REVIEW IN VITAMIN E

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ABSTRACT

Since it was necessary to stop fetal resorption in pregnant, vitamin E-deficient rats fed easily oxidizable diets including lard, vitamin E (α-tocopherol) was discovered about a century ago. The human body prefers α-tocopherol above the other eight vitamin E-related compounds found in the diet, which are all produced by plants and scavenge peroxyl radicals. Vitamin E's biological activity is heavily reliant on regulatory systems that help to excrete non-α-tocopherol forms and retain α-tocopherol. This preference depends on both the metabolism of non-α-tocopherols and the ability of α-tocopherol transfer protein (α-TTP) to enrich plasma with α-tocopherol. α-TTP is critical for human health because mutations in this protein lead to severe vitamin E deficiency characterized by neurologic abnormalities, especially ataxia and eventually death if vitamin E is not provided in large quantities to overcome the lack of α-TTP. α-Tocopherol serves as a peroxyl radical scavenger that protects polyunsaturated fatty acids in membranes and lipoproteins. Although specific pathways and specific molecular targets have been sought in a variety of studies, the most likely explanation as to why humans require vitamin E is that it is a fat-soluble antioxidant.

INTRODUCTION:

Vitamin E: Vitamin E is a fat-soluble vitamin with several forms, but alpha-tocopherol is the only one used by the human body. Its main role is to act as an antioxidant, scavenging loose electrons—so-called "free radicals"—that can damage cells. It also enhances immune function and prevents clots from forming in heart arteries. Antioxidant vitamins, including vitamin E, came to public attention in the 1980s when scientists began to understand that free radical damage was involved in the early stages of artery-clogging atherosclerosis, and might also contribute to cancer, vision loss, and a host of other chronic conditions. Vitamin E has the ability to protect cells from free radical damage as well as reduce the production of free radicals in certain situations. However, conflicting study results have dimmed some of the promise of using high dose vitamin E to prevent chronic diseases.[1]

As a lipid-soluble antioxidant, vitamin E guards against reactive free radicals oxidizing polyunsaturated fatty acids (PUFAs) and other elements of cell and organelle membranes. Furthermore, vitamin E could play significant roles in biological processes like DNA creation that are unrelated to its antioxidant activity. The Scottish Office Agriculture and Fisheries Department provided funding for this research. Requests for reprints should be sent to Dr. Asim K. Dutta-Roy at the Division of Biochemical Sciences, Rowett Research Institute, Aberdeen, AB2 9SB, Scotland, UK. [2]

Accepted on April 18, 1994; received on December 3, 1993. immune response stimulation as well as inflammation suppression. As a result, there is rising knowledge that vitamin E deficiency aids in the emergence of neuropathies and myopathies in animals and that consuming more vitamin E may prevent the advancement of numerous illnesses, such as tardive dyskinesia, arthritis, coronary heart disease, and malignant Hypertherm. However, because vitamin E is widely found in cereals, vegetable oil, and animal fats, vitamin E insufficiency in older babies, children, and adults occurs seldom in industrialized and most developing nations due to diet.[3] Thus, malabsorption of dietary vitamin E as a result of underlying gastrointestinal, pancreatic, and hepatic diseases is the most frequent cause of vitamin E insufficiency that obstruct the absorption or digestion of fat. The main exception is the isolated vitamin E deficiency syndrome, an inborn metabolic mistake that results in clinical vitamin E insufficiency despite adequate intestinal absorption of vitamin E. More reports of a genetically related impairment in vitamin E transport in humans have surfaced recently, and homozygosity mapping has shown that the condition's genetic locus is on chromosome. The other chronic conditions that are most frequently linked to a symptomatic state of vitamin E deficiency are short bowel disease, cystic fibrosis, chronic cholestatic hepatobiliary diseases, abetalipoproteinemia and other disorders of lipoprotein secretion.

Early in the 1930s, vitamin E's antioxidative properties were established. It has now been identified as the primary lipid-soluble antioxidant that shields membranes and lipids from oxidative damage both in vivo and in vitro (Tapped & Zalkin, 1960; Burton & Ingold, 1981; Burton et al. 1982). [4] By definition, antioxidants are substances that interact with free radicals to break up their chain

