GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(RESEARCH ARTICLE)

Check for updates

Assessment of the vasodilator effect of "24-hydroxymethyl-23,26,27-trihydroxy-cucurbit-5-ene-3-yl-acetate" (NC36) isolated from *Sechium edule* (Jacq.) Swartz (Cucurbitaceae) fruits

Marie Nancy Volamiadana RABIA [1, *], Julio Hervé ANDRIAMADIO [2], Soaviherimbola Delore RAZAFIMAHAZORO [1], Roméo RAZANADRABENAFINDRA [1], Nathaniel QUANSAH [1] and Patricia RANDRIANAVONY [1]

[1] *Department of Pharmacology, Sciences of Faculty, University of Antananarivo, Madagascar.*
[2] *Department of Chemistry, Faculty of Sciences, University of Antsiranana, Antsiranana, Madagascar.*

GSC Biological and Pharmaceutical Sciences, 2026, 34(03), 122-127

Publication history: Received on 09 February 2026; revised on 16 March 2026; accepted on 18 March 2026

Article DOI: https://doi.org/10.30574/gscbps.2026.34.3.0107

Abstract

Our previous studies have demonstrated that the hydroalcoholic extract of *Sechium elude* fruits exerts significant antihypertensive and vasodilatory effects. The present study was undertaken to elucidate the mechanism underlying the vasorelaxant activity of NC36 (cucurbitane-type triterpenoid) isolated from this extract. Experiments were performed on isolated aortic rings precontracted with norepinephrine. The results showed that NC36 induced complete (100 %) relaxation in isolated aorta with intact endothelium, whereas no significant relaxation was observed in endothelium-denuded preparations, indicating that the vasodilatory effect of NC36 is endothelium-dependent. Pre-incubation of the aortic rings with indomethacin at the concentrations of 10^{-7}, 10^{-6} and 10^{-5} M induced a significant rightward shift of the concentration–response curves and an increase in NC36 EC_{50} values ($p < 0.05$), indicating the participation of cyclooxygenase-derived metabolites. These findings suggest that NC36 induces endothelium-dependent vasorelaxation, at least in part, through the prostacyclin pathway and most probably NO release.

Keywords: Cucurbitane-Derivative; Fruit; *Sechium elude*; Vasodilation

1. Introduction

Arterial hypertension is a leading risk factor for the development of cardiovascular diseases. In Madagascar, an estimated 2.8 million adults aged 30-79 years, of the 27 533 000 population, were recorded with hypertension and 178 000 deaths, 40 500 attributed to cardiovascular diseases provoked by hypertension are also recorded the same year. Only 16 % are treated according to WHO Guidelines for management of hypertension and 6 % are controlled [1]. Vasodilator drugs, such as calcium-channel blockers, nitro vasodilators, potassium channel activators, and α1-adrenergic blockers are included in the management strategies for hypertension of WHO [2]. *Sechium edule* (Jacq.) SW. (Cucurbitaceae) is a plant endemic to Mexico, known by the vernacular name Sosety in Malagasy, Christophine in French, and Chayote in English. In Madagascar, the fruit of this plant is widely consumed as food and, in traditional medicine, it is used for the treatment of hypertension. Several scientific studies have reported that this species possesses antihypertensive activity. Indeed, Lombardo-Earl and colleagues (2014) demonstrated that the roots of this plant exhibit antihypertensive effects, and in 2025, we also have reported that its fruit shows antihypertensive activity [3, 4]. Moreover, the same year (2025), we have isolated an active compound (NC36 which is a cucurbitane derivate) from the fruit of this plant and demonstrated its vasodilatory activity [5]. However, the mechanism underlying its vasodilatory action has not yet been fully elucidated. Therefore, the vasodilatory effect of this active compound is investigated in the

* Corresponding author: Marie Nancy Volamiadana RABIA

present study using isolated rat aorta with and without endothelium precontracted with norepinephrine. Furthermore, its involvement in prostacyclin pathways was also examined.

