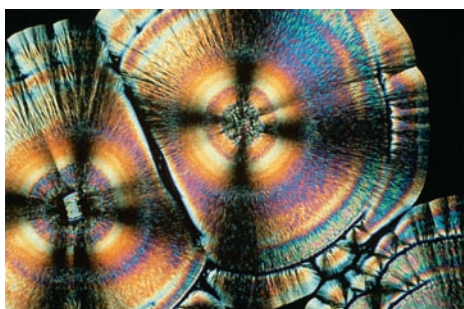


# Vitamin C



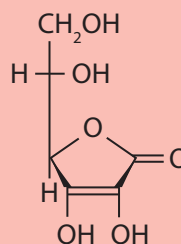
Vitamin C crystals in polarised light

## Synonyms

Ascorbic acid, hexuronic acid, anti-scorbutic vitamin

## Chemistry

L-ascorbic acid (2,3-endiol-L-gulonic acid- $\gamma$ -lactone), dehydro-L-ascorbic acid (2-oxo-L-gulonic acid-  $\gamma$ -lactone).



Molecular formula of vitamin C

## Introduction

Vitamin C is water-soluble, and probably the most famous of all the vitamins. Even before its discovery in 1932, physicians recognised that there must be a compound in citrus fruits preventing scurvy, a disease that killed as many as 2 million sailors between 1500 and 1800. Later researchers discovered that man, other primates and the guinea pig depend on external sources to cover their vitamin C requirements. Most other animals are able to synthesise vitamin C from glucose and galactose in their body.

## Functions

The most prominent role of vitamin C is its immune stimulating effect, which is important for the defence against infections such as common colds. It also acts as an inhibitor of histamine, a compound that is released during allergic reactions. As a powerful antioxidant it can neutralise harmful free radicals and aids in neutralising pollutants and toxins. Thus it is able to prevent the formation of potentially carcinogenic nitrosamines in the stomach (due to consumption of nitrite-containing foods, such as smoked meat). Importantly, vitamin C is also able to regenerate other antioxidants such as vitamin E. Vitamin C is required for the synthesis of collagen, the intercellular “cement” substance which gives structure to muscles, vascular tissues, bones, tendons and ligaments. Due to these functions vitamin C, especially in combination with zinc, is important for the healing of wounds. Vitamin C contributes to the health of teeth and gums, preventing haemorrhaging and bleeding. It also improves the absorption of iron from the diet, and is needed for the metabolism of bile acids, which may have implications

for blood cholesterol levels and gallstones. In addition, vitamin C plays an important role in the synthesis of several important peptide hormones and neurotransmitters and carnitine. Finally, vitamin C is also a crucial factor in the eye's ability to deal with oxidative stress, and can delay the progression of advanced age-related macular degeneration (AMD) and vision-loss in combination with other antioxidant vitamins and zinc.

### Main functions in a nutshell:

- Immune stimulation
- Anti-allergic
- Antioxidant
- “Cement” for connective tissues
- Wound healing
- Teeth and gum health
- Aids iron absorption
- Eye health

## Dietary sources

Vitamin C is widely distributed in fruits and vegetables. Citrus fruits, blackcurrants, peppers, green vegetables (e.g. broccoli, Brussels sprouts), and fruits like strawberries, guava, mango and kiwi are particularly rich sources. On a quantity basis, the intake of potatoes, cab-

bage, spinach and tomatoes is also of importance. Depending on the season, one medium-sized glass of freshly pressed orange juice (i.e. 100 g) yields from 15 to 35 mg vitamin C.

## Absorption and body stores

Intestinal absorption of vitamin C depends on the amount of dietary intake, decreasing with increasing intake levels. At an intake of 30 to 180 milligrams, about 70% to 90% is absorbed; about 50% of a single dose of 1 to 1.5 grams is absorbed; and only 16% of a single dose of 12 grams is absorbed. Up to about 500 milligrams are absorbed via a sodium-dependent active transport process, while at higher doses simple diffusion occurs.

The storage capacity of water-soluble vitamins is generally low compared to that of fat-soluble ones. Humans have an average tissue store of vitamin C of 20 mg/kg body weight. The highest concentration is found in the pituitary gland (400 mg/kg); other tissues of high concentration are the adrenal glands, liver, brain and white blood cells (leukocytes).

