UNIVERSIDADE FEDERAL DO MARANHÃO
CENTRO DE CIÊNCIAS BIOLÓGICAS E DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE
MESTRADO

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EFEITOS DO EXTRATO DE *Euterpe oleracea* Martius (AÇAÍ) NO SISTEMA CARDIOVASCULAR DE RATOS

SÃO LUÍS

2010

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Dissertação apresentada ao Programa de Pós-Graduação em Ciências da Saúde como parte dos requisitos para a obtenção do título de Mestre em Ciências da Saúde.

Orientador: Prof. Dr. – Antônio Carlos Romão Borges

SÃO LUÍS

2010

Barcellos, Priscila Sousa

Efeitos do extrato de *Euterpe oleracea* Martius (açaí) no sistema cardiovascular de ratos. / Priscila Sousa Barcellos. – São Luís, 2010.

35f.

Orientador: Antônio Carlos Romão Borges

Dissertação (Mestrado em Ciências da Saúde) – Universidade Federal do Maranhão, UFMA, 2010.

1. Euterpe oleracea. 2. Doenças cardiovasculares. 3. Ratos SHR. I. Título.

CDU 582.545

Priscila Sousa Barcellos

EFEITOS DO EXTRATO DE *Euterpe oleracea* Martius (AÇAÍ) NO SISTEMA CARDIOVASCULAR DE RATOS

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Para as flores do meu jardim. Que me enchem de cor e perfume. Mãe, vó e tias.

AGRADECIMENTOS

Ao Deus criador de todas as coisas e inspiração de amor ao próximo.

Ao Prof. Dr. ANTÔNIO CARLOS ROMÃO BORGES, por mais uma orientação de parceria e apoio.

À TONICLEY ALEXANDRE DA SILVA pela colaboração nas discussões teóricas e pelo apoio incondicional em todo o processo de desenvolvimento deste trabalho.

Às acadêmicas do curso de nutrição DÂMARIS, NATÁLIA e SAMARA pela colaboração nos trabalhos experimentais e apoio no desenvolvimento deste trabalho.

A todos os colegas do mestrado em Ciências da Saúde e do Laboratório de Farmacologia, por suas importantes sugestões, colaboração e apoio.

À CAPES pela bolsa concedida.

“Vou atirar uma bomba ao destino.”

Álvaro de Campos

RESUMO

A hipertensão arterial é um problema crescente de saúde pública. Para prevenir ou reduzir a hipertensão alguns agentes dietéticos têm sido utilizados. Conhecidos como "alimentos funcionais", esses produtos possuem elevados níveis de compostos antioxidantes. O açaí, fruto da palmeira *Euterpe oleraceae* Martius apresenta vários compostos antioxidantes em sua composição. Neste estudo, o efeito biológico do extrato aquoso de *Euterpe oleraceae* (EA) sobre a reatividade vascular de artérias mesentéricas de ratos SHR foi investigada *in vitro* e *in vivo*, bem como o perfil bioquímico destes animais. Embora, 8 semanas de tratamento com o EA não tenha tido efeito significativo sobre a concentração de glicose sérica e perfil lipídico, atenuou significativamente os efeitos da sensibilidade vascular induzida pela noradrenalina em anéis de artérias mesentéricas em ensaios *in vitro*. Já nas artérias de ratos SHR tratados após 8 semanas, apresentaram redução da reatividade na menor dose utilizada. Estes resultados sugerem que o tratamento com o EA pode interferir na contratilidade das artérias mesentérica de ratos SHR.

Palavras-chave: *Euterpe oleracea*, doenças cardiovasculares, ratos SHR.

ABSTRACT

Hypertension is an increasingly public health issue. To prevent or reduce hypertension some dietary agents have been used. Has known like “functional food” these products possess high levels of antioxidant compounds. Açaí, fruit of *Euterpe oleraceae* Martius palm supplies several of these antioxidant compounds. In this study, biological effect of aqueous extract of açaí (AE) on vascular reactivity of mesenteric arteries from SHR rats was investigated *in vitro* and *in vivo,* as well as biochemistry profile. Although, 8-weeks of treatment with AE extract had no significant effect on the concentration of serum glucose and lipid profile, but it significantly attenuated vascular sensibility effect of noradrenaline in mesenteric arteries rings *in vitro* assays. Mesenteric arteries rings from SHR rats after 8-weeks treated also evaluated and shows similar effect in lowest dose. These results suggest that AE treatment of SHR rats can interfere in contractility through mesenteric arteries.

Keywords: Euterpe oleracea, cardiovascular diseases, SHR rats.

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1 INTRODUÇÃO

No mundo, a hipertensão arterial é a mais frequente entre as doenças não transmissíveis. É ainda, o principal fator de risco para mortalidade, complicações cardiovasculares, como acidente vascular cerebral e infarto agudo do miocárdio, além de um importante fator de risco para o desenvolvimento de doença renal crônica [1-3].