2. Materials And Methods

2.1. Herbs and chemicals

Sechium edule was collected from Antanamitarana and Andranomanitra, two localities in the DIANA region, Madagascar. A voucher specimen was identified at the herbarium of Parc Botanique et Zoologique de Tsimbazaza (PBZT), Antananarivo, Madagascar. All the drugs and reagents used were with the required standard and analytical grade: hexane, chloroform, ethanol, methanol and ethyl acetate were purchased from LABOSI, 141 Rue de JAVEL, Paris 75. Deuterated methanol (MeOD), deuterated chloroform (CDCl3) and ingredients for making Kreb's Henseleit solution were obtained from Sigma-Aldrich Inc. (St. Louis, MO, USA). Standard 5 mm, 7'' NMR tubes (XR-55 series) were purchased from Norell Inc. (Landisville, NJ, USA). Chromatographic preparative plates (Ref 4856-840) were purchased from MERK (39 Rte Industrielle de la Hardt, 67120 Molsheim, France).

2.2. Animal handling

Wistar rats, weighing between 200 and 250 g were used in this work, they were bred at the animal house of Laboratory of General Pharmacology, Pharmacokinetic and Cosmetology of Sciences Faculty, University of Antananarivo, in standard conditions: 12/12 hours cycle of light and darkness, at room temperature of 22 °C and with free access to food and water. Care and use of the animals were approved by the bioethics committee of the Sciences Faculty, University of Antananarivo, Madagascar, registered as CEA/FS-UA/ Registre n° 12/2023.

2.3. Aortic rings preparation

Prior to the isolation of the aorta, Krebs-Henseleit (Krebs) solution (4.7 mM KCl, 118.0 mM NaCl, 2.5 mM $CaCl_2$, 25.0 mM $NaHCO_3$, 1.2 mM KH_2PO_4, 11.0 mM glucose, and 1.2 mM $MgSO_4$, pH 7.4) [6], was prepared and continuously aerated with carbogen (5 % CO_2 and 95 % O_2) in a Petri dish. The rats were sacrificed by injection by injection of 100 mg/kg of phenobarbital intra peritoneally. The thoracic aorta was immediately isolated and placed in Krebs' solution. After removal of the adipose tissues, the aorta was trimmed into 3–4 mm ring segments and mounted in a tissue bath containing Krebs' solution, by using two S-shaped hooks, maintained at the temperature at 37 °C and continuously aerated with carbogen gas. One hook was fixed at the basis of the organ bath, and the second hook was connected to the force-electricity transducer (Statam Gould Isometric Measurement). The mounted aortic rings were allowed to equilibrate for 45 minutes, and the Krebs' solution was renewed every 15 minutes, and the resting tension was readjusted to 1 g. After equilibration period, norepinephrine was injected in the bath to realize 10 µM, at plateau of contraction, acetylcholine was injected in the bath at final concentration of 10 µM. The integrity of endothelium was assured with at least 60 % of relaxation. Then, the aortic rings were rinsed three times with Krebs' solution at 15 minutes intervals before injecting norepinephrine.

2.4. Vascular response to NC36 to precontracted aortic rings

The endothelium-intact aortic ring was precontracted with norepinephrine (10 µM). When the contraction reached a plateau, the isolate was added into the organ bath cumulatively from 4.1×10^{-5} M until complete relaxation. The concentration-response curve, the maximum relaxation and the half maximal effective concentration (EC_{50}) value obtained were assigned as controls and compared to different antagonist pretreated groups [6, 7]

2.5. Vasodilatory effect of NC36 in endothelium-impaired aortic rings

The intima surface of the isolated aortic rings was removed mechanically by gently rubbing with a stainless-steel stick. The integrity of the endothelium-denuded aortic rings was checked by exposure to norepinephrine and injection of acetylcholine at plateau of contraction. Absence of endothelium is assured when no relaxation upon exposure to acetylcholine. The preparation was rinsed, and after equilibration period, the organ was pre contracted with norepinephrine 10 µM, NC36 was added to the organ bath cumulatively at a final concentration of 4.1×10^{-5} M in the bath until complete relaxation [8]

