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Influence of oral dosing with D-isoascorbic acid on L-ascorbic acid content in guinea pig tissues

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The effect of graded doses of D-isoascorbic acid (IAA) on the tissue content of ascorbic acid (AA) in guinea pigs administered a marginal intake of ascorbic acid was studied. Thirty guinea pigs (inbred Hartley-strain) were randomly assigned to three equally sized treatment groups: 1) 1 mg AA (only); 2) 1 mg AA + 20 mg IAA, or 3) 1 mg AA + 100 mg IAA. Ascorbic acid alone or in combination with IAA was orally administered daily to all animals over 42 consecutive days, after which time the animals were sacrificed. Over the study period, animals dosed with 1 mg AA plus 100 mg IAA had a higher rate of weight gain than those dosed with 1 mg AA or 1 mg AA + 20 mg IAA. Tissue concentrations of AA, IAA, and their oxidized forms, dehydroascorbic acid (DHAA) and dehydroisoascorbic acid (DHIAA) were determined by high-pressure liquid chromatography equipped with an electrochemical detector. In guinea pigs dosed with either 20 or 100 mg IAA, AA levels in the plasma, brain, liver, adrenals, lungs. kidneys, spleen, and heart were significantly decreased ($P < 0.05$) compared with the non-supplemented group. IAA content in the guinea pig tissues increased progressively after incremental dosing with IAA. DHAA levels decreased significantly in guinea pigs dosed with 20 mg IAA or 100 mg IAA compared with the corresponding controls in all tissues examined. Thus, in guinea pigs, the co-administration of graded levels of IAA with a marginal AA intake resulted in a decreased bioavailability of AA. © Elsevier Science Inc. 1997
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Keywords: guinea pigs; isoascorbic acid; ascorbic acid; bioavailability; tissues

Introduction

Erythorbic acid (Era) also referred to as D-isoascorbic acid (IAA) or D-araboascorbic acid is one of the stereoisomers of L-ascorbic acid (AA). Owing to its reducing properties, IAA is widely used as an antioxidant in various foods and beverages. Although the antioxidant properties of IAA are very similar to that of AA, the vitamin C activity of IAA in the guinea pig is generally accepted to be 1/20 that of AA.[1] The biological difference in activity is mainly due to the structural difference in the position of the hydroxyl group at carbon 5 of IAA and AA.

The biological properties of IAA have been investigated by many workers. A study conducted by Reiff and Free[2] showed that IAA had a protective effect on AA and a tendency to slow down the development of acute vitamin C deficiency, but did not have significant antiscorbutic activity. In a study with guinea pigs, Hughes and Hurley[3] showed that administration of AA and/or IAA resulted in a better tissue retention with AA than IAA. Hughes et al.[4] reported that IAA was lost more rapidly than AA in the tissues of guinea pigs saturated with AA or IAA. Hornig and Weiser[5] showed that the bioavailability of AA was reduced in the guinea pig after the simultaneous provision of AA and IAA. However, the earlier reports of Hughes et al.[4] and Hornig and Weiser[5] did not measure separately the concentrations of AA and IAA in the tissues because the usual chemical determination methods could not differentiate between these stereoisomers due to their very similar chemical reactivity. The uptake and effect of IAA on tissue AA by organs has never been ascertained.

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Using a HPLC-UV detection system, Suzuki et al.,[6] observed that ascorbic acid levels from tissues of guinea pigs administered AA and IAA were significantly lower than in animals provided only AA. Animal studies have shown that the availability of L-AA is reduced after the co-administration of IAA and AA.[7,8]

Whereas IAA can be eliminated rapidly by guinea pigs,[9,10] humans,[11] monkeys,[12] and mice,[13] it can be incorporated to a significant degree into the tissues of guinea pigs,[5,8,9] which require vitamin C, and of mice,[13] which do not. Both these observations are in agreement with the results of Arakawa et al.,[14] who reported that AA levels in the tissues of guinea pigs administered with AA and IAA were lower than those animals administered only AA. This reduction in bioavailability could be critical for species such as guinea pigs and humans, not capable of synthesizing AA.