A prevalência global da hipertensão em adultos é de 26%, a expectativa é de aumento ao longo das décadas e que a hipertensão arterial acometa adultos cada vez mais jovens. Estima-se que mais de um quarto da população adulta seja hipertensa até 2025, o que representará cerca de 1,56 bilhões de pessoas ou 29%. Só nos Estados Unidos, por exemplo, mais de 50 milhões de pessoas serão hipertensas [4, 5].

O Sétimo Relatório do Comitê da Junta Nacional em Prevenção, Detecção, Avaliação e Tratamento da Hipertensão Arterial (JNC7) Americano define hipertensão como pressão arterial sistólica (PAS) e diastólica (PAD) acima de 140/90 mmHg, respectivamente. Define ainda, que pessoas com pressão arterial acima dos níveis ideais, porém sem hipertensão clínica (PAS de 120-139 mmHg ou PAD de 80-89 mmHg) como tendo pré-hipertensão o que levaria a um risco maior de desenvolver hipertensão que aquelas com baixos níveis pressóricos, além do risco de doenças cardiovasculares independentemente de outros fatores de risco [6, 7].

Apesar de grande parte da população estar exposta aos fatores de risco, alguns grupos mostram-se mais susceptíveis à doença hipertensiva. Indivíduos da raça negra, por exemplo, tem prevalência maior e início precoce que outros grupos étnicos, com pior prognóstico que pacientes brancos; apresentando ainda, resposta terapêutica e resultados clínicos diferentes [8].

A prevalência de síndrome metabólica e diabetes tipo 2 também é significantemente maior em pacientes com pressão arterial não controlada quando comparado com indivíduos hipertensos que controlam os níveis pressóricos [9].

Entretanto, a hipertensão não é um fenômeno isolado. Muitos hipertensos possuem ainda outros fatores de risco, e a coexistência de vários fatores de risco aumenta as chances de desenvolvimento de doenças cardiovasculares [10].

Alguns desses fatores são importantes na determinação da hipertensão arterial, como o excesso de peso, fumo, estresse oxidativo, consumo de álcool e outros, relacionados com o aumento da prevalência da hipertensão, provavelmente devido a uma ação nociva direta sobre o músculo cardíaco. Por outro lado, a atividade física intensa e regular tende a reduzir os valores de pressão sanguínea [4].

Desta forma, mudanças de hábitos de vida tornam-se necessárias para a prevenção e o tratamento da hipertensão. A restrição dietética de sódio para menos de 2300 mg/dia para indivíduos saudáveis e menos de 1500 mg/dia para pacientes hipertensos; a prática de exercícios aeróbicos por 30-60 min de quatro a sete dias por semana; manutenção de peso na faixa de eutrofia (18,5 kg/m² a 24,9 kg/m²) e circunferência da cintura menor que 102 cm para os homens e menor que 88 cm para as mulheres; limitação no consumo de álcool e consumo de dieta pobre em ácidos graxos saturados e colesterol, que enfatize o consumo de frutas, vegetais e produtos pobres em gordura, incluindo fibras solúveis e insolúveis, grãos e proteína de origem vegetal [11].

A terapia medicamentosa pode ser iniciada com inibidores da enzima conversora de angitensina (IECA), antagonistas dos receptores de angiotensina II, bloqueadores dos canais de cálcio ou tiazidas. A terapia de combinação inicial é indicada para pacientes de alto risco onde a redução da pressão arterial desejada seja maior que 20/10 mm Hg. Hipertensão resistente geralmente pede um incremento na dosagem do diurético e/ou adição de diuréticos economizadores de potássio [12].

A prevenção e o controle da hipertensão arterial e doenças cardiovasculares tem muitos modos de intervenção. E embora as estratégias farmacológicas para o controle existam e sejam bem estabelecidas, menos da metade dos hipertensos tem sua pressão sanguínea reduzida para metas relevantes. Devido a este fato, existe ainda um grande interesse no uso de elementos da dieta para prevenir ou reduzir a hipertensão [13-15].

Deste modo, os nutracêuticos ou alimentos funcionais tem atraído um interesse considerável como uma terapia alternativa potencial para o controle da hipertensão nos últimos anos, especialmente para pacientes pré-hipertensos, cujos níveis pressóricos não são altos o suficiente para garantir a prescrição de medicamentos [16, 17].

Vale salientar, que para um alimento ser considerado como “funcional” tem que apresentar benefícios em uma ou mais funções alvo no organismo de forma convincente. Além de adequar qualidades nutricionais, os alimentos funcionais devem também melhorar o estado de saúde e bem-estar e/ou reduzir o risco de doenças. Seu foco primário é nos principais fatores de risco para doenças cardíacas como dislipidemias, diabetes e hipertensão. Não somente os alimentos “in natura”, mas também alguns produtos são enriquecidos com ingredientes “protetores”, acreditando-se melhorar sua ação. Eles podem conter, por exemplo, fibras solúveis (oriunda da aveia e psyllium), usadas para reduzir o colesterol e pressão sanguínea, ou inulinas, efetivas no diabetes [18].

