Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti-inflammatory properties.

Teruo Inoue, MD*, Hiroshi Komoda, MS*, Toshihiko Uchida, MD*, Koichi Node, MD*

Original article
doi:10.1016/j.jcc.2008.06.004
Under an Elsevier user license

Summary

Background

Oxidative stress as well as inflammation plays a pivotal role in the pathogenesis of atherosclerosis. Although, various anti-oxidative dietary supplements have been evaluated for their ability to prevent atherosclerosis, no effective ones have been determined at present. "Camu-camu" (Myrciaria dubia) is an Amazonian fruit that offers high vitamin C content. However, its anti-oxidative property has not been evaluated in vivo in humans.

Methods

To assess the anti-oxidative and anti-inflammatory properties of camu-camu in humans, 20 male smoking volunteers, considered to have an accelerated oxidative stress state, were recruited and randomly assigned to take daily 70 ml of 100% camu-camu juice, corresponding to 1050 mg of vitamin C (camu-camu group; n = 10) or 1050 mg of vitamin C tablets (vitamin C group; n = 10) for 7 days.

Results

After 7 days, oxidative stress markers such as the levels of urinary 8-hydroxy-deoxyguanosine (P < 0.05) and total reactive oxygen species (P < 0.01) and inflammatory markers such as serum levels of high sensitivity C reactive protein (P < 0.05), interleukin (IL)-6 (P < 0.05), and IL-8 (P < 0.01) decreased significantly in the camu-camu group, while there was no change in the vitamin C group.

Conclusions

Our results suggest that camu-camu juice may have powerful anti-oxidative and anti-inflammatory properties, compared to vitamin C tablets containing equivalent vitamin C content. These effects may be due to the existence of unknown anti-oxidant substances besides vitamin C or unknown substances modulating in vivo vitamin C kinetics in camu-camu.

Keywords

Camu-camu; Anti-oxidant; Inflammation; Vitamin C; Smoking

Introduction

Accumulating evidence has demonstrated that oxidative stress (i.e., dysregulation of the cellular redox state) and inflammation play a pivotal role in the pathogenesis of atherosclerosis interacting with each other. Although, various anti-oxidative dietary supplements have been evaluated for their ability to prevent atherosclerosis, no effective ones have been determined at present. Vitamin C is not only the most important dietary anti-oxidant [1] and [2]; but is also suggested to be a potent anti-inflammatory agent [3], [4] and [5]. Several studies have found that dietary vitamin C or plasma vitamin C was associated with a protective effect against coronary artery disease [6], [7], [8] and [9].

"Camu-camu" is an Amazonian fruit that offers high vitamin C content ranging from 9 to 50 g/kg, which is two-fold that of acelora [10]. Additionally, in vitro anti-oxidant activity of 100% camu-camu juice evaluated by DPPH method reaches 50-fold of that of 100% acelora juice (unpublished data), suggesting its potentiality as an effective dietary supplement to prevent atherosclerotic disease. However, the anti-oxidative property has not been evaluated in an in vivo human study. Furthermore, the effects of camu-camu on inflammation have not been elucidated.

This study was designed to establish the anti-oxidative and anti-inflammatory properties of camu-camu in...
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti-inflammatory effects in vivo in humans.

Methods

Study design

Study subjects included 20 healthy male volunteers, all of whom were habitual smokers, being considered to have an accelerated oxidative stress state. All of the participants had neither history of atherosclerotic diseases such as coronary artery disease or cerebrovascular disease nor risk factors such as hypertension, diabetes, or hyperlipidemia except smoking habit by the annual physical checkup. The participants were randomly assigned to take daily 1050 mg of vitamin C tablets (vitamin C group; n = 10) or 70 ml of 100% camu-camu juice, containing 1050 mg of vitamin C (camu-camu group; n = 10) as a dietary supplement for 7 days, and to continued smoking. The dose of 1050 mg/day of vitamin C in both groups was decided, based on previous studies [11,13,19,14,15] and [16]. In all subjects, 10 ml of urine and 15 ml of peripheral blood were sampled at baseline before intake of these dietary supplements, 7 days after the intake, and 1 month after ceasing the intake as a washout stage. The blood samples were immediately centrifuged at 1500 × g for 15 min at room temperature. The urine and serum were frozen and stored at −80 °C until analyzed. We measured urine 8-hydroxy-deoxyguanosine (8-OHdG) levels and serum total reactive oxygen species (ROS) levels as oxidative stress markers, and high sensitivity C-reactive protein (hsCRP) and multiple-cytokine levels as inflammatory markers. The local institutional review board approved the study protocol, and written informed consent was obtained from each participant.

