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Effect of *Aloe vera* preparations on the human bioavailability of vitamins C and E

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Abstract

There are no literature references describing the effect of consumption of *Aloe vera* liquid preparations on the absorption of water- or fat-soluble vitamins. There is a very large population worldwide which consume vitamins and many people also consume Aloe. Thus we report the effect of Aloe on the human absorption of vitamins C and E, the most popular vitamin supplements. The plasma bioavailability of vitamins C and E were determined in normal fasting subjects, with eight subjects for vitamin C and ten subjects for vitamin E. In a random crossover design, the subjects consumed either 500 mg of ascorbic acid or 420 mg of vitamin E acetate alone (control), or combined with 2 oz of two different Aloe preparations (a whole leaf extract, or an inner fillet gel). Blood was collected periodically up to 24 h after consumption. Plasma was analyzed for ascorbate and tocopherol by HPLC with UV detection. There was no significant difference in the areas under the plasma ascorbate–time curves among the groups sincerely due to large differences within the groups. For comparative purposes the control area was 100%. The Aloe Gel area was 304%, and Aloe Whole Leaf 80%. Only Aloe Gel caused a significant increase in plasma ascorbate after 8 and 24 h. For vitamin E, the results for the relative areas were control 100%, Gel 369%, and Leaf (198%). Only the Aloes produced a significant increase in plasma tocopherol after 6 and 8 h. Both Aloes were significantly different from the control after 8 h. Aloe Gel was significantly different from the baseline after 24 h. The Aloes slowed down the absorption of both vitamins with maximum concentrations 2–4 h later than the control. There was no difference between the two types of Aloe. The results indicate that the Aloes improve the absorption of both vitamins C and E. The absorption is slower and the vitamins last longer in the plasma with the Aloes. Aloe is the only known supplement to increase the absorption of both of these vitamins and should be considered as a complement to them.
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Keywords: *Aloe vera*; Vitamin C; Vitamin E; Bioavailability; Plasma

Introduction

The number of people who take vitamin supplements is increasing due to a greater awareness of the benefit. In the USA it is estimated currently that between 51% and 61% of the population consume vitamin supplements (Subar and Block, 1990; Hensrud et al., 1999). The elderly population is greatly increasing in developed nations. This group is especially vulnerable to vitamin deficiency, due to age-related decreases in absorption, reduced food intake, and increased drug use (Fairfield and Fletcher, 2002).

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Vitamin C (ascorbic acid) is a water-soluble vitamin essential to prevent scurvy. It is a common supplement because there is epidemiological evidence that it reduces the risk of cancer, diabetes, cataracts, and Alzheimer's disease. Vitamin C has been proven to increase greatly the absorption of iron and improves poor iron status (Sandstrom, 2001). A recent report showed that *Helicobacter pylori* infection significantly impairs the bioavailability of vitamin C (Woodward et al., 2001). This bacterium infects half of the world's population (Go, 2002) and is especially common in peptic ulcer patients (Vyse et al., 2002; Gisbert and Pajares, 2002). Individuals with kidney problems are deficient in C, and hemodialysis further decreases ascorbate levels (Wang et al., 1999). The amount recommended for vitamin C consumption by the US Government has been increased recently to 75 mg per day for women and 90 mg for men. Smokers should add an additional 35 mg per day because their metabolic turnover of vitamin C is more rapid, as is their rate of oxidative stress (Food and Nutrition Board, 2000). In a comprehensive study of its pharmacokinetics in humans, it was suggested that the amount be increased to 200 mg/day, representing maximum bioavailability (Levine et al., 1996). This amount can be obtained by eating 5 servings of fruits and vegetables. Because the majority of Americans do not consume 5 servings (Stables et al., 2002), then either a supplement of C or ingestion of an agent that can increase the absorption of C may be needed.

