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Assessment of the vasodilatory activity of an isolate from *Moringa oleifera* L. (Moringaceae) seeds on thoracic aorta in rats

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Abstract

Moringa oleifera seeds are widely used to manage hypertension in traditional medicine in the northern part of Madagascar. In this work we studied the vasodilatory activity of a molecule isolated from the seeds for the first time 4'-((3,4,5-trihydroxy-6-(1-hydroxyethyl)-tetrahydro-2H-pyran-2-yl)oxy)benzylamino-3'-(2-hydroxyethane) that we coded N-428. It was isolated from ethyl acetate extract. It relaxes rat thoracic aorta contracted with norepinephrine at 10 µM with EC_{50} equal to $8.92.10^{-5}$ M. Further research revealed that it can dilate endothelium denuded aorta and promotes vasodilation, it provokes a right shift of the concentration-effect curve of norepinephrine without changing the maximal effect, indicating its activity via α1 receptors. Compared to prazosin, a competitive antagonist of norepinephrine its pA_2 is ≈ 5.78 M, versus 8.249 for prazosin, and Kd of $1.25.10^{-6}$ M, versus $5.63.10^{-9}$ M for prazosin. These results indicate that the isolate exhibits good vasodilatory activity, acting as α1 competitive antagonist of norepinephrine and has the potential to be utilized as a lead vasodilator compound.

Keys words: α1 antagonist; Isolated aorta; *Moringa oleifera* seeds; Vasodilator

1. Introduction

Hypertension is a common chronic disease encountered in clinical practice. Based on the related complications, the mortality and disability rate are at the forefront of human diseases, which causes great harm to human health [1, 2]. Current medications for treating hypertension are generally effective and affordable. Nevertheless, not all patients suffering from hypertension have access to these medications. In addition, adherence to treatment is often unsatisfactory. It is estimated that only 21 % to 25 % of people with hypertension have their blood pressure controlled through medication [3]. Therefore, there is still a need for alternative antihypertensive drugs with limited side effects. The use of medicinal plants as alternatives to modern medicine of synthetic origin has shown a remarkable increase in recent years. Traditional and complementary medicine has especially gained popularity for treating mild symptoms or for prophylactic purposes. In addition, there are reports of their use in chronic and more severe conditions, such as hypertension, and even cancer [4].

Moringa oleifera is a plant belonging to the Moringaceae family. It grows in different parts of the world and used as food but also to treat different illness. In recent years, more attention has been paid to the research on elucidating the composition and its activity. Its main ingredients include alkaloids, volatile oils, organic acids, and flavonoids. It has various pharmacological activities, such as regulating fat and weight loss, anti-inflammatory, lowering blood pressure, anti-oxidation, anti-bacterial, anti-spasmodic, hemostasis, and hepatoprotective effects [5, 6]. *Moringa oleifera* leaves are widely studied, and shows lowering blood pressure effect, and have been reported to be involved in vasorelaxation

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[7, 8]. However, there has been no systematic research on antihypertensive ingredients present in its seeds. In this study, we aimed to fill in the knowledge gap on *Moringa oleifera* seeds and elucidate the mechanism of action of a component's vasodilatory activity, to ensure more effective use of them and to provide a basis for its future clinical applications.

Our previous studies have shown anti-hypertensive activity of *Moringa oleifera* seeds [9] as well as its diuretic and vasodilatory activities [10]. We also have identified one vasodilator component [11]. Our objective in this work is to elucidate the vasodilatory mechanism of action of a pure molecule isolated from *Moringa oleifera* seeds, using a rat isolated thoracic aorta as model.

2. Materials and methods

2.1. Extraction procedures

Moringa oleifera seeds were collected in the northern region of Madagascar. They were ground and the powder was extracted respectively with hexane, dichloromethane, ethyl acetate and methanol. Extracts were evaporated under reduced pressure until dry using a rotary evaporator. All dried extracts were stored at –4 °C until use. Each extract was afterwards tested on isolated thoracic aorta of rat contracted with norepinephrine at 10 µM in the organ bath. Previous studies indicate that ethyl acetate was the most effective, and a vasodilator molecule (N-248) was isolated from this fraction [11].

