Production of γ-tocopherol Rich Mixtures

By
Jessica John
Sam VanGordon
Justin Sneed

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Executive Summary

The primary focus of this project is to analyze the methods available for processing soybean oil deodorizer distillate, SODD, to produce various concentrations of tocopherol mixtures for vitamin E dietary supplement uses. An enzymatic distillation process utilizing *Candida rugosa* lipase process SODD to produce an α-rich tocopherol mixture currently sold on the market. The plant will have the capacity to produce 16,500 kg/day of an α-rich tocopherol mixture. The α-rich tocopherol mixture will be processed by column chromatography, in order to produce γ-δ-rich tocopherol, and 99.9% pure γ-tocopherol. The plant will be capable of producing 1,000kg/yr of pure γ-tocopherol, and 15,100 kg/yr of γ-δ-tocopherol mixture. The quantity of γ-δ and γ-tocopherol produced may be varied as sales prices fluctuate.

In order to determine the profitability of producing pure γ-tocopherol, five plant designs were considered.

- Design 1 produces 1kg/yr γ-tocopherol, and 5,510,585 kg/yr γ-δ-tocopherol
- Design 2 produces 10kg/yr γ-tocopherol, and 5,510,563 kg/yr γ-δ-tocopherol
- Design 3 produces 100kg/yr γ-tocopherol, and 5,510,344 kg/yr γ-δ-tocopherol
- Design 4 produces 1,000kg/yr γ-tocopherol, and 5,508,148 kg/yr γ-δ-tocopherol
- Design 5 processes 0 kg/yr γ-tocopherol, and 5,510,588 kg/yr γ-δ-tocopherol

Design 5 is used as a basis of comparison in order to determine the relative profitability of the γ-tocopherol production process. In general, as the production rate of pure γ-tocopherol increases, the net present worth and annual return on investment increases. Design 4, which produced 1,000 kg/yr γ-tocopherol, had a net present worth of $1.2 billion, whereas Design 1, which produced 1 kg/yr γ-tocopherol, had a net present worth of $928 million. The net present worth of Design 5 was $930 million, slightly higher than the net present worth of Design 1, because the revenue generated annually is not substantial enough to make up for the increased capital investment. In order for γ-tocopherol production to be profitable, a minimum of 8.61 kg/yr γ-tocopherol must be produced.

Introduction

Objective

The objective of this project was to design an economic process capable of producing high yields of γ-δ and γ-tocopherol rich mixtures from soybean oil deodorizer distillate, SODD, which were to be marketed as a safe alternative to α-rich tocopherol, also known as vitamin E. SODD is currently processed to produce a tocopherol mixture containing the homologues α, δ, and γ-tocopherol. This α-rich tocopherol mixture is used extensively in pharmaceuticals, cosmetics, and animal feed. Tocopherols are fat-soluble vitamins that neutralize free radicals in the body and play an essential role in reproduction. However, recent studies suggest a link between the consumption of α-tocopherol and increased risk of heart disease. Though γ and δ-tocopherol have health benefits similar to those of α-tocopherol, consumption of these two homologues is not currently associated with an increased risk of heart disease.