2.6. Investigation of the implication of prostacyclin in NC36 vasodilatory activity

To investigate the vasodilatory effect of NC36 in relation to prostacyclin, its effect was evaluated on isolated aorta pre-incubated in a bath containing indomethacin prior to contraction with norepinephrine. After the stabilization period, the aorta was incubated in a bath containing indomethacin at a concentration of 10^{-7} M for 15 minutes. Following this

incubation period, noradrenaline was added to the bath to achieve a final concentration of 10 µM. Once the contraction plateau was reached, NC36 was administered cumulatively to the bath, starting at a concentration of 4.1×10^{-5} M, until complete relaxation of the tissue was achieved. The same experiment was carried out, using indomethacin at concentrations of 10^{-6} and 10^{-5} M. Concentration–response curves were generated in both the absence and presence of indomethacin at various concentrations, and the half-maximal effective concentration (EC_{50}) of NC36 was determined by linear regression.

2.7. Statistical analysis

All the data were expressed as the mean ± S.E.M. The results obtained for antagonist pretreated groups were compared to the control by using one-way ANOVA and Student's t test, and the significance was considered as significative at $p < 0.05$.

3. Results And Discussion

3.1. Effect of NC36 to precontracted aortic rings

When injected to the bath containing isolated aorta precontracted with norepinephrine at a concentration of 10 µM, NC36 induced relaxation in a concentration-dependent manner. This relaxation reached 100 % at a concentration of 9.1×10^{-5} M (Figure 1). These results indicate that this compound exerts vasodilatory effect, with an EC_{50} of 4.38×10^{-5}M.

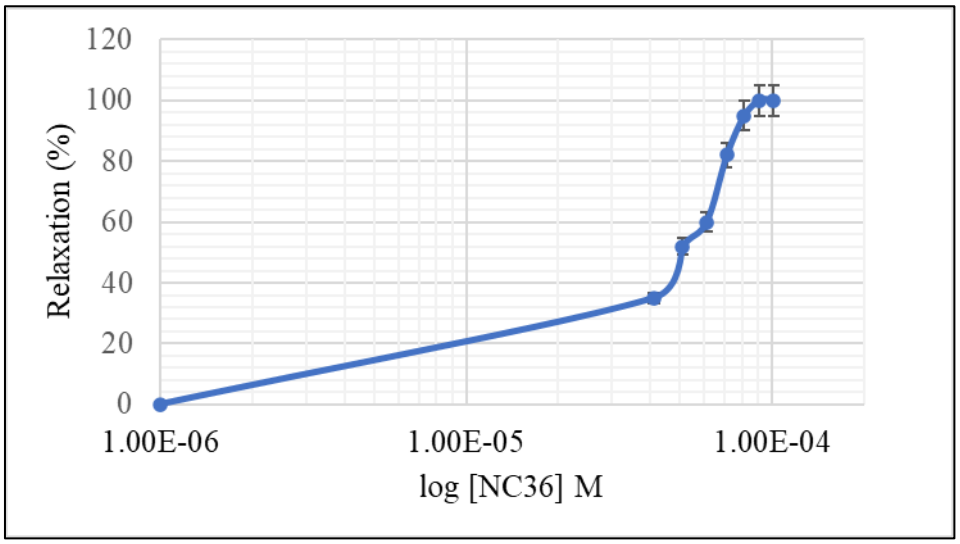

Figure 1 Relaxation of isolated aorta precontracted with norepinephrine at 10 µM, in the presence of NC36 injected in the bath in a cumulative manner ($\bar{x} \pm \bar{\sigma}$; n = 10; $p < 0.05$)

3.2. Role of endothelium in vasodilatory effect of NC36

In the presence of endothelium, NC36 produced 100 % relaxation of isolated aorta precontracted with norepinephrine (Figure1), compared with only 18 % relaxation in the absence of endothelium (Figure 2). According to the results, NC36 completely relaxed endothelium-intact aorta precontracted with norepinephrine. In contrast, it was unable to relax endothelium-denuded aorta contracted with noradrenaline (Figure 2). These results indicate that the vasodilatory effect of NC36 is endothelium dependent.