2.2. Isolated organ preparation

Animals were strictly handled in accordance with the National Institutes of Health Guidelines for the Care and Use of Laboratory Animals (NIH Publication No. 85–23, revised 1996) and the study was approved by the Committee of Animal Ethic of Sciences Faculty, University of Antananarivo, Madagascar (CE/Fac Sciences/02/2025). Rats weighing 250–300 g of both sexes were used for the experiments.

Rats were anesthetized with phenobarbital 125 mg/g, injected intra muscularly. They were exsanguinated by cutting the two carotids, and a laparotomy was practiced. Thoracic aorta was removed and transferred promptly into ice-cold Krebs solution (NaCl 118.0 mM, KCl 4.7 mM, $MgSO_4$ 1.1 mM, KH_2PO_4 1.2 mM, $CaCl_2$ 1.5 mM, $NaHCO_3$ 25 mM, and glucose 10.0 mM in water, pH 7.4 [12]. Surrounding tissue was removed and it was cut into 3–4 mm long annular segment.

The aortic ring was suspended in a tissue bath containing Krebs solution (pH 7.4) and bubbling 95 % O2–5 % CO2 at 37 °C by inserting 2 stainless steel wires into the lumen of the tube under a basal tension of 1 g. One of the extremities was fixed at the base of the organ bath, and the second one was connected to an isometric sensor. Organ was allowed to equilibrate during 60 min, during which the bath was renewed every 15 min. After the equilibration period of 60 min the organ viability was tested by injecting 10 µM of norepinephrine in the bath. After contraction acetylcholine was injected in the bath to get 10 µM, to verify the integrity of endothelium, the preparation was finally rinsed, and the organ was allowed to equilibrate for 30 min, during which the bath was renewed twice [12].

2.3. Evaluation of N-428 effect on thoracic aorta pre contracted with norepinephrine

After the equilibrium period, norepinephrine was injected in the organ bath a concentration of 10 µM. When the contraction reached a plateau, N-428 was added cumulatively in the organ bath from $7.28.10^{-6}$ M until complete relaxation.

In a second series of test, the endothelium was mechanically removed by gently rubbing the surface of the ring back and forth with a plastic tube. Absence of endothelium was tested by injecting acetylcholine at the concentration of 10 µM in the organ bath containing isolated aorta precontracted with norepinephrine. The absence of relaxation following this treatment indicates the absence of endothelium.

To study the vasorelaxation activity of N-428, endothelium-denuded aortic rings were contracted with norepinephrine (10 µM), then at the maximal contraction response, N-428 was added cumulatively into the bath and the changes in the tension were recorded. The relaxation effect was calculated as percentage of the maximum contraction induced by norepinephrine [13].

2.4. Examination of N-428 activity on α1-receptor

To evaluate N-428 mechanism of action, prazosin, an α1-receptor antagonist was used as control. Endothelium-denuded rings were incubated with N-428 at respective concentrations of 4.36. 10^{-5}, 8.73.10^{-5} and 1.31.10^{-4} M for 10 min before exposing them to norepinephrine injected in the bath in a cumulative manner from 10^{-11} M to the maximal contraction. The results were expressed as percentages of maximal contraction, and a comparison was done between the EC_{50} of norepinephrine in the absence and the presence of N-428 [13].

3. Results

3.1. Effect of N-428 on rat thoracic aorta

Injected in the bath, N-428 relaxes completely the organ and exerted concentration-dependent vasorelaxant effect on norepinephrine induced contraction in both endothelium-intact and endothelium-denuded thoracic aorta. Its EC_{50} in the intact endothelium is equal to 8.92.10^{-5} M, and 8.83.10^{-5} M in denuded endothelium. These results indicate that the vasodilatory activity of N-428 is endothelium independent (Figure 1).

