

# Effects of Roselle on arterial pulse pressure and left ventricular hypertrophy in hypertensive patients

Ahmad I. Al-Shafei, MD, PhD, Ola A. El-Gendy, MSc, PhD.

## ABSTRACT

**الأهداف:** وصف آثار التعاطي المنتظم لشاي الكركديه على ضغط الدم وتضخم بطين القلب الأيسر في مرضى ضغط الدم المعتدل.

**الطريقة:** تم إجراء الدراسة الحالية الشبه تجريبية والغير عشوائية في المستشفى العام بمدينة كفر الشيخ بجمهورية مصر العربية لمدة 8 أسابيع، خلال الفترة من سبتمبر إلى نوفمبر 2012م. تم دراسة الآثار المترتبة للتعاطي المنتظم للكركديه لمدة 4 أسابيع على القياسات الأسبوعية لضغط الدم الانقباضي (SBP)، ضغط الدم الانبساطي (DBP)، وضغط الدم النبضي (PP)، وكذلك معدل نبضات القلب (HR) في مجموعتين متماثلتين في العمر والجنس (العدد=50 لكل منهما؛ العمر 50±5 سنوات)؛ إحدى المجموعتين من أشخاص ذوي ضغط دم طبيعي والأخرى تحوى مرضى يعانون من ارتفاع ضغط الدم الأساسي المعتدل ويتعاطون علاجين أو أقل لمعالجة ارتفاع الضغط. تم أيضاً تقييم تضخم البطين الأيسر بواسطة رسم القلب الكهربائي قبل الشروع في تعاطي الكركديه وكذلك عند نهاية كل من فترتي تعاطي وعدم تعاطي الكركديه التي امتدت كل منهما لمدة 4 أسابيع.

**النتائج:** انخفض ضغط الدم النبضي (PP) بشكل ملحوظ من القيم الأساسية بنسبة 10.9% و 21.2%، وانخفض متوسط ضغط الدم الانقباضي (SBP) بنسبة 10% و 19.6%؛ وضغط الدم الانبساطي (DBP) بنسبة 9.5% و 18.7% و معدل ضربات القلب (HR) بنسبة 14.6% و 17.1% بحلول نهاية الأسبوع الرابع من تعاطي الكركديه في المجموعتين ذات ضغط الدم الطبيعي وضغط الدم المرتفع على التوالي. إلا أنه بعد توقف التعاطي المنتظم للكركديه عاد كل من SBP، و DBP، و PP و HR إلى مستوياتها السابقة لتعاطي الكركديه خلال 4 أسابيع. أظهرت النتائج أيضاً أنه قبل التعاطي المنتظم للكركديه، لم يكن هناك تضخماً للبطين الأيسر في أي من أشخاص المجموعة ذات ضغط الدم الطبيعي ولكن 14 مريضاً من مرضى ارتفاع ضغط الدم كان لديهم تضخماً للبطين الأيسر. أدى التعاطي المنتظم للكركديه إلى تراجع تضخم البطين الأيسر في 10 من مرضى ارتفاع ضغط الدم وبقي 4 مرضى لديهم تضخم للبطين الأيسر بعد 4 أسابيع من تعاطي الكركديه. إلا أنه بعد 4 أسابيع من توقف تعاطي الكركديه أصبح العدد 10 مرضى.

**خاتمه:** تشير هذه النتائج تجريبياً إلى آثار حسنة للتعاطي المنتظم للكركديه على القلب والأوعية الدموية.

**Objectives:** To characterize the effects of regular Roselle ingestion on blood pressure and left ventricular hypertrophy (LVH) in patients with established moderate essential hypertension.

**Methods:** This non-randomized quasi-experimental study was conducted in Kafr El-Shaikh, Egypt, for 8 weeks, from September 2012 to November 2012. The effects of a 4-week period of regular Roselle ingestion followed by a 4-week recovery period on systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), and heart rates (HR) was studied in 2 equal, gender- and age-matched groups (n=50 each; average age - 50±5 years) of normotensive subjects, and patients with moderate essential hypertension. Electrocardiographic assessments of LVH were also made prior to, and at the end of both treatment and recovery periods.

**Results:** Pulse pressure (PP) significantly fell from baseline values by 10.9% (normotensive group [NG]), 21.2% (hypertensive group [HG]); SBP by 10% (NG), 19.6% (HG); DBP by 9.5% (NG), 18.7% (HG), and HR by 14.6% (NG), 17.1% (HG) by the end of week 4 of treatment. Following treatment cessation, SBP, DBP, PP, and HR returned to pretreatment levels over 4 weeks. Before intervention, none of the normotensive subjects, but 14 hypertensive patients showed LVH. However, Roselle treatment was associated with regression of LVH in 10 patients with only 4 patients showing LVH after 4 weeks of treatment. This became 10 patients 4 weeks after ceasing treatment.

**Conclusion:** These findings empirically suggest favorable cardiovascular effects of Roselle in patients with established moderate essential hypertension.