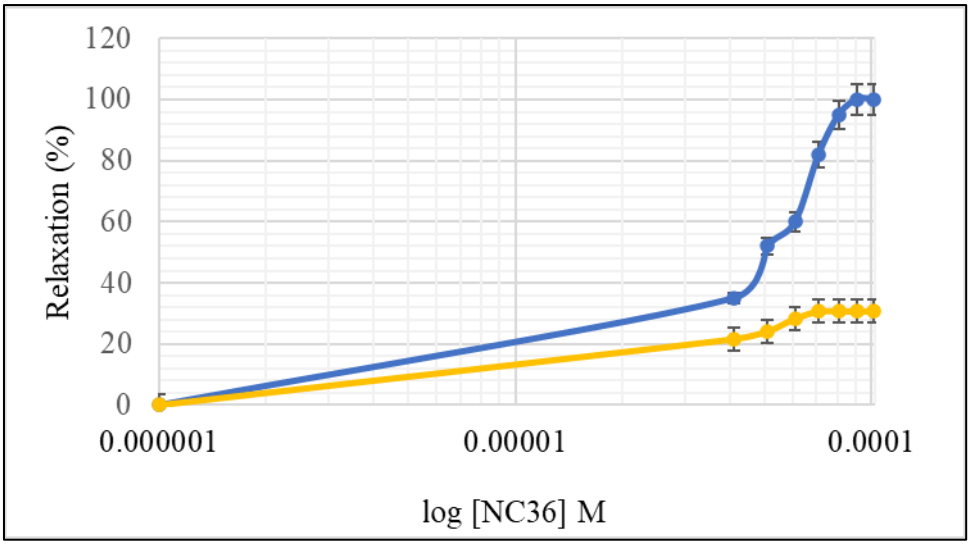

Figure 2 Relaxation of the isolated aorta precontracted with norepinephrine at concentration of 10 µM, induced by NC36 injected in the bath in a cumulative manner, with endothelium ( ) and endothelium free ( ) ($\bar{x} \pm \bar{\sigma}$; n = 10; $p < 0.05$)

These results suggest that NC36 vasodilatory action may involve the release or modulation of endothelial mediators such as prostacyclin or nitric oxide, which are major regulators of vascular tone [10]. To evaluate these possibilities, the implication of prostacyclin was investigated.

3.3. Implication of prostacyclin in NC36 vasodilatory activity

As the vascular endothelium plays a key role in regulating vascular tone through the release of relaxing mediators such as nitric oxide (NO) and prostacyclin, we investigated the vasodilatory effect of NC36 in the presence of indomethacin, a cyclooxygenase inhibitor that blocks prostacyclin synthesis. When aortic rings precontracted with noradrenaline were incubated with increasing concentrations of indomethacin, NC36 continued to induce relaxation of the vascular tissue [12].

However, a rightward shift of the concentration–effect curve was observed without alteration of the maximal response, accompanied by a concentration-dependent increase in EC_{50} values. Specifically, the EC_{50} increased from 4.38×10^{-5} M in the absence of indomethacin to 6.42×10^{-5}, 7.43×10^{-5}, and 8.46×10^{-5} M in the presence of indomethacin at 10^{-7}, 10^{-6}, and 10^{-5} M, respectively ($p < 0.05$) (Figure 3). These findings suggest a competitive interaction between indomethacin and NC36, indicating that prostacyclin partially contributes to the vasodilatory effect of NC36.