### Vitamin C content of foods

Food	Vitamin C (mg/100g)
Acerolas	1600
Blackcurrants	200
Peppers	138
Broccoli	115
Fennel	95
Kiwis	71
Strawberries	64
Oranges	49

(Souci, Fachmann, Kraut)

## Measurement

Vitamin C can be measured in the blood plasma and other body tissues by various techniques. Also dipstick tests for estimation of vitamin C levels in the urine are available. Less satisfying, however, is the evaluation of the analytical data concerning the true reflection of the body status. Threshold values are difficult to define and the subject of controversial discussion. Typical blood plasma levels are in the range of 20 to 100 μmol/L.

## Stability

Vitamin C is sensitive to heat, light and oxygen. In food it can be partly or completely destroyed by long storage or overcooking. Refrigeration can substantially diminish vitamin C loss in food.

### Influence of storage and preparation on vitamin C loss in foods

Food	Storage/Preparation	Vitamin C Loss
Potatoes	1 month	50%
Fruit	1 month	20%
Apples	6-9 months	100%
Milk	UHT	25%
Fruit	Sterilisation	50%
Fruit	Air drying	50-70%
Leafy vegetables	Canning	48%

Modified from Oberbeil, Fit durch Vitamine, Die neuen Wunderwaffen, Südwest Verlag GmbH & Co. KG, München 1993

sants, diuretics, birth control pills and aspirin, deplete the tissues of vitamin C. This is also true of certain habits, for example alcohol consumption.

## Deficiency

Early symptoms of vitamin C deficiency are very general and could also indicate other diseases. They include fatigue, lassitude, loss of appetite, drowsiness and insomnia, feeling run-down, irritability, low resistance to infections and petechiae (minor capillary bleeding). Severe vitamin C deficiency leads to scurvy,

characterised by weakening of collagenous structures, resulting in widespread capillary bleeding. Infantile scurvy causes bone malformations. Bleeding gums and loosening of the teeth are usually the earliest signs of clinical deficiency. Haemorrhages under the skin cause extreme tenderness of extremities and pain during movement. If left untreated, gangrene and death may ensue. Nowadays this is rare in developed countries and can be prevented by a daily intake of about 10-15 mg of vitamin C. However, for optimal physiological functioning much higher amounts are required.

### The development of vitamin C deficiency can be caused by:

- Inadequate storage and preparation of food
- Gastrointestinal disturbances
- Stress and exercise
- Infections
- Smoking
- Diabetes
- Pregnancy and lactation

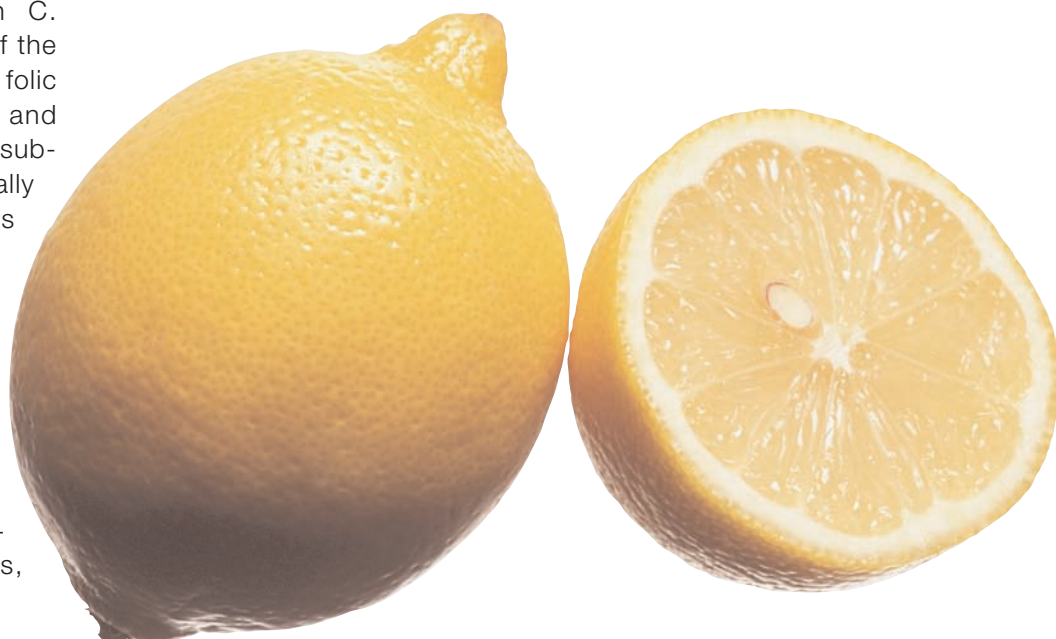
## Interactions

### Positive interactions

The presence of other antioxidants, such as vitamin E and beta-carotene, supports the protective antioxidant action of vitamin C. Other vitamins, such as those of the B-complex (particularly B<sub>6</sub>, B<sub>12</sub>, folic acid and pantothenic acid) and some pharmacologically active substances, as well as the naturally occurring compounds known as bioflavonoids, may have a sparing effect on vitamin C.

