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Review Article

Vitamin E From Microbes: Extraction, Analysis and Application

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Abstract

Different types of important vitamins can't be made or can be generated but not in adequate quantity by the higher species, so they must be received externally through diet. Some of the natural sources that produce vitamins include several plants, animals, vegetable oils, most fishes and certain microorganisms. Due to higher demand, significant use of microorganisms to produce vitamins is under development and research. Vitamin E is an important and significant antioxidant that is fat-soluble and protects the body from free radicals. There are mainly two types of vitamin E: tocopherol and tocotrienol, which are subdivided into a total of eight types. Shikimate and/or MVA (Mevalonate) or MEP (2-C-methyl-D-erythritol-4-phosphate) Pathway synthesise this. Vitamin E is needed to keep skeletal, heart, and smooth muscle structure and function healthy. It also aids in the development of red blood cells and the maintenance of fat-soluble vitamins A and K, iron and other minerals. Vitamin E deficiency can result in anemia, heart disease, serious neurological problems, poor vision, etc. Although various strains of microorganisms like bacteria, yeasts, and algae are known to be isolated for the production of vitamin E. Extraction processes are employed to obtain an extract which is further purified by certain purification techniques. Various quantitative and qualitative analyses of extracts are used to check the quality and quantify the vitamin content of the particular strain. Further characterization by DNA sequencing method is used to identify strains from unknown sources. The sequences are analysed and an online local alignment tool is utilised to find out the organism.

Keywords: Antioxidant; Extraction; HGA-homogentisic Acid; Tocopherol; Tocotrienol

Introduction

Vitamins are requisite organic nutrients. Unlike other nutrients like fats, proteins and carbohydrates they do not provide any energy, however they are obligatory for trouble-free metabolism in the body. Vitamins appear in a large number of natural foods, fishes, cod-liver oil, plants, certain bacteria, yeast and algae. They are micronutrients-in small amount very few milligrams to micrograms quantity has to be taken up in order to accomplish the metabolic function. However, because they are not synthesised by the higher organism, the intake of this small amount is critical. However, there is a Recommended Daily Allowance (RDA) or Daily Value (DV) for each vitamin. The amount of certain quantity of nutrients need to get each day based on your age, gender, pregnant or lactation.

Vitamins have a wide range of chemical and physiological properties. Currently, there are 13 essential vitamins are known. Based on their solubility qualities, vitamins are separated into two classes. A, D, E, and K, as well as more than 45 carotenoids, are fat-soluble vitamins. Vitamin C (ascorbic acid) and all B vitamins, including thiamine (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B8), folic acid (B11 or B9), and cyanocobalamin, are all water-soluble vitamins (B12).

Age	Males Daily value (In mg)	Females Daily value (In mg)	Pregnant Daily value (In mg)	Breast feeding Daily value (In mg)
Up to 1year	4-5	4 -5	-	-
1-13 years	6 -11	6 -11	-	-
14+ adults	15	15	15	19

Table 1: Recommended Dietary Allowances (RDAs) for Vitamin E (α-tocopherol) [22].

Vitamin E is essential bioactive vitamin in human nutrition which is consist of tocochromanols- of two distinct compounds known as tocopherols and tocotrienols [10]. Which are produced by plants, vegetable oils and some of the microorganisms. It has various important functions, the most important of which is as an antioxidant that scavenges free radicals. It is regarded as the lipid soluble antioxidant present in cellular membrane of higher organisms. These definite chemical compounds contain a hydrophobic side chain and a chromanol ring [28]. Vitamin E is a vital fat-soluble vitamin which exists in 8 different is forms namely α-, β-, δ-, γ- tocopherol and α-, β-, δ-, γ- tocotrienol. α-Tocopherol is considered as the typical and biological active form of vitamin E [39,41]. These isoforms are widely found present in vegetables, vegetable oil, nuts (such as almonds), grains (such as corn oil), seeds (such as sunflower), cyanobacteria [30,38], certain bacteria, yeast, algae and fishes.

Alpha-tocopherol is the only vitamin E that is utilised by the human body. Its primary function is to act as an antioxidant, scavenging loose electrons, often known as "free radicals," which can cause cell damage. Vitamin E has the capacity to protect cells from free radical damage and, in some cases, to limit the generation of free radicals.

