02
	GSH	0.61±0.01	1.08±0.03
Acetylcholinestérase (AChE)	Vessels	7.04±0.12	13.68±0.22
Nitric oxide (NO)	Vessels	0.47±0.01	0.07±0.02

Table 2: Effects of Trichilia emetica extracts versus nifedipine on catalase and superoxyde dismutase (SOD) activities

			Heart	Aorta
Catalase	Aqueous extract	100mg/kg bw	2.64±0.02	1.60±0.03
		200mg/kg bw	2.29±0.01	1.54±0.03
	Ethanolic extract	100mg/kg bw	2.34±0.02	1.57±0.02
		200mg/kg bw	1.48±0.02	2.26±0.01
	Nifedipine	10 mg/kg bw	19.34%	17.48%
		20 mg/kg bw	22.62%	20.39%
Super Oxide Dismutase	Aqueous extract	100mg/kg bw	2.74±0.02	2.85±0.02
		200mg/kg bw	2.63±0.02	2.56±0.02
	Ethanolic extract	100mg/kg bw	2.64±0.02	2.60±0.02
		200mg/kg bw	2.56±0.02	2.44±0.02
	Nifedipine	10 mg/kg bw	12.31%	8.64%
		20 mg/kg bw	18.40%	14.42%

Table 3: Compared effects Trichilia emetica extracts versus diastabol on lipids peroxidation markers / TBARS (MDA et GSH)

TBARS (lipids peroxydation)		**MDA**	**GSH**	**P**
Aqueous extract	100mg/kg bw	30.21%	25.00%	<0.05
	200mg/kg bw	32.29%	31.48%	<0.05
Ethanolic extract	100mg/kg bw	33.33%	31.48%	<0.05
	200mg/kg bw	37.70%	38.89%	<0.05
Diastabol	10 mg/kg bw	30.21%	21.30%	<0.05
	20 mg/kg bw	37.70%	31.81%	<0.05

TBARS: Thiobarbituric acid reactive substances
MDA: Malonaldehyde
GSH: Glutathione

Table 4: Effects of Trichilia emetica on acetylcholinesterase (AChE) and nitric oxide in vessels of hypertensive albinos rats versus nifedipine

		Acetyl cholinesterase	**Nitric oxide**	**P**
Aqueous extract	100mg/kg bw	30.70%	53.19%	<0.05
	200mg/kg bw	32.97%	65.96%	<0.05
Ethanolic extract	100mg/kg bw	30.04%	485.71%	<0.05
	200mg/kg bw	54.61%	557.14%	<0.05
Nifedipine	10 mg/kg bw	26.75%	552.34%	<0.05
	20 mg/kg bw	32.68%	570.62%	<0.05

This action induces a dilatation of arterial vessels and a slowing of heart frequency thus decreasing arterial pressure. However, charge of 200 mg/kg bw of ethanolic extracts (Te) was more active in comparison with nifedipine$^{\delta}$ and diastabol$^{\delta}$. These data are in line with literature.[14,23,24] A range of secondary plant metabolites has shown anti-cholinesterase activity including alkaloids, flavonoids and lignans with alkaloids being the largest group of ACh inhibitors.[25–27] Both the ethanolic and the aqueous extracts show a stronger inhibition of AChE than galantamine. Remarkably, the ethanolic extract exhibits an AChE inhibition that is 100-fold stronger than the one observed for galantamine. Usually plants contain a complex profile of secondary metabolites therefore the effect of a plant extract usually cannot be accredited to one single compound. Also, synergistic effects have to be taken into account.[28,29]

