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Consumption of star fruit juice on pro-inflammatory markers and walking distance in the community dwelling elderly

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ABSTRACT

Purpose: This study aimed to evaluate the effect of star fruit juice supplementation on tumor necrosis factor-alpha (TNF-α), interleukin-23 (IL-23) and interleukin-2 (IL-2), nitric oxide (NO), and 6 min walking distance (6MWD) in a group of elderly individuals.
Methods: Twenty-nine individuals (20 males, 9 females) with a mean age of 72.4 ± 8.3 years completed this study. A two-week control period was followed by four weeks of 100 g fresh star fruit juice consumption twice per day after meals.
Results: Plasma TNF-α, IL-23, IL-2, NO and the 6MWD were evaluated twice during the control period (weeks 0 and 2) and once after the star fruit juice consumption (week 6).
Results: The results showed that all parameters in the blood did not change significantly during the control period. After 4 weeks of star fruit juice consumption, a significant reduction in NO, TNF-α and IL-23 was found; however, there was no change in IL-2. Moreover, the 6MWD increased significantly at week 6, when compared to that at week 0 and 2. Furthermore, the results also showed a significantly positive and negative correlation of NO and TNF-α to the 6MWD, but no correlation of IL-23 and IL-2.
Conclusion: This preliminary study concluded that consumption of star fruit juice at 100 g twice daily for one month can significantly depress the pro-inflammation cytokines: TNF-α, IL-23, and NO, while increasing walking distance. Low TNF-α and high NO also present a significant correlation to walking capacity in elderly individuals.

1. Introduction

The increasing trend of Thailand's aging population is predicted to rise from 9.0 million in 2015 to 15.9 million in 2035 (Mahidol University Population Projections for Thailand 2005-2025, 2006). There is a high prevalence of chronic disease in the elderly such as hypertension, cardiac disease, type II diabetes and musculoskeletal problems (Fontana, 2009), as well as a predisposition of increased inflammatory state and impaired immunity associated with the normal aging process (O'Connor et al., 2014). The elderly are often at a greater risk of ill health, due to low caloric intake related to decreased activity levels, less access to food with adequate nutritional content, effects of chronic disease, etc. (Drewnowski & Shultz, 2001). Inflammation is a physiological process for repairing tissue in response to endogenous or exogenous stimulus during the aging process. Age-related change in the immune system is known as immuosenescence, from which dominant increases in secretion of cytokines such as interleukin-6 (IL-6), Interleukin-1 (IL-1), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α) occur (Michaud et al., 2013; Singh & Newman, 2011). The immune system is a complex network of cells, especially T lymphocytes, which have acquired immune recognition and B cell secreting antibodies. In addition, the immune system is highly reliant on cell to cell communication for an optimal function, and during aging, it tends to become impaired after immune cells have been attacked directly by the oxidants in the biological system (Hughes, 1999). Many cytokines are interleukins (IL), secreted by most major systems, especially that for T-lymphocytes (Mitchell, Ulrich, & McTiernan, 2003). Activation of T1 pathways is shown in the release of the cytokines, IL-2 and IFN-γ, which can activate many cells in the body as neutrophils and NK cells (Das, Varalakshmi, Kumari, Patei, & Khar, 2001). Interleukin-23 (IL-23)

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is a cytokine in the family, interleukin-12 (IL-12), and is produced by dendritic cells (DC) and macrophages (Zhou et al., 2007). It correlates to and generates pathogenic T helper cells capable of orchestrating tissue inflammation (Croxford, Kulig, & Becher, 2014). Previous evidence found that increased IL-23 has a strong relationship with autoimmune or psorotic skin diseases and ankylosing spondylitis (AS) (Yawalkar, Tscharner, Hunger, & Hassan, 2009). IL-23 promotes inflammatory responses such as up regulation of the matrix metalloproteinase (MMP)-9, and increases angiogenesis during tumor-promoting pro-inflammatory processes. Thus, low immunity and high oxidative stress have a close relationship. Previous evidence has proposed different mechanisms of active inflammatory factors, especially TNF-α, which can stimulate the superoxide within mitochondria during the function of the electron transport system and NADPH oxidase function. Increased superoxide production is responsible for decreased nitric oxide (NO) bioavailability and endothelial dysfunction, which induces vascular impairment (Assar, Angulo, & Rodriguez-Manas, 2013). The interesting result of high oxidant production and low antioxidant buffering ability is the factor of reducing muscle strength (i.e., sarcopenia), endurance, and function capacity (Gianni, Jan, Douglas, Stuart, & Tarnopolsky, 2004; Rynan et al., 2008).

Functional foods, including grape peel, milk, red and green peppers, garlic, onions, vegetables, and fruit juice (Ferrari, 2007) have been proposed as beneficial for the elderly population. These foods have both antioxidant and immune modulatory effects, due to their probiotic, selenium, and dietary antioxidant (vitamin A, E and C) content (Lopez-Varela, Gonzalez-Gross, & Marcos, 2002). Vitamin C in particular, has the potential to enhance the immune system (Podmore et al., 1998). However, previous evidence showing the relationship between vitamin C and the immune system of healthy elderly subjects has received little attention (Kennes, Dumont, Brohee, Hubert, & Nerve, 1983). An early report demonstrated that supplementation of vitamin C at 500 mg daily for one month, showed an increased proliferative response of T lymphocytes to phytohaemagglutinin (PHA) and concavavalin A (Con A) in 12 women and 8 men aged 70 years and more (Kennes et al., 1983).