reactions. The hydroxylic group at position in the chroman ring is the corresponding functional group in the vitamin E molecule. Since all forms of vitamin E fall into this category, they can all respond as antioxidants—at least in a test tube.
The order of tocopherols' antioxidant capacity when evaluated with organic peroxyl radicals as an oxidizing partner is a-. b- $ g-. d-tocopherol (Burton &Ingold, 1981). This is not by any means a quantitative representation of the bioactivity sequence determined by the fetal resorption–gestation experiment. Additionally, compared to a-tocopherol, a-tocotrienol exhibits up to sixty times greater antioxidant activity against lipid peroxidation in rat liver microsomal membranes caused by Fe2η/ascorbate and Fe2þ/NADPH (Serb Inova et al. 1991). As it does not correlate with its activity in conventional bioassays, this suggests that in vitro antioxidant activity is insufficient to draw conclusions about the in vivo impact.
The widely held belief that vitamin E's antioxidant characteristic is the true foundation of its biological activity has been seriously called into question by this disparity (for reviews, see Azzi & Stocker, 2000; Munteanu et al. 2004; Zingg & Azzi, 2004).Recent reports on clinical trials that refute the efficacy of vitamin E or other antioxidants in preventing cancer, heart disease, or other disorders thought to be caused by oxidative stress highlight the significance of the ongoing controversy (Heart Protection Study Collaborative Group, 2002; Geiringer et al. 2004; Lonn et al. 2005; Poston et al.[5]

Meta-analyses of clinical studies have indicated that vitamin E may even have detrimental effects (Vivekananthan et al. 2003; Miller et al. 2005). Therefore, we must look beyond the biology of free radicals in order to comprehend
The term "vitamin E" refers to a group of lipophilic, naturally occurring substances that contain four tocopherols and four tocotrienols. The molecules that make up the molecule are chromanol rings with side chains at the C2 position.[6] Originally identified as a dietary component necessary for healthy reproduction, vitamin E is today recognized as a significant antioxidant in humans that scavenges free radicals and shields biological components from damaging oxidative changes.

A summary of the origins, purposes, and uses of vitamin E homologues is provided, along with information on their structures and characteristics.

KEYWOARDS: Vitamin E, Source of Vitamin E, Biological activity, Role of Vitamin E, Vitamin and Metabolite excretion, The Role of metabolism in the Antioxidants function of Vitamin E, Metabolism, Interactions requirements & and Functions of Vitamin E in fish, Vitamin E and lipid metabolisms, Emerging aspects and new directions, Bioactivity of Vitamin E.

Source of Vitamin E:

Vitamin E is found in plant-based oils, nuts, seeds, fruits, and vegetables.

- Wheat germ oil
- Sunflower, safflower, and soybean oil
- Sunflower seeds
- Almonds
- Peanuts, peanut butter
- Beet greens, collard greens, spinach
- Pumpkin
- Red bell pepper
- Asparagus
- Mangoes
- Avocados

Figure: Vitamin E Capsule

BIOLOGICAL ACTIVITY:

Strong antioxidant that breaks the chain and stops free radical damage in biological membranes is vitamin E, a peroxyl radical scavenger. Eight naturally occurring molecules—four tocopherols and four tocotrienols combine to form vitamin E. [7] The unsaturated phenyl side chain of tocotrienols sets them apart from tocopherols. The methyl groups on the chromanol nucleus of the four forms of tocopherols and tocotrienols vary (a-has three, /3-, and y-have two, whilst -has I). The antioxidant and biological activities of the different forms of vitamin E are approximately correlated; the proportional peroxyl radical scavenging reactivities of a-, /3-,

The relative order of the biological activities of r n y-, and -tocopherols is the same as that of the traditional fetal resorption experiment in rats, which yielded the following results: 1.5, 0.75, 0.15, and 0.05 mg/l U.

After more examination. The relationship between biological activity and antioxidants breaks disrupted. CT-Tocotrienol has stronger or similar antioxidant activity while having just one-third of a-tocopherol's biological activity. A vitamin analog that has biological activity comparable to RRR-a-tocopherol is 2,4,6,7-tetramethyl-2-(4',8', l2'-trimeth tridecyl)-5-hydroxy-3,4-dihydrobenzofuranj. [8]

After more examination. The relationship between biological activity and antioxidants breaks disrupted. Despite having just one-third of a-tocopherol's biological activity Ct-tocotrienol has stronger or similar antioxidant activity. With biological activity equal to RRR-a-tocopherol and a tetramethyl-2-(4',8', l2'-trimethyltridecyl)-5-hydroxy-3,4-dihydrobenzofuranj, a vitamin analog, with 0.5 times the antioxidant activity. Additionally, eight distinct stereo isomers of a-tocopherol with identical antioxidant activity are present in equal proportions in synthesized vitamin E (all-arc-a-tocopherol), yet each has a distinct biological action. In general, 2-S forms have lower biological activity than 2-R forms

. The highest level of biological activity overall is discovered in compounds with a free hydroxyl on the chromanol ring, three methyl groups, and a phenyl tail that meets the ring in the R orientation [9]. This particular need raises the possibility that vitamin E interacts differently with proteins.