Baseline characteristics

Prior to starting the intake of camu-camu or vitamin C, each participant was interviewed with regard to brand of the cigarette and daily number of cigarettes consumed and daily intake of tar and nicotine was calculated as the content of tar or nicotine for each cigarette brand × daily number of cigarettes consumed. Blood pressure was measured to the nearest 2 mmHg in the same arm at baseline, using a mercury sphygmomanometer with an appropriately sized cuff.

Measurements

Urinary 8-OHdG levels were determined by competitive enzyme-linked immunosorbent assay (ELISA) using the commercially available kit (8-OHdG Check, Japan Institute for the Council of Aging, Fukuroi, Japan) [17]. Serum levels of total ROS were measured using a DEPPD reaction method by Hayashi et al. [18] applying the Fenton reaction on a multi-well plate. The hsCRP levels were measured by particle-enhanced technology on the Behring BN II nephrometer (Dade Behring Inc., Newark, DE, USA) [19]. This assay used monoclonal anti-CRP antibodies and a calibrator that was also traceable to World Health Organization reference materials. The Luminex micro-beads array system was used for a multiplex assay of simultaneous quantification of the following 10 cytokines: interleukin (IL)-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, tumor necrosis factor-α, granulocyte-macrophage colony stimulating factor, and γ-interferon. The assay was conducted as per the manufacturer's instructions (Luminex Corp., Austin, TX, USA), using a commercially available kit (BioSource International, Inc., Camarillo, CA, USA) [20].

Statistical analysis

Values are expressed as the mean ± S.D. for parametric data, and median values and interquartile ranges for non-parametric data. Intergroup comparisons were performed using unpaired t-tests for parametric data and Mann-Whitney's U tests for non-parametric data. Intragroup comparisons for non-parametric data were assessed using Wilcoxon Rank Sum tests. Correlations between two variables were assessed using Spearman rank correlation coefficient. P < 0.05 was considered to be significant.

Results

Baseline characteristics such as the number of cigarettes consumed, daily intake of tar and nicotine, and systolic and diastolic blood pressure were similar in the two groups (Table 1). Overall, at baseline before taking the dietary supplements, urinary 8-OHdG levels (R = 0.47, P < 0.05), but not serum levels of total ROS (R = 0.15, NS) were correlated with the number of cigarettes (Fig. 1). Among 10 cytokines measured, the levels of 8 cytokines (except IL-6 and IL-8) were under the detection limit in almost all subjects, and therefore, were excluded from the analysis. The baseline levels of hsCRP (R = 0.32, NS), IL-6 (R = 0.07, NS), and IL-8 (R = 0.12, NS) were not correlated with the number of daily cigarettes consumed.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vitamin C (n = 10)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>36 ± 4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>171 ± 4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72 ± 10</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25 ± 3</td>
</tr>
<tr>
<td>Number of cigarette (iday)</td>
<td>24 ± 8</td>
</tr>
<tr>
<td>Tar intake (mg/day)</td>
<td>117 ± 93</td>
</tr>
<tr>
<td>Nicotine intake (mg/day)</td>
<td>10 ± 8</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>124 ± 8</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>79 ± 11</td>
</tr>
</tbody>
</table>

Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti-inflammatory properties. In a study, the relationship between baseline levels of oxidative stress markers and the number of cigarettes consumed was examined. Urinary 8-OHdG levels were correlated with the number of cigarettes (left), but total ROS levels were not (right).

In the camu-camu group, 8-OHdG levels (9.0 [4.0, 21.2] to 7.0 [4.6, 14.6] ng/mg Cr, \( P < 0.05 \)) and total ROS levels (128 [116,192] to 123 [110,162] Unit, \( P < 0.01 \)) significantly decreased 7 days after taking the dietary supplements, and were restored at the washout stage (to 11.2 [4.9, 20.9] ng/mg Cr in 8-OHdG, \( P < 0.05 \) and to 131 [121, 186] Unit in total ROS, \( P < 0.01 \)). In the vitamin C group, however, both levels did not change (8.5 [4.1, 22.3], 8.7 [3.0, 20.2], 10.5 [7.5, 14.3] ng/mg Cr in 8-OHdG and 135 [88, 162], 134 [106, 156], 136 [113, 167] Unit in total ROS) (Fig. 2).