The analysis starts with a vitamin extraction from a specific source. The method of extraction chosen is determined by the desired outcome, the source's nature, strain potential (from microorganisms), the current natural or synthetic form of the vitamins, interfering constituents, the vitamin's resistance to certain physical and chemical parameters, and the analytical method's selectivity and specificity. It is important to remove the quantity from the matrix in a form that can be reliably quantified by certain analysis procedures in order to make a good determination.

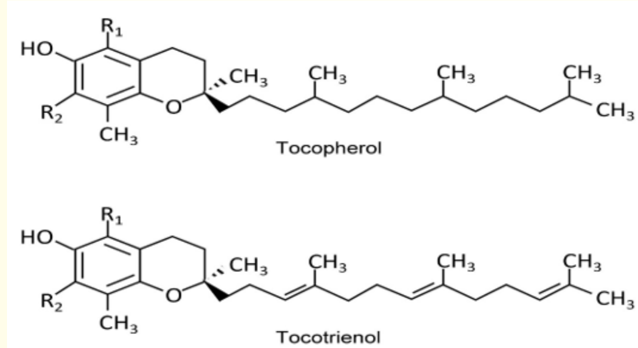

Figure 1: (Vitamin E structure (tocopherol and tocotrienol)) [https://doi.org/10.3390/ma14133691] [14].

Vitamin E types and structure

The vitamin E is functionally very significant, apart from this they are powerful antioxidant. There are eight chemical variants of tocopherol and tocotrienol: 4 tocopherol and 4 tocotrienol. However, the only one able to meet human requirements is alpha tocopherol. Tocopherol and tocotrienol together called as tocochromanol. Vitamin E subsist in 8 chemical forms. A, β, γ, δ-tocopherol and α, β, γ, δ-tocotrienol.

Vitamin E forms	R1	R2
α-Tocopherol/tocotrienol	CH3	CH3
β-Tocopherol/tocotrienol	CH3	H
γ-Tocopherol/tocotrienol	H	CH3
δ-Tocopherol/tocotrienol	H	H

Table 2: Number/positions of ring methyls in α, β, γ, δ- tocopherol and tocotrienol [48].

The 6-chromanol ring structure is methylated to variable degrees at positions 5, 7, and 8, and the C16 saturated phytyl side is linked to the chromanol ring at position 2 in tocopherols. The presence of unsaturated double bonds at the 3,7 and 11 locations of the phytyl side chain distinguishes tocotrienols. The amount and locations of the methyl groups on the 6-chromanol ring change between tocopherols and tocotrienols; alpha-tocopherol/tocotrienol is tri-methylated; beta-tocopherol/tocotrienol and gamma-tocopherol/tocotrienol are dimethylated; and delta-tocopherol/tocotrienol is mono-methylated [48].

Source of vitamin E

Various foods provide vitamin E. The finest source of vitamin E are seeds and fruits. Green leafy veggies are also good sources of vitamin E. Vitamin E can also be synthesized by plants and photosynthetic organisms [32,33]. To synthesis stereospecific tocopherols, enzymes aid in the synthesis: *RRR*-tocopherols [6]. Tocopherols and tocotrienols can be isolated from vegetable oils and other higher plant components and purified or concentrated. Vitamin E can also be found in dietary supplements. The majority of vitamin E pills contain significantly move vitamin E than meals. Vitamin E is frequently esterified in nutritional supplements and fortified foods to extend its self-life while protecting its antioxidant capabilities.

Tocopherols and Tocotrienols quantity and composition in natural oils differ significantly between plants species and even within the same species. Tocotrienols are only found in a few non-photosynthetic tissues of higher plants, but tocopherols are widely distributed. α-Tocopherol is the more abundant tocopherol in palm, olive, and sunflower oils, whereas the contents of γ-tocopherol in some edible oils like corn, rapeseed, and soybean oils are more than α-tocopherol.

Palm, rice and annatto are the most common sources of tocotrienols, with tocopherol-tocotrienol ratios of 25 : 75, 50 : 50, and 0.1 : 99.9, respectively[49]. The tocotrienol α-, γ-, and δ-tocotrienols are abundant in palm oil. γ-Tocotrienol is the most common vitamin E isoform found in the rice bran oil [36]. One of the key isoforms present in wheat germ oil is β-tocopherol. Only tocotrienols, primarily δ-tocotrienol, were found in the lipid fraction of annatto (*Bixa orellana L.*) seeds, but no tocopherols [13].