The objective of this study was to determine the effect of graded levels of IAA on the uptake and retention of AA in guinea pig tissues. Recently, we have developed a sensitive and versatile high performance liquid chromatography analytical method using an electrochemical detection system for the simultaneous determination of AA, IAA, and their oxidized forms [dehydroascorbic acid (DHAA) and dehydroisoascorbic acid (DHIAA), respectively] in food samples and animal tissues.[15] Using this method, we have observed varying levels of IAA added into Canadian food products.[16,17] Thus, this present study was initiated to examine the effect of IAA on AA and DHAA content in tissues of guinea pigs after 42 days of dosing with IAA. In this study, a marginal AA (1 mg AA/day) intake was used with graded levels of IAA in guinea pigs to clarify the effect of IAA on tissue uptake of AA.

Methods and materials

Animals

Weanling male albino guinea pigs (in-bred, Hartley strain purchased from Elm Hill Breeding Labs, Chelmsford, Massachusetts USA) with an initial body weight of approximately 240 g were housed individually in wire cages in a room with controlled temperature (23 ± 2°C), relative humidity (55 ± 2%), and light (lights on, 0600 to 1800 hr). The experiment and animal handling procedures were approved by the Animal Care Committee and were performed in accordance with the guidelines of the Canadian Council of Animal Care (1993) as specified in the *Guide to the Care and Use of Experimental Animals.*

Diets

All animals were fed a synthetic vitamin C-deficient diet (modified Reid-Briggs) as follows: 30% vitamin-free casein; 0.3% L-arginine; 0.3% DL-methionine; 19% corn starch; 11.2% sucrose; 8.45% glucose; 2% corn oil; 15% alphacel, non-nutritive bulk; 6.75% ICN guinea pig mineral mix; 0.5% magnesium oxide; 2.5% potassium acetate; 3% lard, and ICN vitamin fortification excluding ascorbic acid. Water and diets were offered ad libitum with food consumption and body weights recorded daily.

Experimental design

Thirty guinea pigs were randomly assigned into three groups of 10 animals per group. The control animals (group 1) were supplemented orally with 1 mg AA/day (marginal amount to maintain health and prevent scurvy) whereas groups 2 and 3, in addition to receiving 1 mg AA/day orally, were dosed daily with 20 mg IAA or 100 mg IAA, respectively. All guinea pigs were dosed daily for 42 consecutive days. The AA and/or IAA were dissolved in water immediately before use and delivered at the back of the guinea pig's mouth by a plastic syringe through an attached tygon tube. At day 42 of the experimental period, the animals were sacrificed after 24 hr of fasting. Tissues (brain, thymus, heart, lungs, liver, spleen, kidneys, and adrenals) and blood (abdominal aorta) were taken rapidly while the guinea pigs were under halothane anaesthesia (2% in oxygen). The excised tissues were immediately weighed and promptly stored at −75°C. Blood samples (in heparinized tubes) were centrifuged at 1,500 × g for 15 min at 4°C immediately after sampling to obtain plasma. Aliquots of plasma were treated immediately with metaphophoric acid to give a final concentration of 0.85% of acid (wt/vol) and deproteinized plasma was stored at −75°C.

Vitamin C determination

AA and IAA levels and their oxidized forms were determined in the plasma and tissues according to the method of Behrens and Madere.[15] Plasma and tissue Vitamin C analysis were initiated within 1 to 2 days after the sacrifice of the animals. All Vitamin C sample determinations were completed in a 4-week period.

Statistics

Plasma and tissue vitamin C data were analyzed for statistical significance using one-way analysis of variance followed by a least significant differences procedure for multiple comparisons. Values assigned a different superscript letter were significantly different at $P < 0.05$. The data are reported as mean ± SD.

A multivariate analysis of variance was used with the body weight and food consumption data, to test for differences in the rate of growth over the period of the study.[18,19] This statistical approach includes the correlations between successive time points. Contrasts were used between the slopes of the curves to test for significant differences.