*Saudi Med J 2013; Vol. 34 (12): 1248-1254*

*From the Department of Physiology (Al-Shafei), College of Medicine, Al-Imam Muhammad Ibn Saud Islamic University, Riyadh, Kingdom of Saudi Arabia, and the Physiology Section (El-Gendy), Department of Zoology, Women's College for Arts, Science, and Education, Ain Shams University, Cairo, Egypt.*

*Received 25th July 2013. Accepted 11th November 2013.*

*Address correspondence and reprint request to: Dr. Ahmad I. Al-Shafei, Department of Physiology, College of Medicine, Al-Imam Muhammad Ibn Saud Islamic University, Riyadh 13317-4233, Kingdom of Saudi Arabia. Tel. +966 550049027. Fax. 966 (11) 2037108. E-mail: shafei1966@hotmail.com*

Roselle (*Hibiscus sabdariffa*) is a widely cultivated annual okra-like botanical plant with reddish green leaves of length 8-15 cm arranged alternately on smooth or nearly smooth cylindrical red stems, that grows to a height of  $\geq 2$  m and takes ~6 months to mature. The flowers are 8-10 cm in diameter, red to yellow with a dark center, and contain short peduncles with a stout fleshy bright red calyx at the base. The calyx is the main edible part of Roselle; it is increasingly used to make tea in Egypt and elsewhere. Yet, despite the fact that tea is the most widely consumed beverage after water worldwide, there has been remarkably little research on the effects of tea ingestion, including the effect of such Roselle tea on blood pressure. Thus far, hypertension is a common condition associated with a range of undesirable clinical outcomes that include stroke, myocardial infarction, heart failure, renal insufficiency, peripheral vascular disease, and retinopathy.<sup>1,2</sup> Furthermore, recent reports describe actions of an aqueous calyx extract of *Hibiscus sabdariffa* (HS) in producing dose-dependent reductions in both blood pressure and heart rate in rats with experimental hypertension as well as in normotensive controls; nevertheless, greater in the experimental than the controls.<sup>3,4</sup> There have been also few clinical studies reporting the effects of Roselle ingestion on blood pressure in hypertensive patients.<sup>5-7</sup> One study reported significant reductions in the mean systolic blood pressure (SBP) from  $134.4 \pm 11.8$  mm Hg at the beginning of the study to  $112.7 \pm 5.7$  mm Hg after 1 month ( $p < 0.001$ ) in hypertensive patients with type 2 diabetes.<sup>5</sup> The antihypertensive effectiveness and tolerability of a standardized extract from Roselle were compared with captopril in a controlled and randomized clinical trial.<sup>6</sup> The results showed that Roselle treatment decreased the SBP from 139.05 to 123.73 mm Hg (namely, by 11.4%) and the diastolic blood pressures (DBP) from 90.81-79.52 mm Hg (21.4%). The current study complements previous investigations since it included 2 groups; a normotensive group in addition to a hypertensive one. Thus, the effects of regular Roselle ingestion on the SBP and DBP in people with normal blood pressure were also evaluated. The current investigation was run for a duration of 8 weeks and therefore provides a better indicator of the effects of chronic ingestion of Roselle on the SBP and DBP. The present study also investigate the

effects of Roselle treatment on the pulse pressure (PP), heart rate (HR), left ventricular hypertrophy (LVH), and regression in hypertensive patients.<sup>3-9</sup> Clinical definitions of hypertension and current available guidelines for its management employ SBP and DBP, with cardiovascular disease historically assessed using DBP values.<sup>10,11</sup> However, there is a recent interest in PP as an independent predictor for cerebrovascular accident, coronary artery disease, congestive heart failure, and hypertensive mortality.<sup>10-12</sup> Pulse pressure reflects left ventricular ejection and arterial compliance properties. Arterial stiffening thus increases SBP, but decreases DBP accounting for the most common form of hypertension in middle-aged and elderly subjects, in which, PP may then be a more accurate predictor of cardiovascular death than either SBP or DBP alone.<sup>10-13</sup> Emerging evidence suggests that PP is a strong indicator of cardiovascular risk even among normotensive persons and diabetic patients.<sup>14-16</sup> Secondly, a concentric LVH is considered to be the major cardiac change associated with the increased myocardial stress in hypertension.<sup>17,18</sup> Although increasing adaptive contractile forces and maintaining normal wall stress, diminished diastolic compliance leads to impaired diastolic filling.<sup>17-20</sup> Eventually left ventricular systolic function becomes impaired potentially leading to cardiac failure if arterial pressure and ventricular after load are not corrected.<sup>17,21,22</sup> Left ventricular hypertrophy is also associated with an increased prevalence of atrial fibrillation and ventricular arrhythmias, and increased incidences of sudden death even in the absence of epicardial coronary arterial occlusive disease.<sup>22</sup> Antihypertensive therapy should therefore be targeted not only at lowering blood pressure levels, but also at inducing regression or prevention of LVH.<sup>22-24</sup> The current study aims to characterize the effects of regular Roselle ingestion on blood pressure and LVH in patients with established moderated essential hypertension.