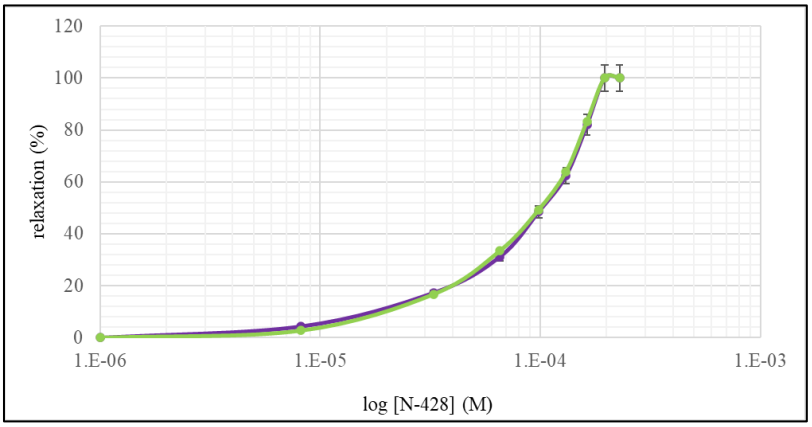

Figure 1 Relaxation of rat isolated thoracic aorta with intact ( ) and denuded endothelium( ) pre contracted with 10 µM of norepinephrine in the presence of N-428 injected in the bath in a cumulative manner ($\bar{x} \pm \bar{\sigma}$; n = 10 ; p < 0.05)

3.2. Effect on α1-receptor activities

Pre-incubation of the isolated aorta with various concentrations of N-428 before injecting norepinephrine does not change the maximal contraction induced by this mediator, while it provokes a right shift of the effect-concentrations curves with increasing of norepinephrine EC_{50} from 4.53.10^{-9} M in the absence of N-428 to 1.61.10^{-8}, 4.39. 10^{-7} and 0.61.10^{-6} M, in the presence de N-428 at concentrations 4.36.10^{-5}, 8.73.10^{-5} and 1.31.10^{-4} M. With pA2 equal to ≈ 5.78 M, versus 8.249 for prazosin. Its dissociation constant Kd is equal to 1.259. 10^{-6} M, versus 5.63.10^{-9} M for prazosin. The right shift of the curve of norepinephrine without reducing its Emax demonstrates that vasodilatory activity of N-428 is related to the α1 -receptor activity (Figure 2).

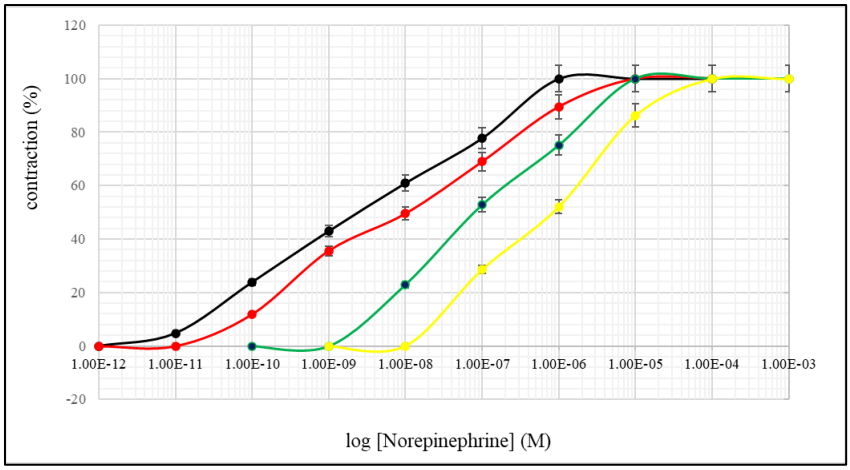

Figure 2 Contraction of rat isolated thoracic aorta induced by norepinephrine (■) injected in the bath in a cumulative manner in the presence of N-428 at concentrations of $4.36.10^{-5}$ (■), $8.73.10^{-5}$ (■) and $1.31.10^{-4}$ M (■) ($\bar{x} \pm \bar{\sigma}$; n = 10; p < 0,05)

4. Discussion

Moringa oleifera seeds are used in traditional medicine in the northern region of Madagascar to manage hypertension. Our previous studies have shown its antihypertensive, diuretic and vasodilation activities [9, 10]. We also have identified one vasodilator compound, isolated from ethyl acetate extract after a bio-guided assays, and its structural elucidation indicated that it belongs to the amide's family [11]. Its mechanism of action was not yet elucidated, therefore this work aimed to do that. Our results indicate that it relaxes isolated thoracic aorta with endothelium and without endothelium precontracted with norepinephrine.

