

# Soursop fruit (*Annona muricata* Linn.) consumption does not increase serum potassium levels and not significant in cardiovascular risk improvements of prehypertension subjects

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## ABSTRACT

Patients with chronic kidney disease (CKD) tend to have hyperkalemia. They worry about the consumption of fruit for fear of increased serum potassium levels and therefore require a restricted potassium diet. Soursop fruit (*Annona muricata* Linn.) is believed to be beneficial for CKD and cardiovascular risk. This study was conducted to investigate the effect of soursop fruit supplement consumption on serum potassium levels and cardiovascular risk in prehypertension subjects from Mlati, Sleman District, Yogyakarta Special Region, Indonesia. A total 143 samples that met to the inclusion and exclusion criteria were subsequently randomized into two groups. Group I was given 2 x 100 g/day of soursop and Group II was without soursop. A laboratory examination from both groups was conducted including potassium, total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL), and triglyceride levels at weeks 0; 7; and 13. Regular soursop consumption was evaluated every 2 weeks for 3 months. Data analysis was performed using an independent t test, a nonparametric Mann-Whitney test, and a chi-square test. No significantly different in serum potassium levels between the soursop and non-soursop groups at week 7 and 13 ( $p=0.073$  and  $p=0.108$ ) was observed. Furthermore, no significantly different in total cholesterol ( $p=0.254$  and  $p=0.932$ ), LDL ( $p=0.221$  and  $p=0.710$ ), HDL ( $p=0.400$  and  $p=0.960$ ), triglycerides ( $p=0.423$  and  $p=0.580$ ) of both groups was also observed. However, in subjects with hypercholesterolemia and hypertriglyceridemia, the mean cholesterol and triglyceride levels decreased compared to no soursop consumption at week 7 and 13. In conclusion, consumption of a soursop fruit supplement of 2 x 100 g/day for 13 weeks does not affect the serum potassium levels of prehypertension subjects. Moreover, the consumption of a soursop fruit supplement is not significantly different compared to those without soursop in improving cardiovascular risk.

## ABSTRAK

Pasien penyakit ginjal kronik cenderung mengalami hiperkalemia. Mereka khawatir konsumsi buah karena takut kalium darahnya naik, oleh karena itu perlu restriksi diet kalium. Buah sirsak (*Annona muricata* Linn.) diduga bermanfaat untuk penyakit ginjal kronik dan risiko kardiovaskular. Penelitian ini dilakukan untuk mengkaji pengaruh pemberian minuman suplemen buah sirsak terhadap kadar kalium darah dan risiko kardiovaskular pada subjek prehipertensi dari Mlati, Sleman, Daerah Istimewa Yogyakarta. Total 143

subjek yang memenuhi kriteria inklusi dan eksklusi dibagi menjadi 2 kelompok. Kelompok I diberi suplemen buah sirsak 2 x 100 g/hari dan Kelompok II tanpa perlakuan. Pemeriksaan laboratorium dilakukan terhadap kalium, kolesterol total, LDL, HDL, trigliserida pada minggu ke 0; 7; dan 13. Evaluasi kepatuhan konsumsi sirsak setiap 2 minggu selama 3 bulan. Analisis data menggunakan uji t, uji nonparametrik Mann-Whitney, dan uji Chi-Square. Tidak ada perbedaan bermakna pada kadar kalium darah pada minggu 7 dan 13 ( $p=0,073$  dan  $p=0,108$ ) antara kelompok sirsak dan non sirsak. Demikian juga tidak dijumpai perbedaan nyata kolesterol total ( $p=0,254$  dan  $p=0,932$ ), LDL ( $p=0,221$  dan  $p=0,710$ ), HDL ( $p=0,400$  dan  $p=0,960$ ), trigliserida ( $p=0,423$  dan  $p=0,580$ ) pada kedua kelompok. Tetapi pada subyek dengan hiperkolesterol dan hipertrigliserida rerata kadar kolesterol dan trigliserida turun pada minggu 7 dan 13 dibanding tanpa konsumsi sirsak. Dapat disimpulkan, konsumsi buah sirsak 2 x 100 g/hari selama 13 minggu tidak mempengaruhi kadar kalium darah subjek preipertensi. Selain itu, konsumsi buah sirsak tidak berbeda bermakna dibandingkan tanpa buah sirsak dalam memperbaiki risiko kardiovaskular.

