ERNA

vitamin E
FACT SHEET



Definition and biological activity

Vitamin E is a generic term covering all tocopherols and tocotrienols which qualitatively exhibit the same biological activity as α-tocopherol. Therefore, vitamin E refers to α-, β-, γ- and δ-tocopherol, plus α-, β-, γ- and δ-tocotrienol.

α-Tocopherol is the form of vitamin E that has the highest biological activity and is the most abundant in the human body. Nevertheless, other tocopherols such as γ-tocopherol may also have specific beneficial roles in human health.[1] The biological activity of the forms of vitamin E vary due to differences in their affinity to a liver protein - the so-called α-Tocopherol-Transfer-Protein (α-TTP).[2]

To account for differences in biological activity of the various forms of vitamin E, the vitamin E content in foods, food supplements and fortified foods should be expressed in 'mg α-Tocopherol Equivalents' (mg α-TE).[3] Some products may, however, still carry the old unit for biological activity of vitamin E: 'International Units' (IU). 1.00 mg α-TE equals 1.49 I.U.

Food supplements and fortified foods may contain either natural source or synthetic vitamin E. As natural source and synthetic vitamin E are not equivalent in chemical structure they differ in biological activity: the biological activity of synthetic vitamin E is lower than that of natural (source) vitamin E, in other words, more synthetic is needed for the same effect.

Conversion factors for the various forms of vitamin E as used by the German, Austrian and Swiss Nutrition Societies and other bodies are given in the table.

Table 1: Vitamin E Activity of various Tocopherols[4]

1 mg α-TE	1 mg RRR-α-tocopherol
	4 mg RRR-γ-tocopherol
	1.36 mg *all-rac*-α-tocopherol
	1.10 mg RRR-α-tocopheryl acetate
	1.49 mg *all-rac*-α-tocopheryl acetate
	1.21 mg RRR-α-tocopheryl succinate

Dietary sources

Vitamin E belongs to the group of fat-soluble vitamins. Vegetable oils, such as wheat germ oil or sunflower oil, are the highest dietary sources, and nuts are another good source. The vitamin E content of fruit and vegetables, as well as of animal foods (meat, fish and dairy products) is relatively low (see Table 2).

Table 2: Food sources of vitamin E[5]

Food (per 100g food)	Fat (g)	Vitamin E (mg α-TE)
Milk	3.6	0.1
Emmental cheese (45% fat/dry matter)	28.4	0.5
Butter	83.2	2.0
Olive oil	100.0	12.0
Soybean oil	100.0	17.0
Rape seed oil	100.0	23.0
Sunflower oil	100.0	63.0
Wheat germ oil	100.0	174.0
Cocoa butter	100.0	1.1
Salmon	13.6	2.2
Pork (muscles only)	1.9	0.4
Wheat whole meal bread	0.9	0.8
Spinach	0.3	1.4
Tomato	0.2	0.8
Orange	0.2	0.3
Apple	0.6	0.5
Peanut	48.1	11.0
Hazelnut	61.6	26.0
Walnut	62.5	6.0

1 Jiang et al., Am J Clin Nutr. 2001;74(6):714-22.
2 Brigelius-Flohe R & Traber MG. FASEB J. 1999;13(10):1145-1155.
3 As established in Directive 2002/46/EC (Food Supplements Directive).
4 For natural (source) vitamin E, both the terms RRR-a-tocopherol and d-a-tocopherol are used. The corresponding terms for synthetic vitamin E are all-rac-a-tocopherol and d,l-a-tocopherol
5 Souci Fachmann Kraut, Food Composition and Nutrition Tables, 6th ed, CRC Press, Boca Raton, 2000.

Intake in Europe

Vitamin E status may be particularly low in people with impaired fat absorption e.g. those with celiac disease, cystic fibrosis, and pancreatic or liver disorders or those on prolonged low-fat diets, since the vitamin E content of foods is linked to the fat content. Genetic defects of lipid (hypo- and abetalipoproteinemia) or vitamin E metabolism (familial isolated vitamin E deficiency, FIVE), or conditions associated with increased oxidative stress, such as diabetes, or chronic inflammatory conditions may also have a negative impact on vitamin E status.

According to data from various surveys, mean vitamin E intakes in Europe are between 7 and 15 mg α-TE.[6] Using data reported for women in the Heidelberg cohort of the EPIC study as example, the statistical distribution of vitamin E intakes was: 10th percentile 4.5 mg α-TE/day, 25th 6.7 mg α-TE/day, 50th 10.3 mg α-TE/day, 75th 15.7 mg α-TE/day, and 90th 22.4 mg α-TE/day. This means that more than 50% of the women had vitamin E intakes below the estimated adequate intake.[7] In Austria, inadequate intake of vitamin E (<80%) was the norm in women aged between 36 and 55 years. Similar intakes were also seen in Austrian men aged over 56 years.[8] In the UK, only 1-3% of the population did not meet national recommendations for vitamin E set in 1991 (3-4 mg/day), More recent recommendations of 12 mg/day would not be met by between 64 and 75% of the population.[9]

Importance for health

Antioxidant and non-antioxidant roles

Vitamin E is long recognised as the body´s major lipid soluble antioxidant, and thus is fundamental in maintaining the integrity and functionality of the cellular membranes of all cells of the human body. As an antioxidant, vitamin E acts within cell membranes, protecting unsaturated fatty acids from oxidation. In doing so, the vitamin is oxidised itself and must be 'recycled' back to its active form, typically by vitamin C. Therefore, the two vitamins are closely interlinked and often investigated jointly.

