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Electrophysiological effects of the aqueous extract of *Averrhoa carambola* L. leaves on the guinea pig heart ☆

C.M.L. Vasconcelos[a,b], M.S. Araújo[a], E.A. Conde-Garcia[a,*]

[a]*Cardiobiophysics Research Laboratory, Department of Physiology, Center of Biological and Health Sciences, Universidade Federal de Sergipe, Aracaju, Sergipe, Brazil*
[b]*Laboratório de Tecnologia Farmacêutica, Universidade Federal da Paraíba, João Pessoa, Paraíba, Brazil*

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Abstract

This work aims to describe some electrophysiological changes promoted by the aqueous extract (AEx) from *Averrhoa carambola* leaves in guinea pig heart. The experiments were carried out on isolated heart or on right atrium–ventricle preparations. In 6 hearts, the extract induced many kinds of atrioventricular blocks (1st, 2nd, and 3rd degrees); increased the QT interval from 229 ± 23 to 264 ± 19 ms; increased the QRS complex duration from 27 ± 3.1 to 59 ± 11 ms, and depressed the cardiac rate from 136 ± 17 to 89 ± 14 bpm. Furthermore, it decreased the conduction velocity of atrial impulse (17 ± 3%); reduced the intraventricular pressure (86 ± 6%), and increased the conduction time between the right atrium and the His bundle (27 ± 6.5%). The conduction time from the His bundle to the right ventricle was not altered. Atropine sulfate did not change either the electrocardiographic parameters or the intraventricular pressure effects promoted by the *A. carambola* AEx. Based on these results, the popular use of such extracts should be avoided because it can promote electrical and mechanical changes in the normal heart.

Keywords: *Averrhoa carambola* L.; Guinea pig atrium; Myocardium; ECG; His electrogram

Introduction

Herbal medicine is an increasingly common form of alternative therapy worldwide. In 1997, it was estimated that 12.1% of adults in the United States used herbal medicine in the previous 12 months, representing an out-of-pocket payment of US$ 5.1 billion (Eisenberg et al., 1998). *Averrhoa carambola* L., known as star fruit ('carambola' in Brazil), belongs to the Oxalidaceae family. According to folk medicine, it is commonly used for treating restlessness, headache, nausea, and cough (Burkhill, 1935). The following symptoms have been reported after fruit ingestion: intractable hiccups, insomnia, mental confusion, and even death in patients who suffered from renal chronic failure (Martin et al., 1993; Neto et al., 1998; Chang et al., 2000). Cecchini et al. (1999) and Carolino et al. (2001) reported the characterization of a potent neurotoxin, isolated from *A. carambola* fruits. It is a water-soluble molecule that

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*Corresponding author. Tel.: +55 79 212 6642; fax: +55 79 246 3377.
E-mail address: egarcia@ufs.br (E.A. Conde-Garcia).

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could induce convulsions and L-glutamate release from rat synaptosomes. Furthermore, infusions prepared from dry *A. carambola* leaves reduced the glucose levels in Wistar rat blood (Martha et al., 2000). Nevertheless, no mention could be found in the specialized literature (Medline/Pubmed: http://www.ncbi.nih.gov/entrez/query.fcgi and Medline/Bireme – http://www.bireme.br, covered period from 1960 to 2004, seeking date: January 7, 2005) dealing with the *A. carambola* myocardial effects. We observed that its leaf aqueous extract (AEx) depressed both the cardiac spontaneous rate and guinea pig left atrium contractility (Vasconcelos and Conde-Garcia, 2002; Vasconcelos et al., 2001). The present paper describes some electrocardiographic and electrophysiological effects of *A. carambola* AEx on guinea pig heart.

Material and methods

Plant characterization

Leaves were collected near the Federal University of Sergipe campus (Aracaju, Sergipe, Brazil) from agrotoxic-free and fumigation-free trees, during the winter season (June–July 2001). Plant identification was made by comparson with voucher specimen no. 24720 deposited in the Herbarium of the Federal University of Pernambuco, Recife, Brazil.