Role of Vitamin E:

Human investigations using deuterium-labeled tocopherols in plasma lipoprotein transport provide one rationale for the significant biological activity of a-tocopherol. The liver secretes very-low-density lipoprotein (VLDL) that is enriched in RRR-a-tocopherol, according to these results and research on emerging lipoproteins released by perfused monkey livers.[10]

1. A hepatic tocopherol transfer protein is probably required for this procedure.

The University of California, Berkeley's Department of Molecular and Cell Biology is the source of the cloned human tocopherol transfer protein.

2. Supported by the Henkel Corporation, LaGrange, IL, and the Palm Oil Research Institute of Malaysia (PORIM) under an NIH grant. [11]

3. Reprint requests should be sent to MG Traber, Department of Molecular Biology, Life Sciences Addition.

4. Research on a unique group of people with vitamin E deficiency for which there is no known cause suggests the importance of the protein. These people cannot maintain plasma RRR CT-tocopherol concentrations and have reduced VLDL synthesis of RRR-a tocopherol. Recent research has shown that these individuals, as well as those suffering from AVED (ataxia with vitamin E deficiency,

are impacted by a genetic mutation in the hepatic tocopherol transfer protein gene. RRR-a-tocopherol's kinetics and turnover measurements reveal that it is always in flux and that the liver quickly absorbs and enters the plasma by resecting it.[12] According to the review in reference, these results highlight the significance of the liver and the function of the tocopherol transfer protein in preserving normal plasma vitamin E concentrations. As a result, the body works extremely hard to keep the amounts of RRR-a-tocopherol in plasma that are accessible for transport to tissues high enough.[13] This result raises the issue of whether RRR a-tocopherol has a structure-specific need that is unrelated to antioxidants.

1.1 Overview:

A previously unknown but essential dietary component for the rat's normal reproduction was discovered by Evans and Bishop (1922).[14] It was thought at the time that the major function of vitamin E was to keep pregnant rats' gestations regular by stopping embryo resorption, which invariably occurred when the vitamin was low. It was found that this unidentified dietary component X was present in green lettuce, dried alfalfa leaves, wheat, and oats. Evans isolated factor X from wheat germ oil, defined the chemical formula $C_{29}H_{50}O_2$, and coined the word "α-tocopherol" in 1936.3. Fernholz published the structural formula for α-tocopherol in 1938.4 The early 1960s saw the discovery of tocotrienols, which were identified considerably later than tocopherol.[15]

Olcott discovered that antioxidants prevented the oxidative degradation of lard in the lipid fractions of vegetable oils.7. Since then, it has been conclusively shown that vitamin E functions as a vital antioxidant both in vivo and in vitro and is crucial in preventing harmful oxidative damage to biological molecules.8–11 The non-antioxidant roles of vitamin E, such as gene regulation, membrane processes, cellular signaling, and neuronal activities, have also drawn a lot of interest in recent times, meanwhile, are still debatable and need more clarification. Understanding the function of vitamin E both in vivo and in vitro requires accurate knowledge supported by strong chemical evidence.[16]

1.2 Vitamin E Structure:

The lipid-soluble chemical known as vitamin E is generated from plants and has a chromanol ring with a side chain at position C2. The term "vitamin E" describes a set of eight distinct substances, which include the four tocotrienols and the tocopherols α, β, γ, and δ. Tocotrienols have an unsaturated iso phenyl side chain with three double bonds at C3′, C7′, and C11′, whereas the four tocopherols have a saturated phytol side chain.[17] The side chain double bonds of tocotrienols at C3′ and C7′ are trans-configured. The α-, β-, γ-, and δ-forms differ in the number and orientation of methyl groups on the chromanol ring. The methyl groups at C5, C7, and C8 of the chromanol ring are present in two, three, and one methyl group, respectively, in the β-, γ-, and δ-forms of tocopherol and tocotrienol.
Nature also has colonels and coronels with a single and two double bond unsaturation, respectively, in addition to tocopherols and tocotrienols. For instance, from palm and rice bran oils, a tocomonoenol containing a single double bond at carbon 11′ was isolated: 2,5,7,8-tetramethy1-2-(4′,8′,12′-trimethyltrideca-11′-enyl)-6-chromanol. Since then, a number of organizations have found tocomonoenols in plants and plant-derived.[18]
Examples of these include α-tocomonoenol found in palm oil, kiwi (Actinidia chinensis) oil, and sunflower oil (Helianthus annuus),γ-tocomonoenol found in pumpkin seed oil, and β–, γ–, and δ-tocomonoenol found in Kalanchoe daigremontianin and Phaseolus coccineas leaves. Salmon tissues also contained a tocomonoenol that had an unsaturation at the isoprenoid-chain terminus. Moreover, it was discovered that palm oil contained tocotrienols with two double bonds at carbon 7′ and 11′. Tocopherols have three chiral carbons: two in the side chain at C4′ and C8′, and one at C2 in the chromanol ring. [19]Chiral carbons may be found in α-tocopherol that occurs naturally in the R-conformation, 2R, 4′R, and 8′R-α-tocopherol. Naturally occurring tocotrienols are found at C2 in the chromanol ring, where the chiral center of α-tocotrienol is situated.
In contrast, an equimolar mixture of eight distinct stereoisomers—RRR, SRR, RSR, RRS, RSS, SSR, SRS, and SSS—is produced during the chemical production of α-tocopherol. All-arc-α-tocopherol is the term for the synthesized form of α-tocopherol. 2-ambo-α-tocopherol is an equimolar combination of RRR-α-tocopherol and SRR-α-tocopherol. Both RRR-α-tocopherol and RRR-α-tocotrienol are identified by their IUPAC designations, which are (2R)-2,5,7,8-tetramethyl-2-[(4R,8R) -(4,8,12-trimethyltridecyl)] (2R)-2,5,7,8-tetramethyl-2-[(3E,7E)-4,8,12-trimethyltrideca-3,7,11-trienyl] and chroman-6-olin that order, 3,4-dihydrochromen-6-ol. Acetate, nicotinate, succinate, and phosphate are examples of the ester forms of tocopherol and tocotrienols that have been synthesized, and their actions and possible uses have been investigated. Heat, light, and an alkaline environment can quickly oxidize vitamin E.[20]