**Keywords:** soursop – potassium – hyperkalemia - chronic kidney disease - cardiovascular

## INTRODUCTION

Many patients with chronic kidney disease (CKD) assume that the consumption of fruit will increase serum potassium levels. Consumption of fruits that contain lots of potassium (apricots and bananas) causes hyperkalemia,<sup>1</sup> especially in patients with impaired renal function. Hyperkalemia can lead to serious cardiac arrhythmias and death.<sup>2</sup> Several studies have suggested that soursop (*Annona muricata* Linn) consumption is beneficial for kidney disease.<sup>3</sup> Surveys-based studies have been conducted in various places including Peru<sup>4</sup> and Bolivia<sup>5</sup> on the use of soursop in the traditional treatment of kidney disease. Sja'bani (2014) reported that the consumption of 2x100 g/day soursop juice in patients with CKD in Yogyakarta, Indonesia decreased uric acid, serum ureum and creatinine, without adverse effects.<sup>6</sup>

The potassium content of soursop fruit is 278 mg/100g.<sup>3</sup> The recommended intake of potassium in a standard diet is 4.7 g/day (120 mmol/day); for mild to moderate CKD is <4.7 g/day, and for severe CKD (including those undergoing dial. Soursop consumption of 2x100 g/day is equivalent to 556 mg/day of potassium, this is well below the recommended dietary amount for mild to severe CKD, even for those undergoing dialysis. However, whether the consumption

of soursop fruit in patients with mild to severe CKD (undergoing hemodialysis) still safe and what is the effect of a soursop fruit supplement on serum potassium levels have not been investigated.

Cardiovascular disease has become a trend in medical talks in both developed and developing countries. Cardiovascular death by 31% from overall mortality rates,<sup>8</sup> otherwise, mortality rates due to infection tend to decrease. Various attempts have been made to reduce mortality due to cardiovascular disease by controlling blood pressure, diabetes, dyslipidemia, and even uric acid.

Hypertension is a major risk factor for increased morbidity and mortality due to cardiovascular, cerebrovascular, and end-stage renal failure.<sup>9</sup> Based on data from the 2011–2012 NHANES survey, about one-third of adults in the United States are hypertensive. Hypertension is uncontrolled in almost half of these 71 million people, and of those with uncontrolled hypertension, about 36% or 13 million are unaware of the diagnosis. Even in patients in whom hypertension is diagnosed and treated, control is attained in only 60%. By convention, hypertension is categorized based on office measurements as stage 1 (140–159/90–99 mm Hg Within 5 years, prehypertension increases the

risk of cardiovascular disease by 45% compared to normal blood pressure.<sup>10</sup> Once the importance of prehypertension became known, the ACC/AHA 2017 grouped it into stage I hypertension.<sup>11</sup> Soursop fruit is expected to reduce blood pressure, decrease uric acid, and improve cardiovascular conditions by lowering cholesterol, LDL, and triglycerides and increasing HDL.<sup>12,13</sup> Soursop fruit contains tannins,<sup>14</sup> which play a role in the reduction of triglycerides.<sup>15</sup> Soursop fruit also contains flavonoids,<sup>13</sup> which can inhibit the activity of the HMG-CoA reductase enzyme in the cholesterol synthesis process. This is the necessary for in-depth research (randomized controlled trials, or RCTs) to determine the effect of soursop fruit supplementation compared to control serum potassium levels and cardiovascular risk.

## MATERIALS AND METHODS

### Design of study

This study represents in-depth epidemiology research on the effect of soursop fruit consumption in prehypertension with high normal uric acid. Prior to the study, the research design was approved by the Medical and Health Research Ethics Committee (MHREC) of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta. After being given information about the study, subjects were asked to fill out and sign a willingness to participate form (informed consent).