**Methods.** Online literature searches using PubMed was the main search method used to find prior related research. PubMed includes more than 23 million citations for biomedical literature from medical and life science journals, and online books. The current study was a non-randomized quasi-experimental investigation that was carried out in the city of Kafr El-Shaikh at Kafr El-Shaikh General Hospital, Egypt, for 8 weeks, during the period from 23 September 2012 to 18 November 2012.

The review board of the Research and Ethics Committees of Kafr El-Shaikh General Hospital, Egypt approved this study. Written informed consent

**Disclosure.** Authors have no conflict of interests, and the work was not supported or funded by any drug company.

was obtained from each participant. As the study involved human subjects, the principals of the Helsinki Declaration were adopted.

The study included normotensive subjects recruited from the general population and hypertensive patients who are used to come to Kafr El-Shaikh General Hospital for their regular checkups. The normotensive subjects and hypertensive patients included both males and females and had an average age of  $50 \pm 5$  years. Potential volunteers were first requested to complete a screening questionnaire. Individuals who were regular consumers of tea or coffee, current smokers or ex-smokers who had stopped smoking within the past 6 months, or who had any history of a major illness including liver, renal, gastrointestinal or thyroid disease were excluded from the study. Inclusion criteria for the hypertensive subjects were a SBP of 150-180 mm Hg and/or a DBP of 95-120 mm Hg, use of 2 or fewer anti-hypertensive drugs and an absence of secondary hypertension. Inclusion criteria for the normotensive subjects included a SBP <140 mm Hg and a DBP <90 mm Hg and absence of diabetes. Participants were then randomly selected from eligible volunteers to have a total of 100 subjects comprising 2 study groups; a normotensive group and a group with moderate essential hypertension, of 50 subjects each ( $n=50$ ). Both groups contained equal numbers of males and females and so subjects from each group were carefully matched for age and gender. Selected participants were finally screened prior to participation and the study design and requirements were thoroughly explained to them. All subjects had their SBP, DBP, PP, and HR, measured before starting the study in order to have baseline data for these parameters. Additionally, all subjects had an ECG at the beginning of the study. The study lasted for a total of 8 weeks. The subjects were instructed to drink 4 standard cups (250 ml each) of Roselle per day for the first 4 weeks of the study. Systolic blood pressure, DBP, PP, and HR were measured in the morning at the end of each 7-day intervention (namely, at the end of each week of treatment). Roselle treatment was then stopped for 4 weeks and all subjects had the above-mentioned parameters rechecked at the end of this period (namely, at the end of the fourth week of stopping treatment). An ECG was also measured for all subjects at the end of the intervention and non-treatment periods. During the study, subjects were instructed to cease intake of caffeine-containing beverages, and not to make any changes to their usual food intake, physical activity and treatment prescribed by their doctors for hypertension. Allowing the hypertensive patients to continue their anti-hypertensive therapy during the study could have

resulted into co-intervention bias. However, designing the study in such a way to include both Roselle treatment and cessation periods and subsequently comparing the results at least partially eliminated that bias since anti-hypertensive therapy continued during both periods. Roselle was obtained from the local market. The method of Roselle preparation was standardized as far as possible. Subjects were instructed to use a standard cup, which holds 250 ml of water to prepare Roselle. Each time a cup of Roselle prepared, 2 g were added into 250 ml of boiled water for 1 min with constant movement. The drink was then consumed without additives, including milk and sugar. A consistent weight of Roselle was achieved by providing subjects with a container that, when filled, contained 2 g of Roselle. Differences in adherence to the planned Roselle treatment regimen across the 2 study groups could have resulted into compliance bias with potential effects on the results. This was minimized by maintaining rigorous regular contact with the participants during the entire treatment period. Furthermore, the study design and requirements were thoroughly explained to the participants at the beginning of the study. Moreover, the participants were seen at the end of each week of the 4 weeks of the intervention period as describe above and the importance of compliance to the treatment protocol was stressed upon and emphasized in each visit. SBP and DBP were measured using an Omron M7 (HEM-780-E) electronic sphygmomanometer (Omron Healthcare Co., Limited, Kyoto, Japan). Subjects rested for approximately 5 min. SBP and DBP were then measured on the right arm on 3 occasions at 5-min intervals. The means of the measurements were used in subsequent analyses. Pulse pressure was calculating by subtracting DBP from the SBP of every individual. Blood pressure measurements were not disclosed to participants during the study. Heart rate was determined by measuring the pulse rate manually and the results were compared with the values given by the electronic sphygmomanometer. There were no differences between pulse rate values determined by both methods. Electrocardiograms were obtained according to protocol at baseline, at 4 weeks of Roselle treatment, and at the end of the 4th week of the non-treatment period. Electrocardiograms were interpreted by observers blinded to other clinical data. The Sokolow-Lyon voltage criteria ( $SV1 + RV5/6$ ) higher than 38 mm were used to identify LVH.<sup>24,25</sup>

Statistical analyses were performed using SPSS software (SPSS, Chicago, IL, USA). Results are presented as means  $\pm$  standard deviations from the means (SD). The independent-samples t-test was

used to compare baseline values between groups and one-way analysis of variance (one-way ANOVA) followed by Tukey's test were used to analyze within-group changes in the measured parameters. LVH 4 weeks after Roselle treatment was compared with LVH 4 weeks after stopping treatment and baseline LVH using Fisher's exact test. A  $p < 0.05$  was chosen as the level of significance in all statistical analysis.