However, compared to the free form, esters are better suitable for use in food, cosmetics, and medicinal applications because they are less oxidation-prone. Because of their amphiphilic qualities, polyethylene glycol conjugates of tocopherols and tocotrienols may form miscible micelles in water, which increases their water solubility and absorption and increases [21]their bioavailability in both humans and animals. RRR-α-tocopherol polyethylene glycol 1000 succinate has been found to function as a secure and efficient vitamin E form for treating or avoiding vitamin E insufficiency in cases of persistent pediatric cholestasis.

1.3 Vitamin E Properties:

At room temperature, the tocopherols are viscous oils that are soluble in ethanol and aprotic solvents but insoluble in water. Vitamin E is a transparent, thick, almost odorless oil that is slightly yellow to amber in color. It oxidizes when exposed to air or light. provides an overview of the physicochemical characteristics of α-tocopherol, which is the most prevalent and potent form of vitamin E in humans. The RRR-α-tocopherol has a melting point of 3 °C. Tocopherols have extremely tiny optical rotations that are influenced by the solvent's properties. The infrared spectra of tocopherols and tocotrienols in ethanol reveal OH (2.8 ± 3.0 μm) and CH (3.4 ± 3.5 μm) stretching along with a distinctive band, whereas the ultraviolet absorption spectra indicate an absorption maximum at 292–298 nm. [22]
8.6 μm. In a hydrophobic solution, α-tocopherol exhibits fluorescence, peaking at around 325 nm in emission. The O-H bond of α-tocopherol has a bond dissociation energy of 77.1 kcal mol−1.31. In a micellar solution, the pike values for α-, β-, γ-, and δ-tocopherol were reported as 13.1, 12.8, 12.7, and 12.6 correspondingly[23] α-Tocopherol's physicochemical characteristics.

IUPAC name: (2R)-2,5,7,8-Tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-3,4-dihydrochromen-6-ol

Molecular formula: C29H50O2

Molecular weight: 430.7 g mol−1

Physical description: Slightly yellow to amber, nearly odorless, clear, viscous oil

Melting point: 3 °C

Boiling point: 235 °C

Solubility: Insoluble in water (1.9 × 10−6 mg L−1 at 25 °C), soluble in ethanol

Density: 0.950 g cm−3 at 25 °C

Partition coefficient: log P = 12.2

Stability: Unstable to UV light, alkaline, and oxidation

Dissociation constant pka:10.8

UV absorption maximum: 292 nm in ethanol

Fluorescence: Excitation 290–295 nm, emission 320–335 nm

BDE (O–H): 77.1 kcal mol−1

The partition coefficient of α-tocopherol is 12.2, while that for ascorbic acid is −1.85,30 showing their lipophilic and hydrophilic characters, respectively.[24]

1.4 Sources:

A wide range of foods contain vitamin E. Fruits and seeds are two of the greatest foods that contain vitamin E. Vegetables with green leaves are also significant sources. Vitamin E can only be synthesized by plants and photosynthetic organisms.[25] Enzymes aid in the manufacture of stereospecific tocopherols, or RRR-tocopherols.35 Vegetable oils and other higher plant materials can be used to extract, purify, or concentrate tocopherols and tocotrienols. Supplements included in food are an additional source of vitamin E. The majority of vitamin E pills have far larger concentrations of vitamin E than meals. Esterification is a common method used to extend the shelf life of vitamin E in dietary supplements and fortified foods while maintaining its antioxidant qualities.
Natural oil composition and tocopherol and tocotrienol concentrations differ significantly throughout plant species and even within the same species. In higher plants, tocotrienols are found only in some non-photosynthetic tissues, while tocopherols are found in large quantities. some samples of natural edible oil contents taken from several publications. In palm, olive, and sunflower oils, α-tocopherol predominates, but in other edible oils, such maize, rapeseed, and soybean oils, γ-tocopherol is present in greater amounts than α-tocopherol.

