Journey at C: Vitamin C in the Body

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Ascorbic acid is vitamin C by definition: Only sources of ascorbic acid can cure scurvy.

Ascorbic acid is the oxidized form of ascorbic acid.

Sodium-dependent Vitamin C Transporters (SVCTs)
- Ascorbic Acid
  - Dehydroascorbic Acid (Oxidized form of Ascorbic Acid)
- Glucose Transporters (GLUTs)

Absorption and Vitamin C Transporters

Remember: There is a limit to vitamin C absorption!
Journey at C

Vitamin C from Circulation to Tissues

Plasma levels peak about 2 hours after a single dose.

Vitamin C is transported into tissues when plasma levels rise.


Journey at C

Vitamin C in Tissues

Note: Tissue ascorbic acid levels on this slide are hypothetical, but are driven by plasma vitamin C levels. As plasma levels increase, different tissues increase vitamin C levels at different rates. The brain is given priority at low vitamin C levels, while less essential organs are saturated with vitamin C only at higher blood ascorbic acid levels.

Journey at C

Vitamin C Urinary Excretion

Vitamin C levels decline in the plasma once kidney reuptake is saturated, which also means that more passes through to the urine.

Kidney reuptake is governed by an SVCT transport protein. Similar to the intestine, this protein can be saturated if too much vitamin C comes through.

Journey at C

Conclusions

- The body can only absorb a limited amount of vitamin C at one time
- All tissues take up vitamin C from the blood, but at different rates
- When the concentration of vitamin C in the kidneys is too high, it is lost into the urine

Vitamin C and Health

Understanding Vitamin C Status

These are cut-off values are the approximate, “steady-state” plasma ascorbate levels the can be achieved after continual ingestion of vitamin C (not just a single dose).

Adapted from Levine et al. PNAS 93:3704-3709, 1996

Vitamin C and Health

Ascorbic Acid is an Electron Donor

Vitamin C is more than an antioxidant!
Functions of Vitamin C
"Recycling" of vitamin C

One-Electron Reduction

Two-Electron Reduction

Vitamin C and Health
Enzyme Function Maximizes at Low Vitamin C Status

Vitamin C deficiency is very rare in developed countries but has been reported in older adults and children on limited diets, alcoholics, people on dialysis, or people with malabsorption issues (including gastric bypass surgery).

Vitamin C and Health
Prevention and Treatment of Scurvy

Loss of the 3 C’s

• Collagen (bleeding, bruising, poor wound healing, abnormal bone growth)
• Carnitine (low energy)
• Catecholamine (mood imbalance)

Low vitamin C can also affect peptide hormone synthesis, responses to hypoxia (low oxygen environments), and DNA methylation – it is not clear how these changes would manifest.

Vitamin C and Health
Vitamin C Status Determines Risk for Disease

Health benefits are often observed when moving from one status category to the one above.

Vitamin C in the Gastrointestinal Tract

Iron Absorption
• Vitamin C can be an effective anemia treatment as it assists the uptake of iron

Nitrates
• Vitamin C can prevent damaging effects from excess dietary nitrates that may result in cancers of the throat and stomach

Effects on gut health and the microbiome
• Large doses of vitamin C can impact gut bacteria, but the health benefits of this are not yet known

Adapted from Levine et al. PNAS 93(37):3704-3709, 1996
Vitamin C and Health
Vitamin C Status Determines Risk for Disease

“Optimal” plasma status means that taking more vitamin C has little effect on plasma levels. It is observed in many people at doses about 200-400 mg/day

The LPI recommends 400 mg/day of vitamin C, enough for most people to achieve optimal vitamin C status

Adapted from Levine et al. PNAS 93:3704-3709, 1996

Vitamin C and Health
Vitamin C as an Antioxidant

- Vitamin C is an outstanding antioxidant:
  - It can react with a wide range of oxidants
  - It is non-toxic or damaging in radical form
  - It can also interact with other antioxidants in the body (like vitamin E, urate, and glutathione).

Vitamin C and Health
Vitamin C as an Plasma Antioxidant

When blood plasma is exposed to an oxidant, vitamin C levels decline first before all other antioxidants present in the blood. Only after vitamin C has been used up does lipid oxidation occur.

Adapted from Frei et al. PNAS 85: 9748-9752 (1988)

Vitamin C and Health
Vitamin C Plays Many Roles in Health

Cardiovascular Immune Function Cancer
Eye Health Diabetes Cognitive Decline

See more at lpi.oregonstate.edu/mic/vitamins/vitamin-C

Vitamin C and Health
Effects Associated with High Vitamin C Status

Many associations are with fruit and vegetable intake (more than just vitamin C!)

Antioxidant functions are assumed for vitamin C, but other mechanisms may exist.

Need more high-quality clinical research trials!
And for that we need more funding!