In the camu-camu group, the levels of hsCRP (0.05 [0.01, 0.62] to 0.02 [0.01, 0.32] mg/dl, \( P < 0.05 \)), IL-6 (6.0 [4.9, 6.9] to 5.1 [4.2, 6.4] pg/ml, \( P < 0.05 \)), and IL-8 (24.8 [22.8, 30.6] to 22.4 [21.6, 24.5] pg/ml, \( P < 0.01 \)) also significantly decreased 7 days after taking the dietary supplements. The levels were restored at the washout stage for hsCRP (to 0.05 [0.01, 0.58] mg/dl, \( P < 0.05 \)) and IL-8 (to 25.4 [23.8, 27.9] pg/ml, \( P < 0.01 \)), but did not for IL-6 (to 5.3 [4.9, 10.8] pg/ml). In the vitamin C group, however, each level did not change (0.03 [0.01, 0.22], 0.06 [0.01, 0.68], 0.05 [0.01, 0.13] mg/dl for hsCRP, 5.3 [4.8, 7.3], 5.1 [4.4, 7.6], 5.5 [4.5, 7.8] pg/ml for IL-6 and 27.3 [24.9, 32.8], 25.1 [23.0, 31.6], 26.4 [24.8, 33.4] pg/ml for IL-8) (Fig. 3).
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti-inflammatory properties. A study investigated the effects of camu-camu juice on oxidative stress and inflammation markers in smokers without atherosclerotic disease. The study found that daily intake of 70 ml of 100% camu-camu juice, including 1050 mg of vitamin C, significantly decreased levels of urinary 8-OHdG and serum total ROS, as well as inflammatory markers hsCRP, IL-6, and IL-8, within 7 days. These changes were restored at the washout stage of 1 month after cessation of intake. In contrast, vitamin C tablets did not produce similar effects. The study concluded that camu-camu juice may have more powerful anti-oxidative and anti-inflammatory activities compared to equivalent doses of vitamin C tablets.

The Discussion section highlights the importance of both oxidative stress and inflammation in the progression of atherosclerosis. Vitamin C has been shown to have antioxidant effects, scavenging ROS and reactive nitrogen species. The Dietary Reference Intake Panel of the US Institute of Medicine recommends a dietary allowance of 90 mg/day for men and 75 mg/day for women. Higher intake of fruit and vegetables as well as vitamin C supplements has been demonstrated to prevent cardiovascular disease. In particular, higher intake of vitamin C is shown to be associated with a decreased risk of coronary artery disease in a population with a high prevalence of smoking. In contrast, Lee et al. reported that supplemental vitamin C increased cardiovascular disease risk in postmenopausal women with diabetes. They considered that this contradictory result might be caused by the fact that vitamin C can also act as a pro-oxidant under certain circumstances. Another in vitro study using the human endothelial cell line ECV 304 and HUVECS demonstrated that vitamin C inhibited nuclear factor κB, a central mediator of altered gene expression during inflammation. In humans, daily intake of 1500 mg vitamin C supplement in runners attenuated an
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti-inflammatory substances in camu-camu. Second, camu-camu may have reported that plasma CRP levels were inversely and significantly associated with concentration of vitamin C after adjustment for age, sex, race-ethnicity, education, body mass index, leisure-time physical activity, and aspirin use. In addition, Wannamethee et al. reported a significant inverse association of dietary and plasma vitamin C and fruit and vegetable intakes with biomarkers of inflammation in a cross-sectional study of 3258 men aged 60-69 years who had no history of cardiovascular disease or diabetes. However, a review of the prospective studies to date found that 4 of the 5 studies with doses ranging from daily 250 to 3000 mg vitamin C in persons with diabetes, hypercholesterolemia, hemodialysis, or coronary artery disease reported no anti-inflammatory effects [12,13,14,15] and [16], corresponding to our results that 1050 mg vitamin C tablets did not decrease the inflammatory markers.

Because of its particularly high vitamin C content, camu-camu is considered to have high nutritional value. Our study provides the first in vivo human data demonstrating the anti-oxidative and anti-inflammatory effects of camu-camu juice. Moreover, the effects of camu-camu were more powerful, compared with those of vitamin C tablets, despite the equivalent vitamin C contents. In this respect, there are two possible mechanisms. First, camu-camu possibly contains other anti-oxidative substances besides vitamin C. In addition to high contents of vitamin C, camu-camu contains carotenoids [33] and anthocyanines [34] as potential anti-oxidants. Otherwise, there may be other unknown contents potentially acting as anti-oxidative and/or anti-inflammatory substances in camu-camu. Second, camu-camu may have substances that increase in vivo availability of vitamin C such as by absorption or excretion. Camu-camu also contains high levels of potassium [35], which is considered to accelerate intestinal absorption of vitamin C [36]. To elucidate these mechanistic issues, the efforts such as search for anti-oxidative or anti-inflammatory substance, or comparison of in vivo vitamin C kinetics between camu-camu juice and vitamin C supplement would be required.