Since a preliminary survey on the occurrence of tocopherols in microorganisms [15], its presence has been demonstrated especially in chlorophyll-containing organisms, though not in all of them [48]. Early, a tocopherol-like antioxidant was found in yeasts and a small amount of a-tocopherol was detected in cells of baker's yeast [7]. a-Tocopherolquinol and a-tocopherolquinone were found in the algae, *Euglena gracilis*, in bacteria and in yeasts [24]. Ruggeri., *et al.* (1985) reported enhancement of a-tocopherol production in temperature-stressed cells of *E. gracilis* Z grown photoheterotrophically [42].

Strain	Mainculturesubstances	Yield
E. gracilis	KH medium. Homogentisate. L-tyrosine	5.10 mg/L
E. gracilis	Methane	8.60 ± 0.22 mg/L
Stichococcus bacillaris	Methyl jasmonate (MeJa). Algal culture	0.60 mg/g (DW)
Nannochloropsis oculata	F/2 medium. Ammonium chloride	2.32 ± 0.04 mg/g (DW)
S. cerevisiae	SD medium	320 mg/L

Table 3: Vitamin E produced from microorganisms [49].

(Key: DW - Dry Weight; SD medium - Synthetic Dextrose Medium).

Figure 2: Biosynthesis pathway of vitamin E in yeast.

[https://doi.org/10.1038/s41467-020-18958-9][43].

Biosynthesis of vitamin E

Proposed tocotrienols synthetic pathway in S. Cerevisiae:- MVA pathway (mevalonate pathway), 4-HPP (4-hydroxyphenylpyruvate), HGA (homogentisic acid), GGPP (geranylgeranyl pyrophosphate),MGGBQ(2-methyl-6-geranylgeranyl benzoquinol), DMGGBQ (2,3-dimethyl-5-geranylgeranyl-benzoquinone), HPPD (4-hydroxyphenylpyruvate dioxygenase), SyHPT (homogentisate phytyltransferase), MPBQMT (2-methyl-6-phytylbenzoquinol methyltransferase), TC(tocopherol cyclase), γ-TMT (γ-tocopherol methyltransferase).

Construction of tocotrienols biosynthetic pathway in yeast

Tocotrienols are formed from two precursors in the vitamin E synthetic pathway in plants: homogentisic acid (HGA) synthesised from 4-hydroxyphenylpyruvate (4-HPP) under the catalysis of 4-hydroxyphenylpyruvate dioxygenase (HPPD) [36] and geranylgeranyl pyrophosphate (GGPP) derived from the 2C-Methyl-D-erythritol-4-phosphate(MEP) pathway. geranylgeranyl pyrophosphate (GGPP) is transferred to homogentisic acid (HGA) by homogentisate geranylgeranyl transferase (HGGT) to generate 2-methyl-6-geranylgeranyl benzoquinol (MGGBQ), which is then methylated and/or cyclized to form tocotrienols. 2-methyl-6-phytylbenzoquinol methyltransferase (MPBQMT) catalyses the methylation of 2-methyl-6-phytylbenzoquinol (MGGBQ)to produce 2,3-dimethyl-5-geranylgeranyl-benzoquinone (DMGGBQ), the second ring of which can be closed by tocopherol cyclase (TC) to form gamma-tocotrienol. The ring closure reaction on MGGBQ can also be catalysed by tocopherol cyclase (TC), resulting in the formation of delta-tocotrienol. gamma tocopherol methyltransferase (TMT) methylates delta-tocotrienol and gamma-tocotrienol, yielding beta-tocotrienol and alpha-tocotrienol, respectively[4].In order to construct a complete biosynthetic pathway for tocotrienols in S. cerevisiae, five exogenous enzymes from photosynthetic organisms, namely HPPD, HGGT, MPBQMT, TC, and gamma-TMT, should be added to the endogenous mevalonate (MVA) pathway leading to the formation of geranylgeranyl pyrophosphate (GGPP) and the shikimate pathway leading to the formation of 4-hydroxyphenylpyruvate (4-HPP). These enzymes were cloned from Arabidopsis thaliana and expressed in S. Cerevisiae utilising an EGFP(Enhanced green fluorescent protein) reporter as a reporter. HPPD, MPBQMT, gamma-TMT, and codon-optimized TC all fluoresced, indicating effective expression. HGGT, on the other hand, showed no fluorescence signal even after codon optimization. homogentisate geranylgeranyl transferase (HGGT)and homogentisate phytyltransferase (HPT) are enzymes that catalyse the production of tocopherol precursor in some photosynthetic organisms [5]. All heterologous enzymes needed for the construction of the tocotrienols synthesis pathway in yeast were obtained in this way.