Vitamin C and Health
Conclusions

- Vitamin C status is important.
- Vitamin C is an electron donor that:
  - Helps run enzymes efficiently.
  - Adds to antioxidant protection.
  - May have other effects not yet discovered.
Getting your Vitamin C

Optimal Vitamin C Status has the Lowest Risk for Disease

[Graph showing optimal, suboptimal, and malnourished blood ascorbic acid levels]

Adapted from Leavitt et al. PNAS 93:3704-3709, 1996

Inadequacy
Suboptimal
Optimal

Getting Your Vitamin C

Daily Recommendations

<table>
<thead>
<tr>
<th>Dietary Group</th>
<th>Recommendations (mg/day)</th>
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<tbody>
<tr>
<td>Infants 0-6 mo</td>
<td>35</td>
</tr>
<tr>
<td>7-12 mo</td>
<td>40 (A)</td>
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<td>15</td>
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<tr>
<td>Lactating</td>
<td>130</td>
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</tbody>
</table>

The upper limit (UL) set by the Institute of Medicine is 2000 mg/day for reports of intestinal issues

*Smokers need 35 mg/day more

Getting Your Vitamin C

Do the Recommendations Fit Everyone?

[Graph showing different curves for smokers, older adults, diabetics, and alcoholics]

Curves can differ for different people
- Smokers
- Older Adults
- Diabetics
- Alcoholics

Getting Your Vitamin C

Sources

- Fresh fruits and vegetables
- Vitamin C additions to packaged foods
- Supplements, alone or in multivitamins
- When cooking or storing, be aware that vitamin C is degraded over time by heat, light, oxygen, and active plant enzymes.
- Vitamin C can be preserved longer in cold storage and with acid.

Getting your Vitamin C

Food Sources of Vitamin C

- Juices
  - 60-90 mg per 6 fl. oz. orange juice
  - 50-70 mg per 6 fl. oz. grapefruit juice
  - 30-35 mg per 6 fl. oz. tomato juice

- Fruits
  - ~180 mg per papaya (304 g)
  - ~70 mg per kiwi fruit (76 g)
  - 35-50 mg per 1/2 cup pineapple, papaya, oranges, or strawberries

- Vegetables
  - ~90-150 mg per sweet pepper, green or red (119 g)
  - ~60-110 mg per hot pepper, green or red (45 g)
  - 35-50 mg per 1/2 cup broccoli, Brussels sprouts, kohlrabi, or edible pod peas

Data from U.S. Department of Agriculture / Agricultural Research Service (USDA / ARS) (2009)
**Vitamin C and Health**

*Vitamin C Supplements*

No vitamin C supplement has been proven to be more bioavailable than ascorbic acid alone!

**Getting Your Vitamin C**

*Changing Vitamin C Status*

We recommend 3-4 weeks of taking vitamin C at a certain dose before achieving lasting changes in vitamin C plasma status.

**Getting Your Vitamin C**

*Regimen for Maximizing Vitamin C Status*

This is a hypothetical situation – it represents a person who has been taking vitamin C for a long period of time (plasma levels are high), who takes one or more additional supplements.

In either case, supplements result in a temporary increase in plasma vitamin C levels. After supplementation stops, vitamin C levels in the body return to the “steady-state” that is determined by the kidney. There is no proven benefit to continuous dosing with vitamin C to maintain high plasma status throughout the day. However, many continue to follow this type of regimen without harm.

**Vitamin C Myths**

**Myth:** “Vitamin C is toxic at high doses”

*Reality:* High doses of vitamin C are generally safe. The most common reported side-effects are bloating, gas, diarrhea, and intestinal discomfort that is often temporary.

**Vitamin C Myths**

**Myth:** “Taking vitamin C supplements leads to kidney stones”

*Reality:* Many individuals have taken large doses of vitamin C without reports of kidney stones. However, those with a history of kidney stone formation might want to limit their vitamin C intake to under 1000 mg/day.
Vitamin C Myths

Myth: “Vitamin C can cure the common cold”

Reality: Taking vitamin C after you already have a cold appears to have little, if any, effect. However, taking vitamin C before a cold (long enough to change your vitamin C status; 3-4 weeks) does seem to reduce cold incidence.

Vitamin C Myths

Myth: “There is no benefit to taking large (megadose) vitamin C”

Reality: This theory posed and practiced by Linus Pauling has not been tested. Although the entirety of a large dose of vitamin C will not enter the body, high levels could still have an impact on the gastrointestinal tract and gut bacteria that could result in beneficial health effects.

Vitamin C Myths

Myth: “We have learned everything about vitamin C already – there is nothing new to discover”

Reality: We learn new things about vitamin C all the time, but the research is not currently well funded. Many dismiss vitamin C as being unimportant, and for many reasons this slows research progress.

Vitamin C Myths

Myths: “Research on vitamin C in animals or cell culture is the same as giving vitamin C to people”

Reality: Ascorbic acid is not a vitamin for most animals, so much of the research in those models (like mice and rats) is questionable. Cell culture papers with vitamin C are also very hard to interpret. If you have any questions about a study, it is best to contact an expert in the field.

Vitamin C Myths

Myth: “Vitamin C has no role in cancer therapy”

Reality: We do not yet know the true potential of vitamin C as a cancer therapy. Intravenous vitamin C has shown some cancer fighting properties, and even oral vitamin C can improve cancer patient quality of life.

Functions of Vitamin C

$H_2O_2$ Production by High IV Doses
Helpful Websites

Micronutrient Information Center (MIC):
http://lpi.oregonstate.edu/mic/vitamins/vitamin-C

http://lpi.oregonstate.edu/mic/micronutrients-health/skin-health/nutrient-index/vitamin-C

http://lpi.oregonstate.edu/mic/vitamins/vitamin-C/supplemental-forms