Tocopherol to tocotrienol ratios in palm, rice, and annatto are 25:75, 50:50, and 0.1:99.9, respectively, making them the main sources of tocotrienols. Significant levels of α-, γ-, and δ-tocotrienols are present in palm oil. The main vitamin E isoform found in the rice bran oil is γ-tocotrienol, however one of the main isoforms present in wheat germ oil is β-tocopherol. It's interesting to note that tocotrienols—primarily δ-tocotrienol—and no tocopherols were found in the lipid fraction of annatto (Bixa Orellana L.) seeds.[26]

1.5 Chemical Synthesis:

Owing to its numerous uses in the food, pharmaceutical, and cosmetic sectors, around 35,000 tons of vitamin E are produced year globally. The most significant product in the industry is all-racemic-α-tocopherol, also known as all-arc-α-tocopherol, which is an equimolar combination of all eight stereoisomers and may be made either naturally or by complete synthesis. It is mostly used as an ester of acetate. The creation of 2,3,5-trimethylhydroquinone, the synthesis of the side chain component, and the condensation reaction are the three mains of steps in the commercial synthesis.[27]
Semi-synthesis is a chemical method used to produce pure RRR-α-tocopherol. Large-scale refining and isolation of vegetable oils using several separation techniques result in combinations of RRR-tocopherols that are then methylated to form RRR-α-tocopherol. The methods and procedures used to create tocopherols.

1.6 Analysis:

In addition to trace levels of tocotrienols and tocomonoenols, natural goods also include mixes of isomeric tocopherols and tocotrienols. They undergo oxidation and metabolism to create a wide variety of chemicals. Complex mixes of vitamin E isoforms, metabolites, and oxidation products can be found in the biological samples. Clarifying the roles and activities of vitamin E isoforms and their products requires their identification and quantification. Given that sample preparation is the primary cause of mistakes in analysis, it is both the most time-consuming and crucial phase. Many analytical techniques have, including colorimetric, fluorometric, gas chromatographic (GC), high performance liquid chromatographic (HPLC), GC-MS, and HPLC-MS. Regarding publicly available documentation for the quantitative technique of determining the presence of vitamin E in active components in pharmaceuticals, the United States and Europe. [28]
Whereas Japanese pharmacopeia uses the HPLC method, GC is used in pharmacopeia. Each of these approaches has advantages and disadvantages. Currently, HPLC techniques are the most often used.
Reviews of HPLC settings for vitamin E analysis have been written. and Direct extraction, solid-phase extraction, and saponification are methods used to extract vitamin E and its byproducts from natural items, food matrices, and biological materials. Preparing samples and conducting analyses should be done with caution to prevent artifactual oxidation and breakdown. Compared to traditional UV detection, the use of electrochemical (amperometry), fluorometric (Ex. 290–295 nm, Em. 320–330 nm), or MS detection is far more sensitive and specific. 2-methyl-2-(4,8,12-trimethyltridecyl) Tobol.[29]
Since 6-chromanol shares many properties with vitamin E, it might be the most appropriate chemical to utilize as an internal standard. In MS analysis, deuterium-labelled α-tocopherol acetate is frequently employed as a standard. The positive ionization mode of air pressure chemical ionization (APCI) is utilized in the majority of vitamin E studies. It should be mentioned that a "greener" analytical method for the identification and quantification of vitamin E homologues has been suggested: supercritical-fluid chromatography using NH2 as the stationary phase, CO2 and ethanol as the mobile phase, and mass spectrometry.