Vários estudos epidemiológicos sugerem que o consumo regular de alimentos funcionais ricos em flavonóides está associado a uma redução no risco de várias patologias que vão desde a hipertensão à doença coronariana, acidente vascular cerebral, demência e comprometimento da função endotelial, propriedade de elasticidade das grandes artérias, importantes determinantes do desempenho cardiovascular, diretamente relacionada ao envelhecimento e a associação entre a diminuição da perfusão cerebral [19].

O açaí, fruto da palmeira de *Euterpe oleraceae* Martius, é tradicionalmente consumido no Brasil e tem ganhado popularidade como alimento funcional. Apesar de ainda existirem poucas informações acerca dos seus benefícios, destaca-se por apresentar grandes quantidades de componentes antioxidantes como polifenóis, antocianinas, carotenóides, taninos e ácido ascórbico [20-23].

2 OBJETIVOS

Objetivo Geral

Avaliar os efeitos do extrato aquoso de *Euterpe oleracea* Martius no sistema cardiovascular de ratos espontaneamente hipertensos.

Objetivos Específicos

- Analisar os parâmetros bioquímicos e hematológicos sangüíneos de animais tratados com o EA;
- Avaliar o efeito da administração crônica do EA na pressão arterial de ratos SHR;
- Estudar o efeito do EA na reatividade de músculo liso vascular.

3 CAPÍTULO I

EFFECTS OF EXTRACT *Euterpe oleracea* Martius IN CARDIOVASCULAR SYSTEM OF SPONTANEOUSLY HYPERTENSIVE RATS

Para Submissão para Revista The Journal of Nutrition

ABSTRACT

Hypertension is a serious public health issue. To prevent or reduce hypertension some dietary agents have been used. Has known like “functional food” these products possess high levels of antioxidant compounds. Açaí, fruit of *Euterpe oleraceae* Martius palm supplies several of these antioxidant compounds. In this study, biological effect of aqueous extract of *Euterpe oleraceae* (AE) on vascular reactivity of mesenteric arteries from SHR rats was investigated *in vitro* and *in vivo,* as well as biochemistry profile. Although 8-weeks of treatment with AE extract had no significant effect on the concentration of serum glucose and lipid profile, it significantly attenuated vascular sensibility effect of noradrenaline (NA) in mesenteric arteries rings *in vitro* assays. Mesenteric arteries rings from SHR rats after 8-weeks treated were also evaluated and showed similar effect in lowest dose. These results suggest that AE treatment of SHR rats can interfere in contractility through mesenteric arteries.

Keywords: *Euterpe oleracea*, cardiovascular diseases, SHR rats.

Introdution

Hypertension is an increasingly important medical and public health issue. Worldwide, arterial hypertension is the leading risk factor for mortality and it is a strong risk factor for the development of heart failure, myocardial infarction, kidney failure, stroke, and death [7, 10].

Some factors are important in the determination of arterial hypertension, like excess weight, smoking, oxidative stress and vasoconstrictive effect associated with the incensement in inflammations related to hypertension; alcohol consumption, has been associated with an increase in hypertension prevalence, probably due to the fact that it has a direct harmful action on the cardiac muscle[4].

The prevention and treatment of cardiovascular disease have used many interventional modalities. Although effective pharmacological strategies for the

treatment of hypertension exist, there is a great deal of interest in using dietary agents to prevent or reduce hypertension [13, 14].

Recently, much attention has been paid to its antioxidant capacity and possible role as a “functional food” or food ingredient. Dietary intake of berry fruits has been demonstrated to positively impact human health. Interest in exploring new and exotic types of berries has grown in recent years. Açai, fruit from *Euterpe oleraceae* Martius palm, has been demonstrated to possess high levels of these antioxidant compounds. [20, 21, 24].

Açai is a fruit from the Amazon region, common especially in Pará, Amazonas, Tocantins, Maranhão and Amapá states. The pulp of açai fruit is largely consumed in a variety of beverages and food preparations, like juice, ice-cream and sweets, mainly in Brazil. This fruit supplies several antioxidant compounds such as polyphenols, tannins, anthocyanins, carotenoids, and ascorbic acid [20, 22, 25, 26].

Although açai fruit is rich in phytochemicals that possesses high anti-oxidant activities, and has anti-inflammatory, anti-cancer and anti-cardiovascular disease properties little is known about these potential properties especially at the biological level[27].

Nowadays, it is widely accepted that if these phytochemicals anthocyanins in special have any preventive or curative activity through their ingestion, this effect must involve, not only their antioxidant potential, but also the modulation of multiple cellular pathways that are crucial in the pathogenesis of those diseases[28].

Therefore the aim of this work is to investigate the biological effects of aqueous extract of açai on vascular reactivity of mesenteric rings and biochemistry profile from rats SHR.

2 Materials and methods

2.1 Extract

Fresh pulp of *Euterpe oleracea* fruit was purchased from a retail food store (São Luís, Maranhão) in november 2008. Aqueous extract of açai (AE) was obtained from a mix of açai fruit with water in a pulp machine that separates açai stones from

juice. The AE was frozen immediately at - 20º C, lyophilized and ground to obtain a fine powder. Then, it was homogenized in filtered water in different concentrations.