### Protocol of study

Data was taken from Mlati Study 10 years ago; the selected subjects still have prehypertension, are 30–59 years old, and are located in the region of Mlati, Sleman, Yogyakarta, Indonesia. A random sample of the study was conducted using simple random sampling with SPSS 22 software. There were 143 samples that conform to the inclusion criteria of prehypertension, high normal uric acid ( $\geq 5$  to  $< 7$  mg/dL),

negative urine protein, and negative urine reduction. Exclusion criteria included a history of diabetes, chronic renal failure, use of hormonal contraception, pregnancy, hypertension, ages  $< 30$  or  $> 59$  years old, the consumption of uric-acid-lowering drugs (allopurinol, probenecid), uric acid levels  $< 5$  mg/dL or  $\geq 7$  mg/dL, creatinine levels  $> 1.5$  g/dL, and fasting blood glucose (FBG)  $> 126$  g/dL. From 143 samples randomized to two groups, Group I was given 2x100 g/day of soursop supplement and Group II was without soursop. Laboratory examinations of serum potassium, total cholesterol, LDL, HDL, and triglycerides were performed at weeks 0, 7, and 13 in the soursop and non-soursop groups. Compliance with the soursop consumption was evaluated every 2 weeks for 3 months. The study was conducted with RCTs.

### Statistical analysis

Data analysis was performed using an independent *t* test, a nonparametric Mann–Whitney test, and a chi-square test.

## RESULTS

The study involved 143 subjects, consisted 71 subjects soursop and 72 subjects non-soursop groups. The 71 subjects soursop group was 15 subjects (21%) are drop out at week 7 and 17 subjects (23%) at week 13. The 72 subjects non-soursop group was 12 subjects are drop out (16%) at week 7 and 14 subjects (19%) at week 13. The mean age of the soursop group is  $46.30 \pm 7.95$  years old, and the mean age of the non-soursop group is  $44.44 \pm 7.52$  years old. There was no significant difference between the mean age of the two groups soursop and non-soursop ( $p=0.107$ ). The gender breakdown in the soursop group is 56 (79%) males and 15 (21%) females, while the number of males in the non-soursop group is 51 (71%) and the number of females is 21 (29%). There was no significant difference between the males and females of the two groups soursop and non-soursop ( $p=0.268$ ; TABLE 1).

TABLE1. Age and gender in the soursop and non-soursop groups.

Variable	Total	Soursop	Non-soursop	p
	n=143	n=71	n=72	
Age (mean ± SD years)	45.36 ± 7.76	46.30 ± 7.95	44.44 ± 7.52	0.107 <sup>a</sup>
Gender [n (%)]				
• Male	107 (74.8)	56 (39.2)	51 (35.7)	0.268 <sup>a</sup>
• Female	36 (25.2)	15 (10.5)	21 (14.7)	

Note: <sup>a</sup>t test, <sup>b</sup>Mann–Whitney test.

TABLE 2. Mean potassium, total cholesterol, LDL, HDL, and triglycerides [mean (SD mg/mL)] at weeks 0; 7; and 13 in the soursop and non-soursop groups.

Variable	Week 0			Week 7			Week 13		
	Soursop n=71	Non- soursop n=72	p	Soursop n=56	Non- soursop n=60	p	Soursop n=54	Non- soursop n=58	p
Potassium	3.90 (0.35)	3.88 (0.32)	0.905 <sup>b</sup>	4.09 (0.37)	3.99 (0.32)	0.073 <sup>a</sup>	4.04 (0.30)	3.95 (0.36)	0.108 <sup>a</sup>
Cholesterol	164.76 (34.20)	167.81 (34.33)	0.596 <sup>a</sup>	191.59 (27.86)	187.77 (31.91)	0.254 <sup>a</sup>	182.81 (21.84)	185.86 (28.26)	0.932 <sup>a</sup>
LDL	108.51 (26.74)	109.04 (30.78)	0.912 <sup>a</sup>	127.57 (21.72)	121.67 (28.57)	0.221 <sup>a</sup>	124.33 (18.92)	121.95 (27.21)	0.710 <sup>a</sup>
HDL	41.54 (10.11)	42.85 (10.54)	0.449 <sup>a</sup>	44.18 (9.28)	44.30 (11.85)	0.40 <sup>a</sup>	45.30 (10.03)	47.12 (13.00)	0.960 <sup>a</sup>
Triglycerides	118.54 (69.25)	124.47 (74.55)	0.634 <sup>b</sup>	147.54 (86.42)	168.32 (198.05)	0.423 <sup>b</sup>	138.81 (60.82)	164.66 (168.12)	0.580 <sup>b</sup>