1.7 Functions and Applications:

Vitamin E is a micronutrient that is physiologically necessary and has applications in medicine, pharmaceutics, cosmetics, and food. It is believed that vitamin E is crucial for maintaining good health as well as for the prevention and treatment of a number of illnesses 15mg.
The antioxidant properties of vitamin E have been shown or suggested, and it also plays a role in membrane stabilization by forming complexes with destabilizing molecules to prevent disruption of the amphipathic balance within the structure, physiological regulation of enzyme activity, cellular signaling, cell proliferation, and gene expression, which is not directly related to antioxidant action, and membrane stabilization.
The sixth is the biocompatible modifier of biomaterials and medical devices, such as high molecular weight polyethylene used in hip and knee implants.[30] The other five are the inhibition of platelet coagulation, the prevention of diseases such as neurological disorders, cardiovascular diseases, age-related eye and skin damage, and infertility. Beyond the benefits of tocopherols, it has been suggested that tocotrienols offer other health benefits, such as boosting the immune system and reducing blood cholesterol.
Of these, vitamin E's action as an antioxidant against lipid peroxidation driven by free radicals has been well proven, and it seems to be the most significant physiological role of the vitamin. In order to prolong the shelf life of foods, oils, and industrial products, vitamin E also prevents air oxidation.[31]
Future research is needed to determine the physiological importance of additional activities unrelated to antioxidant of platelets coagulation, the prevention of diseases such as neurological disorders action.
As a dietary supplement, vitamin E is frequently used either alone or in combination with other micronutrients like vitamin C to support good health and lower the risk of or prevent illnesses thought to be caused by harmful oxidative alteration of biological components. Certain foods and beverages are fortified with vitamin E.
Vitamin E shortage is rare since normal diets seem to provide enough levels of the nutrient, yet malnourishment and hereditary diseases can cause deficiencies. Babies born prematurely and with extremely low birth weights may be vitamin E deficient. Additionally, individuals with hereditary and fat-malabsorption diseases

Conditions where the liver's α-tocopherol transfer protein (α-TTP) is missing or defective or where sialoprotein levels are lowered more likely to result in vitamin E deficiency and necessitate large dosages of vitamin E supplements.[32] There has been discussion about vitamin E's possible protection against sarcopenia, nonalcoholic steatohepatitis, and periodontal diseases. The severity of periodontal disease was found to be substantially correlated with inadequate consumption of micronutrients, including phosphorus and vitamins. Vitamin E and lycopene significantly improved periodontal indices, according to a comprehensive study. Sarcopenia may be lessened by vitamin E because it may improve muscle regeneration and reduce age-related skeletal dysfunction.

Biomedical materials also employ vitamin E. In order to increase stability and functionality for patients receiving chronic hemodialysis, α-tocopherol is mixed with the dialysis membrane. Ultra-blended vitamin E[33]
UHMWPE, or ultra-high molecular weight polyethylene, is a polymer that has been developed for use in total hip and knee replacements. It is acknowledged that α-tocopherol enhances resistance to oxidation while preserving
The use of vitamin E has been severely restricted due to its weak water solubility. Many studies have been conducted to improve the formulations and oral and topical encapsulation of vitamin E. To address this issue and increase the vitamin's solubility, permeation, and bioavailability, many delivery methods for vitamin E have been created. Among these are liposomes, nano-emulsions, and lipid nanoparticles Both tocopherol phosphate and the tocopherol ester of polyethylene glycol are soluble in water. Tocotrienol conjugates with polyethylene have also been investigated.[34]
When dietary polyphenols like quercetin are absorbed into the body, they are transformed into conjugated metabolites that appear in the bloodstream as glucoside and/or sulfate derivatives, or their O-methyl counterparts. The in vivo formation of tocopherol metabolites, such as glucoside, sulfate, and O-methyl derivatives, has not been documented. However, α-tocopherol glucoside was produced by trans glycosylating maltose and 2-hydroxymethyl-2,5,7,8-tetramethylchroman-6-ol using α-glucosidase from Saccharomyces species.2-(α-d-glucopyranosyl) methyl-2,5,7,8-tetramethylchroman-6-ol, the glycosylated product, is soluble in water and functions as an antioxidant that scavenges free radicals. The preparation of δ-tocopherol glucoside and its topical use on skin were investigated.
Whether or whether each vitamin E isoform performs a unique function that is distinct from that of other isoforms is a crucial question. [35]Some have contended that tocopherol interferes with the activities of tocotrienol and that tocotrienol performs some tasks that tocopherol does not. Future research must clarify these crucial problems.

1.8 Stability:

While vitamin E is stable in room temperature, it is easily oxidized under high temperatures, bright light, or alkaline environments. One of the most popular ways to prepare food is frying. When food is fried, typically at a temperature of 160 to 190 °C, vitamin E is oxidized, resulting in complex mixtures of products such as cored (5,6-tocopheryl Dione) and dimers, which are thought to be formed by the recombination of tocopherol radicals. [36] Ferric and cupric transition metal ions, such as Fe3+ and Cu2+, oxidize α-tocopherol to α-tocopherol radical.