Due to its role as an antioxidant, a crucial role of vitamin E has been suggested for all conditions associated with increased oxidative stress, such as cardiovascular disease, diabetes, disorders involving chronic inflammation, preeclampsia, cancer, neurologic disorders, endurance exercise, increased exposure to oxidants, and others.

In addition to its antioxidant function, recent research demonstrated specific roles of vitamin E in signal transduction, gene expression, and regulation of other cellular functions.[10]

Immune function

Immune functions decline with age, which may relate to an increased vulnerability in elderly people to infections and other diseases. Numerous studies suggest a role for vitamin E in maintaining optimal immune status later in life.[11]

Heart health

Vitamin E has long been ascribed a role in preventing atherosclerosis and heart disease due to its beneficial effects on various mechanisms involved in atherosclerosis development (such as inhibition of LDL oxidation, anti-inflammatory effects, inhibition of smooth muscle cell proliferation). Nevertheless, the role of vitamin E in the prevention of heart disease is currently a matter of debate: A large body of evidence from epidemiology and experimental studies suggests that greater intake of vitamin E is associated with a reduced risk of heart disease.[12] Even though the efficacy of vitamin E in patients with heart disease has been mixed, there is a high biological plausibility that vitamin E is beneficial if taken before the disease starts to develop. Therefore, vitamin E should not be considered as magic bullet to treat diseases or to make up for decades of unhealthy lifestyles, but rather as valuable addition in supporting and maintaining life-long optimal health.

6 EC Scientific Committee on Food, Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Vitamin E (expressed on 4 April 2003)
7 Schulze et al., Ann Nutr Metab. 2001;45(5) 181-9
8 Institut für Ernährungswissenschaften, Österreichischer Ernährungsbericht (1998).
9 UK Office for National Statistics, The National Diet & Nutrition Survey (NDNS): adults aged 19 to 64 years (2003).
10 Azzi et al., FEBS Lett. 2002;519(1-3):8-10.
11 For summaries of the literature see Serafini, Int J Dev Neurosci. 2000;18(4-5):401-10) and Meydani, Am J Clin Nutr. 2000 ;71(6 Suppl):1665S-8S
12 Gey et al., Am J Clin Nutr. 1991;53(1 Suppl):326S-334S., Stampfer et al., N Engl J Med. 1993;328(20):1444-9, Rimm et al., N Engl J Med. 1993;328(20):1450-6.



Safety

Unlike other fat-soluble vitamins such as vitamin A and vitamin D, vitamin E is generally safe even at higher intakes, and may be considered one of the safest vitamins, along with vitamin C.

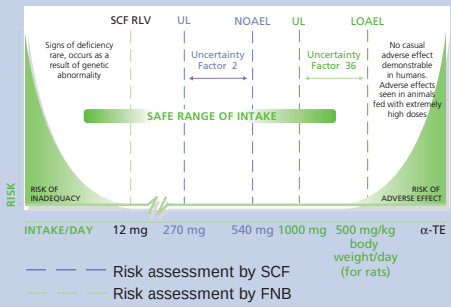
Three international expert groups have recently evaluated the safety of vitamin E: The EC Scientific Committee on Foods (SCF) 2003, the UK Expert group on Vitamins and Minerals (EVM) - a scientific committee of the UK Food Standards Agency- 2003, and the Antioxidant Panel of the Food and Nutrition Board (FNB), Institute of Medicine of the US National Academy of Sciences (2000). Although all three expert groups draw on the same body of published data, the Tolerable Upper Intake Levels (UL) set by these groups differ considerably:

The SCF, in accordance with the other two groups, identified hemorrhagic effects as the critical adverse events, and used a placebo controlled dose response supplementation study in 88 healthy humans (Meydani et al., 1998) to set the NOAEL (No Observed Adverse Effect Level) at 540 mg α-TE, the highest dose used in the study. Considering an uncertainty factor (UF) of 2 to cover for interindividual differences in sensitivity, the SCF established an UL of 270 mg α-TE for adults, which was rounded to 300 mg α-TE.[6]

The EVM established a NOAEL of 540 – 970 mg α-TE based on three placebo controlled human studies: Gillilan et al. 1977 (48 patients with stable angina pectoris, 1072 mg α-TE for 6 month); Meydani et al. 1998 (s.a., 88 healthy subjects, 34, 134 or 537 mg α-TE for 4 months), and Stephens et al. 1996 (CHAOS trial, 2002 atherosclerosis patients, 537 or 268 mg α-TE for a median of 510 (3- 981) days). A UF to account for interindividual differences was not considered necessary since the results of the larger trial by Stephens et al. support a NOAEL of 540 mg α-TE, so that the UL was established as 540 mg α-TE for supplemental vitamin E.[13]