2.2 Animals and experimental protocol

There were used male and female Spontaneousy Hypertensive (SHR) rats weighing 135 to 175 g, with 45 to 50 days old in the beginning of the experiment. The animals were obtained from the of Federal University of Maranhão (UFMA) Biotery. They were maintained in groups of five animals, housed in rooms with controlled temperature (25 ± 2 °C) and a light/dark cycle of 12 hours, with water and food *ad libitum*. After a basal period of 14 days, the animals were divided into 4 groups: control (CT, water), aqueous extract of *Euterpe oleracea* 0.1 g/kg (AE 0.1), 0.25 g/kg (AE 0.25) and 0.5 g/kg (AE 0.5). The experimental protocol consisted of daily treatment for eight weeks, with acai extract or water and measurements (heart rate and systolic blood pressure) always before the gavage. Following a chronic treatment, animals were put down for removal of the retroperitoneal and epididimal fat and organs (heart, lung, spleen, kidney, liver and superior mesenteric artery) which were visually inspected, weighted and evaluated *in vitro* reactivity of mesenteric artery. All protocols were approved by Animal Ethics Committee of State University of Maranhão (UEMA) protocol number P07/06.

2.3 Blood Pressure and Heart Rate Measurements

The systolic blood pressure (SBP) and heart rate (HR) were measured according of noninvasively [29] three times a week in unanesthetized rats, by a tail-cuff method using an automated blood-pressure meter (LE 5007, Letica, PanLab, Barcelona, Spain). Each of these parameters was measured in triplicate, and the mean was regarded as the value of each parameter in each animal. To improve recording, the animals were kept at 45 ºC for 5 min before measurement. The animal's weight, food and water intake were determined weekly and the SBP and HR measurements always preceded the animal treatment.

2.4 Reactivity of mesenteric artery

To measure of mechanical response, the superior mesenterics artery were removed carefully and placed in freshly prepared Krebs solution containing (mM): NaCl, 118; $NaHCO_3$, 25; glucose, 5.6; KCl, 4.7; KH_2PO_4, 1.2; $MgSO_4$, 1.17 and

$CaCl_2$, 2.5. The arteries were cleaned of all adherent tissue and cut into rings of approximately 4 mm. Each ring was suspended between two wire hooks and mounted in 5-mL organ chambers with Krebs solution at 37 °C, pH 7.2, and continuously aerated with a mixture of 95% O_2 and 5% CO_2 under a resting tension of 1 g. The other end of each wire attached by a cotton thread to a F-60 isometric force transducer connected to MK-IV-P physiograph. The rings were allowed to equilibrate for 60 min under a resting tension of 1 g before experiments were started. During the equilibration period, the rings were washed every 30 min. Successful removal of the endothelium was confirmed by the loss of acetylcholine (10^{-3} M)-induced relaxation in preconstricted rings by noradrenaline (NOR, 10^{-6} M). At the end of the equilibration period, concentration–response curves were obtained with NA in mesenteric rings with or without AE. NOR was added in a cumulative manner until a maximum response was achieved. After addition of each concentration, a plateau response was obtained before addition of a subsequent concentration. Consecutive concentration–response curves were taken at 30-min intervals, during which the Krebs solution was changed at least three times. Nonlinear regression analyses to determine the parameters Emax, log EC_{50} and n were done using GraphPad Prism [30].

2.5 Biochemical Analysis

After 8 weeks of treatment animals were anesthetized and blood samples were obtained from retro orbital puncture by Pasteur pipette and collected blood was immediately stored on ice and centrifuged within 10 min at 2500 RPM; 15 min at 4°C. There were determined blood lipid concentrations (triglycerides, HDL and cholesterol); glucose; enzymes (AST and ALT) and catabolites (urea and creatinin).

2.6 Data and statistical analysis

All values were given as mean ± S.E.M. Contractile response to noradrenalin was expressed as grams of tension. Statistical analyses were performed by sigmoid non-linear regression of concentration-response curves and was carried out using GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com. There were used Student's *t*-test and one-way analysis of variance (ANOVA) followed by Newman-

Keuls post-test when parametrical test can be used and Kruskal-wallis followed by Dunns post-test when non-parametric were selected. Statistical *P* value 0.05 was considered significant.

3 Results

3.1 Effects of Euterpe oleracea aqueous extract on SHR rats corporal weight

SHR rats after cronic daily oral treatment with aqueous extract of *Euterpe oleracea* (açai) did not show weight statistical differences from control group studied. The weight mean values were: control (172.1±7.6 g); AE 0.1g/kg (174.2±4.0 g); AE 0.25g/kg (163.5±7.8 g) and AE 0.5g/kg (164.5±8.4 g).

3.2 Effects of aqueous extract of açai on SHR rats blood pressure and heart rate

In SHR rats, the mean value of systolic blood pressure from control group did not present differences in weekly means from groups submitted at daily oral administration of AE in all doses during 8 weeks (Figure 1).