The results of the test that we have done demonstrate the vasorelaxant activity of N-428 in both endothelium-intact and endothelium-denuded aortic rings. The persistence of complete relaxation after mechanical endothelial removal suggests that pathways involving endothelial mediators such as nitric oxide, prostacyclin, or EDHF are unlikely to be the primary contributors to this relaxation activity. These results are characteristic of vasodilators acting directly on vascular smooth muscle rather than dependent on endothelial signalling [14, 15].

The concentration-response analysis provides further insight into the mechanism of action. Pre-incubation of the organ in a bath containing N-428 before contracting with norepinephrine produced a progressive, concentration-dependent rightward shift of norepinephrine-induced contractions curves, without altering the maximal response. According to classical receptor pharmacology, such parallel shifts accompanied by preservation of Emax are defining features of competitive antagonism at the receptor level [16]. The increase of norepinephrine EC_{50} in the presence of N-428 confirms that its affinity for α1-receptors is reduced in the presence of the isolate, without change in maximal efficacy.

These findings show the isolate mechanism of action which behaves as a competitive α1-antagonist, but with markedly modest affinity compared with prazosin, a classical agent. Quantitative affinity parameters further consolidate this conclusion. The pA_2 of the isolate (≈ 5.78) is substantially lower than that of prazosin (8.249), a standard α_1-antagonist known for its high receptor affinity and clinical potency [17]. Similarly, the dissociation constant of the isolate (Kd = $1.259.10^{-6}$ M) is higher than that of prazosin ($5.63.10^{-9}$ M), indicating comparatively weak α_1-receptor binding typical of antagonists with moderate binding kinetics [16, 18]. From a mechanistic standpoint, its ability to attenuate adrenergic vasoconstriction despite weaker affinity places it within the category of mild-to-moderate antagonists capable of reducing vascular tone without completely abolishing sympathetic responsiveness. As antagonist α1 with lower affinity, it may theoretically generate fewer orthostatic or reflexogenic side effects, a concern well documented for potent α_1-blockers [19].

Nevertheless, the comparatively high EC_{50} values required for N-428 to exert its vasorelaxant action raise critical questions about its pharmacological viability. Higher effective concentrations may reflect suboptimal receptor interactions or limited membrane permeability - issues frequently observed with highly polar or hydrophilic small molecules. Additionally, the gap between its affinity and that of prazosin suggests that this isolate may require substantial structural optimization before consideration as a therapeutic lead [20, 21].

5. Conclusion

In summary, these results indicate that N-428 isolated from *Moringa seeds* possesses vasodilatory activity, acting directly on vascular smooth muscle and independently of endothelial function, primarily mediated by competitive antagonism of α1-adrenergic receptors. This isolate may offer effective and consistent blood pressure reduction in hypertensive patients, even in the presence of endothelial dysfunction, by directly modulating vascular smooth muscle tone. This study validates the traditional use of *Moringa oleifera seeds* in hypertension treatment by demonstrating the significant vasodilatory effects of a bioactive compound.

Compliance with ethical standards

Acknowledgments

All authors approved the final manuscript. We would like to thank Marc ANDRIANOME for his support.

Disclosure of conflict of interest

The authorswork.re that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Statement of ethical approval

They were strictly handled in accordance with the National Institutes of Health Guidelines for the Care and Use of Laboratory Animals (NIH Publication No. 85-3, revised 1996) and the study was approved by the Committee of Animal Ethic of Faculty of Sciences, University of Antananarivo, Madagascar (CE/Fac Sciences/04/2025).

Author contributions

Patricia and Yodan designed the study. Yodan and Tiananiaina performed the experiments and analysed results. Yodan and Quansah wrote the manuscript. Patricia and Rivoarison supervised the work.

References

[1] World Health Organization. First detailed report on the devastating consequences of hypertension and ways to overcome it. World Health Organization. September 2023. 1-5.

[2] Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nature Reviews Nephrology. April 2020; 16 (4): 223-237.

[3] World Health Organization. Global report on hypertension 2025: high stakes: turning evidence into action. WHO Newsletter. Ed. WHO. September 2025; p 342.