Note: <sup>a</sup>t test, <sup>b</sup>Mann–Whitney test

The mean potassium level at baseline (week 0) of the soursop group was 3.90 ± 0.35 mg/dL, and for the non-soursop group it was 3.88 ± 0.32 mg/dL. There was no significant difference in the baseline potassium levels in the two groups (p=0.905). At week 7, the potassium level of the soursop group was 4.09 ± 0.37 mg/dL, and in the non-soursop group it was 3.99 ± 0.32 mg/dL. There was no significant difference in the two groups (p=0.073). At week 13, the soursop group level was 4.04 ± 0.30 mg/dL, and the non-soursop group level was 3.95 ± 0.36 mg/dL. There was no significant difference in the two groups (p=0.108; TABLE 2).

The mean total cholesterol level at baseline (week 0) of the soursop group was 164.76 ± 34.20 mg/dL, and it was 167.81 ± 34.33 mg/dL in the non-soursop group. There was no significant difference in the

baseline total cholesterol levels in the two groups (p=0.596). At week 7, the soursop group level was 191.59 ± 27.86 mg/dL, and the non-soursop group level was 187.77 ± 31.91 mg/dL. There was no significant difference in the two groups (p=0.254). At week 13, the soursop group level was 182.81 ± 21.84 mg/dL, and the non-soursop group level was 185.86 ± 28.26 mg/dL. There was no significant difference in the two groups (p=0.932; TABLE 2).

The mean LDL level at baseline (week 0) of the soursop group was 108.51 ± 26.74 mg/dL, and for the non-soursop group it was 109.04 ± 30.78 mg/dL. There was no significant difference in baseline LDL levels in the two groups (p=0.912). At week 7, the soursop group level was 127.57 ± 21.72 mg/dL, and in the non-soursop group it was 121.67 ± 28.57 mg/dL. There was

no significant difference in the two groups ( $p=0.221$ ). At week 13, the soursop group level was  $124.33 \pm 18.92$  mg/dL, and the non-soursop group level was  $121.95 \pm 27.21$  mg/dL. There was no significant difference in the two groups ( $p=0.710$ ; TABLE 2).

The mean HDL level at baseline (week 0) of the soursop group was  $41.54 \pm 10.11$  mg/dL, and in the non-soursop group it was  $42.85 \pm 10.54$  mg/dL. There was no significant difference in the baseline HDL levels in the two groups ( $p=0.449$ ). At week 7, the soursop group level was  $44.18 \pm 9.28$  mg/dL, and the non-soursop group level was  $44.30 \pm 11.85$  mg/dL. There was no significant difference in the two groups ( $p=0.400$ ). At week 13, the soursop group level was  $45.30 \pm 10.03$  mg/dL, and the non-soursop group level was  $47.12 \pm 13.00$  mg/dL. There was no significant difference in the two groups ( $p=0.960$ ; TABLE 2).

The mean triglyceride level at baseline (week 0) of the soursop group was  $118.54 \pm 69.25$  mg/dL, and in the non-soursop group

it was  $124.47 \pm 74.55$  mg/dL. There was no significant difference in baseline triglyceride levels in the two groups ( $p=0.634$ ). At week 7, the soursop group level was  $147.54 \pm 86.42$  mg/dL, and the non-soursop group level was  $168.32 \pm 198.05$  mg/dL. There was no significant difference in the two groups ( $p=0.423$ ). At week 13, the soursop group level was  $138.81 \pm 60.82$  mg/dL, and the non-soursop group level was  $164.66 \pm 168.12$  mg/dL. There was no significant difference in the two groups ( $p=0.580$ ; TABLE 2).