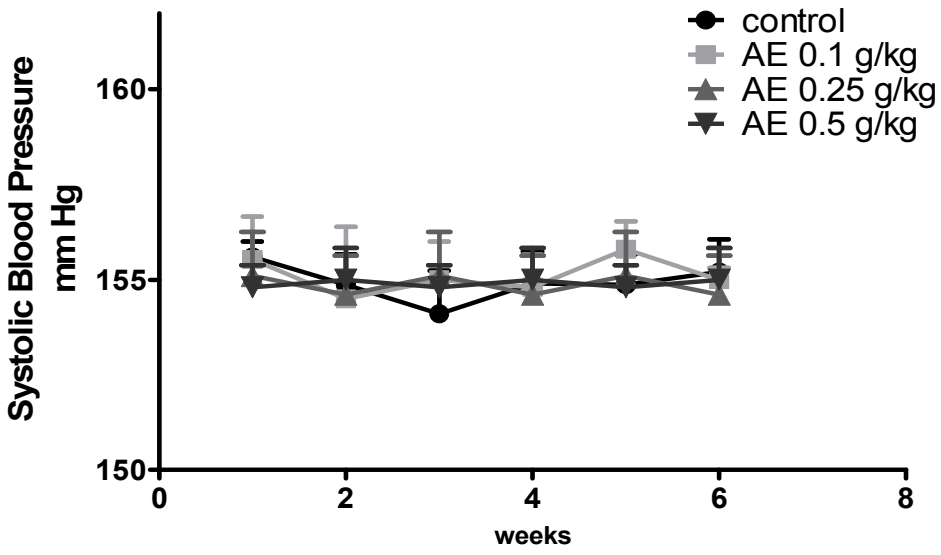

Figure 1: Systolic blood pressure of SHR rats treated with aqueous extract of *Euterpe oleracea* fruit in 0.1 (AE 0.1), 0.25 (AE 0.25) and 0.5 (AE 0.5) g/kg doses during 6 weeks. Data correspond to the average ± standard error of 5 animals/group. Data were tested by one-way ANOVA.

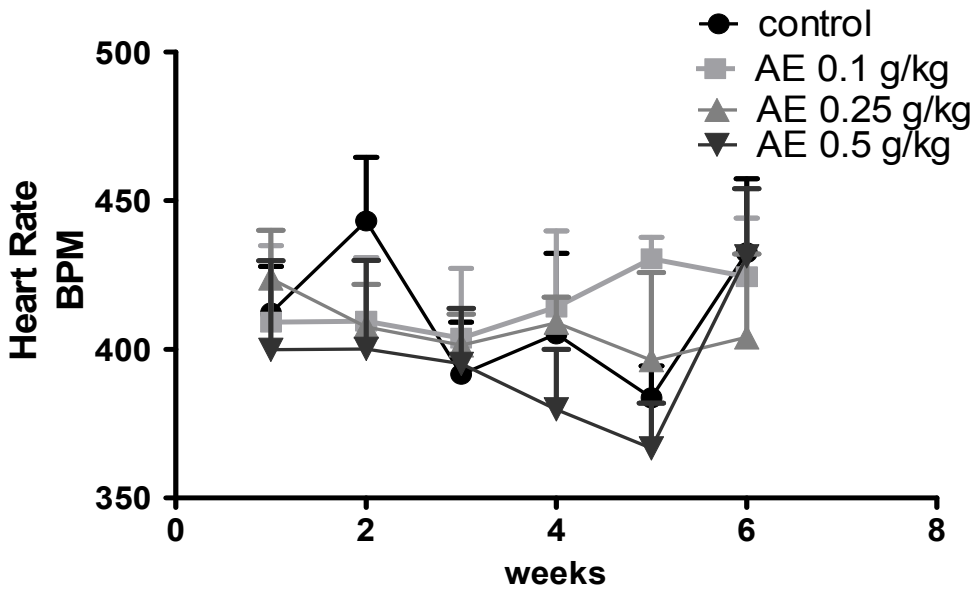

Figure 2: Heart rate of SHR rats treated with aqueous extract of *Euterpe oleracea* fruit in 0.1 (AE 0.1), 0.25 (AE 0.25) and 0.5 (AE 0.5) g/kg doses during 8 weeks. Data correspond to the average ± standard error of 5 animals/group. . Data were tested by one-way ANOVA.

3.3 *Effect of cronic treatment with EA in organs weight*

Oral administration with aqueous extract of *Euterpe oleracea* fruit did not induced any changes in organs weight analyzed (heart, lung, spleen, kidney, liver) nor in fat weight (retroperitoneal and periepididymal) in 0.1; 0.25; and 0.5 g/kg doses in 8 weeks treatment.

Table 1: Organs weight evaluation and total fat of SHR rats treated with aqueous extract of *Euterpe oleracea* fruit in 0.1 (AE 0.1), 0.25 (AE 0.25) and 0.5 (AE 0.5) g/kg during 8 weeks treatment.