**Results.** Table 1 compares baseline SBP, DBP, PP, and HR values of the normotensive and hypertensive groups, showing significantly higher SBP, DBP, and PP in the hypertensive group. Mean SBP values were  $162.7 \pm 10.0$  and  $128.2 \pm 8.3$  mm Hg for hypertensive and normotensive groups respectively ( $p < 0.001$ ). Corresponding DBP values were  $105.2 \pm 9.4$  and  $82.2 \pm 7.4$  mm Hg ( $p < 0.001$ ). Peripheral PP, determined by subtracting DBP from the SBP was also significantly higher ( $p < 0.001$ ) in the hypertensive ( $57.5 \pm 8.5$  mm Hg) compared with the normotensive group ( $45.9 \pm 7.0$  mm Hg). In contrast, baseline HR was significantly lower ( $p < 0.001$ ) in the hypertensive ( $70 \pm 6$  beat/min) compared with the normotensive group ( $82 \pm 7$  beat/min).

The effects of Roselle treatment over 4 weeks in the 2 study groups are summarized in Table 1. In the normotensive group, Roselle significantly lowered SBP from baseline values by 5.4 ( $p = 0.001$ ), 8.6 ( $p < 0.001$ ), 11.0 ( $p < 0.001$ ), and 12.8 mm Hg ( $p < 0.001$ ) after the 1st, 2nd, 3rd, and 4th weeks of treatment respectively resulting in a significant (10%) reduction by the end of 4

weeks. Stopping treatment then significantly ( $p < 0.001$ ) increased SBP from this level by 9.7 mm Hg (8.4%) over 4 weeks, returning it to a value indistinguishable from baseline ( $p = 0.07$ ). DBP decreased by 2.3 ( $p = 0.11$ ), 4.8 ( $p < 0.001$ ), 6.8 ( $p < 0.001$ ) and 7.8 mm Hg ( $p < 0.001$ ) respectively, and returned by 7.6 mm Hg (10.2%) to a value indistinguishable from baseline ( $p = 0.87$ ). PP decreased by 3.0 mmHg ( $p = 0.07$ ), 3.6 ( $p = 0.02$ ), 4.1 ( $p = 0.01$ ), and 5.0 mm Hg ( $p = 0.01$ ) and resulted in a return by 2.2 mm Hg (5.4%) to a value indistinguishable from baseline ( $p = 0.12$ ).

In the hypertensive group, Roselle treatment significantly lowered SBP from baseline values by 10.2 ( $p < 0.001$ ), 19.3 ( $p < 0.001$ ), 25.6 ( $p < 0.001$ ), and 31.9 mm Hg ( $p < 0.001$ ) after the 1st, 2nd, 3rd, and 4th weeks of treatment respectively therefore resulting in a 19.6% reduction by the end of the 4th week of regular ingestion of Roselle. Stopping treatment elevated SBP significantly ( $p < 0.001$ ) by 29.6 mm Hg (22.6%) over 4 weeks from this final value to a level indistinguishable from the baseline ( $p = 0.24$ ). Diastolic blood pressure correspondingly fell by 5.2 ( $p = 0.01$ ), 10.2 ( $p < 0.001$ ), 14.7 ( $p < 0.001$ ), and 19.7 mm Hg ( $p < 0.001$ ) to give an overall 18.7% fall. Stopping treatment significantly ( $p < 0.001$ ) raised the DBP by 16.1 mm Hg (18.8%) to a level statistically indistinguishable from baseline values ( $p = 0.05$ ). Finally, PP significantly fell by 5.1 ( $p = 0.01$ ), 9.0 ( $p < 0.001$ ), 10.9 ( $p < 0.001$ ), and 12.2 mm Hg ( $p < 0.001$ ) respectively to give a 21.2% reduction after fourth weeks, and rose again significantly ( $p < 0.001$ ) by