## DISCUSSION

The recommended intake of potassium in a standard diet is 4.7 g/day (120 mmol/day); for mild to moderate CKD it is <4.7 g/day, and in severe CKD (including those undergoing dialysis) it is <3 g/day (TABLE 3).<sup>7</sup> Those with low-potassium diets are at risk for cardiac arrhythmias and constipation.

TABLE 3. Recommended dietary potassium intake in normal and CKD

Variable	Normal	Mild to moderate CKD	Severe dialysis CKD
Potassium (g/day)	4.7 (120 mmol/day)	< 4.7 (< 120 mmol/day)	< 3 (< 77 mmol/day)

At week 7, the mean potassium levels of the soursop group increased from  $3.90 \pm 0.35$  to  $4.09 \pm 0.37$  mg/dL, but in the non-soursop group there was also an increase from  $3.88 \pm 0.32$  to  $3.99 \pm 0.32$  mg/dL. In the statistical analysis, there was no significant difference between the soursop and non-soursop groups ( $p=0.073$ ). At week 13, the mean potassium levels of the soursop group increased from  $3.90 \pm 0.35$  to  $4.04 \pm 0.30$  mg/dL, but in the non-soursop group there was also an increase from  $3.88 \pm 0.32$  to  $3.95 \pm 0.36$  mg/dL. In the statistical analysis, there was no significant difference between the soursop and non-soursop groups ( $p=0.108$ ). This study indicate soursop consumption 2x100 g/day for 3 months there was no significant difference in serum potassium levels between

the soursop and non-soursop groups. Soursop consumption of 2x100 g/day is equivalent to 556 mg/day of potassium; this is well below the recommended dietary intake for mild to severe CKD, even for those undergoing dialysis (TABLE 3). This means that the consumption of soursop fruit for patients with mild to severe CKD (dialysis) is still safe.

Several studies have suggested that soursop consumption is beneficial for kidney disease.<sup>3</sup> Surveys-based studies have been conducted in various places including Peru<sup>4</sup> and Bolivia<sup>5</sup> on the use of soursop in the traditional treatment of kidney disease. Sja'bani,<sup>6</sup> reported that the consumption of 2x100 g/day soursop juice in patients with CKD in Yogyakarta, Indonesia can decrease

uric acid, serum ureum and creatinine, without causing negative effects.<sup>6</sup>

In a review journal of the NKF (National Kidney Foundation), the issue of whether a high-potassium diet restriction can prevent hyperkalemia in patients undergoing hemodialysis was explored. After study and data collection, it was found that a high-potassium diet restriction was required to prevent hyperkalemia in patients undergoing hemodialysis.<sup>16</sup> Patients with CKD tend to have hyperkalemia.<sup>17</sup> They worry about the consumption of fruit for fear of increased serum potassium levels and therefore require a restricted potassium diet. Soursop fruit is beneficial for CKD,<sup>6</sup> and in this study the consumption of soursop was found to have no significant effect on potassium levels compared to the group without soursop. So the consumption of soursop on CKD is safe because it does not cause hyperkalemia and is beneficial because several other studies have stated about the benefits of soursop on kidney disease.

This cardiovascular risk study aims to examine the effect of the consumption of 2x100 g/day of soursop supplement on cardiovascular risk (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides). Soursop fruit contains tannins,<sup>14</sup> which play a role in the reduction of triglycerides.<sup>15</sup> Soursop fruit also contains flavonoids,<sup>13</sup> which can inhibit the activity of the HMG-CoA reductase enzyme in the cholesterol synthesis process. The inhibition of this enzyme activity results in the absence of mevalonate from HMG-CoA; mevalonate will be converted to squalene, lanosterol, dihydrolanosterol, D 8-dimethylsterol, 7-dihydrocholesterol, and eventually cholesterol. In addition, flavonoids also have a positive effect in decreasing total cholesterol levels through the increased excretion of bile acids with feces. Tannins, riboflavin, and cyanide acid have a hypoglycemic effect that can lower cholesterol and triglyceride blood levels in mice.<sup>15,18</sup>