### Negative interactions

Due to toxic compounds in smoke, the vitamin C requirement for smokers is about 35 mg/day higher than for non-smokers. Also several pharmacologically active compounds, among them some anti-depres-



## Disease prevention and therapeutic use

Dozens of prospective studies suggest that vitamin C plays a role in preventing a variety of diseases. It is also used to treat certain diseases in orthomolecular medicine. As this nutrient is important for a variety of diseases, only a selection of them are presented here in detail.

### Cardiovascular diseases (CVD) (heart disease and stroke)

The data for the CVD protective benefits of vitamin C are inconsistent. While some studies have failed to find significant reductions in the risk of coronary heart disease (CHD), numerous prospective cohort studies have found inverse associations between dietary vitamin C intake or vitamin C plasma levels and CVD risk. Vitamin C may protect coronary arteries by reducing the build-up of

plaque, as this helps to prevent the oxidation of LDL cholesterol (the “bad” cholesterol), especially in combination with vitamin E. Some data has shown that vitamin C may also boost blood levels of HDL cholesterol (the “good” cholesterol), which is also considered positive for the prevention of heart diseases. The risk of stroke may be reduced by an adequate intake of vitamin C through fruits, vegetables and supplements. However, due to the inconsistency of the data and its lack of specificity to vitamin C, the interpretation of these results is difficult.

### Cancer

The role of vitamin C in cancer prevention has been studied extensively, and until now no beneficial effect has been shown for breast, prostate, or lung cancer. However, a number of studies have associated higher intakes of vitamin C with decreased incidence of cancers of the upper digestive tract, cervix, ovary, bladder, and colon. Studies finding significant cancer risk reduction by dietary intake recommended at least 5 servings of fruits and vegetables per day. Five servings of most fruits and vegetables provide more than 200 mg vitamin C per day. Just significant cancer risk reductions were found in people consuming at least 80 to 110 mg of vitamin C daily.

### Common cold

Numerous studies have shown a general lack of effect of prophylactic vitamin C supplementation on the incidence of common cold, but they do show a moderate benefit in terms of the duration and severity of episodes in some groups, especially those who are exposed to substantial physical and/or cold stress. The improve-

ment in severity of colds after vitamin C supplementation may be due to the antihistaminic action of mega doses of vitamin C.

### Wound healing

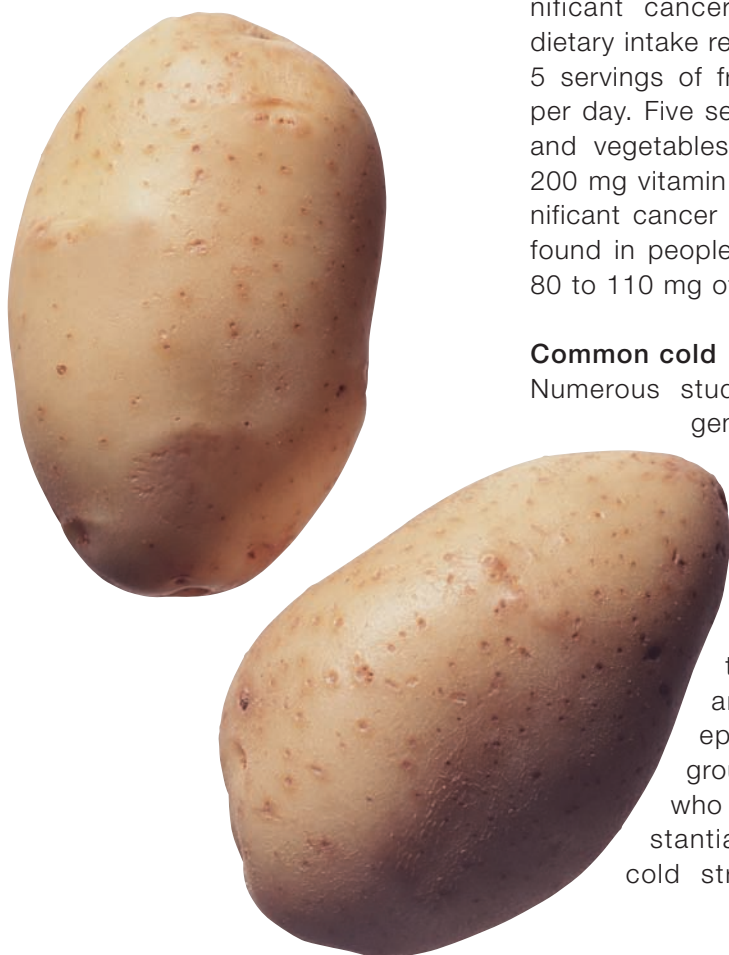
During a postoperative period, or during healing of superficial wounds, supplemental vitamin C contributes to the prevention of infections and promotes skin repair.