Results

The rate of growth of guinea pigs fed the three treatments is presented in *Figure 1*. There was no significant difference in the weights of guinea pigs at the beginning of the study (range, 230–250 g). There was a slight weight loss during the initial 2 to 3 days of the experimental period, but thereafter, the body weights of all groups increased continuously over the entire study period.

In our study, guinea pigs supplemented with 100 mg IAA, showed a higher ($P < 0.05$) rate of weight gain than those animals receiving 20 mg IAA or the control group given only 1 mg AA (*Figure 1*). There was no difference ($P > 0.05$) in the rate of growth between guinea pigs dosed with 1 mg AA alone or 1 mg AA + 20 mg IAA. The standard errors of the slopes of the curves are as follows: group 1 (control) versus group 2 (20 mg IAA), 0.49; group 1 versus group 3 (100 mg IAA), 0.44; group 2 (20 mg IAA) versus group 3 (100 mg IAA), 0.50; respectively. The estimates of differences in slopes of group 1 (control) versus group 3 (100 mg IAA), and group 2 (20 mg IAA) versus group 3 (100 mg IAA) were −0.88 and −1.10, respectively.

Data on weekly mean food consumption are summarized

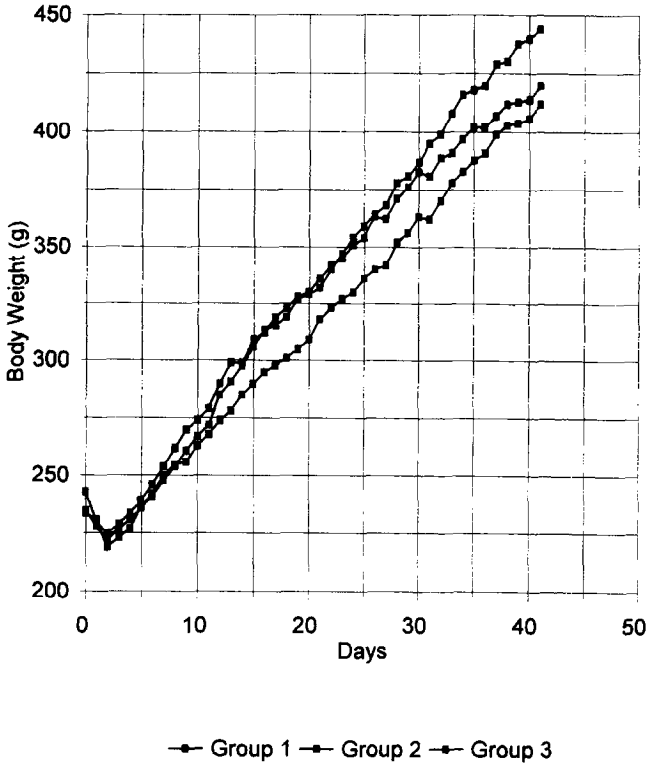

Figure 1 Growth rate of guinea pigs after continuous oral dosing with 1 mg AA alone (group 1) or in combination with 20 mg IAA (group 2) or 100 mg IAA (group 3) over 42 days. N = 10 animals/treatment. The slope of the curve of group 3 was significantly different (P < 0.05) from groups 1 and 2.

in *Table 1*. The food intake increased steadily during the first 3 weeks and remained fairly constant thereafter until the end of the study. Over the course of the study, there were no significant differences in feed intake ($P > 0.05$) between the three dose groups. When averaged across the treatments, the guinea pigs ate approximately 20 g/day.

Dosing with either 100 or 20 mg IAA resulted in decreased ($P < 0.05$) total AA levels (AA + DHAA) in all tissues except the thymus as compared with the control animals (*Table 2*). Supplementation with 100 mg IAA resulted in lower ($P < 0.05$) total AA (AA + DHAA) levels in all tissues, except for the liver and spleen than dosing with 20 mg IAA.