Flavonoids in soursop leaves and fruit are antioxidants that have the ability to reduce fat emulsion and cholesterol

synthesis. Decreasing fat emulsions and cholesterol synthesis will lower the levels in the blood.<sup>18</sup> Soursop fruit also contains many antioxidants.<sup>13</sup> Most fruit is rich in antioxidant compounds that can prevent and inhibit damage from fats, proteins, and nucleic acids.<sup>19</sup> The abundant antioxidants in fruit are polyphenols and vitamins (A, B, C and E) including flavonoids.<sup>20</sup>

The consumption of a soursop fruit supplement of 2x100 g/day for 3 months led to no significant difference in total cholesterol at week 7 ( $p=0.254$ ) and week 13 ( $p=0.932$ ) between the soursop and non-soursop groups. For LDL cholesterol there was no significant difference at week 7 ( $p=0.221$ ) and week 13 ( $p=0.710$ ). For HDL cholesterol there was no significant difference at week 7 ( $p=0.400$ ) and week 13 ( $p=0.960$ ). There was no difference in triglyceride levels at week 7 ( $p=0.423$ ) and week 13 ( $p=0.580$ ) between the soursop and non-soursop groups.

No similar research has been conducted on the effect of soursop consumption on cardiovascular risk in humans, only in animals. Firmansyah *et al.*<sup>21</sup> who administered soursop leaf extract to hyperglycemic rats, found that it did not lower total cholesterol and triglycerides significantly, but it decreased the blood sugar of mice. However, the administration of soursop leaf extract with ethyl acetate solvent can significantly decrease total blood cholesterol levels in mice.<sup>22</sup> Likewise, Posangi *et al.*<sup>23</sup> concluded that administering soursop leaf extract can reduce total cholesterol in mice.<sup>23</sup>

Pratiwi *et al.*<sup>24</sup> found that the essential oil of soursop leaves (*A. muricata* Linn.) contains terpenoid, alkaloid, and phenolic compounds. Terpenoids, alkaloids, and phenolics serve as antioxidants and anti-inflammatories in the right dosage. If the dose is high and administered for a long time, the terpenoids, alkaloids, and phenolics will become toxic and result in increased LDL and decreased HDL. A dosage of soursop leaf oil of 2.5 mg/kgW is a safe dose that does not increase LDL levels and decreases subchronic HDL levels in normal male and

female rats.<sup>24</sup>

Tia *et al.*<sup>25</sup> reported the percentages of decrease in the LDL cholesterol serum levels of white rats from various dosages of soursop juice: a dose of 0.9 g/200 g BW is equal to 46.19%, a dose of 1.8 g/200 g BW is equal to 52.30%, and a dose of 2.7 g/200 g BW is equal to 61.62%. There is an effect of administering various doses of soursop juice on the decrease in LDL cholesterol serum levels in white mouse dyslipidemia. The greater the dose of soursop juice, the greater the decrease in LDL cholesterol levels in the serum of white rats with dyslipidemia.<sup>25</sup>

de la Cruz *et al.*<sup>26</sup> concluded that dried soursop fruit significantly lowers cholesterol, triglycerides, and LDL cholesterol in hyperlipidemic rats. The dosages of soursop fruit used were 500, 1000, 2000 mg/kgW. The higher the dose, the greater the decrease in cholesterol, triglyceride levels, and LDL levels. Syahida *et al.*<sup>27</sup> showed that the higher the provision of soursop extract given to rats, the higher the level of antioxidants. Yuliantari *et al.*<sup>28</sup> investigated the influence

of temperature and extraction on the flavonoid content and antioxidant activity of soursop leaves. They showed that the best result is at a temperature of 45°C and a time of extraction of 20 min. The total yield is 19.14% flavonoid 903.90 mgQE/g extract material, and the lowest antioxidant activity is 258.155 mg/L.<sup>28</sup>

Tugiyanti *et al.*<sup>18</sup> showed that a soursop leaf supplement in male ducks of 8.36% showed the highest HDL level of 99.89 mg/dL. However, a soursop flour supplement up to 15% had not been able to reduce triglycerides, cholesterol, and LDL blood levels in male ducks aged 10 weeks. Soursop leaves have antioxidant flavonoid content. Tugiyanti *et al.*<sup>18</sup> stated that antioxidants can affect fat content. Wulandari *et al.*<sup>29</sup> concluded that soursop leaf extract with ethanol solvent can lower triglyceride levels and increase HDL levels in male wistar rats. How does this study compare with other research on the effect of soursop on cardiovascular risk? TABLE 4 summaries briefly the study of soursop on cardiovascular risk.