Extraction Methods of Vitamin-E From Microorganisms

Centrifugation

A centrifuge works on the concept of sedimentation, which states that substances separate according to density and particle size under the influence of gravitational force (g-force). Particles are concentrated as a pellet at the bottom of the centrifuge tube and separated from the residual fluid, referred to as supernatant, in this step. It's one of the most common and helpful techniques in the molecular biology lab for collecting cells, precipitating DNA, purifying viral particles, and detecting minor variations in molecule conformation.

For Extraction of Vitamin-E (From Supernatant)

1 mL fermented broth was collected from shaking flasks or the bioreactor and placed in a centrifuge tube, which was centrifuged at 7,000RPM for 10 minutes at 4° C. The cell-free supernatant was collected into a fresh microfuge tube after centrifugation. The absorbance of the supernatant was determined using spectrophotometry.

For Extraction of Vitamin-E (From Pellet)

1 mL fermented broth was collected from shaking flasks or the bioreactor and placed in a centrifuge tube, which was centrifuged at 7,000RPM for 10 minutes at 4°C. The supernatant was removed after centrifugation, and PBS buffer (phosphate-buffered saline) was added to the pellet and combined by vortexing. The pellet was rinsed three times with PBS buffer, vortexed, and centrifuged. Under ice, the bacterial cell pellet was resuspended in 1 ml PBS and ultrasonically disrupted five times at 1 min intervals. The mixture was cleared by centrifugation (7,000RPM; 10 min) and the lysed cells were extracted from the supernatant [3].

Soxhlet Extraction Method for Algae

In 1879, Franz von Soxhlet created a piece of scientific equipment called a Soxhlet extractor. When the target product has a low solubility in a solvent and the impurity is insoluble in that solvent, a Soxhlet extraction is usually required. Typically, a solid material containing part of the desired ingredient is placed into a thimble composed of thick filter paper and poured into the Soxhlet extractor's main chamber. The extraction solvent is placed in a flask with the Soxhlet extractor. A condenser is then added to the Soxhlet. The solvent is brought to a state of reflux. The solvent vapour ascends a distillation arm and floods the chamber containing the solid thimble. Any solvent vapour cools and drips back down into the chamber containing the solid substance, thanks to the condenser. Warm solvent progressively fills the compartment housing the solid substance. In the heated solvent, some of the desired chemical will dissolve. When the Soxhlet chamber is nearly filled, a syphon side arm automatically empties the chamber, allowing the solvent to flow back down to the distillation flasks. This cycle can be repeated several times over the course of hours or days. A fraction of the non-volatile component dissolves in the solvent throughout each cycle. The target component is concentrated in the distillation flask after numerous cycles. The solvent is removed from the extracted chemical using a rotary evaporator after extraction.

Prepare a number of different solvent systems. By combining 20 grammes of Spirulina powder with 300 millilitres of a solvent such as acetone, chloroform, or methanol in an extractor flask for vitamin-E. After the cycle was completed, the extract was collected in a screw-capped vial and stored at 4°C. This extract was used in further analysis.

Analytical methods of vitamin E

Colorimetric Estimation of Vitamin E

After the Emmerie-Engel reaction, colorimetric measurement of vitamin-E (tocopherols) is performed. This reaction is based on tocopherols reducing ferric to ferrous ion, which subsequently produces a red colour when combined with 2,2-dipyridyl reagent.

Preparation of standard

Dissolve commercially available tocopheryl acetate capsule (EBION) in 10 ml methanol.

