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Effects of Consumption of Noni (*Morinda citrifolia*) in Rats Fed a High-Fat Diet

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Abstract

Objective: To evaluate the effects of noni consumption on risk factors for cardiovascular disease, fasting glucose and hepatic and renal function in rats fed a high-fat diet. **Methods:** 18 Wistar rats were divided into three groups. Group control (C) was fed with high-fat diet and water. Group's noni juice (NJ) and noni infusion (NI) received the same diet and noni juice and infusion, respectively, for 4 weeks. After this time were assessed anthropometric measurements, adiposity, organ weights and biochemical measurements. **Results:** Groups NJ and NI had higher waist circumference compared to group C (C=11.0 cm, NJ=12.8 cm and NI=14.0 cm, $p<0.05$), lower serum creatinine (C=0.8 mg/dL, NJ=0.2 mg/dL and NI=0.3 mg/dL, $p<0.05$), and higher blood urea nitrogen/creatinine ratio (C=92.7, NJ=349.3 and NI=230.4, $p<0.05$). Noni infusion consumption promoted higher serum total cholesterol (C=59.7 mg/dL, NJ=60.1 mg/dL and NI=99.8 mg/dL, $p<0.05$) and LDL (C=48.5 mg/dL, NJ=42.0 mg/dL and NI=78.7 mg/dL, $p<0.05$). **Conclusion:** Consumption of noni, either as juice or as infusion, promoted higher waist circumference and blood urea nitrogen/creatinine ratio. Furthermore, noni infusion consumption promoted increased of serum total cholesterol and LDL

Keywords: Morinda, hyperlipidemias, cardiovascular diseases, rats

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1. Introduction

Proper nutrition can act in the prevention and treatment of diseases. On the other hand, an unhealthy diet, combined with physical inactivity and excessive use of tobacco and alcohol, causes metabolic changes that contribute to the development of non-communicable diseases (NCDs). In 2008, 63% of deaths worldwide were due to NCDs, and cardiovascular disease accounted for 48% of the number of deaths caused by these diseases, representing the leading cause of mortality worldwide (World Health Organization, 2011).

In Brazil, cardiovascular diseases are also the leading cause of death, accounting for about 20% of all deaths in people over 30 years old (Mansur & Favarato, 2012), accounting for high costs in the health sector and imposing challenges for control of their risk factors (Ribeiro et al., 2012).

The adoption of a balanced diet, promoting physical activity and smoking cessation are associated with the prevention of cardiovascular disease. Regarding diet, the consumption of unsaturated fatty acids, phytosterols and dietary fiber are associated with decreased serum levels of cholesterol and triglycerides and accordingly to the prevention of dyslipidemias (Simão et al., 2013), leading to the development of research for the verification and proof of beneficial properties of food.

Noni is a fruit from the Polynesia and its different parts have traditionally been used in folk medicine for the treatment of various diseases and metabolic disorders (Kamiya et al., 2004). The main components found in noni that can contribute to beneficial physiological effects are phenolic and organic acids, amino acids, vitamins and minerals (Chan-Blanco et al., 2006). However, it is necessary that studies be carried out to guarantee its benefits, as well as cytotoxic components (Lv et al., 2011).

Due to noni having no consumption history in Brazil, its commercialization was vetoed in the country by the National Health Surveillance Agency (Brazil, 2007). However, this fruit has been widely marketed in Brazil, both in nature and in the form of juices and infusions, making it necessary to carry out studies for the verification of their possible beneficial and toxic effects. Based on the above, this study aimed to evaluate the effects of noni consumption on risk factors for cardiovascular disease, fasting glucose, and hepatic and renal function in rats fed a high-fat diet.

2. Methods

There were 18 weanling male *Wistar* rats, weighing 50±5g. The animals were randomly divided into three equal groups (n=6) and kept in collective cages, in a light-dark cycle of 12 hours and at a controlled temperature of 23ºC.