TABLE 4. Comparison of this study with other soursop research on cardiovascular risk.

	Haidar <i>et al.</i> , 2018	Tia <i>et al.</i> , 2014	Tugiyanti <i>et al.</i> , 2016	de la Cruz <i>et al.</i> , 2016
Material	Soursop fruit juice	Soursop fruit juice	Soursop leaf flour	Dried soursop fruit
Subject	Healthy human	Dyslipidemia mice	Healthy ducks	Dyslipidemia mice
Given by	Oral	Oral	Oral	Oral
Dose	2 x 100 g/day	0.9 g/200 g BW 1.8 g/200 g BW 2.7 g/200 g BW	Fodder+5%; 10%; 15% Soursop leaf flour	500 mg/kg BW 1000 mg/kg BW 2000 mg/kg BW
Method	Cohort, 3 months, RCT	Control group design	Completely randomized design, 5 weeks	Completely randomized design, 30 days
Evaluation	Every 2 weeks	Pre- and post-test	Pre- and post-test	Pre- and post-test
Result	No significant effect on the decrease in total cholesterol, LDL, or triglycerides and an increase in HDL at week 7 and 13 in the soursop and non-soursop groups.	There is the effect of giving various doses of soursop juice on the decrease in LDL cholesterol levels. The greater the dose, the greater the decrease in LDL cholesterol levels.	Cannot lower triglycerides, cholesterol, and blood LDL and triglyceride levels	Significantly lower cholesterol, triglycerides, and LDL. The higher the dose, the greater the decrease.

In a study on dyslipidemia in mice, Tia *et al.*<sup>25</sup> found that soursop juice can lower LDL. Research by de la Cruz *et al.*<sup>26</sup> on dyslipidemia in mice concluded that soursop can lower cholesterol, triglycerides, and LDL. This study found that soursop juice in healthy humans had no significant effect in decreasing cholesterol, LDL, or triglycerides, and HDL increased in the 7<sup>th</sup> and 13<sup>th</sup> weeks for the soursop and non-soursop groups. Why is there no significant difference in total cholesterol, LDL, HDL,

or triglycerides among the soursop and non-soursop groups at weeks 7 and 13? We suspect that the subjects of the study were healthy subjects rather than subjects with cardiovascular disorders (dyslipidemia) as in other studies. When the subjects who had dyslipidemia (hypercholesterolemia, high LDL, low HDL, and hypertriglyceridemia) are compared to the soursop and non-soursop groups, the results are as presented in TABLE 5.

TABLE 5. Subject dyslipidemia [mean (SD)] in the soursop and non-soursop groups.

	Week 0(n = 22)		Week 7(n = 17)		Week 13(n = 17)	
	Soursop (n = 10)	Non-soursop (n = 12)	Soursop (n = 7)	Non-soursop (n = 10)	Soursop (n = 7)	Non-soursop (n = 10)
Hypercholesterol (mg/dL)	221.30 (17.30)	223.25 (15.88)	213.57 (19.67)	223.70 (25.06)	197.57 (33.64)	220.70 (18.06)
	Week 0(n = 81)		Week 7(n = 63)		Week 13(n = 61)	
	Soursop (n = 42)	Non-soursop (n = 39)	Soursop (n = 33)	Non-soursop (n = 30)	Soursop (n = 32)	Non-soursop (n = 29)
High LDL (mg/dL)	126.86 (16.75)	131.69 (21.53)	135.73 (20.44)	137.07 (24.38)	130.53 (18.20)	134.24 (26.61)
	Week 0(n = 60)		Week 7(n = 49)		Week 13(n = 46)	
	Soursop (n = 32)	Non-soursop (n = 28)	Soursop (n = 26)	Non-soursop (n = 23)	Soursop (n = 25)	Non-soursop (n = 21)
Low HDL (mg/dL)	32.50 (5.00)	32.54 (4.69)	40.15 (8.63)	40.61 (10.57)	41.12 (7.73)	42.19 (13.43)
	Week 0(n = 35)		Week 7(n = 29)		Week 13(n = 28)	
	Soursop (n = 18)	Non-soursop (n = 17)	Soursop (n = 14)	Non-soursop (n = 15)	Soursop (n = 14)	Non-soursop (n = 14)
Hypertriglyceride (mg/dL)	205.28 (83.52)	233.47 (77.80)	183.07 (90.76)	339.67 (342.53)	188.29 (64.51)	324.21 (276.16)