Preparation of test sample

Fill a flask with 2.5 grammes of Spirulina powder. Slowly pour in 40 mL of 0.1N sulfuric acid, stirring constantly. Allow the content to sit for at least one night. Shake the contents briskly the next morning and filter through Whatman filter paper No-1. In three tubes, pipette 5ml of unknown (Test), 5ml of standard, and 5ml of distilled water (Blank). 2 mL 2, 2-dipyridyl solution, mixed thoroughly in each tube Then, in each tube, add 1 mL ferric chloride solution and well mix. Take the absorbance at 525nm and compare it to a blank.

Thin-layer chromatography (TLC)

Izmailov and Shraiber were the first to introduce thin-layer chromatography in 1938. The stationary phase in thin-layer chromatography (TLC) is an absorbent solid such as alumina, silica gels, cellulose powder, or other absorbent solid material that is spread over a glass plate to form a 2 mm thick and firm adhesive layer of this absorbent solid material, and the mobile phase is a liquid (solvent). TLC is a separation technique in which the components of a mixture are separated by differential migration via a stationary phase's flat bed, with the mobile phase flowing by capillary forces.

To dissolve the residue, a tiny amount of chloroform (20-50μL) was added to the tubes, and the solution was spotted on silica gel G plates. Pure α-tocopherol was also spotted as standard. The plate was then developed in a benzene-ethyl acetate 2:1 solvent system, or, more ideally, in a benzene-ethanol 99:1 solvent system. The tocopherol band was observed after development by spraying the plate with methanolic 0.001% Rhodamine 6G and examining it under UV light. The separation is expressed in terms of a 'RF value,' which is a unit of measurement.

$$RF = \frac{\textit{Distance travelled by solute from the origin}}{\textit{Distance travelled by solvent from the origin}}$$

High-performance liquid chromatography (HPLC)

Because this equipment operates at a high pressure (5.55*107pa), HPLC is sometimes known as high pressure liquid chromatography. HPLC can only evaluate compounds that are dissolved in solvents. HPLC separates compound dispersed in a liquid sample and allows for qualitative and quantitative examination of which components are present in the test sample, as well as how much of each component is present. The mobile phase is the solvent used to separate components in a liquid sample for HPLC examination. At a constant flow rate controlled by the solvent delivery pump, the mobile phase is transported to a separation column, also known as the stationary phase, and subsequently to the detector. The substances in the sample are separated once a particular amount of sample is put into the column. A detector downstream of the column detects the chemicals separated in the column, and each compound is identified and quantified. Shimadzu (LC-20AD) is an ocratic pump with UV (Ultraviolet) detector (SPD-20A) that was run on the LC-solution (Liquid chromatography-soluttion) software for the HPLC analysis. The phenomenex C18 column (250*4.6m* 5 m) was employed, and detection was done at 292nm. For UV visible analysis, Shimadzu (UV1800) was employed.

Fourier transform infrared (FTIR) spectroscopy

The infrared spectrum of absorption, emission, and photoconductivity of solids, liquids, and gases is obtained using the FTIR (Fourier transform infrared spectroscopy) technique. It offers a wide range of applications in the elucidation of structures that are either chemically generated or of natural origin. It's a mathematical method for converting a time domain spectrum to a frequency domain spectrum. The existence of organic and inorganic components in a sample can be determined using FTIR. The specific chemical groups present in the sample will be determined using spectrum data in the automated spectroscopy software based on the infrared absorption frequency range 600-4000 cm-1.

Characterization of isolate by DNA sequencing

For further characterisation, isolate organisms that produce vitamin E must be sequenced. The sequencing is evaluated, and the online local alignment tool BLAST (Basic local alignment search tool) is used to search the NCBI (National center for biotechnology information) database for organisms with similar or identical sequences.