Tissue AA of animals receiving 20 mg IAA (group 2) decreased significantly ($P < 0.05$) in the brain, liver and adrenals (*Table 2*) compared to the nonsupplemented control group. Except for the thymus, spleen and plasma, AA content in all tissues decreased significantly ($P < 0.05$) in guinea pigs dosed orally with 100 mg IAA compared with the controls. Animals given 100 mg IAA had significantly lower ($P < 0.05$) AA levels in the adrenals, brain, kidneys, and lungs than in the group dosed with 20 mg IAA. Our data show that IAA was found in all the tissues of IAA supplemented animals, and except for spleen and thymus, IAA concentration increased considerably when additional IAA was given to the guinea pigs. However, only in the brain and plasma were IAA levels found to be statistically higher ($P < 0.05$) after dosing with 100 mg IAA than 20 mg IAA. Our observations demonstrate that with the exception of liver, the total tissue AA + IAA content of animals administered both AA and IAA (group 2 and group 3) was higher than the guinea pigs given only AA (group 1).

Reduced ($P < 0.05$) DHAA levels were observed in all tissues except the thymus when guinea pigs were dosed with either 20 or 100 mg IAA compared with the control group. Tissue DHAA concentrations were all lower after administration with 100 mg IAA than 20 mg IAA although, only heart and lung were significantly ($P < 0.05$) reduced.

Whereas DHIAA levels were higher in organs of animals given 100 mg IAA as compared with 20 mg IAA, the difference was significant ($P < 0.05$) only for the brain, liver and lung. As shown in *Table 2*, ratios of DHAA to AA were quite different among the various tissues. The tissue DHAA/AA ratios decreased significantly ($P < 0.05$) in guinea pigs dosed with 1 mg AA + 100 mg IAA (group 3) when compared with control (group 1) except for liver, thymus, and spleen. For guinea pigs treated with 1 mg AA + 20 mg IAA, tissue DHAA/AA ratios decreased significantly ($P < 0.05$) in the brain, adrenals, heart, kidney, and plasma when compared with animals dosed with 1 mg AA.

No significant differences were found in any tissue in the ratio of DHIAA/IAA, except for the brain and thymus ($P < 0.05$), where animals dosed with 1 mg AA + 100 mg IAA had a higher ratio than in animals dosed with 1 mg AA + 20 mg IAA.

Table 1 Food consumption patterns (grams) in guinea pigs dosed with 1 mg AA alone (group 1); 1 mg AA + 20 mg IAA (group 2) or 1 mg AA + 100 mg IAA (group 3) over 42 consecutive days

Week	1 mg AA	1 mg AA + 20 mg IAA	1 mg AA + 100 mg IAA
1	$9.02^{a} \pm 5.50$	$8.03^{a} \pm 3.51$	$4.54^{a} \pm 3.47$
2	$15.62^{b} \pm 5.13$	$18.55^{b} \pm 6.41$	$17.56^{b} \pm 5.09$
3	$18.52^{bd} \pm 6.71$	$19.17^{b} \pm 9.74$	$17.44^{b} \pm 7.41$
4	$22.67^{c} \pm 3.96$	$21.43^{b} \pm 7.02$	$21.80^{bc} \pm 5.86$
5	$23.15^{c} \pm 3.96$	$24.45^{b} \pm 8.24$	$24.37^{c} \pm 6.37$
6	$22.23^{cd} \pm 3.22$	$25.92^{b} \pm 5.95$	$26.63^{c} \pm 6.24$
7	$25.48^{c} \pm 6.02$	$22.07^{b} \pm 8.07$	$25.81^{c} \pm 9.54$

n = 10 animals/group
Values are mean ± SD
[a,b,c,d]Mean in the same vertical column with different letters differ (P < 0.05)