Superoxide dismutase (SOD) and catalase are both enzymes present in aorta, heart, liver and kidney where they play enzymatic antioxidant activities. Results reached in this study showed a significant increase of their activities in hypertensive rats. Hypertension induces a decreasing in endothelium relaxation facilitating peripheral vascular resistance. Endothelial dysfunction associated to a great oxidation stress generate overproduction of reactive oxygen species (ROS) in different tissues and organs. Thus, there is an important enzymatic activities of superoxide dismutase and catalase in hypertensive-induced rats.[30,31] SOD has been characterized to convert oxygen free radicals, produced by xanthine oxidase, into oxygen and hydrogen peroxide. SOD is regarded as the main intracellular antioxidant defense against free radicals.[32] Superoxide dismutase plays a major role in defense against oxygen radical-mediated toxicity in aerobic organisms. In plants, environmental adversity such as drought, high or low temperature, flood, presence of heavy metal and macronutrient deficit often leads to the increased generation of reduced oxygen species and, consequently, SOD is suggested to play an important role in plant stress tolerance.[33,34] Moreover, catalase acts by inhibiting oxidative abilities of H_2O_2 transforming it into H_2O and O_2.[32] Extracts of Trichilia emetica given to hypertensive rats decreased significantly superoxide dismutase activities and catalase comparatively to hypertensive rats naïve of treatment. Although oxidative stress being implicated in different hypertensive patterns, results emerging from numerous studies are in line with the concept that they intervene more in aggravating than in genesis of high blood pressure.[35] High blood pressure arouses a dysfunction in vascular endothelium that induces some modification such as lowering of nitric oxide release into different organs. In fact, superoxide anions react quickly with endothelial nitric oxide, which constantly reduce vascular resistance. It's also notified that excessive reactive oxygen species (ROS) production could directly or indirectly alters mechanisms responsible for relaxing effect of nitric oxide on smooth muscle cells.[36] This corroborates our results because adrenaline injected to rats conducted a significant lowering of nitric oxide concentration in heart and aorta of hypertensive rats. Aqueous or ethanolic extracts of Trichilia emetica increased the biodisponibility of nitric oxide responsible of arterial vasodilatation. Through its action, extracts could have protective effects against endothelial dysfunction induces by high blood pressure.

Acetylcholinesterase catalytic enzymatic activities augment tremendously during high blood pressure and/or metabolic disorders such as diabetes. Acetylcholinesterase is such enzyme that hydrolyzes acetylcholine in acetate and in choline few seconds after its releasing in synaptic cleft. Once secreted in mammalian, acetylcholine give rise to peripheral vasodilatator consecutive to a stimulation of M2 receptors binded to G protein that leads to a vasodilatator substance called Endothelium Derived Relaxing Factor (EDRF) or nitric oxide.[37,38]

Treatment of rats become diabetics with extracts reduced level of malonaldehyde (MDA) and glutathione (GSH). This trend suggests that extracts could have induced an inhibition of lipid peroxidation and free radicals, thus decreasing of MDA and GSH. Similarly, the charge of 200 mg/kg bw of ethanolic extracts of Trichilia emetic was more important in comparison with diastabol used as antidiabetic drug. Alloxan administration to rats has also lead to increase Thiobarbituric Acid Reactive Substances Assay (TBARS). Rising of MDA and GSH rate for sick animals is a good indicator of overproduction of reactive oxygen species further to alloxan administration.

Lipid peroxidation is the polyunsatured fatty acids oxidation in free fatty acids through free radicals, given that cellular membrane riches in polyunsatured fatty acids are prone to be targeting by peroxidation.[39] The overproduction of free fatty acids promotes ceramides synthesis which will activate nitric oxide synthetase. Excessive nitric oxide formed accentuates the production of nitric oxide radical, which will inhibit cytochrome C oxidase, leading to the opening of the Permeability Transition Pore (PTP) of the inner mitochondrial membrane. This breach of the PTP leads to the escape of protons and in turn leads to mitochondrial swelling, the release of cytochrome C into the cytosol and the activation of caspases, a phenomenon in link with the death of the pancreatic beta cell.[40] Since treatment of rats with different extracts, particularly 200mg/kg bw of ethanolic extract, reduced MDA and GSH concentration, we conclude that Trichilia emetica could have prevent lipid peroxidation and reactive oxygen species production, hence the effects on biological markers of oxidative stress.

6. Conclusion

Plants using as medication to treat several diseases is a reality worldwide and in Africa in particular. Their role as

alternative medicine is not discussing because their bring lots of bioactive compounds in our body. Plants produce a high diversity of secondary metabolites representing a complex mixture of compounds from different chemical classes, so their action is probably due to the pleiotropic effects of the secondary metabolites contained in the plant. Antioxydative effects obviously is one of the most important action they could have. In our study, the ethanolic and aqueous extracts of Trichilia emetica trunk bark was investigated.

The results obtained showed that the extracts have the potential to reduce the rate of reactive oxygen species and free radicals in rats with alloxane-induced diabetes or adrenaline-induced hypertensive. However, further large studies are needed to investigate the specific action and particularity of Trichilia emetica that could justify these activities and also in the design of therapeutic alternatives for treatment of chronic diseases.

7. Ethical Approval

The experimental procedures and protocols used in this study were approved by the Ethical Committee in accordance with the European Council Legislation 87/607/EEC for the protection of experimental animals. All efforts were made to minimize animal suffering and reduce the number of animals used.

8. Limitations

Size of sample and study duration due to self-funding.

9. Source of Funding

None.

10. Conflict of Interest

The authors stated that there is no conflict of interest.