There were 22 subjects with hypercholesterolemia at week 0 and 17 at weeks 7 and 13. The mean value for subjects with hypercholesterolemia who consumed soursop at week 7 showed decreased cholesterol averages from 221 to 213 mg/dL. At week 13, the average value for cholesterol decreased from 221 to 197 mg/dL when compared with week 0. From week 7 to week 13, the average cholesterol value decreased from 213 to 197 mg/dL.

Regarding the mean value for subjects with hypercholesterolemia without soursop

consumption, at week 7 cholesterol did not decrease (it stayed at 223 mg/dL). At week 13, the value of the cholesterol average decreased from 223 mg/dL to 220 mg/dL when compared with week 0. Without soursop consumption in subjects with hypercholesterolemia, there was almost no change for 13 weeks. From this study, it can be concluded that the consumption of soursop fruit in subjects with hypercholesterolemia can reduce cholesterol averages at weeks 7 and 13 compared to the group without the consumption of soursop.



There were 81 subjects with high LDL at week 0, 63 subjects at week 7, and 61 subjects at week 13. The mean value for high LDL subjects in the soursop consumption group at week 7 increased from 126 to 135 mg/dL and at week 13 from 126 to 130 mg/dL. Regarding the mean values for high LDL subjects without soursop, at week 7 the average LDL increased from 131 to 137 mg/dL. At week 13, the mean LDL value increased from 131 to 134 mg/dL when compared with week 0. From this research, it can be concluded that the consumption of soursop fruit in subjects with high LDL did not lower mean LDL at weeks 7 and 13 compared to the group without the consumption of soursop.

There were 60 subjects with low HDL at week 0, 49 subjects at week 7, and 46 subjects at week 13. The mean value for low HDL subjects with soursop consumption increased at week 7 and week 13 from 32 to 40 and 41 mg/dL, respectively. Regarding the mean value for low HDL subjects without soursop consumption, at weeks 7 and 13 it increased from 32 to 40 and 42 mg/dL, respectively. From this study, it can be concluded that the consumption of soursop fruit does not increase mean HDL cholesterol compared to the non-soursop group.

There were 35 subjects with hypertriglyceridemia at week 0, 29 subjects at week 7, and 28 subjects at week 13. The mean value for hypertriglyceridemia subjects with the consumption of soursop decreased from 205 to 183 mg/dL and 188 mg/dL, respectively, at weeks 7 and 13. Regarding the mean value for hypertriglyceridemia subjects without soursop consumption, at weeks 7 and 13, it increased from 233 to 339 mg/dL and 324 mg/dL, respectively. From this study, it can be concluded that the consumption of soursop fruit can lower mean triglyceride levels compared to the group without soursop consumption.

## CONCLUSION

In conclusion, consumption of a soursop fruit supplement of 2 x 100 g/day for

13 weeks does not affect the serum potassium levels of prehypertension subjects. Moreover, the consumption of a soursop fruit supplement is not significantly different compared to those without soursop in improving cardiovascular risk as expressed by the decrease total cholesterol, LDL, and triglycerides and the increase HDL. However, in subjects with hypercholesterolemia and hypertriglyceridemia, the consumption of soursop fruit for 13 weeks decreases the cholesterol and triglyceride levels at weeks 7 and 13 compared to those without soursop fruit supplement.

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