### Blood pressure

Several studies have shown a blood pressure lowering effect of vitamin C supplementation at about 500 mg per day due to improved dilation of blood vessels.

## Recommended Dietary Allowance (RDA)

The recommended daily intake of vitamin C varies according to age, sex, risk group and criteria applied in individual countries. The RDAs in the USA for vitamin C were recently revised upwards to 90 mg/day for men and 75 mg/day for women, based on pharmacokinetic data. For smokers, these RDAs are increased by an additional 35 mg/day. Higher amounts of vitamin C are also recommended for pregnant (85 mg/day) and lactating women (120 mg/day). The RDAs are in a similar range in other countries. Recent evidence sets the estimate for the maintenance of optimal health in the region of 100 mg daily.



## Safety

As much as 6-10 g vitamin C per day (more than 100 times the RDA) has been ingested regularly by many people with no evidence of side effects. Although a number of possible problems with very large doses of vitamin C have been suggested, none of these adverse health effects have been confirmed, and there is no reliable scientific evidence that large amounts of vitamin C (up to 10 g/day in adults) are toxic. In the year 2000 the US Food and Nutrition Board recommended a tolerable upper intake level (UL) for vitamin C of 2 g (2,000 mg) daily in order to prevent most adults from experiencing osmotic diarrhoea and gastrointestinal disturbances.

## Supplements and food fortification

Vitamin C is offered in conventional tablets, effervescent and chewable tablets, time-release tablets, syrups, powders, granules, capsules, drops and ampoules, either alone or in multivitamin-mineral preparations. Buffered vitamin C forms are less acidic, which can be an advantage in terms of preventing gastric irritation. Vitamin C can also be used in the form of injections (Rx). A number of fruit juices, fruit flavour drinks and breakfast cereals are enriched with vitamin C. On average in Europe, vitamin C supplements provide between 5.8% and 8.3% of total vitamin C intake.

## Uses in food technology

The food industry uses ascorbic acid as a natural antioxidant. This means that ascorbic acid, added to food-stuffs during processing or prior to packing, preserves colour, aroma and nutrient content. This use of ascorbic acid has nothing to do with its vitamin action. In meat processing, ascorbic acid makes it possible to reduce both the amount of added nitrite and the residual nitrite content in the product. The addition of ascorbic acid to fresh flour improves its baking qualities, thus saving the 4-8 weeks of maturation flour would normally have to undergo after milling.

## Industrial production

The synthesis of ascorbic acid was achieved by Reichstein in 1933, and this was followed by industrial production five years later by Hoffman La Roche Ltd. (the vitamin division of which is now DSM Nutritional Products Ltd.). Today synthetic vitamin C, identical to that occurring in nature, is produced from glucose on an industrial scale by chemical and biotechnological synthesis.

