REFERENCE SHEET:

Vitamin C

Pronunciation

Vitamin C (ascorbic acid, ah-score-bick ah-syd)

Summary

Vitamin C is an essential, water-soluble vitamin. It is well-known for its antioxidant properties and ability to reduce free radicals by donating electrons through reduction reactions. The discovery of vitamin C has been attributed to the treatment of scurvy in sailors and the potato famine in Ireland. Administration of approximately 0.01 grams per day can prevent scurvy. In the North American diet, some of the highest concentrations of vitamin C are present in citrus juices, fruit, and a variety of vegetables.

Main Medical Uses

Evidence exists for the use of vitamin C in the treatment of many conditions. Vitamin C administration has been used in atrial fibrillation, the common cold, complex regional pain syndrome, cardiovascular conditions, gout, osteoarthritis, cataracts, blood pressure regulation, glycemic control, upper respiratory tract infections, and inflammation. It is an adjuvant used to prevent and treat iron deficiencies and tyrosinemia. There is mixed evidence for its use in physical and exercise performance.

Dosing and Administration

The Recommended Dietary Allowance (RDA) of vitamin C for adults is 75 mg per day for females and 90 mg per day for males. It is recommended that smokers increase their intake by an additional 35 mg per day. The optimal intake for the majority of the adult population, without increasing risk of inadequacy or adverse effects, is 200 mg per day.

Condition	Dosing & Administration	Outcome	Class of Evidence
Post Operative Atrial Fibrillation	2.0 g pre-op + 1.0-2.0 g post-op	↓ risk of AF	A
Common Cold	1.0 g per day	↑ immunity	A
	1.0-2.0 g per day	↓ duration, severity	A
	3.0-4.0 g per day	↑ recovery	A
Complex Regional Pain Syndrome	0.5 g per day	↓ risk CRPS after fracture	A
	1.0 g per day	↓ risk CRPS after surgery	A
	2.0 g per day	↓ post-operative morphine consumption	A
Gout	0.5 g per day	↓ serum uric acid	A
Blood Pressure	0.5 g per day	↓ systolic & diastolic BP	A
Osteoarthritis	1.0 g per day	↓ pain	B

For an explanation of the classes of evidence, please see the Rating Scales for Evidence-Based Decision Support.

Adverse Effects

Vitamin C is considered to be safe and tolerable. Exceeding the Tolerable Upper Intake Level (UL) of 2000 mg per day for adults can lead to gastrointestinal disturbances and osmotic diarrhea. The daily UL for children aged 1 to 3 is 400 mg, aged 4 to 8 is 650 mg, and aged 9 to 13 is 1800 mg.

Forms

Form	Dose	Effects	Class of Evidence
Natural/Food	Equal bioavailability to supplemental sources in humans	Equal bioavailability to supplemental sources in humans	D
Ascorbic Acid (AA)			
Unformulated	Safe for general population up to 2.0 g doses	See Dosing & Administration	A
	Single 0.2 g dose produces a plateau in plasma concentration, with little effect of higher doses	↑ doses increased oxalate & urate excretion. Neutrophils, monocytes, & lymphocytes saturated at 100 mg	D
Sustained-Release Formulation	0.25 g twice per day increased plasma reduced AA 54% after two months compared with 32% of ascorbic acid	↑ malondialdehyde (MDA) formation; no effect on lipid peroxidation	D
	Single 0.50 g dose with a disintegration time of 60 mins produced the highest bioavailability	↑ AA absorption especially in 60 min disintegration tablet	D
	Single 1.0 mg dose	↑ plasma concentration by 180% compared to AA	D
Vitamin C with Bioflavonoids	200 ml orange juice (OJ) 3x per day for 4 weeks (vitamin C +phytonutrients)	OJ led to an antioxidant effect correlated with plasma hesperetin and decrease in ROS	C
	0.50 g for two weeks	No difference in bioavailability with AA	D

