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# CARDIOVASCULAR PROPERTIES OF AQUEOUS EXTRACT FROM *TAPINANTHUS DODONEIFOLIUS* DC DANSER.

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## Abstract

Aqueous extracts of *Tapinanthus dodoneifolius* DC Danser. (Loranthaceae) (AETD) were investigated for cardiovascular activities on isolated rat aorta and heart. AETD did not affect heart rate but significantly enhanced heart contraction force and relaxation capacity. AETD (0.001-1mg/ml) elicited a dose-dependent relaxation on arteries which was previously contracted with phenylephrine [$10^{-6}$M] (rat aorta). AETD induces relaxation in endothelium dependent manner. When Indomethacin failed to inhibit AETD vasodilatory activity, in the presence of L-NAME, the vasodilatory activity of AETD was completely abolished. These results suggest a cardiotropic activity without any tachycardia as a side effect for AETD. However, AETD elicited vasodilatory activity which involved NO from endothelium.

**Key words :** *Tapinanthus dodoneifolius* , endothelium , vasodilator , rat.

## Introduction

*Tapinanthus dodoneifolius* DC Danser (Loranthaceae) is an ubiquist plant, especially parasitizing Mimosaceae ; these plants are largely growing in West Africa (Kerharo and Adams, 1974 ; Boussim, 2002). Those parasitizing *Vittelaria paradoxa* CF Gaertn (Sapotaceae) are used alone or in association with other traditional remedies in Burkina Faso for the treatment of variety of disorders, particularly cardiovascular and respiratory diseases (Nacoulma/Ouédraogo, 1996).
Spasmolytic and anti-inflammatory activities of aqueous extract from *T. dodoneifolius* has been reported (Traoré 2000). Cepleanu et al. (1994), reported larvicidal and

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molluscicidal activities of this plant. Here we studied the effects of the aqueous extract from *T. dodoneifolius* on cardiovascular preparation.

## Experimental

### Plant and extract

*T. dodoneifolius* (stems and leaves) was collected from the region of loumbila, Burkina Faso (zone of savanna) in February 2002 (dry season). Plant materials were verified to be identical samples at the specimen herbarium of the laboratory of vegetal biology, University of Ouagadougou. A voucher specimen (n° 002) was previously deposited at this herbarium.

The aqueous extract was prepared as follows : the dried powder (100 g) of whole plant of *T. dodoneifolius* was extracted in 500 ml of distilled water. Raw material was boiled during 15 minutes and filtered, frozen and lyophilized.

### Tissue preparations

This investigation conforms to authorization number 01918 given by the French government Department of Agriculture.

### Isolated perfused heart

Male Wistar rats (12-14 weeks old) were used. Rats were anaesthetized with pentobarbital (60 mg/kg, i.p.) mixed with 500 UI of heparin. Heart was rapidly excised and transferred into ice-cold Krebs-Henseilet buffer with the following composition (mM): NaCl 118; $NaHCO_3$ 24; KCl 4.7; $KH_2PO_4$ 1.2; $MgSO_4$ 1.2; $CaCl_2$ 1.7; glucose 10. Then, the heart was immediately mounted and cannulated in the retrograde mode according to Langendorff method as already described (Langendorff , 1985). Perfusion pressure was maintained constant at 100 cm $H_2O$ with Krebs-Henseilet buffer gassed with 95% $O_2$, 5% $CO_2$ at 37°C and was controlled with a pressure transducer connected to the perfusion circuit immediately before the heart. The heart was then placed in semi-closed, circulating water warmed air chamber. Then, a water-filled latex balloon (Ealing S.A.R.L, France) connected to an Isotec pressure transducer (Hugo-Sachs, Germany) was inserted into the left ventricle for measurement of ventricular pressure. Transducers were connected to a computer via an amplifier and a MacLab™ (ADI Instruments, Australia) for on-line recording and analysis of parameters. Left ventricular and diastolic pressure was set to 10-15 mmHg by adjusting the volume of the balloon. The heart was then allowed to equilibrate for 20 min. Cardiac parameters were recorded continuously : left ventricular developed pressure [(LVDP) difference between systolic and diastolic pressure, positive of LVDP (+ $dP/dt_{max}$)] and heart rate. Coronary perfusion was controlled with an another pressure transducer connected to the circuit immediately before the heart.

