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Vitamin C

Updated: July 27, 2017.

OVERVIEW

Introduction

Vitamin C (ascorbic acid) is a water soluble vitamin found in citrus fruits and green vegetables and deficiency of which is the cause of scurvy. There is no evidence that vitamin C, in physiologic or in moderately high doses, causes acute liver injury or jaundice.

Background

Vitamin C is a water soluble vitamin known chemically as L-ascorbic acid (as kore' bik as' id). The major role of ascorbic acid is as an electron donor and intracellular antioxidant protecting critical intracellular molecules and enzymes systems against reactive oxygen species. Vitamin C also plays a role as a cofactor in many biochemical synthetic reactions, in collagen cross linking, the synthesis of neuropeptides and hormones, and in non-heme iron absorption. Vitamin C is found in many foods, particularly citrus fruits, green vegetables, tomatoes and potatoes. The recommended daily allowance of vitamin C is 90 mg in adult men and 70 mg in women, an amount that is provided by most American diets. Intakes of more than 2 grams daily are considered excessive and should be avoided. Vitamin C deficiency is the cause of scurvy which is marked by fatigue, spongy gums, loss of teeth, ecchymosis, petechiae and excessive bleeding including bleeding from the gums, into joints and into internal organs. Scurvy is now rare in the developed world, seen predominantly with severe malnutrition and chronic alcoholism. Vitamin C is available in many over-the-counter forms in concentrations ranging from 25 to 1000 mg and is a component of virtually all multivitamins, typically in concentrations of 60 to 180 mg. Parenteral formulations are available for administration with parenteral nutrition. Despite many claims, there is no convincing evidence that vitamin C supplementation decreases the rate of cancer, heart attacks or strokes or prevents common colds or other viral infections. Physiologic and even excessive intakes up to 2 grams daily have virtually no side effects. Higher doses of vitamin C can be associated with diarrhea, nausea, abdominal discomfort, flushing, dizziness and headache and may be associated with transient serum aminotransferase elevations.

Hepatotoxicity

Neither normal nor moderately high intakes of vitamin C are associated with liver injury or liver test abnormalities. In long term clinical trials, serum enzyme and bilirubin elevations were no more frequent with vitamin C therapy than with placebo. Indeed, in many animal models, vitamin C is protective against hepatotoxic substances and provides antioxidant and cytoprotective activity to hepatocytes. Single large doses of vitamin C, however, can cause symptoms of nausea, abdominal pain and diarrhea and higher doses have been reported to result in serum ALT elevations, but not to clinically apparent liver injury with jaundice.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Mechanism of Injury

The serum ALT elevations that occur with extremely high doses of vitamin C are likely due to a direct but minimal toxic effect on the liver. The injury is, however, short lived and has not been linked to cases of acute or chronic hepatitis, acute liver failure or cirrhosis.

Drug Class: Vitamins

Other Drugs in the Class: Vitamin A, Vitamin B, Vitamin D, Vitamin E, Vitamin K, Folate, Niacin

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Vitamin C – Generic, Combination Products

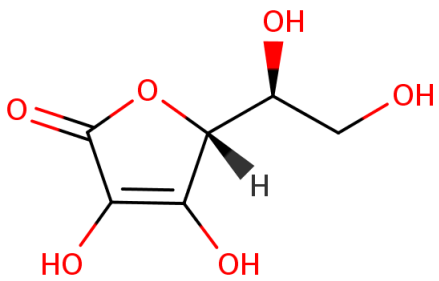
DRUG CLASS

Vitamins

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO	MOLECULAR FORMULA	STRUCTURE
Ascorbic Acid	50-81-7	C6-H8-O6	

ANNOTATED BIBLIOGRAPHY

References updated: 27 July 2017

Zimmerman HJ. Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999.

(Expert review of hepatotoxicity published in 1999; does not discuss vitamin C).

Seeff L, Stickel F, Navarro VJ. Hepatotoxicity of herbals and dietary supplements. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013: pp, 631-57.

(Review of hepatotoxicity of dietary supplements; does not discuss vitamins and minerals).

Jacob RA. Vitamin C. In, Shils ME, Olson JA, Shike M, Ross AC, eds. Modern nutrition in health and disease. 9th ed. Baltimore: Williams & Wilkins, 1998; pp 467-484.

(Textbook of nutrition).

Food and Nutrition Board, Institute of Medicine. DRI dietary reference intakes: for vitamin C, vitamin E, selenium and carotenoids. Washington DC: National Academy Press, 1998.

(Reports from the Food and Nutrition Board of the Institute of Medicine on dietary reference values for vitamin C intake, replacing the previously published Recommended Dietary Allowances).

Vitamin C. Available at: https://ods.od.nih.gov/factsheets/VitaminC-HealthProfessional/

(Fact sheet on vitamin C maintained and regularly updated by the Office of Dietary Supplements, National Institutes of Health).

Dykes MH, Meier P. Ascorbic acid and the common cold. Evaluation of its efficacy and toxicity. JAMA 1975; 231: 1073-9. PubMed PMID: 1089817.

(Review of the literature on the safety and efficacy of high doses of vitamin C in prevention and treatment of the common cold found little or no evidence of either efficacy or significant toxicity).

Rivers JM. Safety of high-level vitamin C ingestion. Ann N Y Aca Sci 1987; 498: 445-54. PubMed PMID: 3304071.

(Review of literature on toxicity of high doses of vitamin C focusing on calcium-oxalate stones, uric acid excretion, iron overload and increased mutagenic activity; no mention of ALT elevations or hepatotoxicity).

Bendich A, Langseth L. The health effects of vitamin C supplementation: a review. J Am Coll Nutr 1995; 14: 124-36. PubMed PMID: 7790686.

(The safety of higher doses of vitamin C has been shown in 8 placebo controlled trials).

Levine M, Rumsey SC, Daruwala R, Park JB, Wang Y. Criteria and recommendations for vitamin C intake. JAMA 1999; 281: 1415-23. PubMed PMID: 10217058.

(Review of the role of vitamin C in metabolic pathways, its absorption and pharmacokinetics, adverse events and beneficial dose effects).

Shekelle P, Morton S, Hardy ML. Effect of supplemental antioxidants vitamin C, vitamin E, and coenzyme Q10 for the prevention and treatment of cardiovascular disease. Evid Rep Technol Assess (Summ) 2003; (83): 1-3. PubMed PMID: 15040141.

(A systematic review of four placebo controlled trials of vitamin C for its effects in decreasing the rate of cardiovascular disease showed no evidence of benefit, but also no evidence for toxicity of vitamin C).

Shekelle P, Hardy ML, Coulter I, Udani J, Spar M, Oda K, Jungvig LK, et al. Effect of the supplemental use of antioxidants vitamin C, vitamin E, and coenzyme Q10 for the prevention and treatment of cancer. Evid Rep Technol Assess (Summ) 2003; (75): 1-3. PubMed PMID: 15523748.

(A systematic review of placebo controlled trials of vitamin C for its effects in decreasing the rate of cancer showed no evidence of benefit, but also no evidence for toxicity of vitamin C).

Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology 2010; 52: 2065-76. PubMed PMID: 20949552.

(Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 were attributed to drug induced liver injury, but none were attributed to vitamins including vitamin C).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al.; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology 2015; 148: 1340-1352. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, 7 were attributed to niacin, but none were attributed to any other vitamin including vitamin C).