Form	Dose	Effects	Class of Evidence
Buffered/Mineral Ascorbates			
Calcium Ascorbate (CA)	1.0 g Ester-C® for 3 days	↑ tolerability rating, ↓ adverse events	B
	Ester-C® (no dose)	↑ bioavailability compared with AA	D
	0.44 mg/kg per day of Ester-C® for 24 days	↑ weight gain, ↓ scorbutic signs in Osteogenic Disorder Shionogi compared with AA	D
	1.0 g CA for two weeks	↓ osteoarthritic pain	B
	Single 1.0 g dose CA	↑ the concentration of AA in leukocytes compared with unformulated	C
	Single 100 mg/kg CA	↑ 150% in AUC compared with AA; similar ↑ in antioxidant activity without high gastric acidity	D
	Unspecified	↓ expression of NF κ B, CRP, TNF- α, IL-1 β & IL-6; ↑ expression of the anti-inflammatory cytokines, IL-4 & IL-10	D
Sodium Ascorbate (SA)	Topical SA (10% concentration for 6 months	↓ dark circles of the lower eyelid by increasing dermal thickness	D
Magnesium Ascorbate (MA) & Potassium Ascorbate (PA)	No available evidence.	No available evidence.	n/a
Liposomal	Single 4.0 g dose of liposomal-encapsulated AA	↑ bioavailability compared with AA and placebo, ↑ protection from ischemia-reperfusion mediated oxidative stress	D
	Proliposomal formulation	↑ vitamin C release reliability (compared with regular liposomal formulation), antioxidant activity, ↓ MDA	E
Ascorbyl Palmitate	Ascorbyl palmitate (no dose)	↑ bioavailability compared with AA	D

Mechanism of Action and Metabolism

The main functions of ascorbic acid occur by substrate reduction. As it donates electrons, ascorbic acid becomes a free but stable, ascorbyl radical. Two molecules of this newly formed radical can then be simultaneously reduced to form ascorbate or oxidized to form dehydroascorbic acid (DHA).

Action	Mechanism
Ascorbate	↑ cellular viability, extracellular substrate reduction, vasorelaxation, synthesis of collagen, carnitine, and enzymes of iron homeostasis ↑ immune system via accumulation in lymphocytes, monocytes and neutrophils, maintaining bacterial activity of phagocytes, in maintaining neutrophil clearance and apoptosis, in increasing IL-12p70 in lipopolysaccharide-induced dendritic cells, in increasing lymphocyte levels, in increasing resistance to apoptosis via T cells, in decreasing TH17 and Th2 cytokine secretion, in increasing IL-17 in TH17 cells, in maturing T cells, in increasing NK cell expression, and in stabilizing Foxp3 expression ↓ glutathione and vitamin E oxidation, free radicals, reactive oxygen and nitrogen species
DHA	↓ glucose transporter, hexokinase, glyceraldehyde-3-phosphate dehydrogenase, and glucose-6-phosphate dehydrogenase activity ↑ synthesis of NADPH and glutathione, killing of cells susceptible to oxidative stress and be recycled ascorbic acid as needed

Vitamin C is absorbed by the lumen in the small intestine, as well as by renal tubules through sodium-dependent vitamin C transporters for ascorbate. These transporters are located throughout the body and promote cellular accumulation of ascorbate. Similarly, ascorbate that is oxidized to DHA outside of cells can be transported through GLUT1 and GLUT 3 transporters, which are also widely distributed throughout the body. While renal reabsorption of vitamin C occurs, the precise mechanism of efflux in the kidney is yet to be.

Associated Interactions

Class of Drug	Vitamin C Dose	Effect	Class of Evidence
β-blockers, Statins	Unspecified	↓ Post-Operative Atrial Fibrillation risk, intensive care unit length of stay, hospital length of stay, adverse event risk	A
β-blockers (atenolol, propranolol, or metoprolol)	2.0 g pre-op, 1.0 g 2x per day post op for 5 days	↓ Post-Operative Atrial Fibrillation risk	B
Statins (atorvastatin)	2.0 g pre-op, 1.0 g per day post-op	↓ Post-Operative Atrial Fibrillation risk	B
Iron Chelators (deferoxamine, deferiprone or deferasirox)	0.10 g per day	↓ transfusion index, serum iron, serum ferritin, transferrin saturation (Tsat), & liver iron concentration ↑ hemoglobin and cardiac MRI T2	B