Background

γ-Tocopherol

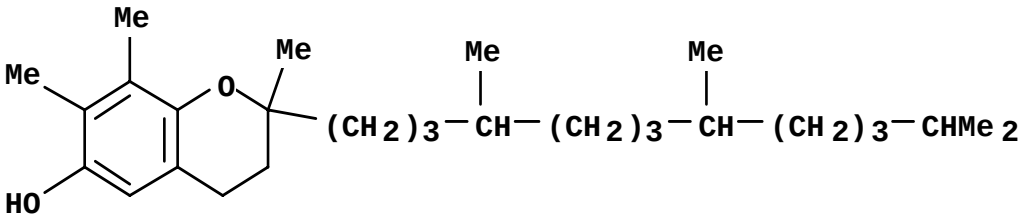


Figure 1. γ -tocopherol chemical structure

Tocopherols exist in various plants, such as soybeans, in a mixture of homologues: alpha, beta, gamma, and delta tocopherol. When these tocopherol-containing plants are processed, tocopherols may be extracted with other materials from the plant matter. This mixture may be further processed to remove the tocopherol homologues for use in pharmaceuticals, animal feed, human dietary supplements, and other areas. Tocopherols are fat-soluble antioxidants that are essential for normal reproduction and neutralize free radicals in the body. Preliminary studies revealed that α-tocopherol is a powerful antioxidant which protects human cells from oxidation and neutralizes damaging unstable free radicals. Practically all supplemental tocopherol is d-alpha-tocopherol, also known as vitamin E. Vitamin E is the second best selling vitamin in the U.S., with multi-vitamins being the top seller. Sales of vitamin E topped the $706 million for 2003[9]. Recent studies indicate that γ-tocopherol type may help prevent prostate cancer and heart disease, whereas α-tocopherol may actually increase risk of heart disease. In addition, studies show that α-tocopherol has a higher affinity in the body than γ-tocopherol. Therefore, the presence of α-tocopherol inhibits the absorption rate of

γ-tocopherol. Consequently, in order for a γ-tocopherol mixture to be truly effective, there must be no more than a trace amount of α-tocopherol present in the mixture. For these reasons, industrial emphasis is shifting towards production of γ-tocopherol mixtures containing little alpha homologues, and away from production of the more common α-tocopherol.

γ-tocopherol vs. α-tocopherol

According to Hensley[2], α-tocopherol is generally stated to be "more biological active" than the desmethyl tocopherols. This statement is perhaps a generalization arising from misinterpretation of older literature taken out of historical context. Past studies showed α-tocopherol as a fertility maintenance agent. In standard fertility-restoration assays, γ-tocopherol is only 10% as active as α–tocopherol. However, there is no prior reason to expect that tocopherol efficacy as a fertility agent would correlate with other biological activities. There is some evidence that supplementation with α-tocopherol depresses the serum level γ-tocopherol and is therefore undesirable. A goal of this process is to obtain a mixture containing γ-tocopherol and relatively free of α-tocopherol.

Raw Materials

The source of tocopherols for this process is soybean oil deodorizer distillate, SODD, a byproduct of soybean oil production. Tocopherols found in soybeans are removed during the soybean oil process via the deodorizer distillate. SODD may be purchased from numerous soybean processing factories across the United States. SODD normally contains anywhere from 10% to 15% tocopherols, 60% of which are γ-

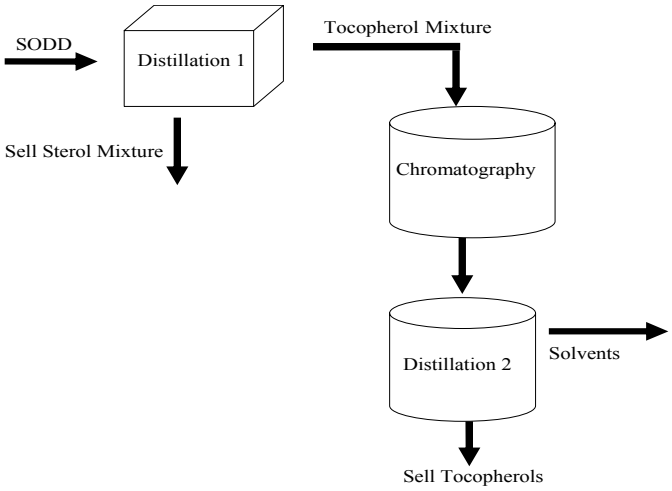
tocopherol, 20% of which are α-tocopherol the remainder being δ-tocopherol. AG Processing, Inc., located in Nebraska, and Bunge North America, located in Indiana, are two providers of SODD. SODD is usually shipped by truck loads of 48,000 lbs., and sold at a price of $0.14/kg.