Initially the animals went through an adjustment period of three days, when they were fed with commercial diet for rats (Nuvilab CR1®) and water *ad libitum*. The experimental model used in this study was adapted from Gong et al. (2010), wherein the high-fat diet consisted of 10% powdered egg yolk, 7.5% pork fat, 1% cholesterol, 0.25% cholic acid and 81.25% of commercial diet for rats. In 100 g, the diet contained 380.9 kcal, 37.7 g carbohydrate, 21.3 g protein, 16.1 g lipids and 1237.7 mg cholesterol.

All groups were fed with this diet and the control group (C) received water, the noni juice (NJ) received noni pulp juice and the noni infusion (NI) received fruit infusion for 4 weeks. The diet and liquid intake was *ad libitum* throughout the experiment, but monitored. The noni used in the study was donated by Seko Sonho da Amazônia® Company. Both juice and infusion were prepared in accordance with the manufacturer's instructions.

After the trial period, the anthropometric measures were assessed - weight, nasoanal length and waist circumference. The body mass index was determined by Lee index, which consists in dividing the cubic root weight (g) by nasoanal length (cm), with multiplication of the result by 1000. The fasting glucose was obtained by puncture of the vena cava, using the Accu-Chek kit (Roche®).

The animals were anesthetized with intraperitoneal application of 1.0 mL/kg ketamine hydrochloride 10% (Cetamin®) and 0.5 mL/kg of xylazine hydrochloride 2% (Xilazin®). A laparotomy was performed and individual blood samples were collected in test tubes containing EDTA and were centrifuged for the separation of serum. It was transferred to Eppendorf test tubes and stored at -20°C for determination of total cholesterol, LDL, HDL, VLDL, triglycerides, AST (aspartate aminotransferase), ALT (alanine aminotransferase), urea, creatinine and urea ratio/creatinine, using laboratory kits (Labtest®). After blood collecting, the retroperitoneal, epididymal and epicardial fat and certain organs - heart, liver and right and left kidneys - were collected.

For weighing of fats and organs a semianalytical balance (Marte® model AS2000) with maximum load of 2000g and sensitivity and reproducibility of 0.01g was used. The weight of each fat and organ was presented in percentage terms in relation to body weight.

Furthermore, it was calculated the coefficient of feed efficiency, obtained through the relation between the total weight gain of each animal (g) and the total diet intake (g) (Moreira & Mancini-Filho, 2004). In order to check the difference in the results between experimental groups, the Kruskal-Wallis test was applied followed by Tukey post-hoc test, adopting as significant $p<0.05$. The data are presented as median and interquartile range [Md (IQR)]. Statistical analyzes were performed using SPSS software version 20.0.

The project was approved by the Ethics Committee on Animal Use of Mackenzie Presbyterian University, under process 094/02/2013.

3. Results

Animals that consumed noni showed a higher waist circumference compared to those that received water during the trial period, with no difference in relation to other anthropometric parameters, the adiposity, and weight of the heart, liver, right kidney, and left kidney in relation to body weight, as shown in Table 1.

Table 1: Anthropometric profile, adiposity, and relative weight of organs of rats fed with high-fat diet receiving water or noni for 4 weeks.