Vitamin E deficiency

Low levels of vitamin E can lead to

- **Muscle weakness:** The central nervous system need vitamin E to function properly. It is one among the body's most important antioxidants, and a lack of it causes oxidative stress, which can cause muscular weakness.
- **Coordination and walking difficulties**: Certain neurons, known as Purkinje neurons, might die down as a result of a deficit, impairing their capacity to send messages.
- **Numbness and tingling:** Damage to nerve fibres can impede nerves from properly transferring messages, resulting in these symptoms, sometimes known as peripheral neuropathy.
- **Vision deterioration:** Light receptors in the retina and other cells in the eye can be weakened by a vitamin E deficit. This can result in eyesight loss over time.
- **Immune system problems:** According to some studies, a deficiency of vitamin E might impair immune cells. Senior citizens may be particularly vulnerable

Causes of deficiency

Genetics

Vitamin E insufficiency is commonly inherited. Learning about your family's medical history might help you diagnose some uncommon, hereditary disorders. Congenital abetalipoproteinemia and familial isolated vitamin E insufficiency are two of these disorders that are persistent and cause severely low vitamin E levels.

Medical conditions

Vitamin E insufficiency can also occur as a result of disorders that significantly limit fat absorption. This is due to the fact that the body requires fat to properly absorb vitamin E.

Some of these diseases include

- Chronic pancreatitis
- Celiac disease
- Cholestatic liver disease Trusted Source
- Citric fibrosis

Deficiency is also frequent in newborns and babies born prematurely, who have lower birth weights and fat levels. Because an undeveloped digestive tract might interfere with fat and vitamin E absorption, premature newborns are especially vulnerable. Vitamin E deficiency in young babies can cause hemolytic anaemia, which causes red blood cells to die.

Diagnosis

- Physical examination
- Sometimes blood tests

Vitamin E deficiency is diagnosed based on symptoms, the existence of risk factors, and the findings of a physical examination. To confirm the diagnosis, blood tests to evaluate vitamin E levels may be performed.

Treatment

Vitamin E supplements

Vitamin E deficiency is treated by taking vitamin E tablets orally. Supplements may be given to premature neonates to avoid the onset of diseases. Vitamin E is abundant in breast milk and commercial formulae, thus most full-term neonates do not require supplements.

Biological role of vitamin E

Vitamin E is an essential anti-inflammatory chemical because it affects a variety of components that impact the immune system, either directly or indirectly. Vitamin E has the ability to reduce inflammation in a variety of ways: It has an effect on proinflammatory enzymes including (cyclooxygenase) COX, which is responsible for the creation of prostaglandins (PG) E2 [40,43]; (PG) E2 is a proinflammatory mediator linked to a number of senile illnesses, including cancer, arthritis, and cardiovascular disease [26]. It regulates the proliferation and activation of immune cells such as T cells, lymphocytes, and natural killer cells (natural killer) NK cells [29]. Finally, it inhibits the release of proinflammatory cytokines including (Interleukin 6) IL-6 and (tumor necrosis factor) TNF. Vitamin E is essential in the prevention of chronic inflammation [40,29]. Chronic inflammation is inextricably connected to oxidative stress [17], and it is the primary cause of age-related illness and cancer in conjunction with it [40]. The biological role of vitamin E is depicted schematically in the image below.

Figure 3: Biological role of vitamin E.
[https://doi.org/10.3390/ma14133691][14].

Biomedical Applications of Vitamin E

In Prosthetic Implants

Vitamin E is being studied as a chemical that might be integrated or utilised as a coating on prosthetic materials to give them extra qualities.

In Blend Form or through Bulk Diffusion

Tocopherol's greatest effective application to far has been as an antioxidant in the stabilisation of high molecular weight polyethylene (UHWMPE), making vitamin E a helpful chemical in the biomedical area. Prior to implantation, UHWMPE inserts were sterilised with gamma rays until the late 1990s. Unfortunately, this method of sterilisation posed a significant oxidative problem for the polymer, as the radiation increases the likelihood of oxidative destruction, making it more unstable and brittle, resulting in severe implant loosening [34].

As a Coating

The issue of joint replacement due to loosening is one of the most prevalent biomedical implant issues. Infections and wear are common causes of failure, with debris forming in the particular region of the prosthesis causing persistent inflammation. A coating with anti-inflammatory and anti-bacterial properties can surely assist to decrease these occurrences, hence minimising the occurrence of septic or aseptic loosening of prosthesis. As a result, while still in the research phase, some studies advise treating metal surfaces with vitamin E to provide antibacterial and anti-inflammatory characteristics or to aid Osseo integration [16,26].