Production Processes

Overall Production

The production of γ-tocopherol rich mixtures includes three main processes as shown in Figure 2. SODD is first purified by using molecular distillation coupled with enzymatic reactions. The molecular distillation removes unwanted components from the SODD mixture while the enzymatic reactions convert unwanted components into molecules that can be more easily distilled. This process purifies the original SODD mixture containing 10% tocopherols into a mixture that contains 75% tocopherols, while creating a byproduct stream of free fatty acids, sterols, and sterol esters which are then sold. This new tocopherol rich mixture is then further purified by high performance chromatography. Tocopherol homologues exhibit different acidities in weakly self-dissociating solvents. Basic anion exchange resins and non-ionic exchange resins are used in the chromatography to exploit these chemical differences. The chromatography is able to produce a product comprised of mostly γ-tocopherol, 77%, and small amounts of α-tocopherol, 5%, as well as a product with 99% γ-tocopherol. Next, these to products are distilled, evaporating the solvents from the chromatography and leaving the tocopherols behind for sale.

Figure 2. Overall Production Flow



Distillation of Crude Soybean Oil Deodorizer Distillate

The distillation of crude soybean oil deodorizer distillate is a multiple unit process consisting of two primary types of stages (1) enzyme reaction and (2) molecular distillation. This is illustrated in Figure 3. The molecular distillation removes unwanted components from the SODD mixture, while the enzymatic reactions using *Candida rugosa* lipase convert unwanted components into molecules that can be more easily distilled. This process purifies the original SODD mixture containing 10% tocopherols into a mixture that contains 75% tocopherols, while creating a byproduct stream of free fatty acids, sterols, and sterol esters which are then sold. The distillation process was designed with and without methanol induction. The whole distillation process yields a 90% recovery of tocopherols from crude SODD. Other leading industrial methods, such as liquid-liquid extraction using cold ethanol, only achieve a maximum recovery of 75% of tocopherols from crude SODD[3,4].

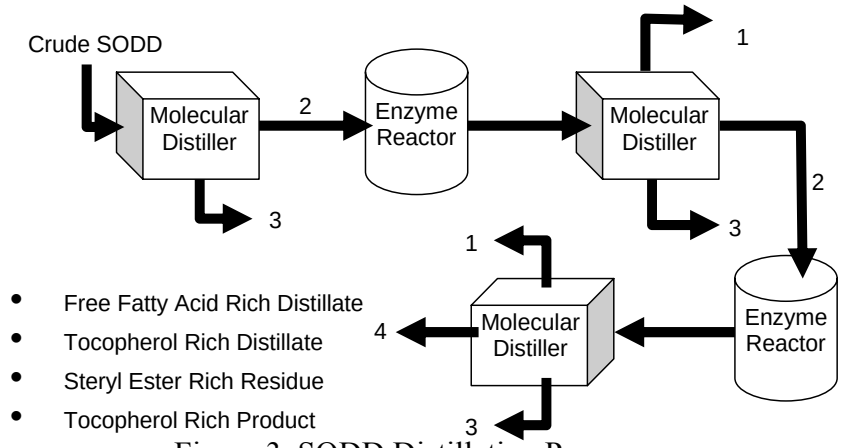


Figure 3. SODD Distillation Process

Enzyme Reaction

The purpose of the enzyme reaction is to transform substances in the process mixture that have molecular weights similar to tocopherols. Altering the molecular structure of the substances changes the molecular weight of the substances, thus creating substances that have a higher or lower boiling point than the tocopherols. This allows the use of heat for separation of unwanted substances from the tocopherols. Sterols are the main substances that can not be separated out from SODD by molecular distillation because their molecular weight is very similar to that of tocopherols.

Lipases are a group of enzymes that catalyze the hydrolysis of fats into glycerol and fatty acids. During the enzyme reaction *Candida rugosa* lipase hydrolyzes acylglycerols. The lipase also bonds FFAs (organic acids) and sterols (alcohols) together to form steryl esters (inorganic salts) in a process known as esterification. This is useful because steryl esters have a higher boiling point than tocopherols. Therefore vaporization can be used for the separation of tocopherols from the mixture. The vaporization is performed under vacuum to prevent the decomposition of tocopherols under heating conditions. Because water is necessary for hydrolysis of the acylglycerols, water is added to the reactors.