Aqueous extract preparation

The AEx was obtained in a Soxhlet apparatus by extracting dry leaves with the following solvents (P.A.-A.C.S): hexane, chloroform, acetone, ethanol, methanol, and water. Each extract was concentrated in a rotative evaporator (BUCHII RE 111, Buchi Laboratoriums-Technik AG, Flawil, Schweiz) and stored at $27 \pm 3\,^{\circ}C$ in a dry atmosphere without light protection until (storage time: 1–6 months).

Phytochemistry screening

Phytochemical screening was performed on AEx according to the technique proposed by Domínguez (1973).

Isolated heart experimental assembly

Guinea pigs (*Cavia porcellus*) of both sexes (300–500 g each) were sacrificed by cervical stroke 30 min after a subcutaneous administration of heparin (1000 IU, Liquemine, Roche, São Paulo, SP, Brazil). The animal chest was opened, the heart carefully removed and mounted on a constant-flow (Milan Peristaltic Pump, Milan Equipamentos Científicos Ltda., Curitiba, PR, Brazil) aortic perfusion system (Langendorff technique, Döring, 1990). The heart was perfused by a modified Tyrode solution (NaCl 137.0, KCl 5.0, $MgCl_2$ 0.5, $NaHCO_3$ 12.0, $CaCl_2$ 1.8, Glucose 6.0, NaH_2PO_4 1.8, in mM, substances of analytical grade purchased from Merck S.A. Indústrias Químicas, Rio de Janeiro, Brazil), oxygenated and buffered by carbogen mixture (95% O_2 + 5% CO_2, error less then 0.2%, purchased from Aga S.A., São Paulo, Brazil or White Martins Gases Industriais S.A. São Paulo, Brazil), kept at $34 \pm 0.1\,^{\circ}C$ (Haake F3, Berlin, Germany), and filtered through a cellulose acetate membrane (0.45 μm) to prevent microembolia (Harrison and Raymond, 1951). When the heart was electrically driven, suprathreshold DC current pulses, isolated from the ground were used (Anapulse Stimulator 302-T, WPI Instruments, Inc., 60 Fitch Street, POX 3110, New Haven, Connecticut 06515, USA; Digitimer D4030, Digitimer DS2, Digitimer Limited, Tewin Road, Welwyn Garden City, Hertfordshire, England). The stimuli were delivered through a pair of stainless steel electrodes connected to the right atrium appendage. The whole preparation was maintained immersed in Tyrode (50 ml) in which three electrodes (Ag/AgCl/NaCl 1 M) were placed for sensing the heart electrical signal, the electrocardiogram (ECG) to be recorded. Those signals were amplified (HP8811B, HP7754A, HP7754B, Hewlett-Packard, Chicago, IL, USA) and stored in a computer for off-line processing (DI-205, DI-400, Windaq Pro, Dataq, 241 Springside Drive Suite 200, Akron, OH 44 333, USA). Before beginning the experimental procedures, the biological preparation was allowed to stabilize for 1–2 h. To investigate whether the parasympathetic pathways were involved in the cardiodepressor effects of AEx, some hearts were atropinized by adding atropine sulfate (10 μM) to the perfusion fluid 20 min before starting the test with the AEx.

Heart rate measurements

For studying the effect of AEx on cardiac rate, the isolated heart was allowed to beat spontaneously. The ECG was recorded in a computer and the heart rate was determined, beat-to-beat, from the stored data. To accomplish that, successive R–R intervals during control, test (AEx, 1 g/l), and washout, were determined (Calculate and Windaex softwares from Dataq, 241 Springside Drive Suite 200, Akron, OH 44 333, USA).

Intraventricular pressure

Left intraventricular pressure was measured using a water-filled balloon. This device, coupled to a pressure transducer (HP 1290A, HP8805B), sent its signals to an