Vitamin E (tocopherol), a lipid-soluble vitamin, is needed in much smaller amounts than C. E is present mainly in oils that are often avoided in the diet of individuals with weight problems. Vitamin E can reduce cognitive decline (Morris et al., 2002) and improve the immune system (Meydani, 2002) in older persons. Higher intakes of vitamin E were shown recently to be associated with a lower risk of Alzheimer's disease (Engelhart et al., 2002) and prostate cancer (Fleshner, 2002). Age-related cataract and age-related macular degeneration are delayed by consumption of antioxidant nutrients such as vitamins C and E (Jacques, 1999). Epidemiological studies indicate vitamin E may also reduce the risk of cardiovascular disease, although results from supplementation studies are mixed (Blumberg, 2002). Dietary fiber (Hoffmann et al., 1999) and low fat meals (Dimitrov et al., 1991) reduce the bioavailability of E as do the long-term consumption of Orlistat (a fat absorption inhibitor used for weight loss), and Olestra, a fat substitute (Melia et al., 1998).

The genus *Aloe* belongs to the Asphodelaceae Alooidea sub family, and includes ~420 species of succulent plants (Smith and Van Wyk, 1998). The correct name is *Aloe vera* (L.) Burm f. Its chemical and therapeutic properties have recently been reviewed (Coats and Ahola, 1979; Shelton, 1991). In commerce the full botanical name, *A. vera*, is used to refer to gel products. The Aloe plant has yellow flowers and triangular leaves arranged in a rosette configuration. The leaves are triangular and, when mature, are filled with a gel that exudes from the clear central mucilaginous pulp. The Arabic word Aalloeh means shining and bitter. The peripheral bundle sheath cells give rise to a bitter, yellow exudate (latex) that is responsible for the cathartic effect. For 3000 years it has been used externally (initially in Mesopotamia and Egypt) for skin infections and wounds, and internally as a cathartic. Careful processing of aloe gel is necessary to maintain activity.

Aloe is processed using the hand-filleted technique or whole leaf procedure (Goldberg, 1999). Hand-filleted processing removes the inner gel while avoiding the yellow latex found next to the rind. Whole leaf extracts for consumption are prepared after sterilization and blending by grinding the entire leaf and then removing the bitter yellow component (alloin) by charcoal filtration. Aloin and its derivatives are anthraquinones. Polysaccharides are considered to be the active ingredients for Aloe's anti-inflammation and immune modulation effects (Pugh et al., 2001). The major carbohydrate fraction isolated from aloe gel, "Aacemannan," is composed of β-1,4-linked acetylated mannan interspersed with *O*-acetyl groups. (Pugh et al., 2001).

Materials and methods

Materials

The two Aloe products were selected by The International Aloe Science Council (Irving, TX 75062) from commercial samples, blinded upon receipt, and certified by the Council. These products passed quality control certification, which consisted of testing for total solids, calcium and magnesium content and L-malic acid (a marker for processing in a timely fashion without excess heat, time, and pressure). NMR was used to detect acetylated polysaccharides, acids, and suspected adulterants. The gel product is designated AVG and the whole leaf AVL. Both were kept in a refrigerator until use. Vitamin C tablets (500 mg) and vitamin E acetate soft capsules (420 mg) were prepared by Summa Rx Laboratories, Inc. (Ft. Worth, TX 76116), an FDA-registered contract drug and supplement manufacturer.

Subjects

There were 11 healthy subjects in the study pool, ranging in age from 21 to 42. They were not taking vitamin supplements. Eight volunteers participated in the vitamin C study and 10 (5 males and 5 females) in

the vitamin E study. Every subject completed the study for each vitamin given in 3 supplements. This study was approved by the University of Scranton Institutional Review Board according to the Declaration of Helsinki. All volunteers gave their written informed consent prior to study inclusion.