	ORGANS WEIGHT (g)					
	Heart	**Lung**	**Spleen**	**Kidney**	**Liver**	**Fat**
GROUPS						
Control	1.11 ± 0.07	1.68 ± 0.16	0.40 ± 0.02	1.22 ± 0.06	6.91 ± 0.44	2.47 ± 0.27
AE 0.1	1.14 ± 0.10	2.17 ± 0.17	0.41 ± 0.02	1.22 ± 0.04	7.43 ± 0.56	1.99 ± 0.39
AE 0.25	1.12 ± 0.06	2.02 ± 0.19	0.46 ± 0.04	1.17 ± 0.08	6.89 ± 0.65	2.34 ± 0.42
AE 0.5	1.12 ± 0.23	2.00 ± 0.26	0.43 ± 0.04	1.16 ± 0.11	6.46 ± 1.12	2.34 ± 0.12

Data correspond to the average ± standard error of 5 animals/group evaluated at the end of the 8 weeks. . Data were tested by one-way ANOVA.

3.4 Biochemical parameters – glucose and lipid profile

As will be shown in Table 2, at the end of 8 weeks of AE treatment, the lipid profile (total cholesterol, HDL cholesterol and triglycerides) and glucose concentration of SHR rats serum did not presents significance difference when comparison with control group.

Table 2: Biochemistry evaluation of SHR rats serum treated with aqueous extract of *Euterpe oleracea* fruit in 0.1 (AE 0.1), 0.25 (AE 0.25) and 0.5 (AE 0.5) g/kg during 8 weeks.

GROUPS	BIOCHEMISTRY EVALUATION (mg/dL)			
	Cholesterol	HDL	Triglycerides	Glucose
Control	107.2 ± 11.4	70.2 ± 7.4	81.2 ± 5.2	111.4 ± 18.1
AE 0.1	117.8 ± 26.4	70.6 ± 10.6	78.4 ± 7.6	133.6 ± 23.6
AE 0.25	97.8 ± 22.8	57.0 ± 9.2	76.8 ± 5.6	99.4 ± 11.0
AE 0.5	150.5 ± 1.5	90.0 ± 1.0	100.0 ± 3.0	128.5 ± 49.5

Data correspond to the average ± standard error of 5 animals/group evaluated at the end of the 8 weeks. . Data were tested by one-way ANOVA

3.5 Biochemical parameters – enzyme profile – Toxicity

Determination of enzymes, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), inflammatory markers unspecific and specific of liver cells, respectively, did not show differences when compared with control group.

Urea and creatinine, markers of kidney function also did not show statistical difference, nor does uric acid, catabolic of protein metabolism, what can indicate that AE haven't kidney toxicity action.

Table 3: Determinations of enzymes and catabolites of SHR rats serum treated with aqueous extract of *Euterpe oleracea* fruit in 0.1 (AE 0.1), 0.25 (AE 0.25) and 0.5 (AE 0.5) g/kg during 8 weeks.

GROUPS	ENZYMES AND CATABOLITES (mg/dL)				
	AST	ALT	Urea	Creatinine	Uric acid
Control	191.8 ± 16.8	64.8 ± 4.5	81.6 ± 5.1	0.48 ± 0.06	1.98 ± 0.12
AE 0.1	167.8 ± 18.5	76.4 ± 5.7	82.8 ± 1.8	0.46 ± 0.04	1.98 ± 0.06
AE 0.25	185.8 ± 6.7	75.0 ± 7.6	74.6 ± 9.0	0.52 ± 0.04	1.98 ± 0.11
AE 0.5	165.5 ± 7.5	79.0 ± 24.0	85.0 ± 3.0	0.60 ± 0.10	1.85 ± 0.05

Data correspond to the average ± standard error of 5 animals/group evaluated at the end of the 8 weeks. (*) $p < 0.05$ when compared to control group. Data were tested by one-way ANOVA.

3.6 Hematological parameters determination

Analysis from hematological profile just presents statistical differences in monocytes numbers of SHR animals treated with AE 0.25 g/kg dose. Elevation in these immunologic cells, precursor from macrophage cells, can represent protective elevation against infection process.

Other types of immunologic cells (leucocyte, neutrophils, lymphocytes, eosinophils and basophils) were also studied but did not show differences from control. Although blood compound hemoglobin, although did not show statistical significance they had a trend of elevation.

Table 4: Hematological analysis of SHR rats blood treated with aqueous extract of *Euterpe oleracea* fruit in 0.1 (AE 0.1), 0.25 (AE 0.25) and 0.5 (AE 0.5) g/kg during 8 weeks.

	HEMATOLOGICAL ANALYSIS ($10^3/mm^2$)							
GROUPS	Leucocyte	Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils	Hemoglobines	Platelets
Control	5.45 ± 0.45	0.59 ± 0.19	4.05 ± 0.22	0.44 ± 0.13	0.11 ± 0.03	0.25 ± 0.07	14.13 ± 0.19	726.0 ± 47.8
AE 0.1	7.16 ± 0.97	1.07 ± 0.46	5.17 ± 0.72	0.51 ± 0.19	0.07 ± 0.01	0.34 ± 0.11	14.77 ± 0.18	783.0 ± 9.8
AE 0.25	7.14 ± 0.26	0.22 ± 0.02	4.41 ± 0.37	1.82 ± 0.13*	0.05 ± 0.01	0.64 ± 0.17	15.03 ± 0.58	787.0 ± 13.9
AE 0.5	4.46 ± 0.23	0.19 ± 0.02	3.32 ± 0.23	0.59 ± 0.08	0.06 ± 0.01	0.29 ± 0.06	15.10 ± 0.04	575.0 ± 85.0

Data correspond to the average ± standard error of 5 animals/group evaluated at the end of the 8 weeks. (*) $p < 0.05$ when compared to control group. . Data were tested by one-way ANOVA; Turkey's post hoc test was performed to determine the specific differences between mean values.