Star fruit (*Averrhoa carambola* L.) is one of many native fruits grown all over Thailand, as well as in Malaysia, Taiwan, Israel, the U.S.A., Indonesia, India, Sri Lanka, etc. Typical characteristics of this fruit are its five-pointed cross section forming a star, green to yellowish skin, and flavor that is fresh, sour, and slightly sweet (O'Hare, 1993). Previously updated reviews show interesting evidence of both chemical constituents and nutritional values, including traditional uses (Dasgupta, Chakraborty, & Bala, 2013; Manda, Vyas, Pandya, & Singhal, 2012). Star fruit contains saponins, alkaloids, flavonoid C-glycosides, tannin and has a high antioxidant activity (Thomas et al., 2008; Yang, Xie, Jia, & Wei, 2015), as well as containing L-ascorbic acid, (−) epicatechin and gallic acid (Shui & Leng, 2004; Dasgupta et al., 2013). The reviewed data show various traditional applications for humans such as anti-pyretic, laxatives, appetite stimulants, diuretics and digestives including treating throat inflammation, mouth ulcer, toothache, cough, asthma, and eye related problems (Dasgupta et al., 2013; Manda et al., 2012). With little research of star fruit consumption in aging people, a previous study by Krone and Ely (2004) showed that ascorbic acid could suppress glycation and reduced glycohemoblogin in all proteins in their aging participants. A further benefit of ascorbic acid is its ability to decrease the osmotic fragility of erythrocytes from oxidative stress (Arora, Maurya, & Shaarma, 2004). This body of evidence confirms the benefits of ascorbic acid for anti-oxidant status, and star fruit is an excellent source of ascorbic acid. However, it creates less interest and is not consumed as much as other fruits such as banana, guava or orange, and is undervalued as a healthy functional food. Currently, there is no evidence that star fruit supplement benefits elderly individuals, especially regarding oxidative stress and functional capacity. Therefore, this preliminary study was designed to evaluate the effects of star fruit juice consumption on pro-inflammatory cytokines and walking capacity in an elderly population.

2. Methods

2.1. Study design and recruitment of participants

This research protocol was approved by the Human Ethics Committee at the Faculty of Associated Medical Sciences, Chiang Mai University, Thailand, and performed in accordance with the Helsinki Declaration (2001) (Ethical approval number 027E/52). All approved participants, comprising 40 healthy elderly subjects (20 men and 20 women) aged between 54 and 87 years from the elderly community of Chiang Mai province, were nonsmokers, understood the research protocol, and provided written consent before enrolling in the study. All participants were capable of performing basic daily activities independently and they lived on their own. Before and during the study period, their regular activities, such as diet and behavioral aspects, were controlled, including taking supplementary multi-vitamins. Six weeks prior to the study, all participants were screened for inclusion into this research by a physician using hospital records and a physical examination.

2.2. Experimental design

The study design was divided into two periods: (1) a 2 week control period in which the participants continued their life as per usual without the consumption of star fruit, and (2) a 4 week period of having star fruit juice added to their daily diet. Star fruit was purchased from a local farmer in Chiang Mai province, and made available for consumption 2 weeks after it was harvested. One hundred grams of fresh star fruit juice were contained in a glass, prepared by fine homogenization using a blender, and consumed immediately after breakfast and dinner daily for the 4 week study period. All parameters of pro-inflammatory cytokines, such as TNF-α, IL-23, interleukin-2 (IL-2) and NO, as well as the 6-minute walking distance (6MWD) for physical capacity, were evaluated three times (at week 0 and 2 for the controls and week 6, after 4 weeks of star fruit juice consumption).

2.3. Pro-inflammatory cytokines and nitric oxide evaluation

Ten milliliters of blood were taken from the anterior cubital vein and put into sterile tubes containing ethylene diamine tetraacetic acid (EDTA). After centrifugation at 3000 × *g* for 10 min, the serum was transferred to 1.5 mL sterile tubes and stored at −80 °C until further analysis. Fresh serum was separated for basic evaluation of the complete blood count and NO. The plasma concentration of TNF-α, IL-23, and IL-2 was determined using the sandwich ELISA technique (Quantikine ELSA-kit, R&D system, USA) and expressed as units in pg/mL.

2.4. Pro-inflammatory cytokine assay

The method for determining the TNF-α, IL-2 and IL-23 in plasma was performed by following the guidelines in the Quantikine, Human TNF-α, IL-2 or IL-23 Immunoassays (Quantikine®, R&D systems, Inc., Minneapolis, MN, USA). One hundred microliters of diluent solution with 50 μL of external standard TNF-α (125 pg/mL), standard IL-2 (25 pg/mL), and standard IL-23 (100 pg/mL) were loaded onto an anti-TNF-α,