After 20 min period of stabilization, the protocol consisted of perfusing the heart with increasing concentrations of AETD ( 0.001-1mg/mL).

### Aortic preparation and mounting

Male wistar rats (12-14 weeks old) were killed by cervical dislocation and then exsanguinated by carotid artery transection. The thoracic aorta was removed and mounted as previously described in a physiological salt solution (Andriambelson et al.

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1997). Aortic rings with and without functional endothelium were pre-contracted to the same tension (i.e. 80% of maximal response obtained in vessel with functional endothelium) with phenylephrine $10^{-6}$ or 5 x $10^{-8}$M respectively. When the contraction reached a steady state, increasing concentrations of AETD were added cumulatively.
In order to characterize the involvement of NO and cyclooxygenase (COX) products, some arteries with functional endothelium were exposed to the NO synthase inhibitor, $N^G$-nitro-L-arginine methyl ester (L-NAME : 3 x $10^{-4}$M) or to the COX inhibitor indomethacin ($10^{-5}$M), added to the bath 15min before phenylephrine. In the case of L-NAME, the concentration of phenylephrine was adjusted in order to obtain the same level of pre-contraction as in the absence of L-NAME.

**Drugs and chemicals**

NaCl, $NaHCO_3$, KCl, $KH_2PO_4$, $MgSO_4$, $CaCl_2$, glucose (Sigma Chemical Co, Grenoble, France). Phenylephrine, Indomethacin, L-NAME (Sigma Chemical Co, Grenoble, France). Indomethacin ($10^{-5}$M) was dissolved in 5 % $NaHCO_3$.

**Statistical analysis**

All data were expressed as mean ± S.E.M. Two way ANOVA and Student's *t*-test were used to determine significant differences between groups. Mean values were considered significantly different when $P<0.05$.

## Result and Discussion

In rat isolated hearts, AETD induced an increase in cardiac contraction represented by an enhancement of dP/dt value ; (Figure. 1 A). In the same condition, AETD did not significantly modify heart rate (Figure. 1 B) ; coronary flow value was 12.08 ± 0.75 and 11.60 ± 1.01 mL/min in the presence and in the absence of AETD respectively.

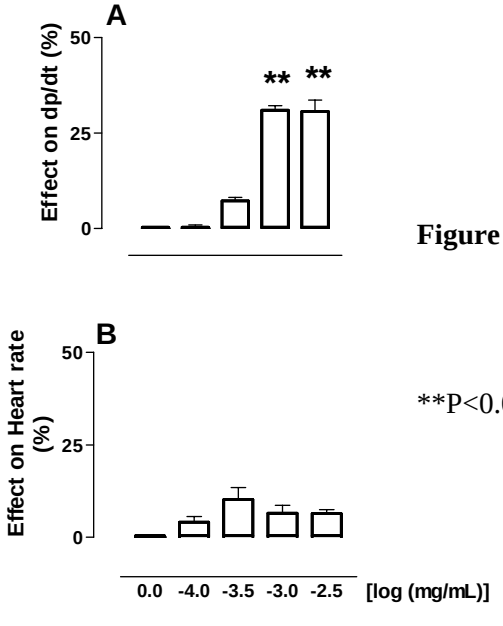


**Figure 1 :** Non-cumulative concentration-response to AETD treatment on isolated rat heart dP/dt (A) and rate (B). Bars represent the mean ± S.E.M. of at least 6 experiments.
**P<0.01, with respect to the control.

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Thus AETD induced an increase in cardiac contraction without any significant modification on heart rate. These results suggest that AETD possess a cardiotropic activity without any tachycardia.