Vitamin E and metabolite excretion:

Vitamin E excretion

One important route of vitamin E loss in vivo is fecal excretion. According to earlier research assessing the amount of radioactive at that is fecal recovered after being taken orally, about 30% of the art is not absorbed. Additionally, it has been demonstrated that both a and CT are easily eliminated from the bile of both humans and rats of these, some enterohepatic circulation occurs (about 60% in rats), and the remainder is most likely lost by the fecal pathway. [37]

Vitamin E metabolism and drug interactions:

Vitamin E is processed by the same mechanism as many medications and xenobiotics. Specifically, it has been hypothesized that over half of the medicinal drugs that undergo oxidative metabolism are metabolized by CYP3A, one of the CYP450 isoforms indicated for vitamin hydroxylation. Because of this, some have questioned whether vitamin E, particularly in populations consuming large doses of supplementary vitamin E, might reduce the effectiveness of drugs by causing the expression of xenobiotic degradation mechanisms. Other dietary supplements, such St. John's wort, have also been linked to this kind of negative impact. According to in vitro research, some vitamin E isomers may bind to the pregame X receptor (PXR) and cause CYP3A4 production.[38]
Studies on mice have also demonstrated that high-dose, long-term supplementation can enhance the expression of CYP3a11, the murine equivalent of human CYP3A4, in the liver. Perhaps as a result of its quick conversion to c-CEHC, which avoided its buildup in the liver, another vitamin E isomer, c-tocotrienol, did not raise CYP3a11 expression in mice. Daily subcutaneous injections of at least for eighteen days raised the expression of CYP3A, 2B, and 2C proteins in the liver, according to a recent study conducted on rats. Additionally, the injection boosted the expression of MDR-1, a transporter protein that helps the liver excrete foreign substances by biliary excretion.

Recent research indicates that vitamin E supplementation, either in isolation or in combination with other antioxidants, may lower the levels of cyclosporine A, an immunosuppressant that is known to be metabolized by CYP3A4, in both healthy individuals and recipients of kidney transplants. Reductions in cyclosporine A concentration may cause transplant recipients to reject their organs more frequently. All of these findings point to the urgent need for more study to determine if vitamin E supplements may affect how drugs are metabolized in humans.[39]

The role of metabolism in the antioxidant function of vitamin E:

By capturing reactive oxygen radicals, vitamin E (α-tocopherol), the primary antioxidant that breaks down chains in cellular membranes, stops oxidative damage caused by carcinogens and toxicants. Despite the apparent lack of direct metabolic regulation, α-tocopherol antioxidant reactions might be facilitated by redox cycles, which supply reducing equivalents for antioxidant reactions and connect antioxidant activity to cellular metabolism. This study explains the chemistry of α-tocopherol as an antioxidant and assesses experimental data supporting the idea that cellular metabolism is linked to the turnover of α-tocopherol through redox cycles. Antioxidant synergism between α-tocopherol and ascorbate, reduced glutathione, NADPH, and cellular electron transport proteins has been shown in several in vitro tests.[40] However, there is conflicting information about the regeneration of α-tocopherol from the tocopherol radical by a one-electron redox cycle. The challenge of distinguishing between direct and recycled tocopheroltioxidant actions of other antioxidants has complicated interpretation of the available data. It is possible for a two-electron redox cycle to transpire, but it would need enzymatic catalysis in vivo. This cycle would include α-tocopherol oxidation to 8a-substituted topophones and topophone reduction to α-tocopherol. The reductive metabolism of α-tocopherol quinone, an α-tocopherol oxidation product, produces α-tocopherol hydroquinone, which may also offer antioxidant protection, whereas the metabolism of antioxidant-inactive α-tocopherol esters releases α-tocopherol.[41]

Metabolism, interactions, requirements and functions of vitamin E in fish:

Tocopherols and tocotrienols are a class of lipid-soluble compounds that are collectively known as vitamin E. They may have additional, more specialized biological roles in addition to shielding organisms from lipid oxidation. Similar to other vertebrates, fish also preferentially retain α-tocopherol (TOH) over the other tocopherols in their bodies. This is likely due to the liver's tocopherol transfer protein (TTP), which binds tocopherols with varying affinities and releases them back into the bloodstream. Bile has a higher number of tocopherols that are expelled than those that bind poorly to TTP. Because α-TOH interacts with other nutrients, the amount needed varies depending on the makeup of the food. [42]
The need is increased by high concentrations of polyunsaturated fatty acids and low concentrations of astaxanthin, vitamin C, and selenium. Lipid oxidation and antioxidant defiance, in which oxidized vitamin E is recycled by other antioxidants, are both dynamic processes that are responsible for this. The interactions also dictate immunological responses, the manifestation of vitamin E deficiency symptoms, and the impact on the quality of the meat. Some of the theories put out in this study address the debate in the field of mammalian nutrition research over the role of vitamin E, [43] which centers on whether it is primarily an antioxidant or a particular regulator of cell signaling through regulation of enzyme activity and gene expression.