Study design and methodology

The study was designed as a randomized, double-blind, cross-over trial. On study days at least a week apart, each volunteer had a baseline blood sample taken after an overnight fast. They then consumed in a random fashion a 500-mg vitamin C tablet or a 420-mg vitamin E capsule with 60 ml (2 oz) of either water (control), AVL, or AVG that was slowly sipped over 5 min. Further blood sampling was at 1, 2, 4, 6, 8, and 24 h (fasting) post-dosing. Subjects were allowed to eat their normal lunch and evening meals. One week and 2 weeks later, the other liquid was consumed with vitamins C or E and the sampling repeated. Blood was converted to plasma, mixed with metaphosphoric acid preservative only for vitamin C, and stored at −80 °C.

Analysis

Ascorbic acid in plasma was measured by HPLC using a Brownlee (Perkin Elmer, Norwalk, CT) Pecosphere C18 cartridge column (3 μm, 33 × 4.6 mm) operating at 1 ml/min using 0.05 KH_2PO_4 (pH 2.5) as a solvent and a wavelength of 245 nm. Tocopherol was extracted from 100 μl of plasma with 500 μl methanol/butanol (50/50). The same column as above was used with a mobile phase of formic acid/water/acetonitrile (10/81/9) at flow rate of 0.5 ml/min. and a wavelength of 295 nm. Plasma concentrations were determined from a standard curve plotted on the same day as the sample. The area under the curve was determined using integration software (Kaleidagraph7, Synergy Software, Reading, PA 19606). Statistics were analyzed using a *t*-test for normal distributions and a Mann–Whitney Rank Sum test for non-normal distributions with SigmaStat7, (SPSS Science, Chicago, IL 60606).

Results

Vitamin C

The baseline plasma ascorbate was 40.8 ± 8.4 (standard error of the mean, s.e.m.), 51.2 ± 9.8, and 52.4 ± 11.0 μM for control, AVL, and AVG, respectively. For easier comparison purposes the changes in plasma ascorbate from the baseline were calculated and the results shown in Fig. 1. All the supplements except AVL caused an increase in plasma ascorbate that was significantly different from the baseline ($p < 0.05$) at 1 and 2 h. All the supplements were different from the baseline at 4 h, but only AVG showed a significant increase after 8 h. The largest increase from baseline occurred at 2 h for the control, and 8 h for AVL and AVG. The AVL and AVG groups had another smaller maximal change at 4 h. Presumably the two maxima for the Aloes are due to the re-release from the liver (first-pass effect). The control and AVL group returned to the baseline after 24 h and an overnight fast, but the AVG