**Table 1** - Effects of Roselle treatment on blood pressures and heart rates over 4 weeks in the 2 study groups.

Parameter	Baseline	One week after treatment	Two weeks after treatment	Three weeks after treatment	Four weeks after treatment	Four weeks after stopping treatment
<i>Systolic blood pressures (mm Hg)</i>						
Normotensive group	128.2 ± 8.3	122.8 ± 8.2 <sup>aa</sup>	119.6 ± 7.4 <sup>aaa</sup>	117.2 ± 5.8 <sup>aaa</sup>	115.4 ± 6.8 <sup>aaa</sup>	125.1 ± 8.5 <sup>bbb</sup>
Hypertensive group	162.7 ± 10.0*	152.5 ± 9.0 <sup>aaa</sup>	143.4 ± 9.7 <sup>aaa</sup>	137.1 ± 10.2 <sup>aaa</sup>	130.8 ± 10.4 <sup>aaa</sup>	160.4 ± 9.4 <sup>bbb</sup>
<i>Diastolic blood pressures (mm Hg)</i>						
Normotensive group	82.2 ± 7.4	79.9 ± 6.9	77.4 ± 6.6 <sup>aaa</sup>	75.4 ± 6.1 <sup>aaa</sup>	74.4 ± 6.0 <sup>aaa</sup>	82.0 ± 7.0 <sup>bbb</sup>
Hypertensive group	105.2 ± 9.4*	100.0 ± 9.5 <sup>aa</sup>	95.0 ± 8.5 <sup>aaa</sup>	90.5 ± 8.9 <sup>aaa</sup>	85.5 ± 6.0 <sup>aaa</sup>	101.6 ± 8.9 <sup>bbb</sup>
<i>Pulse pressures (mm Hg)</i>						
Normotensive group	45.9 ± 7.0	42.9 ± 9.4	42.3 ± 8.8 <sup>a</sup>	41.8 ± 7.5 <sup>aa</sup>	40.9 ± 8.4 <sup>aa</sup>	43.1 ± 11.0
Hypertensive group	57.5 ± 8.5*	52.4 ± 7.9 <sup>aa</sup>	48.5 ± 8.8 <sup>aaa</sup>	46.6 ± 8.8 <sup>aaa</sup>	45.3 ± 8.9 <sup>aaa</sup>	58.8 ± 10.3 <sup>bbb</sup>
<i>Heart rate (beat/minute)</i>						
Normotensive group	82 ± 7	78 ± 6 <sup>a</sup>	76 ± 7 <sup>aaa</sup>	72 ± 7 <sup>aaa</sup>	70 ± 5 <sup>aaa</sup>	78 ± 8 <sup>a, bbb</sup>
Hypertensive group	70 ± 6*	68 ± 5 <sup>a</sup>	64 ± 6 <sup>aaa</sup>	60 ± 5 <sup>aaa</sup>	58 ± 6 <sup>aaa</sup>	68 ± 7 <sup>bbb</sup>

Data are presented as means ± standard deviations; the independent-samples t-test was used to compare baseline values between groups; \* $p < 0.001$ , † $p < 0.01$  and ‡ $p < 0.05$  (comparing the baseline parameters of the hypertensive and normotensive groups). One-way analysis of variance followed by Tukey's test were used to analyze within-group changes in the measured parameters; <sup>aaa</sup> $p < 0.001$ , <sup>aa</sup> $p < 0.01$  and <sup>a</sup> $p < 0.05$  (comparing values after the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> weeks of treatment and value 4 weeks after stopping treatment with the baseline value); <sup>bbb</sup> $p < 0.001$ , <sup>bb</sup> $p < 0.01$  and <sup>b</sup> $p < 0.05$  (comparing the value 4 weeks after stopping treatment with the value after the 4<sup>th</sup> week of treatment).

13.5 mm Hg (29.8%) to a level indistinguishable from its baseline value when treatment was stopped ( $p=0.50$ ).

Regular Roselle ingestion thus progressively but reversibly reduced the SBP, DBP, and PP of both study groups with maximal reductions achieved at the end of the fourth week of treatment but with an almost 2-fold greater influence on these variables in the hypertensive group. Thus, PP significantly fell from baseline values by 10.9% and 21.2% ( $p=0.01$ ); SBP fell by 10% and 19.6% ( $p<0.001$ ); DBP by 9.5% and 18.7% ( $p<0.001$ ) by the end of the 4th week of treatment in the normotensive and hypertensive groups respectively.

Table 1 also demonstrates that Roselle consumption progressively lowered the HR of the normotensive group by 4 ( $p=0.02$ ), 6 ( $p<0.001$ ), 10 ( $p<0.001$ ), and 12 beat/minute ( $p<0.001$ ) after the 1st, 2nd, 3rd, and 4th weeks of treatment respectively resulting in a 14.6% reduction by the end of the 4th week of treatment. Stopping Roselle treatment significantly ( $p<0.001$ ) elevated the HR by 8 beat/minute (11.4%) restoring HR to a level significantly ( $p=0.02$ ) lower than its baseline value 4 weeks after stopping treatment. In the hypertensive group, HR fell by 2 ( $p=0.02$ ), 6 ( $p<0.001$ ), 10 ( $p<0.001$ ), and 12 beat/minute ( $p<0.001$ ) to give a final, 17.1% reduction. Stopping treatment for 4 weeks then significantly ( $p<0.001$ ) raised the HR of the hypertensive group by 10 beat/minute (17.2%) returning it to a level not significantly different from baseline ( $p=0.11$ ). Thus, the normotensive subjects had significantly higher HR than the hypertensive subjects throughout the treatment and non-treatment weeks of the study. Furthermore, regular Roselle treatment had greater influence on the HR in the hypertensive group than in the normotensive group; HR fell by 14.6% and 17.1% ( $p<0.001$ ) by the end of the 4th week of treatment in the normotensive and hypertensive groups respectively. Before Roselle treatment none of the normotensive subjects, but a significant ( $p<0.001$ ; Fisher's exact test) number (14) of the hypertensive subjects showed LVH. Four weeks of Roselle consumption significantly ( $p=0.01$ ) reduced this incidence to 4 hypertensive patients, indistinguishable from normotensive group ( $p=0.07$ ). Stopping Roselle treatment for 4 weeks returned this incidence to pre-treatment levels ( $p=0.03$ ) where LVH redeveloped in 6 to give a total incidence of 10 hypertensive patients by the end of the 4th week of the non-treatment period.