Discussion

The AA requirement for the young growing guinea pig is considered to be 5 mg/day to support optimum growth.[20] In this study, a marginal amount of AA (1 mg/day) was provided, which is the amount required to maintain health and prevent scurvy. In a 16-day guinea pig experiment, Suzuki et al.[21] observed a decrease in weight gain in guinea pigs administered only 1 mg AA/day as compared with those receiving 5 mg AA/day. In our present study, the data show that guinea pigs receiving 1 mg AA + 100 mg IAA had a higher rate of growth ($P < 0.05$) than controls or animals supplemented with 20 mg IAA. There were no significant differences in the rate of growth between controls and those animals supplemented with 20 mg IAA over the 42-day period. Differences in the response of growth from the three

Table 2 The influence of oral daily dosing with D-Isoascorbic acid (20 mg or 100 mg) on L-Ascorbic acid levels in plasma (μg/mL) and tissue (μg/g, fresh) of guinea pigs following a 42 days of administration

		Total AA		AA		DHAA	
Organ	Group	Mean	SD	Mean	SD	Mean	SD
adrenal	1	200.7[a]	±35.3	146.84[a]	±33.6	55.25[a]	±13.9
	2	137.6[b]	±39.9	116.13[b]	±36.4	21.49[bc]	±12.2
	3	86.0[c]	±18.8	73.85[c]	±17.9	12.22[c]	±4.8
brain	1	75.5[a]	±13.5	67.88[a]	±12.1	7.65[a]	±2.7
	2	51.6[b]	±10.6	48.07[b]	±10.4	3.53[bc]	±1.2
	3	32.9[c]	±3.7	30.73[c]	±3.8	2.24[c]	±0.8
heart	1	12.2[a]	±2.62	2.94[a]	±1.06	9.26[a]	±1.71
	2	7.93[b]	±3.17	2.32[ab]	±1.45	5.62[b]	±1.84
	3	4.29[c]	±0.90	1.47[b]	±0.68	2.83[c]	±0.52
kidney	1	17.86[a]	±2.97	11.16[a]	±4.43	6.71[a]	±4.49
	2	12.58[b]	±3.77	9.92[ab]	±3.99	2.66[bc]	±0.97
	3	6.39[c]	±1.63	5.25[c]	±1.46	1.15[c]	±0.66
liver	1	21.84[a]	±8.13	14.26[a]	±6.46	7.58[a]	±3.50
	2	10.58[bc]	±6.63	6.99[bc]	±6.52	3.60[bc]	±0.93
	3	5.26[c]	±3.04	2.89[c]	±2.78	2.37[c]	±0.80
lung	1	67.15[a]	±19.52	25.77[a]	±12.33	41.39[a]	±12.64
	2	50.49[b]	±16.09	23.93[ab]	±14.40	26.56[b]	±3.37
	3	23.14[c]	±6.77	12.03[c]	±5.00	11.11[c]	3.27
plasma	1	0.49[a]	±0.06	0.17[a]	±0.12	0.33[a]	±0.12
	2	0.38[b]	±0.09	0.18[a]	±0.10	0.20[bc]	±0.07
	3	0.25[c]	±0.06	0.10[a]	±0.09	0.15[c]	±0.06
spleen	1	91.1[a]	±14.48	32.39[a]	±21.44	58.80[a]	±14.21
	2	64.8[bc]	±17.88	26.56[a]	±14.92	38.32[bc]	±9.06
	3	55.7[c]	±22.22	22.82[a]	±16.29	32.98[c]	±9.17
thymus	1	31.20[a]	±17.52	4.39[a]	±7.22	26.82[a]	±13.18
	2	43.94[a]	±24.15	16.64[b]	±16.26	27.31[a]	±15.73
	3	21.88[a]	±15.97	6.67[ab]	±12.25	15.22[a]	±10.55