[4] Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. Journal of Natural Products. March 2020; 83 (3): 770-803.

[5] Anwar F, Latif S, Ashraf M, Gilani AH. Moringa oleifera: A food plant with multiple medicinal uses. Phytotherapy Research. January 2007; 21 (1): 17-25.

[6] Leone A, Spada A, Battezzati A, Schiraldi A, Aristil J, Bertoli S. Cultivation, genetic, ethnopharmacology, phytochemistry and pharmacology of Moringa oleifera leaves: An overview. International Journal of Molecular Sciences. June 2015; 16 (6): 12791-12835.

[7] Aekthammarat D, Pannangpetch P, Tangsucharit P. (2019). Moringa oleifera leaf extract lowers high blood pressure by alleviating vascular dysfunction and decreasing oxidative stress in L-NAME hypertensive rats. Phytomedicine. February 2019; 54: 9-16.

[8] Menichetti F, Berteotti C, Schirinzi V, Poli C, Arrighi R, Leone A. *Moringa oleifera* and Blood Pressure: Evidence and Potential Mechanisms. Nutrients. April 2025; 17 (7): 1-18.

[9] Ralahiravo DY, Randimbivololona F, Randrianavony P. Étude comparative de l'effet vasodilatateur des graines de *Moringa oleifera* et d'écorce d'*Anacardium occidentale*. Revue des Sciences, de Technologies et de l'Environnement. November 2021; 5: 237-246.

[10] Ralahiravo DY, Rakotoarison O, Randimbivololona F, Quansah N, Randrianavony P. Antihypertensive activity of *Moringa oleifera* seeds hydroalcoholic extract on high sodium diet-induced hypertension in Wistar Rat. World Journal of Biology Pharmacy and Health Sciences. February 2023; 13 (02): 350-356.

[11] Donkor PO, Andriamadio JH, Ralahiravo DY, Rakotondrasoa T, Randrianavony P, Randrianasolo R. (2025). Isolation of a vasodilator molecule from *Moringa oleifera* L. (MORINGACEAE) seeds using bioassay-guided fractionation. World Journal of Chemical and Pharmaceutical Sciences. December 2025; 07 (01): 009-016.

[12] KITCHEN I. Textbook of in vitro Practical Pharmacology. Ed. Blackwell Scientific Publications, Oxford. 1984; 1-6.

[13] Mengistu M, Abebe Y, Mekonnen Y, Tolessa T. In vivo and in vitro hypotensive effect of aqueous extract of Moringa Stenopetala. African Health Sciences. December 2012); 12 (4): 545-551.

[14] Félétou M, Vanhoutte PM. (2006). Endothelium-derived hyperpolarizing factor: Where are we now? Arteriosclerosis, Thrombosis, and Vascular Biology. June 2006; 26 (6) 1215-1225.

[15] Rang HP, Dale MM, Ritter JM, Flower RJ, Henderson G. Rang & Dale's Pharmacology 9th Ed. Elsevier. November 2020; 1-65.

[16] Kenakin T. A Pharmacology Primer: Techniques for More Effective and Strategic Drug Discovery. 6th ed. London: Academic Press (Elsevier). April 2014; 71-95.

[17] Bryson CL, Psaty BM. A Review of the Adverse Effects of Peripheral Alpha-1 Antagonists in Hypertension Therapy. Current Controlled Trials in Cardiovascular Medicine. April 2002; 3 (1), 1-7.

[18] Clark RB, Titeler M. Binding characteristics and regulation of α_1-adrenergic receptors. Journal of Pharmacology and Experimental Therapeutics. 1986; 237 (2): 600-606.

[19] Sica DA. (2005). Alpha-1 adrenergic blockers: current usage considerations. Journal of Clinical Hypertension (Greenwich). December 2005; 7 (12): 757-762.

[20] Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. (2001). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews. March 2001; 46 (1-3): 3-26.

[21] Gleeson MP, Hersey A, Montanari D, Overington, J. Probing the links between in vitro potency, ADMET and physicochemical parameters. Nature Reviews Drug Discovery. March 2011; 10 (3): 197-208.