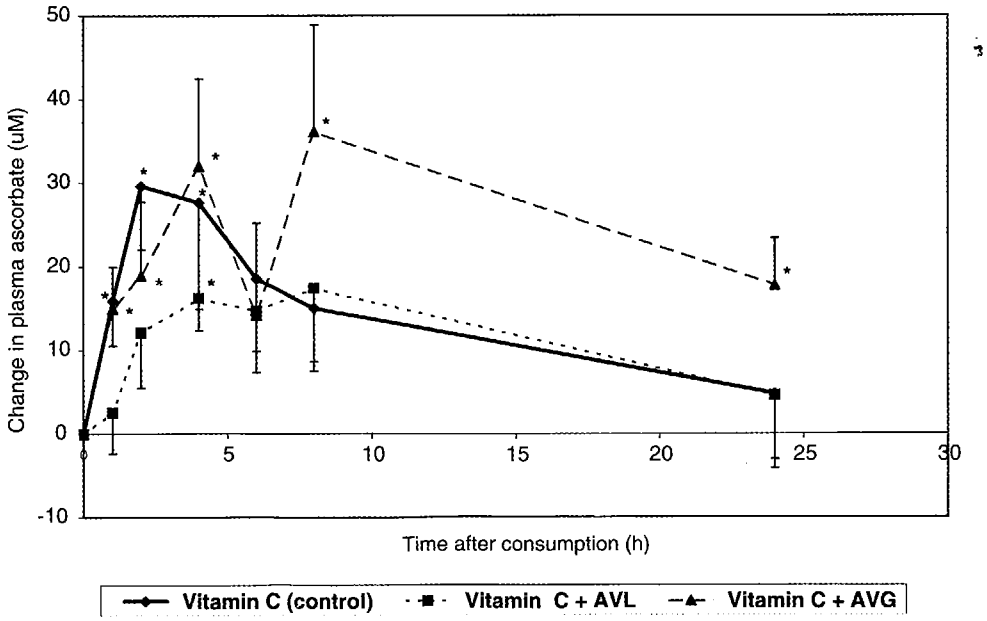

Fig. 1. Bioavailability of vitamin C. Eight subjects consumed 500 mg of ascorbic acid alone (control) or with 60 ml of Aloe (AVG gel or AVL whole leaf extract). Data are mean ± standard error of the mean. *$p < 0.05$ vs. 0 h.

group was still significantly greater than baseline at 24 h ($p<0.05$). The areas under the plasma ascorbate–time curves are shown in Table 1. There was no significant difference in areas due to the large differences between individuals in each group. No significant difference existed between the two Aloes.

Vitamin E

The baseline plasma tocopherol was 15.1±2.6 (s.e.m.), 13.3±2.5, and 12.2±2.3 μM for control, AVL, and AVG, respectively. The changes in plasma tocopherol from the baseline were calculated and the results shown in Fig. 2. Aloe AVG was significantly different from the baseline at 1 h. Both Aloe supplements, but not the control, caused a substantial increase in tocopherol which was significantly different from the baseline after 6 and 8 h. Both Aloes were significantly different from the control at 8 h. The largest increase from baseline occurred at 4 h for the control, 6 h for AVL, and 8 h for AVG. The AVL and AVG groups had another smaller maximal increase at 2 h. Both Aloes caused a significantly greater increase in plasma E after 8 h than the control without Aloe. The AVG group was also significantly higher than the baseline after 24 h. The areas under the plasma tocopherol–time curves are displayed in Table 1. There was no significant difference in areas due to the large differences between individuals in each group. Again, there was no significant difference between the two Aloes.

Table 1. Areas under the plasma concentration–time curves for vitamins C and E alone or with Aloe gel (AVG) or Aloe whole leaf extract (AVL)

Supplement	Area under the curve (μM h)
Vitamin C (500 mg)	339±124
Vitamin C+AVL	272±144
Vitamin C+AVG	1031±513
Vitamin E (420 mg)	19.3±23.2
Vitamin E+AVL	38.3±17.0
Vitamin E+AVG	71.3±22.5

Data are mean±s.e.m.

Discussion

Vitamin C

Comparing the areas under the curves, Aloe AVG was 3 times more bioavailable than the control, while AVL was 80% of the control curve. Fig. 1 clearly indicates that both Aloes, the gel and the whole leaf extract, slowed down the absorption of vitamin C and the gel kept plasma ascorbate significantly elevated even after 24 h. The effect of AVG was most evident at (a) 8 h when the average increase was 36 μM, and control only 15 μM, and (b) 24 h when the increase was 18 μM for AVG, and only 5 μM for control. Both the Aloes act as time-release agents for vitamin C. The factors that affect ascorbate bioavailability have recently been reviewed (Bates, 1997). The phytochemicals in the Aloes may protect ascorbate from degradation in the intestinal tract and then *in vivo*. That is the mechanism by which