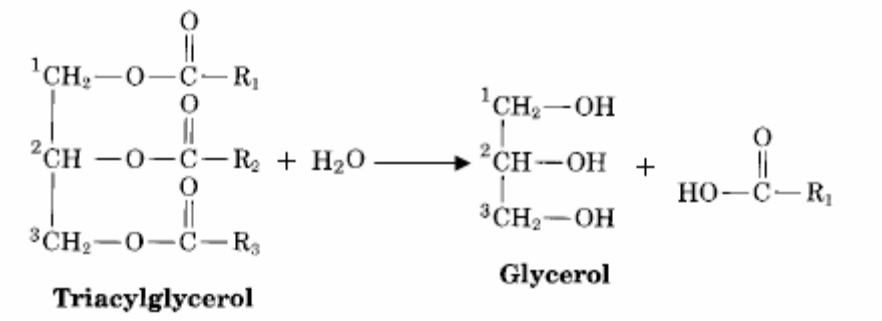


Figure 4. Hydrolysis: where R_1, R_2, and R_3 are fatty acid residues.

In one of the setups, methanol, an alcohol, is added to the reactors. Methanol is added to the reactors in a ratio of 2 mol of methanol per 1 mol FFA, to esterify additional FFAs. This creates a mentholated free fatty acid (FAME) which as a lower boiling point than the tocopherols. By creating FAME, more impurities can be removed from the process mixture which further concentrates the tocopherols. This creates a product advantage over the non-methanol setup. The use of methanol can create a tocopherol mixture product containing 75% tocopherols while the non-methanol setup only creates a 65% tocopherol mixture, which is the same product that an industrial liquid-liquid extraction process would achieve. Methanol is a simple alcohol but other alcohols can be used in its place.

In order to keep the process continuous, the enzyme reactions take place in multiple tanks. While one tank is being prepped and filled for the start of the enzyme reaction, another tank where the enzyme reaction is at the end of its gestation or reaction time is emptying out. A tank remains empty at all times, in case deviations in flowrates require overflow to the next tank in the system. A simple diagram of this can be seen in Figure 5. This creates a system of X+2 tanks, where X is determined from available tank sizes and system flows into the enzyme reaction phase.