### Current recommendations in the USA

#### Dietary Reference Intakes\*

Infants	< 6 months	40mg (Adequate Intake, AI)
Infants	7-12 months	50mg (AI)
Children	1-3 years	15mg
Children	4-8 years	25mg
Children	9-13 years	45mg
Males	14-18 years	75mg
Females	14-18 years	65mg
Males	> 19 years	90mg
Females	> 19 years	75mg
Pregnancy	< 18 years	80mg
Pregnancy	> 19 years	85mg
Lactation	< 18 years	115mg
Lactation	> 19 years	120mg

\*The Dietary Reference Intakes (DRIs) are actually a set of four reference values: Estimated Average Requirements (EAR), Recommended Dietary Allowances (RDA), Adequate Intakes (AI), and Tolerable Upper Intake Levels, (UL) that have replaced the 1989 Recommended Dietary

Allowances (RDAs). The RDA was established as a nutritional norm for planning and assessing dietary intake, and represents intake levels of essential nutrients considered to meet adequately the known needs of practically all healthy people

## History

**Ca.**

- 400 BC** Hippocrates describes the symptoms of scurvy.
- 1747** British naval physician James Lind prescribes oranges and lemons as a cure for scurvy.
- 1907** Scurvy is experimentally produced in guinea pigs by Hoist and Frohlich.
- 1917** A bioassay is developed by Chick and Hume to determine the anti-scorbutic properties of foods.
- 1930** Szent-Györgyi demonstrates that the hexuronic acid he first isolated from the adrenal glands of pigs in 1928 is identical to vitamin C, which he extracts in large quantities from sweet peppers.
- 1932** In independent efforts, Haworth and King establish the chemical structure of vitamin C.
- 1932** The relationship between vitamin C and anti-scorbutic factor is discovered by Szent-Györgyi and at the same time by King and Waugh.
- 1933** In Basle, Reichstein synthesises ascorbic acid identical to natural vitamin C. This is the first step towards the vitamin's industrial production in 1936.
- 1937** Haworth and Szent-Györgyi receive a Nobel prize for their research on vitamin C.
- 1940** In a self experiment, Crandon proves the mandatory contribution of vitamin C in wound healing
- 1970** Pauling draws worldwide attention with his controversial bestseller "Vitamin C and the Common Cold".
- 1975-79** Experimental studies in vitro illustrate the antioxidant and singlet-oxygen quenching properties of vitamin C.
- 1979** Packer and coworkers observe the free radical interaction of vitamin E and vitamin C.
- 1982** Niki demonstrates the regeneration of vitamin E by vitamin C in model reactions.
- 1985** The worldwide requirement for vitamin C is estimated at 30,000-35,000 tons per year.
- 1988** The National Cancer Institute (USA) recognises the inverse relationship between Vitamin C intake and various forms of cancer, and issues guidelines to increase vitamin C in the diet.

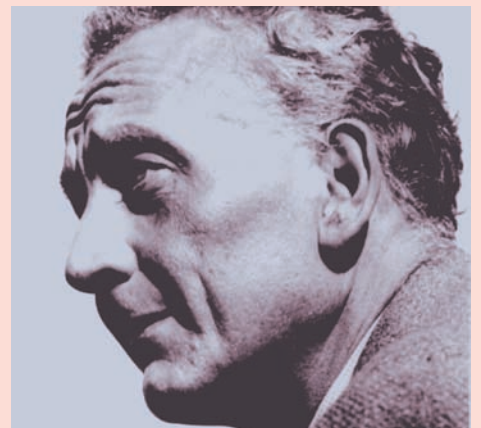
- 1998/99** Three studies show that supplementation with vitamin C can dramatically lower lead levels.
- 2004** A systematic review of thirty studies addressing the effect of supplemented vitamin C on the duration of colds revealed that there was a consistent benefit, with a reduction in duration of 8% to 14%.
- 2005** Levine calls for a re-evaluation of vitamin C as cancer therapy, especially intravenous vitamin C
- 2006** A 5 year Japanese study showed that the risk of contracting three or more colds in the five-year period was decreased by 66% by daily intake of a 500-mg vitamin C supplement.



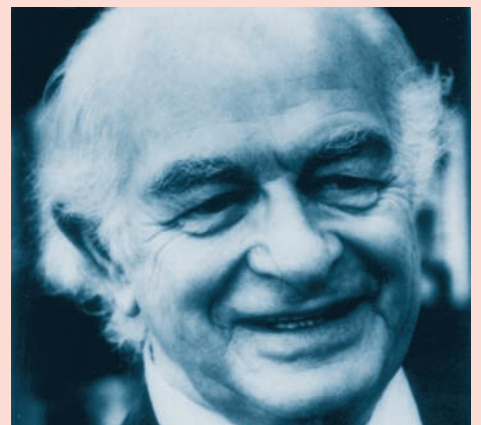
Tadeusz Reichstein



Charles Glen King



Albert Szent-Györgyi



Linus Carl Pauling