Variable	Experimental group		
	C	NJ	NI
Anthropometric profile			
Weight (g)	213,7 (202,3-220,9)a	214,7 (214,4-216,3)a	209,1 (200,4-212,8)a
Nasoanal length (cm)	19,5 (18,3-20,0)a	19,3 (19,0-19,8)a	19,3 (18,9-19,9)a
Lee index	306,7 (295,7-330,3)a	311,1 (301,5-315,0)a	305,2 (298,9-314,1)a
Waist circumference (cm)	11,0 (11,0-11,8)a	12,8 (12,1-13,0)b	14,0 (12,5-14,0)b
Adiposity			
Retroperitoneal fat (%)	0,4 (0,4-0,5)a	0,4 (0,3-0,5)a	0,7 (0,5-0,9)a
Epididymal fat (%)	0,3 (0,3-0,4)a	0,3 (0,3-0,4)a	0,6 (0,6-0,6)a
Epicardial fat (%)	0,2 (0,2-0,2)a	0,2 (0,1-0,2)a	0,1 (0,1-0,2)a
Organs			
Heart (%)	0,4 (0,4-0,4)a	0,4 (0,4-0,4)a	0,3 (0,3-0,4)a
Liver (%)	4,4 (4,3-4,5)a	4,2 (4,1-4,3)a	4,1 (4,0-4,3)a
Right kidney (%)	0,4 (0,4-0,4)a	0,3 (0,3-0,4)a	0,4 (0,4-0,4)a
Left kidney (%)	0,4 (0,4-0,4)a	0,3 (0,3-0,4)a	0,3 (0,3-0,3)a

Different letters in the horizontal direction indicate significant difference ($p < 0.05$).

The noni infusion consumption promoted higher serum total cholesterol and LDL compared to other groups. Moreover, the intake of both juice and noni infusion provided a higher urea/creatinine ratio (Table 2).

Table 2: Biochemical measures of rats fed with a high fat diet that received water or noni for 4 weeks.

Biochemical measure	Experimental group		
	C	NJ	NI
Glycemia			
Fasting glucose	120,5 (118,5-125,5)a	124,5 (121,8-125,8)a	124,0 (120,8-131,8)a
Lipid profile			
Total cholesterol (mg/dL)	59,7 (51,4-66,7)a	60,1 (53,8-63,7)a	99,8 (99,1-100,1)b
LDL (mg/dL)	48,5 (39,4-58,4)a	42,0 (35,5-44,9)a	78,7 (71,9-88,3)b
HDL (mg/dL)	10,5 (10,5-10,8)a	11,5 (11,1-12,0)a	11,3 (11,2-11,5)a
VLDL (mg/dL)	8,1 (6,2-8,4)a	6,9 (5,5-8,9)a	9,0 (7,9-9,5)a
Triglycerides (mg/dL)	40,6 (31,0-42,1)a	34,7 (27,6-44,6)a	45,2 (39,3-47,7)a
Liver function			
AST (U/L)	297,0 (162,7-365,4)a	232,1 (173,0-242,1)a	112,1 (95,4-127,2)a
ALT (U/L)	88,6 (73,1-112,7)a	95,9 (83,4-135,9)a	59,9 (57,2-71,7)a
Renal function			
Urea (mg/dL)	76,1 (75,9-76,7)a	76,0 (75,9-76,4)a	71,4 (69,4-75,6)a
Creatinine (mg/dL)	0,8 (0,8-0,8)a	0,2 (0,2-0,3)b	0,3 (0,3-0,4)b
Urea/creatinine ratio	92,7 (88,9-98,7)a	349,3 (259,2-441,0)b	230,4 (185,8-266,9)b

Different letters in the horizontal direction indicates statistically significant difference ($p < 0.05$).

There were no statistically significant difference compared to the fasting glucose and serum levels of HDL, VLDL, triglycerides, AST, ALT and urea, according Table 2. Diet and liquid intake was similar between groups as shown in Table 3. Moreover, the coefficient of feed efficiency did not differ between the groups, where C=0.4 (0.4-0.5), NJ=0,4 (0.4-0.4) and NI=0.5 (0.4-0.5), p = 0.58.

Table 3: Mean daily consumption of diet and liquid of experimental groups for 4 weeks.