Vitamin E and lipid metabolism:

PRESENT Elgin project, designed to investigate the tocopherol needs of man, is now iii its sixth year. Some previously reported general conclusions' 'can be summarized as follows: Tocopherol requirements are a function of the amounts of certain peroxidizable lipids in the diet and in the tissues. The fatty acid composition of the lipids in all the tissues tested to date can be altered, within limits, by varying the fatty acid composition of the diet. Linoleic acid appears to be the most significant oxidizable lipid component in diets of normal human beings. Other easily peroxidized fatty acids, such as arachidonic, and some of the higher molecular weight unsaturated in fish oils may also be important.[44] When peroxidizable fatty acids in the diet are low, the demand for tocopherol drops to very low levels, however the need for tocopherol must be assessed in light of previous dietary practices that may have altered tissue composition. A detailed description of the current Elgin project's structure and procedures was provided beforehand.

Vitamin E: Emerging aspects and new directions:

In 2022, the discovery of vitamin E will celebrate its centennial. However, there are still many unanswered concerns about the nutrient's biological roles and importance to human health. In the 1980s, vitamin E—which had previously been found to be crucial for rat fertility was found to have signaling and gene regulatory effects in addition to being a fat-soluble antioxidant. The cytochrome P-450 dependent metabolism of vitamin E was defined during the same years, and the 1990s saw the initiation of a series of investigations on short-chain carboxyethyl metabolites, which led to the idea that this metabolism had a biological purpose. [45]
substitute for the catabolism of vitamin E. Over the past ten years, other physiological metabolites of vitamin E have been discovered, including α-tocopherol phosphate and long-chain metabolites produced by cytochrome P-450's ω-hydroxylase activity. Current research in several experimental models, including inflammatory, neuronal, and hepatic cells, as well as in vivo in animal models of acute

inflammation, is in line with the gene regulation and homeostatic roles of these metabolites. Numerous labs are looking into the molecular processes driving these reactions, and a quick peek at studies on other fat-soluble vitamins might help advance this field more quickly. Additional cutting-edge topics covered in this review article include neuroprotection, immunomodulation and antiallergic effects, and new insights into the processes reducing cardiovascular risk. (46)
characteristics in models of spine-cerebellar injury and glutamate excitotoxicity, hepatoprotection and liver toxicity prevention through many causes, and even therapeutic applications in non-alcoholic steatohepatitis.
Here, we address these subjects in an effort to pique the curiosity of scientists and encourage more study projects that might contribute to commemorating the anniversary of vitamin E with a thorough understanding of its role as a vitamin. [47]

Bioactivity of vitamin E:

Even now, nearly eight decades after vitamin E's necessity for mammals was established, its chemical mechanism of action remains mysterious. Out of the eight distinct forms of vitamin E, the body only retains α-tocopherol. This is partly because the α-tocopherol transfer protein specifically selects RRR-α-tocopherol, and partly because it degrades and eliminates more slowly than the other vitamers. Its antioxidant capacity cannot, at least not solely, account for its essentiality, as the tocopherols have similar antioxidant qualities and certain tocotrienols are even more efficient at scavenging radicals.[48] Over the past ten years, a significant amount of so-called unique functionalities of practically all forms of vitamin E, including the control of gene expression and cellular communication, have been shown. While γ-tocopherol seems to be quite successful in avoiding processes connected to cancer, α-tocopherol appears to be primarily active in gene regulation. It seems that tocotrienols can help to slow down neurodegeneration. The majority of the unique roles that each form of vitamin E possesses have only been shown in vitro and still need to be verified in vivo. We address the different bioactivities of the different vitamers, taking into account their metabolism and the possible roles of metabolites.[49]

CONCLUSIONS:

Vitamin E concentrations in plasma and tissue are impressively constant in healthy individuals. The body exhibits a definite preference for something that has nothing to do with its antioxidant function, pointing to the possibility of a strictly regulated regulatory system. But after reexamining the processes behind vitamin E tissue distribution and intracellular trafficking, we discover that the seeming controlled nature of these processes may be deceptive. A large portion of vitamin kinetics seems to be associated with one of its basic characteristics, lipid solubility.[50] This characteristic makes it easier for vitamin E to diffuse among the components of membranes. Tissue lipid contents also have a significant impact on vitamin E tissue distribution, and concentrations of vitamin E seem to moderate rather than directly control intracellular trafficking and tissue distribution. Additionally, as is Due to its relative lipid solubility, vitamin E may redistribute from plasma and other tissues to adipose tissue. This phenomenon is typical for fat-soluble medicines and may have more physiological relevance than is currently understood. The vitamin E distribution method that the body uses to distribute it is metabolically efficient, but at the expense of "losing" 90% of the total amount of vitamin to adipose tissue, which might lead to a distribution that is not ideal.[51]

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