Nevertheless, the persistence of a significant relaxation despite cyclooxygenase inhibition strongly suggests the involvement of additional endothelium-dependent or endothelium-independent mechanisms. In particular, nitric oxide (NO) may play a central role, as it is a major endothelial-derived relaxing factor capable of inducing smooth muscle relaxation via activation of the guanylate cyclase–cGMP pathway. Moreover, other vasorelaxant pathways could be implicated, including endothelium-derived hyperpolarizing factor (EDHF), modulation of calcium influx in vascular smooth muscle cells, or direct action on potassium channels.

This interpretation is consistent with the findings of Chung et al. (2023), who reported that the vasodilatory effect of the chloroform fraction of Crinum amabile is endothelium-dependent and mediated, at least in part, by prostacyclin [13]. Taken together, our results suggest that while prostacyclin contributes to NC36-induced vasorelaxation, but it is not the only mediator, other pathways—particularly NO-related mechanisms—are likely to be involved, since cucurbitane-type triterpenoids are known to enhance nitric oxide (NO) release [14].

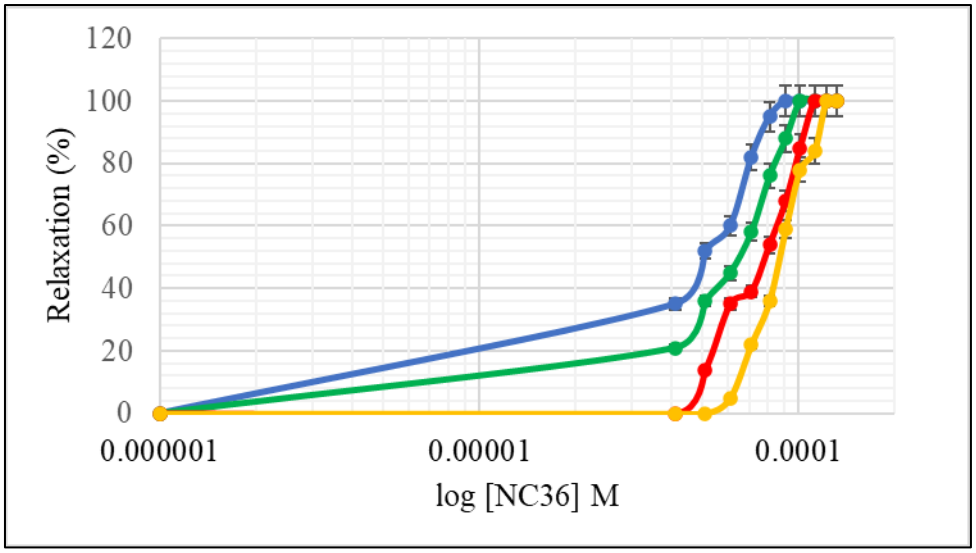

Figure 3 Relaxation of isolated aorta precontracted with norepinephrine at 10 µM, induced by NC36 injected in the bath in a cumulative manner in the absence of indomethacin ( ) and in its presence at concentrations of 10^{-7} ( ), 10^{-6} ( ) and 10^{-5} M ( ) ($\bar{x} \pm \bar{\sigma}$; n = 10; p < 0,05)

4. Conclusion

The present findings demonstrate that NC36, isolated from *Sechium edule* fruit, exerts a significant vasorelaxant effect on noradrenaline-precontracted aortic rings. This activity could be attributed to partial contribution of prostacyclin. However, the persistence of relaxation despite cyclooxygenase inhibition suggests that additional mechanisms are involved. Overall, these results highlight that NC36 contributes to anti-hypertensive activity of *Sechium edule* fruit.

Compliance with ethical standards

Acknowledgments

All authors have contributed according to their speciality to the work

Disclosure of conflict of interest

Declaration of competing interest: All authors declare that No conflict of interest exists.

Statement of ethical approval

Care and use of the animals were approved by the bioethics committee of the Sciences Faculty, University of Antananarivo, Madagascar, registered as CEA/FS-UA/ Registre n° 12/2023.