References

1. Angelos MG, Kutala VK, Torres CA, He G, Stoner JD, Mohammed M, et al. Hypoxic reperfusion of the ischemic heart and oxygen radiacal generation. *Am J Physiol Heart Circ Physiol*. 2006;290(1):341–7.
2. Baldwin JS, Lee L, Leung TK, Murugananda m A. Identification of the site of non-enzymatic glycation of glutathione peroxidase: rationalization of the glycation-related catalytic alterations on the basis of the three-dimensional protein structure. *Biochim Biophys Acta*. 1995;1247(1):60–4.
3. Lenzen S, Drinkgern J, Tiedge M. Low antioxidant enzyme gene expression in pancreatic islets compared with various other mouse tissues. *Free Radic Biol Med*. 1996;2(3):463–6.
4. Hartnett ME, Stratton RD, Browne RW, Rosner BA, Lanham RJ, Armstrong D. Serum markers of oxidative stress and severity of diabetic retinopathy. *Diabetes Care*. 2000;23(2):234–40.
5. Khavandi K, Amer H, Ibrahim B, Brownrigg J. Strategies for preventing type 2 diabetes: an update for clinicians. *Ther Adv Chronic Dis*. 2013;4(5):242–61.
6. Yuan H, Ma Q, Ye L, Piao G. The traditional medicine and modern medicine from natural products. *Molecules*. 2016;21(5):599.
7. Traditional medicine strategy launched; 2002.
8. Koduru S, Grierson DS, Afolayan AJ. Ethnobotanical information of medicinal plants used for treatment of cancer in the eastern Cape Province, South Africa. *Curr Sci*. 2007;92(7):906.
9. Mahdavi MRV, Roghani M, Baluchnejadmojarad T. Mechanisms responsible for the vascular effect of aqueous Trigonella foenumgraecum leaf extract in diabetic rats. *Indian J Pharmacol*. 2008;40(2):59–63.
10. Meddah B, Ducroc R, Faouzi M, Eto B, Mahraoui L, Benhaddou-Andaloussi A, et al. Nigella sativa inhibits intestinal glucose absorption and improves glucose tolerance in rats. *J Ethnopharmacol*. 2009;121(3):419–24.
11. Tripathi UN, Chandra D. The plant extracts of Momordica charantia and Trigonella foenum graecum have antioxidant and antihyperglycemic properties for cardiac tissue during diabetes mellitus. *Oxid Med Cell Longev*. 2009;2(5):290–6.
12. Long HS, Tilney PM, Van W. The ethnobotany and pharmacognosy of Olea europaea subsp. africana (Oleaceae). *S Afr J Bot*. 2010;76(2):324–31.
13. Madureira AM, Ramalhete C, Mulhovo S, Duarte A, Ferreira MJ. Antibacterial activity of some African medicinal plants used traditionally against infectious diseases. *Pharm Biol*. 2012;50(4):481–9.
14. Prisca DA, Félix YH, Françis YA. Assessment of Cardioprotective Effects of Aqueous and Ethanolic Extracts of Stem Barks from Trichilia emetica against Cardiotoxicity Induced by Doxorubicin in Wistar Rats. *Cardiol Angiol*. 2016;5(4):1–7.
15. Prisca DA, Luc DKA, Kahissié M, Félix YH, Georges TG. Antidiabetic Activity of Aqueous and Ethanolic Extracts of Stem Barks from Trichilia emetica (Meliaceae) in Alloxan-Induced Diabeticalbinos Rats. *Int J Biochem Res Rev*. 2020;29(3):17–24.
16. Zihiri GN, Kra AM, Guede-Guina F. Evaluation de l'activité antifongique de Microglossa pyrifolia (LA MARCK) O.KUNTZE (Astéraceae) «PYMI» sur la croissance in vitro de Candida albicans. *Rev Med et Pharm Afr*. 2003;17:11–8.
17. Diatewa M, Samba CB, Assah TC, Abena AA. Hypoglycemic and antihyperglycemic effects of diethyl ether fraction isolated from the aqueous extract of the leaves of Cogniauxia podoleana Baillon in normal and alloxan-induced diabetic rats. *J Ethnopharmacol*. 2004;92(2-3):229–32.
18. Worek F, Thiermann H, Szinicz L, Eyer P. Kinetic analysis of interactions between human acetylcholinesterase, structurally different organophosphorus compounds and oximes. *Biochem Pharmacol*. 2004;68(11):2237–48.
19. Van ZPA. Comparative mechanism of action of diuretic drugs in hypertension. *Eur Heart J*. 1992;13(Suppl G):2–4.
20. Elia AC, Galarini R, Taticchi MI, Dörr AJM, Mantilacci L. Antioxidant responses and bioaccumulation in Ictalurus melas under mercury exposure. *Ecotoxicol Environ Saf*. 2003;55(2):162–7.
21. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. *Anal Biochem*. 1979;95(2):351–8.
22. Ellman GL. Plasma antioxidants. *Arch Biochem Bioph*. 1959;82:70–7.
23. Tom ENL, Thèse de Doctorat. Effets antihypertenseurs des extraits de Terminalia superba Engler & Diels (Combretaceae) : étude in vivo et in vitro. France; 2011.
24. Tiekpa WJ, Koutou A, Bahi C, N'guessan JD, Coulibaly A. Evaluation of the Effect of "Wakouba " on the Lipid Profile, Systolic Blood Pressure (SBP) Diastolic (DBP) and Blood Glucose in Hypertensive Rabbits. *IJABPT*. 2014;5(4):87–95.
25. Kaufmann D, Dogra AK, Tahrani A, Herrmann F, Wink M. Extracts from Traditional Chinese Medicinal Plants Inhibit Acetylcholinesterase, a Known Alzheimer's Disease Target. *Molecules*. 2016;21(9):1161.
26. Na TM, Dat M, Ngoc NT, Youn TM, Kim U, Min HJ, et al. Cholinesterase inhibitory and anti-amnesic activity of alkaloids from Corydalis turtschaninovii. *J Ethnopharmacol*. 2008;119(1):74–80.
27. Jung M, Park M. Acetylcholinesterase inhibition by flavonoids from Agrimonia pilosa. *Molecules*. 2007;12(9):2130–9.