**Discussion.** Systemic arterial hypertension is an important modifiable risk factor for coronary artery disease, stroke, and other adult cardiovascular disease

complications.<sup>1,2</sup> The condition is currently defined in terms of SBP and DBP rather than PP levels. A number of randomized trials of antihypertensive therapy have demonstrated the benefits of DBP control although there is increasing interest in isolated systolic hypertension as an important predictor of CVD morbidity and mortality.<sup>11,13</sup> However, several follow-up studies showed that SBP increases with age, that would in turn result in an increased left ventricular pressure load and a consequent hypertrophy (LVH),<sup>17,18</sup> and diastolic, followed by systolic dysfunction failure.<sup>17,19-21</sup> DBP also increases with age only until age 57.5 y after which it decreases by 1-2 mm Hg per decade of age, both findings likely reflecting a progressively declining aortic compliance. Consequently, PP increases slowly with age up to around 60 but then rises rapidly with increasing age. Increased PP may thus be more predictive of cardiovascular risk than either SBP or DBP alone and that ideal antihypertensive therapy should be aimed at rigorous control of both SBP and DBP in order to maintain the PP within a normal narrow range.<sup>13</sup> The calyxes of Roselle (*Hibiscus sabdariffa*) are used to make a beverage called karkade, currently used by Egyptians to lower blood pressure, on the basis of evidence from folk medicine. We report a simple non-randomized quasi-experimental study (pre-post intervention) characterizing the effects of regular ingestion of Roselle on PP and LVH in hypertensive patients for the first time to best of our knowledge. Lack of randomization and placebo effect were the main limitations of the current study. It thus has a lower level of credibility than the randomized controlled investigations. It could have been appropriately complemented by randomizing each of the 2 study groups into 2 subgroups; one subgroup ingests Roselle and the other one ingests hot water for the duration of the treatment period. The subgroups ingesting hot water would then serve as control subgroups. However, such randomization was difficult because some of the participants used to leave the Roselle tea to cool and then ingest it. The pretreatment baseline values as well as the post-treatment recovery levels of the studied parameters could be then considered as control levels in the 2 study groups. Given that Roselle is increasingly used to make tea in Egypt and that all participants would know its taste, it was equally difficult to consider the placebo effect in the current study. Blinding of clinical data was maintained during the study by ensuring that blood pressure measurements were not disclosed to participants and interpreting the electrocardiograms by observers blinded to other

clinical data. Blinding of group affiliations was another limitation of the study. The current study shows that regular consumption of 4 standard cups (250 ml each) of Roselle per day for 4 weeks resulted in significant reversible reductions in the SBP, DBP and PP of both normotensive subjects and hypertensive patients over 4 weeks of treatment without causing hypotension, with stronger effects in the hypertensive patients. Similarly, regular consumption of Roselle seems to have a strong negative chronotropic influence. Stopping Roselle treatment returned all these parameters to pretreatment values over 4 weeks. The results of the present study are generally consistent with the few recent clinical studies evaluating the effects of Roselle treatment on essential hypertension.<sup>5-7</sup> In our opinion, the current study is more comprehensive. First, we included a normotensive group in addition to the hypertensive one whereas the other studies included only hypertensive patients. This protocol was essential to investigate the effects of regular Roselle ingestion on the SBP and, DBP in normotensive people. Second, the current investigation was run for a duration of 8 weeks and is therefore a better indicator of the effects of chronic ingestion of Roselle on the SBP, DBP, and PP. Third, the present study also characterized the effects of Roselle treatment on the PP, HR and LVH regression in hypertensive patients.

Several animal studies were conducted to elucidate the mechanisms of the antihypertensive effects of Roselle. Their findings suggest that the antihypertensive effect of Roselle could be mediated through acetylcholine-like and histamine-like mechanisms, direct vaso-relaxant effects, and a vasodilator effect mediated through the endothelium-derived nitric oxide-cGMP-relaxant pathway and inhibition of calcium (Ca<sup>2+</sup>)-influx into vascular smooth muscle cells.<sup>8,26</sup> Electrocardiographic LVH is a strong predictor of cardiovascular (CV) morbidity and increases the risk of sudden cardiac death.<sup>24</sup> Interestingly enough, we found that chronic consumption of 4 standard cups (250 ml each) of Roselle per day for 4 weeks induced significant and early regression of LVH in the hypertensive patients possibly by improving blood pressure and thereby reducing left ventricular pressure overload. The regression of LVH with Roselle treatment might also be the result of a direct action of Roselle on the myocardium. These findings are in agreement with a recent animal study confirming that chronic administration of Roselle attenuates hypertension and induces early reversal of cardiac hypertrophy in Sprague-Dawley hypertensive