Variable	Experimental group		
	C	NJ	NI
Diet consumption (g)			
Week 1	59,7	56,9	58,0
Week 2	70,3	73,7	65,9
Week 3	89,2	96,7	87,5
Week 4	78,6	76,8	65,1
Liquid consumption (mL)			
Week 1	111,4	122,6	114,6
Week 2	108,1	119,1	119,5
Week 3	198,6	213,6	211,4
Week 4	177,0	178,0	171,0

4. Discussion

Rats fed a high-fat diet and that have received noni, either as juice or as infusion, had higher waist circumference and lower serum creatinine levels, resulting in increased urea/creatinine ratio. Furthermore, the animals that received noni infusion exhibited higher serum levels of total cholesterol and LDL. Although animals that have consumed noni have presented a greater waist circumference than the control group, there was no statistically significant difference in relation to the relative weight of the retroperitoneal fat between the groups.

The larger waist circumference, then, may have been due to the increase of some organs of the abdominal cavity, not evaluated. In the present study, it was not observed difference in fasting glucose between groups. In turn, Nerurkar et al. (2012) found that fermented noni juice was able to improve glucose metabolism in rats fed a diet rich in lipids by regulating of FoxO1. In diabetic rats, noni was also benefit by modulation of PPAR-γ receptor and AMPK (Lee et al., 2012).

Lin et al. (2012) found that supplementation with fermented noni juice promoted lower serum level of total cholesterol and triglyceride in hamsters fed a high fat diet. In turn, Mandukhail et al. (2010) demonstrated that different parts of the fruit (pulp, leaves and aqueous extract) promoted an improvement in the lipid profile in rats fed a high-fat diet, attributing such effect to the inhibition, biosynthesis, secretion and absorption of lipids.

In the present study, it was not identified the efficacy of noni in the improvement of the lipid profile of rats fed a high-fat diet. In contrast, rats that consumed the noni infusion showed serum levels of total cholesterol and LDL greater than the other groups.

Supplementation with fermented noni juice, as in the study by Lin et al. (2005), may have beneficial effects of noni or prebiotics resulting from fermentation, which may contribute to the improvement of the lipid profile (Beserra et al., 2015). As for the study by Mandukhail et al. (2010), the benefits found were for the pulp, the leaves, and the aqueous extract of the fruit. In the present study, higher serum levels of total cholesterol and LDL were identified in the group that ingested whole fruit infusion, and may indicate that some part of the noni may have some component responsible for such increase. In addition, the infusion was made from dehydrated fruit, which can modify fresh fruit components.

In addition, the experimental models in these and in the present study were different, which may justify the difference in the results. In addition, it was found that the groups that consumed noni had lower serum creatinine levels and, in turn, a higher ratio of urea/creatinine, which may indicate the presence of processes leading to a decrease in renal blood flow, such as dehydration, congestive heart failure and prolonged febrile conditions (Sodré et al., 2007; Bastos, 2011).

No studies were identified in which there was worsening of the lipid profile or alteration of the renal blood flow. Although the present study did not identify any indication of hepatic injury, there are reports of toxicity due to its consumption in humans (Millonig et al., 2005; Stadlbauer et al., 2005; Andrada et al., 2007, Yu et al., 2011). In rats, fruit ingestion has been shown to impair prenatal development (Müller et al., 2009; Marques et al., 2010).

It is important to also take into consideration the processing of the fruit. The powdered pulp used in the study was obtained industrially by spray dryer. For the preparation of the infusion, the dehydrated fruit and boiling water were used. All these processes use high temperatures, which can favor the oxidation and loss of nutrients and bioactive compounds (Naves et al., 2010; Barreto et al., 2013). As a limiting factor of the present study, the time of the experiment stands out. Administration of the fruit for a longer period could reveal other effects that were not identified with noni consumption for 4 weeks.

5. Conclusion

Consumption of noni, both in the form of juice or infusion, promoted higher waist circumference and urea/creatinine ratio. In addition, noni infusion intake increased serum levels of total cholesterol and LDL.

The results of the present study indicate that the consumption of noni can have an opposite effect to that used popularly, at least in the presence of hypercholesterolemia, emphasizing the necessity of this type of study and pointing out the indiscriminate use of certain foods and compounds with claims of beneficial properties.

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