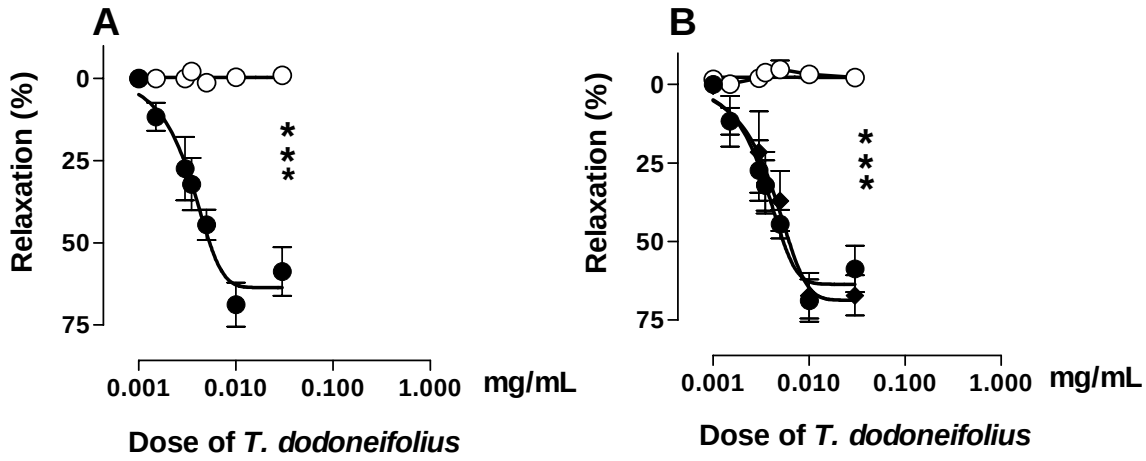


**Figure 2 : A** : Cumulative concentration-response curves to AETD on isolated rat aorta, previously contracted with phenylephrine ($10^{-6}$M) in the presence or in the absence of endothelium (filled and open circles respectively). **B** : Cumulative concentration-response curves to AETD on isolated rat aorta, previously contracted with phenylephrine ($10^{-6}$M) (filled circles), in the presence of indomethacin $10^{-5}$ M (filled squares) or indomethacin $10^{-5}$ M + L-NAME $310^{-4}$ M (open circles). Each point represents the mean ± S.E.M. of 5 to 8 rats. ***P<0.001 Control with respect to absence of endothelium (A) or to L-NAME treatment.

Effect of AETD was then investigated on isolated rat aorta. On this vessel pre-constricted by phenylephrine ($10^{-6}$M), AETD (0.001-1mg/mL) induced a concentration-dependent relaxation. This relaxation was observed in endothelium-intact aortic rings (Figure. 2 A, solid circles). The maximal effect (74.07 ± 0.89) was observed with 0.01mg/ml concentration. In endothelium-denuded arteries, AETD failed to relaxe phenylephrine-induced contraction (Figu.2 A ; open circles).

Up to 0.01 mg/ml, the relaxation in response to AETD was exclusively dependent on the endothelium. It is widely know that one of the most important vasorelaxing mechanisms depends on nitric oxide (NO) and prostacyclin (Palmer et al. 1987 ; Moncada et al. 1988), released from endothelium. We examined the relative contribution of endothelial nitric oxide (NO) and cyclo-oxygenase (COX) metabolites in relaxation to AETD.

The addition of indomethacin ($10^{-5}$M) in the organ bath failed to influence the AETD decreases tension developed by phenylephrine ($10^{-6}$M) in rat aorta (compare solid square and circle in Figure 2 B). The maximal inhibition response to AETD (0.01 mg/ml) amounted to 74.07 ± 0.89% in the absence and 73.78 ± 0.99% in the presence of indomethacin. The presence of LNAME ($3.10^{-4}$M) abolish the relaxant effect of the AETD (Figure 2B, open circles).

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The COX inhibitor, indomethacin, failed to influence the AETD decreases tension developed by phenylephrine in rat aorta. (see Fig.2 B).These results suggest that COX metabolites were not involved in the response to this plant extracts. To test whether NO is involved in the endothelium-dependent relaxation to AETD, the effect of the NO-synthase inhibitor, L-NAME, was studied in the presence of indomethacin. In these conditions, L-NAME abolished the relaxation to AETD in rat aorta with endothelium. The involvement of NO in these effects of the extract was suggested by the obligatory role of endothelium for the relaxant action, and confirmed by the inhibition of the effects, observed after the treatments with L-NAME.

The results of this study allow us to conclude that aqueous extract (AETD) elicited vasodilatory activity in rat aorta. The mechanism may involve NO from endothelium. Moreover, AETD also increases the cardiac contraction without significant change in heart rate. This could be the basis of its ethnomedical use against cvs disorders traditionally. Further studies are necessary in order to determine which of the constituents of the extract from *T. dodoneifolius* are responsible for the decrease in tension development in response to agonist.

## Acknowledgements

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