rats within 6-8 weeks.<sup>9</sup> Furthermore, in a rabbit model of LVH, aortic banding for 8 weeks resulted in robust LVH as a result of pressure overload. Such LVH was subsequently reversed completely or partially within 8 weeks following debanding of the ascending aorta.<sup>27</sup> Interestingly, it was recently reported that treatment with the cardioselective beta-blocker esmolol induces some degree of regression of LVH within 48 hours in an experimental rat model of primary hypertension.<sup>28</sup>

The present study thus suggests that regular ingestion of Roselle has cardiovascular protective effects as evidenced by the remarkable reductions in SBP, DBP, and PP, and regression of LVH induced by Roselle treatment in hypertensive subjects. However, further studies are required to review the mechanisms of the antihypertensive effects and elucidate the mechanism of the LVH regression effects of Roselle.

**Acknowledgment.** *The authors wish to thank Dr. Mohammad Salama for the use of his clinic while conducting the study, and Professor Christopher Huang for his kind help and support.*

## References

1. Webb AJ, Fischer U, Metha Z, Rothwell PM. Effects of antihypertensive-drug class on inter-individual variation in blood pressure and risk of stroke: a systemic review and meta-analysis. *Lancet* 2010; 375: 906-915.
2. Winter KH, Tuttle LA, Viera AJ. Hypertension. *Primary Care* 2013; 40: 179-194.
3. Mohan M, Khade B, Shinde A. Effect of A-HRS on blood pressure and metabolic alterations in fructose-induced hypertensive rats. *Nat Prod Res* 2012; 26: 570-574.
4. Seujange Y, Leelahavanichkul A, Yisarakun W, Khawsuk W, Meepool A, Phamonleatmongkol P, Saechau W, Onlamul W, Tantiwarattanatikul P, Oonsook W, Eiam-Ong S. *Hibiscus sabdariffa* Linnaeus aqueous extracts attenuate the progression of renal injury in 5/6 nephrectomy rats. *Renal Failure* 2013; 35: 118-125.
5. Mozaffari-akhosravi H, Jalali-Khanabadi Bam Afkhami-Ardekani M, Fatehi F, Noori-Shadkam M. The effects of sour tea (*Hibiscus sabdariffa*) on hypertension in patients with type II diabetes. *J Hum Hypertens* 2009; 23: 48-54.
6. Herrera-Arellano A, Flores-Romero S, Chavez-Soto MA, Tortoriello J. Effectiveness and tolerability of a standardized extract from *Hibiscus sabdariffa* in patients with mild to moderate hypertension: a controlled and randomized clinical trial. *Phytomedicine* 2004; 11: 375-382.
7. McKay DL, Chen CY, Saltzman E, Blumberg JB. *Hibiscus sabdariffa* L. tea (tisane) lowers blood pressure in prehypertensive and mildly hypertensive adults. *J Nutr* 2010; 140: 298-303.
8. Mojiminiyi FB, Dikko M, Muhammad BY, Ojobor PD, Ajagbonna OP, Okolo RU, Igbokwe UV, Mojiminiyi UE, Fagbemi MA, Bello SO, Anga TJ. Antihypertensive effect of an aqueous extract of the calyx of *Hibiscus sabdariffa*. *Fitoterapia* 2007; 78: 292-297.