The FNB considered data from several large human intervention trials as well as other clinical trials, but nevertheless concluded that there is insufficient human data pertaining to dose-response relationships – a key element in scientific safety assessment. Therefore, the panel used animal data to establish the LOAEL (Lowest Observed Adverse Effect Level), considered several aspects to be combined into the UF (severity of effects, pharmacokinetics in humans and animals, duration of studies and others, including an UF of 2 to extrapolate from the LOAEL to the NOAEL) and, in this way, set a Tolerable Upper Intake Level (UL) for adults at 1000 mg/day of any form of supplemental α-tocopherol.[14]

The extrapolation of considerably different ULs from the same databases is problematic for risk managers who need to take measures on the basis of this work, i.e, who may wish to set limits for the use of vitamin E in food supplements and fortified foods. It would therefore be desirable for different risk assessment bodies to consolidate their work to arrive at a single harmonized UL.



Fortified foods

The most common types of foods currently fortified with vitamin E are soft drinks (such as multivitamin juices, 'ACE-juices', sports drinks), cereals and dairy spreads. Typical vitamin E concentrations in ACE-drinks are in the range of 1 – 2.5 mg/100 ml. The addition of vitamin E to oils and food rich in unsaturated fatty acids is in general not considered to be a fortification as such since the addition most often balances previous losses due to the refining or the production process.

13 Safe Upper Levels for Vitamins and Minerals. UK Expert Group on Vitamins and Minerals (2003).

14 Institute of Medicine, Food and Nutrition Board, Vitamin E. In: Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium and Carotenoids, National Academy Press, Washington, (2000).

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Food supplements

A Gallup survey of 6 European countries in 1999 showed that 23% of the population use food supplements (France 21%, Germany 27%, Italy 15%, Spain 16%, and UK 36%). Of these users, 19% claim to take a vitamin E supplement, vitamin E being most popular in Germany (21% of users). 42% of users took dosages of less than 100 mg, 17% between 100 mg and 400 mg and 18% took between 400 and 1000 mg. On average, food supplements provide between 5.5 and 11.9% of total vitamin E intake.[15]

In Germany, users of food supplements have, on average, an intake approximately 22% higher than non-users.[16] The UK data indicates a highest average daily intake of vitamin E from supplements of 270 mg in women aged between 50 and 64 years with highest intake (97.5 percentile).

Table 3 provides a review of the range of vitamin E content in food supplements currently sold freely in the EU, i.e. those that the consumer can find on the shelves of supermarkets and health stores (including products that in some countries may be registered as medicines). Food supplements sold in pharmacies and subject to specific controls are not included.

Table 3: Daily content range of vitamin E in food supplements on free sale (via health stores and supermarkets) in the major EU markets[17]

Country	Vitamin E (mg α-TE)
Germany	10-540
Denmark	10-335
Finland	10-44.8
Ireland	10-270
Netherlands	10-350
Portugal	10-400
Sweden	10-825
UK	10-670

Recommended intakes

Several Nutrition Societies in EU Member States, or governmental bodies, have established recommendations for intakes of vitamin E. Although these may vary between countries, there is general consensus that the vitamin E requirements depend on the intake of unsaturated fatty acids: increased intake of unsaturated fatty acids results in increased incorporation of such fatty acids into body cell membranes, thus increasing the need for antioxidant protection by vitamin E, the body´s major lipid-soluble antioxidant.

Most recommendations for vitamin E intakes – or 'estimations for adequate intakes' - are largely based on the observation that vitamin E deficiency symptoms are usually not observed, so that the current intakes seem to meet the needs of the population. With the further development of biomarkers for vitamin E status and requirements it will eventually become possible to establish science-based recommendations for vitamin E intakes to support optimal health.

Table 4: Recommended Dietary Allowances of Vitamin E (mg α-TE) for adults in Europe[18]

Country/Organisation	Male	Female
Belgium, 2000	10	10
France, 2001	12	12
DACH,* 2000	15	12
Italy, 1996	>8	>8
Netherlands, 2000	11.8	9.3
Nordic countries, 1996	10	8
Spain, 1994-98	12	12
UK. 1991	>4	>3
EU Reference Labelling Value, 2003	12	12

*Recommendation for Germany, Austria and Switzerland.

15 Irish Universities Nutrition Alliance, The North-South Ireland Food Consumption Survey, Food Safety Promotion Board, Dublin (2001).

16 Robert Koch Institut, Was essen wir heute?: Beiträge zur Gesundheitsberichterstattung des Bundes. (2002)

17 Market survey undertaken by the European Responsible Nutrition Alliance in 2001-2003.

18 Scientific Committee on Food: Opinion of the EC Scientific Committee on Food on the revision of reference values for nutrition labelling. European Commission, Brussels, 5.3.2003.