28. Wink M. Evolutionary advantage and molecular modes of action of multi-component mixtures used in phytomedicine. *Curr Drug Metab*. 2008;9(10):996–1009.
29. Wink M. Modes of Action of Herbal Medicines and Plant Secondary Metabolites. *Medicines (Basel)*. 2015;2(3):251–86.
30. Landmess U, Dikalov S, Price SR, McCann L, Fukai T, Steven SM, et al. Oxidation of tetrahydrobiopterin leads to uncoupling of endothelial cell nitric oxide synthase in hypertension. *J Clin Invest*. 2003;111(8):1201–9.
31. Iijima O, Nakamura Y, Ogat Y, Tanaka K, Sakurai N, Suda K, et al. Metabolite annotations based on the integration of mass spectral information. *Plant J*. 2008;54(5):949–62.
32. Miller AF. Superoxide Dismutases. In: Encyclopedia of Biophysics. Berlin, Heidelberg: Springer; 2013. Available from: https://doi.org/10.1007/978-3-642-16712-6_50. doi:10.1007/978-3-642-16712-6_50.
33. Bela K, Bangash SAK, Riyazuddin, Csiszár J. Plant glutathione peroxidases: Antioxidant enzymes in plant stress responses and tolerance. *J Plant Physiol*. 2017;176:113–26.
34. Stepheniea S, Changb YP, Gnanasekaranc A, Esad CNM, Gnanaraj C. An insight on superoxide dismutase (SOD) from plants for mammalian health enhancemen. *J Func Foods*. 2020;68. doi:10.1016/j.jff.2020.103917.
35. Thomas SR, Chen K, Keaney JF. Oxidative stress and endothelial nitric oxide bioactivity. *Antioxid Redox Signal*. 2003;5(2):181–94.
36. Cuzzocrea S, Mazzon E, Dugo L, DiPaola R, Caputi AP, Salvemini D. Superoxide: a key player in hypertension. *Faseb J*. 2004;18:94–101.
37. Damas J. L'acétylcholine endothelial. *Rev Med*. 2002;57:104–6.
38. Jiang ZG, Nutall AL, Zhao H, Dai CF, Guan BC, Si JQ, et al. Electrical coupling and release of K+ from endothelial cells co-mediate Ach-induced smooth muscle hyperpolarization in guinea-pig inner ear artery. *J Physiol*. 2005;564(Pt 2):475–87.
39. Inoguchi T, Li P, Umeda F, Yu H, Kakimoto M, Imamura M, et al. High glucose level and free fatty acid stimulate reactive oxygen species production through protein kinase C-dependent activation of NADPH oxidase in cultured vascular cells. *Diabetes*. 2000;49(11):1939–45.
40. Detaille D, Guigas B, Leverve X, Wiernsperger NF, Devos P. Obligatory role of membrane events in the regulatory effect of metformin on the respiratory chain function. *Biochem Pharmacol*. 2002;63(7):1259–72.

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