After 8-weeks treatment, isolated rings of mesenteric artery from control group were contract with noradrenalin and presents pD2 and E_{max} (5.23 ± 0.12 and 0.82 ± 0.05 g). When compared with isolated rings of mesenteric artery from treated groups pD2 values did not show statistical differences from control group (5.24 ± 0.23; 5.6 ± 0.37 and 5.86 ± 0.22 respectively) but reduced E_{max} effect in AE 0.1 g/kg group (0.43 ± 0.05 g).

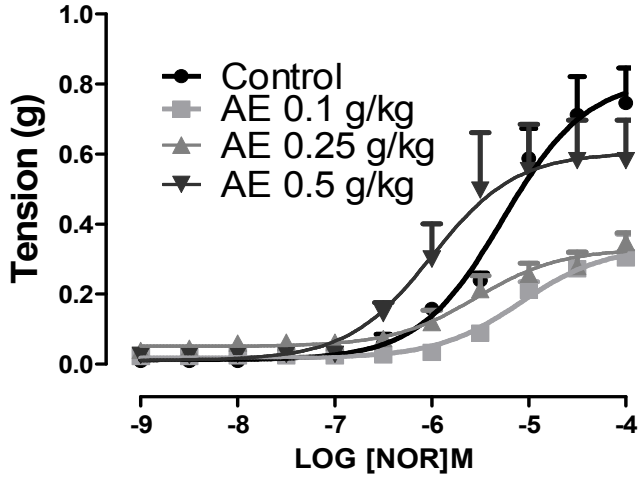

Figure 3: Effect of aqueous extract of *Euterpe oleracea* fruit in 0.1 (AE 0.1), 0.25 (AE 0.25) and 0.5 (AE 0.5) g/Kg doses on cumulative concentration-response curves for noradrenaline in mesenteric arteries preparations 8 weeks after treatment.

The isolated rings of the mesenteric artery contract with noradrenalin presented pD2 and E_{max} 6.1 ± 0.18 and 0.43 ± 0.02 g, respectively; the value pD2 was shifted right after AE addition in all concentration utilized from AE 0.1; 0.25 and 0.5 mg/ml (5.29 ± 0.2; 5.21 ± 0.2; 5.17 ± 0.2, respectively) although did not reduced the E_{max} of the cumulative concentration –response curves to NE (0.38 ± 0.04; 0.42 ± 0.04; 0.45 ± 0.05), respectively (Figure 3).

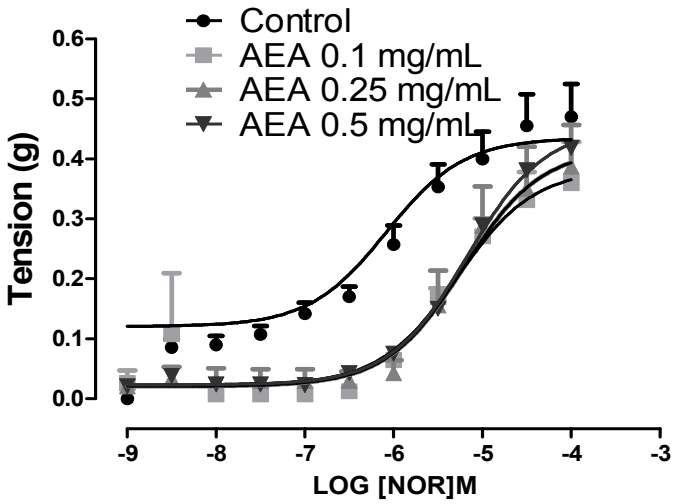

Figure 4: Mesenteric arteries rings were contract with noradrenalin. After washes mesenteric arteries from SHR rats were exposed at AE for 30 minutes and again contract by noradrenalin *in vitro*. Data correspond to the average ± standard error of 7 animals/group evaluated.

4 Discussions

The blood pressure lowering effect of a fruit and vegetable-rich diet is a necessary dietary lifestyle measure included the guidelines for the management of arterial hypertension [31].

These influence of dietary habits on cardiovascular mortality and morbidity is well documented. Diets rich in fruit and vegetables can reduce cardiovascular risk, contribute to weight loss and directly lower blood pressure. Analyzing the effect of AE on SHR rats biochemistry profile and blood pressure[32]. In this study, it was shown that açai extract treatment *in vivo* did not change the hypertension screen in doses studied with diary consume by 8 weeks.

Results demonstrated that incubation of aqueous extract of açai was unable reduced reactivity (E_{max}) of cumulative concentration-response curves to NA in mesenteric artery isolated rings *in vitro* assays. However, in all concentration studied mesenteric artery isolated rings from SHR rats were less sensitivity, showed by pD_2 values - log EC50 from NA curves shifted to right (Figure 3). Rocha [25] demonstrated that vessels contracted with NA induced rapid and transient decrease of perfusion pressure, in presence of aqueous extract of açai, sustained vasodilator effect.