References

[1] World Health Organization. Global report on hypertension: the race against a silent killer [internet]. Geneva, Switzerland: World Health Organization; © 2023; p. 1–291. [cited 2023 sept 19]. Available from https://www.who.int/publications/i/item/9789240081062

[2] Moick S, Sommer I, Gartlehner G. WHO Guideline for the Pharmacological Treatment of Hypertension in Adults. Gesundheitswesen. 2023; 85(2):139-142.

[3] Lombardo-Earl G, Roman-Ramos R, Zamilpa A, Herrera-Ruiz M, Rosas-Salgado G, Jaime Tortoriello J, JiménezFerrer E. Extracts and Fractions from Edible Roots of *Sechium edule* (Jacq.) Sw. with Antihypertensive Activity. Evid Based Complement. Alternat Med. 2014; 1-9.

[4] Rabia MNV, Razanadrabenafindra R, Rakotondrasoa T, Quansah N, Andriamadio JH, Randrianavony P. Evaluation of antihypertensive activity of the hydroalcoholic extract of *Sechium edule* (Jacq.) SW. (CUCURBITACEAE) fruit in rat. GSC Adv Res Rev. 2025; 22(03):207-213.

[5] Donkor PO, Rabia MNV, Randrianavony P, Razafimahazoro SD, Quansah N, Rajaonarison JF. Identification of a vasodilator compound isolated from the fruit of *Sechium edule* (Jacq.) Swartz (CUCURBITACEAE). Int J Adv Chem Res. 2026; 8(3):1-5.

[6] Kitchen I. Textbook of in vitro Practical Pharmacology. 1st Ed Scientific Blackwell: Oxford; 1984.p. 1-6.

[7] Vergara-Galicia J, Jimenez-Ramirez LÁ, Tun-Suarez A, Aguirre-Crespo F, Salazar-Gómez A, Estrada-Soto S, Sierra-Ovando Á, Hernandez-Nuñez E. Vasorelaxant activity of extracts obtained from *Apium graveolens*: Possible source for vasorelaxant molecules isolation with potential antihypertensive effect. Asian Pac J Trop Biomed. 2013; 3(10):776-779.

[8] Knox M, Vinet R, Fuentes L, Morales B, Martínez JL. A Review of Endothelium-Dependent and -Independent Vasodilation Induced by Phytochemicals in Isolated Rat Aorta. Animals (Basel). 2019; 9(9):623-631.

[9] Lopez-Canales JS, Lozano-Cuenca J, Munoz-Islas E, Aguilar-Carrasco JC, Lopez-Canales OA, Lopez-Mayorga RM, Castillo-Henkel EF, Valencia-Hernandez I, Castillo-Henkel C. Mechanisms involved in the vasorelaxant effects produced by the acute application of amfepramone in vitro to rat aortic rings. Braz J Med Biol Res. 2015; 48(6):537-544.

[10] Vanhoutte PM, Félétou M, Tang EHC. Endothelium-dependent contractions in hypertension. Br J Pharmacol. 2005; 144(4):449-458.

[11] Félétou M, Vanhoutte PM. Endothelium-dependent hyperpolarizations: Past beliefs and present facts. Pharmacol Rev. 2006; 58(3):289-329.

[12] Brown L, Smith J, Taylor P, Johnson R. Prostacyclin synthesis and vascular tone regulation. Cardiovasc J. 2008; 33(6):512-520.

[13] Lim CP, Fei YM, Asmawi MZ, Chin VK, Khairuddin NH, Yong YK, Lawal1 MG, Basir R. Endothelium-dependent vasorelaxation effects of F5 fraction of *Crinum amabile* chloroform extract. J Basic Appl Sci. 2023; 12:1-13.

[14] Chen JC, Chiu MH, Nie RL, Cordell GA, Qiu SX. Cucurbitacins and cucurbitane glycosides: structures and biological activities. Natural Product Reports. 2005; 22(3): 386-399.