In Tissue Engineering

Tocopherol has been a fascinating study topic in the field of wound healing and tissue regeneration due to its antioxidant and anti-inflammatory properties. Vitamin E has been mixed, encapsulated, or blended with several types of polymeric materials that have been handled as scaffolds, hydrogels, or films in the literature.

In Wound Healing

Wound healing is a physiological process that occurs after an injury to the skin, such as a laceration or a burn. Inflammation, proliferation, and maturation are the phases that make wound healing a difficult and time-consuming process [27,31]. It is feasible to create a polymeric wound dressing that leverages the antioxidant potential of vitamin E to aid and speed the healing process by combining vitamin E with polymers commonly used in biomedicine. Hydrogels and scaffolds are the recommended dressing medium for full skin regeneration because they are three-dimensional and encourage cell adhesion and development.

In Tissue Regeneration

Tissue repair is the process of a tissue's compensatory regeneration, which results in the restoration of its structure and function. Tissues can be healed by implanting three-dimensional constructs, such as scaffolds, that can encourage cell growth and adherence, allowing for full tissue regeneration [26]. In this case, the same materials as before are utilised, which can sustain the tissue both mechanically and cellularly, and which may disintegrate in a physiological environment when they've done their job.

Vitamin E in drug delivery

Pharmaceutical Use

Vitamin E has recently acquired prominence as a result of its shown anticarcinogenic properties, making it a promising option for use as an adjuvant or preventative anticancer therapy. According to the research, and tocopherols are more powerful inducers of apoptosis than and tocopherols; in fact, despite its antioxidant properties, tocopherol does not appear to be cytotoxic.

As a delivery system

The bulk of approved anti-cancer drugs, such as paclitaxel and docetaxel, are lipophilic, making bioavailability and, as a result, absorption by target tissues challenging [8]. The phenolic component of tocopheryl etherlinked acetic acid (TEA) and tocopherol succinate (TOS), both of which have been discovered to be potent anti-cancer agents, is frequently converted to esters using acetic or succinic acid to expand the hydrophilic part and optimise the amphiphilic structure, resulting in more stable esterified compounds that can be easily used for drug delivery [1,35]. D-a-tocopheryl polyethylene glycol succinate (TPGS) is produced by esterifying tocopherol succinate (TOS) with the important biomaterial polyethylene glycol (PEG), which is widely used in drug delivery as a nonionic surfactant and micellar stabiliser, capable of forming micelles in water at concentrations as low as 0.02 wt percent. Another interesting synthetic polymer is made by esterifying alphatocopherol succinate with the glucidic polymer inulin (INU), resulting in amphiphilic molecules called INVITE, which are based on inulin with hydrolyzable groups and a vitamin E-based radical chain.

Figure 4: Chemical structure of different forms of vitamin E used for drug delivery system. [https://doi.org/10.3390/ma14133691][14].

As dietary supplements

Because of the increasing prevalence of lifestyle problems caused by nutrition and a sedentary lifestyle, there is a rising awareness of health issues and, as a result, a large market for wellness goods and supplements. It promotes immunological function and maintains vitamin A levels, among other things, as a health supplement. Natural and synthesised versions of vitamin E, particularly RRR a-tocopherol ether-linked acetic acid analogue, are well recognised for their anti-cancer properties (α -TEA).

In cosmetic industry

Natural Vitamin-E is commonly utilised in cosmetics and skin care products, such as lotions, creams, lipsticks, and sunscreens, as an antioxidant. It shields the skin from damaging UV rays and inhibits melanin deposition. It reduces the indications of ageing, heals scars and acne, and enhances the moisture content and texture of the skin. It also makes lipid-based cosmetics more stable.

Figure 5: Dietary role of Vitamin E in humans.
[https://www.iari.res.in/files/Bulletins/VitEbulletin%20_31012020.pdf] [48].

Conclusion

This review focused to isolate microbes which can produce vitamin E, for future enrichment of such isolates to solve vitamin E deficiency in our society. Vitamin E has a various number of relevant biological actions (like anti-inflammatory properties, antioxidant properties, etc.), and having positive impacts on immune system, bone health, age-related diseases, cancer and protection of skin. Antimicrobial action of vitamin E and its derivate compounds is still under discussion.

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Competing Interests

The authors declare that there is no conflict of interests.

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