9. Odigie IP, Ettarh RR, Adigun SA. Chronic administration of aqueous extract of *Hibiscus sabdariffa* attenuates hypertension and reverses cardiac hypertrophy in 2K-1C hypertensive rats. *J Ethnopharmacol* 2003; 86: 181-185.
10. Assmann G, Cullen P, Evers T, Petzinna D, Schulte H. Importance of arterial pulse pressure as a predictor of coronary heart disease risk in PROCAM. *Eur Heart J* 2005; 26: 2120-2126.
11. Johnson RJ, Feig DI, Nakagawa T, Sanchez-Lozada LG and Rodriguez-Iturbe B. Pathogenesis of essential hypertension: historical paradigms and modern insights. *J Hypertens* 2008; 26: 381-391.
12. Lovett JK, Howard SC, Rothwell PM. Pulse pressure is independently associated with carotid plaque ulceration. *J Hypertens* 2003; 21: 1669-1676.
13. Protogerou AD, Safar ME, Iaria P, Safar H, Le Dudal K, Filipovsky J, Henry O, Ducimetiere P, Blacher J. Diastolic blood pressure and mortality in the elderly with cardiovascular disease. *Hypertension* 2007; 50: 172-180.
14. Nakano S, Konishi K, Furuya K, Uehara K, Nishizawa M, Nakagawa A, Kigoshi T, Uchida K. A prognostic role of mean 24-h pulse pressure level for cardiovascular events in type 2 diabetic subjects under 60 years of age. *Diabetes Care* 2005; 28: 95-100.
15. Mannucci E, Lambertucci L, Monami M, Fedeli A, Chiasserini V, Marchionni N, Masotti G, Ungar A. Pulse pressure and mortality in hypertensive type 2 diabetic patients. A cohort study. *Diabetes Metab Res Rev* 2006; 22: 172-175.
16. Ungar A, Pepe G, Lambertucci L, Fedeli A, Monami M, Mannucci E, Gabbani L, Masotti L, Marchionni N, Di Bari M. Low diastolic ambulatory blood pressure is associated with greater all-cause mortality in older patients with hypertension. *J Am Geriatr Soc* 2009; 57: 291-296.
17. Meijs ME, de Windt LJ, de Jonge N, Cramer MJ, Bots ML, Mali WP, Doevendans PA. Left ventricular hypertrophy: a shift in paradigm. *Curr Med Chem* 2007; 14: 157-171.
18. Katholi RE & Couri DM. Left ventricular hypertrophy: major risk factor in patients with hypertension: update and practical clinical applications. *Int J Hypertens* 2011; 495349.
19. Apostolakis EE, Baikoussis NG, Parissis H, Siminelakis SN and Papadopoulos GS. Left ventricular diastolic dysfunction of cardiac surgery patients: a point of view for the cardiac surgeon and cardio-anesthesiologist. *Cardiothorac Surg* 2009; 24: 67.
20. Masugata H, Senda S, Inukai M, Murao K, Hosomi N, Iwado Y, Noma T, Kohno M, Himoto T and Goda F. Differences in Left Ventricular Diastolic Dysfunction between Eccentric and Concentric Left Ventricular Hypertrophy in Hypertensive Patients with Preserved Systolic Function. *J Int Med Res* 2011; 39: 772-779.
21. Imbalzano E, Zito C, Carerj S, Oreto G, Mandraffino G, Cusmà-Piccione M, Di Bella G, Saitta C and Saitta A. Left ventricular function in hypertension: new insight by speckle tracking echocardiography. *Echocardiography* 2011; 28: 649-657.
22. Okin PM, Wachtell K, Devereux RB, Harris KE, Jern S, Kjeldsen SE, Julius S, Lindholm LH, Nieminen MS, Edelman JM, Hille DA, Dahlöf B. Regression of electrocardiographic left ventricular hypertrophy and decreased incidence of new-onset atrial fibrillation in patients with hypertension. *JAMA* 2006; 296: 1242-1248.
23. Devereux RB, Wachtell K, Gerds E, Boman K, Nieminen MS, Papademetriou V, Rokkedal J, Harris K, Aurup P, Dahlöf B. Prognostic significance of left ventricular mass change during treatment of hypertension. *JAMA* 2004; 292: 2350-2356.
24. Okin PM, Devereux RB, Jern S, Kjeldsen SE, Julius S, Nieminen MS, Snapinn S, Harris KE, Aurup P, Edelman JM, Wedel H, Lindholm LH, Dahlöf B. Regression of electrocardiographic left ventricular hypertrophy during antihypertensive treatment and the prediction of major cardiovascular events. *JAMA* 2004; 292: 2343-2349.
25. Bacharova L, Estes EH. Electrocardiographic diagnosis of left ventricular hypertrophy: depolarization changes. *J Electrocardiol* 2009; 42: 228-232.
26. Ajay M, Chai HJ, Mustafa AM, Gilani AH, Mustafa MR. Mechanisms of the anti-hypertensive effect of *Hibiscus sabdariffa* L. calyces. *J Ethnopharmacol* 2007; 109: 388-393.
27. Zhao Z, Chen L, Xiao YB, Hao J, Tang CZ, Zheng DZ. A rabbit model to study regression of ventricular hypertrophy. *Heart Lung Circ* 2013; 22: 373-382.
28. Quintana-Villamandos B, Delgado-Martos MJ, Sánchez-Hernández JJ, Gómez de Diego JJ, Fernández-Criado Mdel C, Canillas F, Martos-Rodríguez A, Delgado-Baeza E. Early regression of left ventricular hypertrophy after treatment with esmolol in an experimental rat model of primary hypertension. *Hypertens Res* 2013; 36: 408-413.

#### Related Articles

Bayoumy NM, Al-Sharaidh AS, Babay ZH, Abdulgader AM. The role of interleukin-6 promoter polymorphism-174G/C in Saudi women with hypertensive disorders of pregnancy. *Saudi Med J* 2013; 34: 689-694.

Huang GZ, Tang YH, Wang BY, Zhang B, Hu TJ, Zhang L, et al. Effects of telmisartan on insulin resistance and visceral fat distribution in Chinese hypertensive patients with obesity. *Saudi Med J* 2011; 32: 1017-1021.

Al-Bannay R, Husain AA. Hypertensive crisis. Clinical presentation, comorbidities, and target organ involvement. *Saudi Med J* 2010; 31: 916-920.