Although the mechanisms are not clear, camu-camu juice has more powerful anti-oxidative and anti-inflammatory properties, compared to vitamin C tablets containing equivalent vitamin C contents, and thus may be expected as a dietary supplement to prevent atherosclerosis.

Acknowledgments
We acknowledge Mr. Sin Takei, Kinos Co., Tokyo Japan, for generously providing us camu-camu juice. We also thank Koji Yamaguchi, Ph.D., General Institute, Fancl Corp., Kawasaki, Japan, for helpful suggestions.

References
Ascorbate is an outstanding antioxidant in human blood plasma
Proc Natl Acad Sci USA, 86 (1989), pp. 6377–6381
Vitamin C: antioxidant or prooxidant in vitro?
C-reactive protein concentration and concentrations of blood vitamins, carotenoids, and selenium among United States adults
Eur J Clin Nutr, 57 (2003), pp. 1157–1163
Effects of vitamin C on intracytoplasmic cytokine production in human whole blood monocytes and lymphocytes
Cytokine, 27 (2004), pp. 101–106
Vitamin C inhibits NF-κB activation by TNF via the activation of p38 mitogen-activated protein kinase
Relation of serum ascorbic acid to mortality among US adults
Vitamin C deficiency and risk of myocardial infarction: prospective population study of men from eastern Finland
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...

---

Carotenoids, vitamin C and E and mortality in an elderly population

Vitamin C intake and mortality among a sample of the United States population
Epidemiology, 3 (1992), pp. 194–202

High-performance liquid chromatography (HPLC) analysis of phenolic compounds in berries with diode array and electrospray ionization mass spectrometric (MS) detection: Ribes species

Influence of vitamin C supplementation on cytokine changes following an ultramarathon

Plasma C-reactive protein concentration in active and passive smokers: influence of anti-oxidant supplementation

Effect of ascorbic acid on microcirculation in patients with type II diabetes: a randomized placebo-controlled cross-over study

Effects of oral vitamin C supplementation on oxidative stress in haemodialysis patients

Long-term combined supplementations with aloha-tocopherol and vitamin C have no detectable anti-inflammatory effects in healthy men
J Nutr, 133 (2003), pp. 1170–1173

Vascular endothelium and inflammatory process, in patients with combined type 2 diabetes mellitus and coronary atherosclerosis: the effects of vitamin C

Quantitative immunohistochemical determination of 8-hydroxy-2-deoxyguanosine by a monoclonal antibody H45.1: its application to ferric nitrotetrate-induced renal carcinogenesis model

[18] T. Hayashi, Y. Morishita, I. Hayashi
Rapid and multi-sample determination of reactive oxygen species in human sera
Jpn J Clin Lab Anal, 30 (2005), pp. 216–220

Analytical evaluation of particle-enhanced immunopheometeric assays for C-reactive protein, serum amyloid A, and mannose binding protein in human serum

Simultaneous quantification of 15 cytokines using a multiplex flow cytometric assay
J Immunol Methods, 227 (1999), pp. 41–52


Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti-inflammatory properties, which can reduce the risk of cardiovascular diseases. The nutritional content of camu-camu and its potential health benefits are discussed in these articles:


Nutritional composition and vitamin C stability in stored camu-camu (Myrciaria dubia) pulp
Arch Latinoam Nutr, 50 (2000), pp. 405–408

N.R. Stevenson

Active transport of L-ascorbic acid in the human ileum
Gastroenterology, 67 (1974), pp. 952-956

Corresponding author. Tel.: +81 952 34 2364; fax: +81 952 34 2089.
Copyright © 2008 Published by Elsevier Ireland Ltd.

Recommended articles
Antioxidant compounds and antioxidant capacity of...
2010, Food Chemistry

Nutritional compositions and health promoting phyt...
2011, Food Research International

Carotenoid composition from the Brazilian tropical f...
2007, Food Chemistry

View more articles »

Citing articles (25)

Related book content
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...

Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...
Tropical fruit camu-camu (Myrciaria dubia) has anti-oxidative and anti...