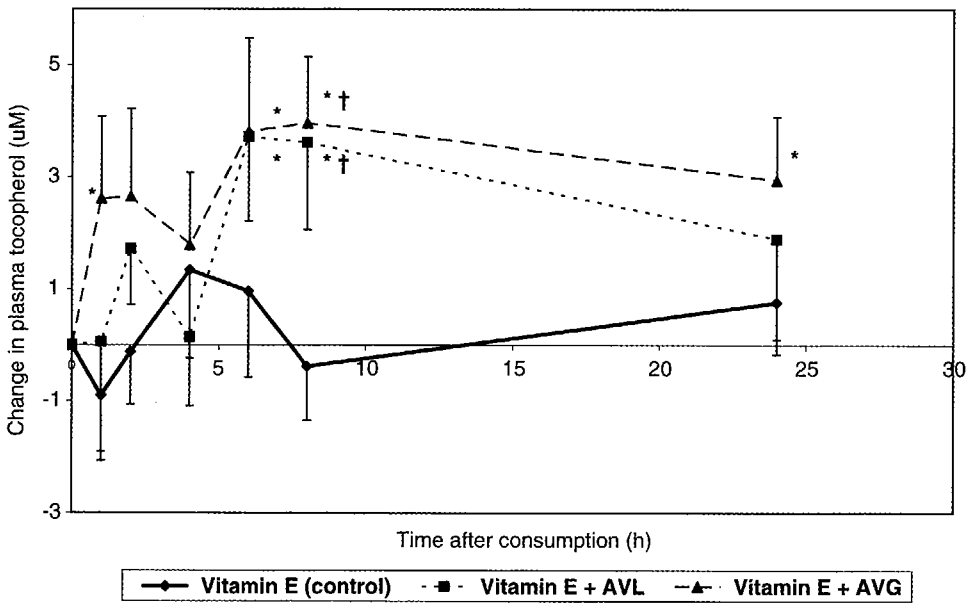

Fig. 2. Bioavailability of vitamin E. Ten subjects consumed 400 mg of tocopherol acetate alone (control) or with 60 ml of Aloe (AVG gel or AVL whole leaf extract). Data are mean±standard error of the mean. *$p<0.05$ vs. 0 h, †$p<0.05$ vs. control.

flavonoids are believed to operate. For instance, blackcurrant juice significantly improved the absorption of vitamin C (Jones and Hughes, 1984), as did a concentrated citrus extract containing a high concentration of flavonoids (Vinson and Bose, 1988). The latter also slowed down ascorbate absorption and excretion. Aloes are known to contain flavonoid antioxidants (Lee et al., 2000). Treatment of mice with low doses (30–60 μl/day) caused a reduction of lipid peroxides and an increase in thiols, clearly an *in vivo* antioxidant effect (Singh et al., 2000). The Aloe polysaccharides are also antioxidants and act to reduce oxidative DNA damage in mouse liver cells (Kim et al., 1999). Another factor that might influence absorption is gastric emptying time. Ascorbate given with a meal that slows gastric emptying time, was found to be better absorbed than when consumed on an empty stomach (Yung et al., 1981). However, Aloes are not known to affect gastric emptying time (Shelton, 1991). The polysaccharides in the Aloes have been shown to bind to the mucosal cells in the stomach (Yagi et al., 2001) and also may bind to the ascorbic acid, slowing down its absorption.

Vitamin E

The data from this study indicate clearly that vitamin E was poorly absorbed in our fasting subjects, especially with the control (water). A recently reported study with 400 mg of tocopherol acetate (similar to the dose in this study) found that only a 0.7 μM maximal increase in plasma E resulted when the capsule was consumed on an empty stomach (Leonard et al., 2002). The increase was 1.3 μM with water in the present study, a comparable result. Comparing the areas under the curves, Aloe AVG was 3.7 times more bioavailable than the control, while AVL was 2 times more bioavailable than the control. Both of the Aloes slowed down the absorption of vitamin E and kept it at higher concentration for a longer period of time than the control. The mechanism for the beneficial effects of the Aloes for vitamin E may well be the same as mentioned for vitamin C, namely decreased degradation in the stomach or binding to the polysaccharides.

Conclusions

For both the water-soluble vitamin C and the fat-soluble vitamin E, both Aloes had a salutary effect. For vitamin C, the Aloe gel extract was especially effective in slowing down and increasing the absorption of ascorbate. It prolonged its plasma concentration significantly, even for 24 h, and following an overnight fast. Both the gel and whole leaf Aloe extracts improved the absorption of vitamin E and prolonged its plasma concentration, especially after 8 h. Aloe is unique in its ability to improve the absorption of both of these vitamins and should be considered as an adjunct for people who take vitamin supplements.

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