	DHAA/AA**		IAA		DHIAA		DHIAA/IAA**	
Organ	Mean	SD	Mean	SD	Mean	SD	Mean	SD
adrenal	0.40[a]	±0.14	—	—	—	—	—	—
	0.19[bc]	±0.09	131.01[a]	±59.7	37.39[a]	±33.30	0.30[a]	±0.18
	0.17[c]	±0.07	179.91[a]	±66.30	72.95[a]	±53.9	0.39[a]	±0.15
brain	0.11[a]	±0.037	—	—	—	—	—	—
	0.08[bc]	±0.030	34.14[b]	±11.7	3.39[b]	±1.14	0.10[a]	±0.03
	0.07[c]	±0.030	59.56[c]	±13.2	7.38[c]	±2.3	0.13[b]	±0.05
heart	3.52[a]	±1.44	—	—	—	—	—	—
	2.50[bc]	±0.73	1.62[a]	±1.29	4.34[a]	±2.23	2.39[a]	±0.61
	1.84[c]	±0.68	2.09[a]	±1.63	6.84[a]	±3.23	2.73[a]	±0.75
kidney	0.90[a]	±1.04	—	—	—	—	—	—
	0.33[bc]	±0.21	6.23[a]	±3.33	2.23[a]	±1.80	0.44[a]	±0.40
	0.24[c]	±0.16	9.49[a]	±5.12	2.77[a]	±2.05	0.32[a]	±0.22
liver	0.62[a]	±0.34	—	—	—	—	—	—
	1.42[a]	±1.94	2.42[a]	±2.47	1.82[a]	±0.98	1.20[a]	±0.85
	1.21[a]	±0.78	4.09[a]	±5.89	3.99[b]	±1.65	2.27[a]	±2.24
lung	2.28[a]	±1.77	—	—	—	—	—	—
	1.46[ac]	±0.72	15.80[a]	±12.70	19.69[a]	±7.33	1.65[a]	±0.71
	1.09[c]	±0.67	27.28[a]	±14.52	32.86[b]	±5.36	1.64[a]	±1.21
plasma	1.13[a]	±0.31	—	—	—		—	—
	0.81[bc]	±0.27	0.45[a]	±0.29	0.61[a]	±0.30	1.09[a]	±0.41
	0.60[c]	±0.26	0.74[b]	±0.33	0.79[a]	±0.44	1.09[a]	±0.33
spleen	3.50[a]	±4.05	—	—	—	—	—	—
	2.08[a]	±1.35	32.58[a]	±25.89	45.24[a]	±17.87	2.40[a]	±1.78
	2.21[a]	±1.36	15.84[a]	±13.50	21.93[b]	±7.58	2.56[a]	±1.81
thymus	5.85[a]	±5.02	—	—	—	—	—	—
	2.59[a]	±2.72	10.92[a]	±13.10	24.30[a]	±15.10	2.45[a]	±2.03
	2.35a	±1.54	4.45[a]	±7.87	39.42[a]	±43.48	15.70[b]	±11.81

Group 1 = 1 mg AA (control)
Group 2 = 1 mg AA + 20 mg IAA
Group 3 = 1 mg AA + 100 mg IAA
Results are means ± SD
n = 10 guinea pigs/group
AA = Ascorbic Acid
DHAA = Dehydroascorbic Acid
IAA = Isoascorbic acid
Total AA = Ascorbic acid + Dehydroascorbic acid
DHIAA = Dehydroisoascorbic acid
*Means for individual organs assigned different superscript letters within each column were significantly different ($P < 0.05$)
**Ratios for DHAA/AA and DHIAA/IAA were calculated from each corresponding animal, respectively, from which the means were derived.

dose groups cannot be explained by feed intake patterns as similar consumption ($P > 0.05$) were observed in the dose groups. It might be suggested that supplemental dosing with 100 mg IAA (group 3), provided additional "Vitamin C activity" resulting in an enhanced growth rate than dosing solely with a marginal amount of AA (1 mg AA). The different weight response observed in groups supplemented with 100 mg IAA compared with 20 mg IAA, could be explained that a greater amount of IAA was absorbed with the larger dose, which supported an increased growth rate. Previous studies have shown that normal growth of guinea pigs can be maintained by IAA, provided that a sufficiently high concentration of IAA is present in the tissues.[1,4] Similarly, Goldman et al.[22] and Pelletier and Godin[8] reported that in AA-deficient guinea pigs with body weight loss, administration of 100 mg IAA and 40 mg, respectively, were able to restore the growth of the animals and may be able to replace AA in its functions. However, Reif and Free[2] reported no effect on body weight loss in AA-deficient guinea pigs after administration with 100 mg IAA.