Although treatment did not affect blood pressure and reactivity of mesenteric arteries from SHR rats treated could not dislocate pD_2 (log EC50) in doses used, after 8-weeks of treatment with AE 0.1 g/kg could reduced E_{max} effect in noradrenaline curves (Figure 4). These redution can suggest vasodilator proprieties. Studies about influence of extracts from parts of *Euterpe oleracea* in NO production, [33], demonstrated that extracts inhibited LPS/IFN□ induced NO production. These effects could influence vasodilator effects finds.

Circulatory and cardiovascular diseases may be reduced by the antioxidant actions of anthocyanins, by the increased resistance to hydrogen peroxide-induced ROS generation of red blood cells (RBC) treated with these antioxidant compounds. Although anthocyanin-rich food have significant influence on health, it becomes important to consider levels in commonly eaten foods that could realistically be incorporated into the human diet. An additional difficulty in determining human health implications of anthocyanin-rich foods, is that the anthocyanins are not found as isolated compounds, but rather as a component of often complexmixtures [34].

Açai powder product is also a hypercaloric food, 489.39 kcal/ 100 g lyophilized pulp, specially to the high lipid contents (40.75%) [35]. However, after 8 weeks of treatment animals weight mean did not show differences from control group. And although açai have a high perceptual of lipids this is not able to change serum lipid profile.

Açai can be considered a fair source of vitamin C and good source of natural antioxidants. However, in regard to the correlation with the antioxidant activity

some of antioxidant compounds can did not presented positive and significative correlation[36].

Oliveira [37], in studies with rats fed with hypercholesterolemic diet supplementing with açai show that 6 weeks treatment caused a hypocholesterolemic effect by reducing total and non-high-density lipoprotein cholesterol. In previous study from our department with swiss mice with açai 4 week treatment decrease in triglycerides levels were identified. In contrast with this information, in spontaneous hypertensive rats models utilized, açai 8 week treatment did not change serum lipid levels.

Cyanidin 3-glucoside is the predominant anthocyanin in açai. In the presence of hydrogen peroxide açai is less stable than red grape, display lower color stability in a temperature-dependent manner [38]. Although hydrogen peroxide is related with inflammatory process, liver inflammatory markers (AST, ALT) have not different from control levels and compared with aqueous açai extract that mimics açai juice consumed by region population.

Studies that investigated antioxidant effects from açai juice and pulp in human health, demonstrated that anthocyanins in an acute human consumption trial were not significantly altered uric acid plasmatic concentrations [23]. Similar data were found in SHR rats that did not altered uric acid urea and creatinine, catabolic of protein metabolism that used like kidney function markers.

In conclusion, the findings obtained in this study showed that chronic treatment of SHR rats with açai extract *in vitro* and *in vivo* induced a reduction of the vascular hyperreactivity to phenylephrine, without changes body weight, organs weight, biochemical and hematological parameters that suggest safe use.

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5 CONSIDERAÇÕES FINAIS

Após 8 semanas de tratamento com extrato aquoso de *Euterpe oleracea* (açaí) observamos que o tratamento sub-crônico do extrato aquoso de açaí não foi capaz de alterar o consumo de ração, o peso corpóreo, pressão arterial sistólica e frequência cardíaca.

O peso dos órgãos dos animais estudados (coração, pulmão, baço, rins fígado) e gordura corpórea ao final do tratamento também não apresentaram alterações quando comparadas ao grupo controle.

O tratamento com o extrato aquoso de *Euterpe oleracea* (açaí) não teve efeito significativo sobre a concentração de glicose sérica e perfil lipídico dos animais tratados. Nem tampouco provocou alterações nas enzimas e metabólicos avaliados, marcadores inflamatórios específicos e inespecíficos, o que nos sugere que as alterações macroscópicas encontradas não se devem ao processo inflamatório e que outras hipóteses devem ser investigadas.

Já os anéis de artérias mesentérica de ratos SHR tratados com extrato após 8 semanas, apresentaram redução da reatividade na menor dose utilizada e quando submetidos à exposição do extrato atenuou significativamente os efeitos da sensibilidade vascular induzida pela noradrenalina (NA) em anéis de artérias mesentéricas em ensaios *in vitro*.

Este trabalho buscou contribuir com os estudos acerca do potencial antioxidante do fruto de *Euterpe oleracea* açaí, bem como da toxidade de seu uso diário e prolongado no modelo hipertensivo haja vista que é um alimento que faz parte do hábito regional da população. Os resultados sugerem que o tratamento com extrato aquoso de *Euterpe oleracea* (açaí) pode interferir na contratilidade das artérias mesentérica de ratos SHR, com um possível efeito de vasorelaxamento.

Mais estudos são necessários, no entanto, a fim de confirmar a segurança de seu uso para esta população específica e melhor dose-efeito em sua forma tradicionalmente de preparada e consumida pela população em geral.

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