The same pattern of weight gain was reported by Arakawa et al.,[14] who stated that administration of IAA had antiscorbutic activity and decreased AA utilization in guinea pigs simultaneously administered with AA and IAA. Thus, as has been suggested, IAA supplementation in a considerable excess may be able to replace AA in the function of growth.[6]

As has been reported by Arakawa et al.,[14] the level of AA in the tissues of the guinea pigs administered both AA and IAA was always lower than in animals administered solely AA. The rate of disappearance of AA from the tissues of the IAA supplemented animals indicated that IAA may have a depressing effect on AA content. This is in agreement with a report by Arakawa et al.,[14] who postulated that a decreased tissue AA content may be caused either by IAA inhibition of AA absorption from the gastrointestinal tract or by IAA inhibition of AA transport through the tissue membrane or both. Further, these workers reported that the sum of AA and IAA in tissues of guinea pigs given 5 mg AA + 100 mg IAA was lower than the total AA in guinea pigs given only AA and suggested that AA is not replaced by IAA in the tissues and, at the same time, IAA may inhibit AA storage in the tissues. The difference in tissue content between the AA and IAA may be due to a difference in their retention mechanism in the tissues. This suggests that maybe IAA is being utilized in tissues and probably interferes in AA tissue storage in guinea pigs receiving marginal AA.

Our guinea pig data show that IAA supplementation at either 20 mg or 100 mg in combination with a marginal intake of AA, resulted in a marked depression in tissue AA levels compared with those animals receiving solely AA. In addition to this, IAA was substantially incorporated in the tissues. Our results are somewhat contradictory to an earlier guinea pig study by Suzuki et al.,[23] who examined the influence of oral dosing with IAA and a marginal AA intake (1 mg/day) upon vitamin C status. In that study, Suzuki et al.[23] observed a slight depression on AA tissue content as well as a relatively small incorporation of IAA after dosing with 1 mg AA plus 20 mg IAA to that reported in this present study. A partial explanation for the differences observed between our study and that of Suzuki et al.[23] could be related to the length of time of dosing with the two stereoisomers. Suzuki et al.[23] carried out their study for only 16 days, as compared with our 42-day period, which might have not allowed enough time to observe the changes in AA and IAA tissue status.

It is well established that DHAA exhibits some Vitamin C activity.[24,26] As suggested by Tolbert and Ward,[26] the activity of DHAA is about 70% and absorbed DHAA is probably as effective as AA in meeting nutritional needs. In the in vivo oxidation of AA, the first chemically stable product is DHAA. DHAA is part of the AA/DHAA-reducing/oxidizing couple, and it is known that DHAA to be reversibly converted to AA in animal tissues.[26] Our data suggests that IAA supplementation modified the redox state (dehydroascorbic acid/ascorbic acid) of Vitamin C in the tissues. However, in view of the paucity of data published on DHAA/AA in guinea pigs, it is difficult to interpret the results obtained from these ratios and are provided as observational. Although only speculative, the lowering of DHAA/AA observed in the tissues with IAA supplementation might indicate either a conservation or protection of AA stores perhaps through an enhanced conversion of the oxidized form of AA to its reduced state or alternatively an enhanced oxidation of DHAA to irreversible products. Future studies would be required to probe these potential scenarios. It is possible that DHIAA could alter tissue levels of DHAA or ratios of DHAA/AA, which might interfere with the metabolism of the cell and regulation of growth.[27]

In conclusion, the present data show that the administration of IAA, in conjunction with marginal AA intake, reduced the bioavailability of AA in guinea pig tissues. Moreover, the amount of IAA incorporation in the tissues was relatively high.

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