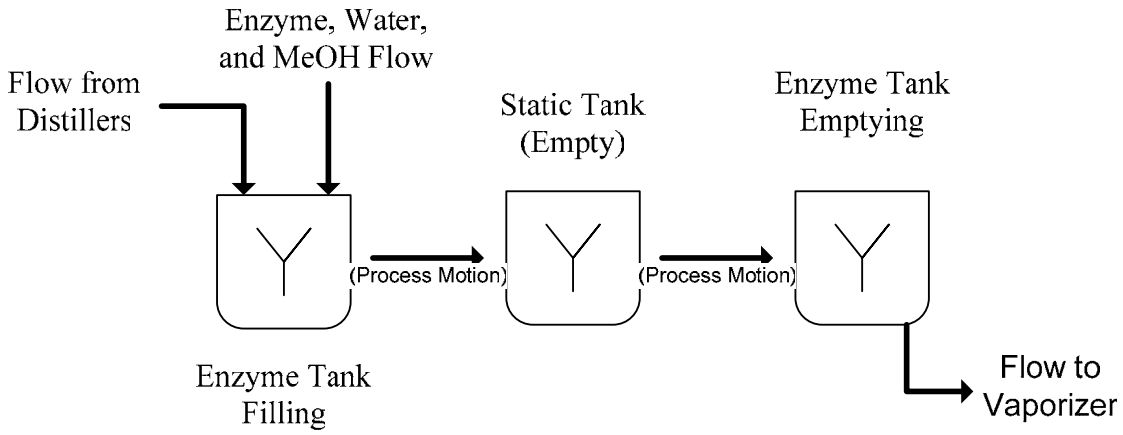
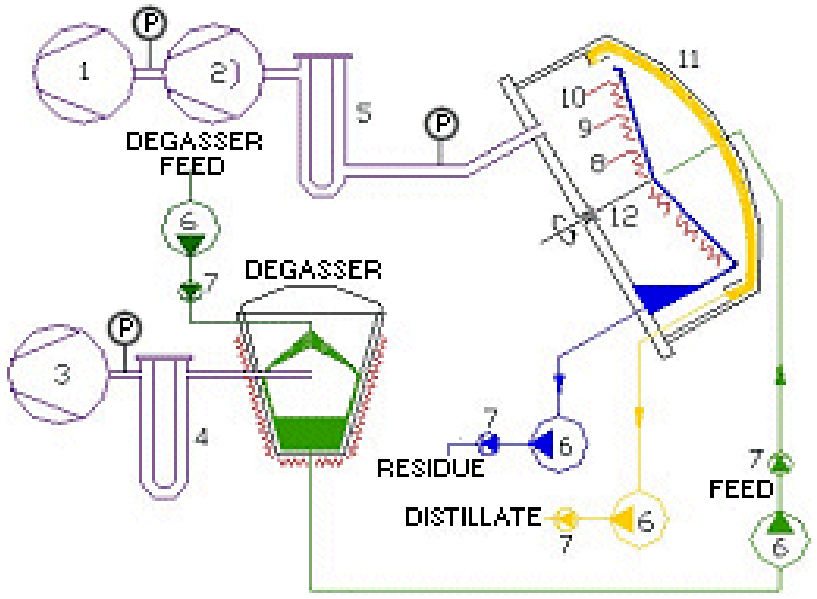


Figure 5. Tank Flow Schematic

Molecular Distillation

Molecular distillation, also known as short-path distillation, is the separation of materials using differences in the boiling points of the materials under vacuum conditions (see Appendix B). Molecular distillation uses heat in order to bring the substances to their boiling points. All materials, both liquid and solid, are capable of vaporization under extreme low pressure conditions (i.e. pressure ~0.001 mm Hg), provided a high enough temperature can be employed. The reduction in the pressure lowers the interaction and collisions of chemicals with inert gases, gasses that do not react with the components in the process mixture, present in the reaction chamber. By applying a vacuum to a system, inert gasses are removed from the reaction chamber. Also, by putting the process in vacuum, less heat is needed to vaporize a substance, thus lowering boiling points by approximately 150 ºC. Molecular distillation is most useful in separating molecules of large molecular weight because larger molecules begin to break down under extreme heats (over 250 ºC) at atmospheric pressure (760 mm Hg.)

For the molecular distillation mechanism to operate properly and effectively, molecules need to be removed from interaction areas. Interaction areas include, but are not restricted to, condensing surfaces and inert molecules in gas pathways. Some methods of molecule removal from molecular distillers include condensation, reaction, adsorption, and pumps. Creating a short unobstructed path to condensing surfaces improves the operation of molecular distillation. Ideally the condensing surface of a molecular distiller should cover all the paths an evaporated molecule can take.



1. Backing/Roughing Vacuum Pump
2. Diffusion Ejector Pump (High Vacuum)
3. Roughing Vacuum Pump (Degasser Option)
4. Trap (Degasser Option)
5. Chamber Trap
6. Liquid Transfer Pump
7. Check Valve Rotor
8. Inner Heater Rotor
9. Middle Heater Rotor
10. Outer Heater
11. Domed Condenser
12. Rotor

P - Vacuum Pressure Gauge

Figure 6. Macro 36 Molecular Distillation Still Diagram (centrifugal still)[13]

Centrifugal molecular distillation is the molecular distillation used in the enzyme distillation process. Centrifugal molecular distillers operate with a feed entering at the center of a rotating disk. The disk rotates, moving the feed out to the ends of the disk and creating a film layer across the disk. Heating elements raise the temperature of the film on the disk causing components in the film to vaporize away from the film. The vapor condenses on a condensing plate, or dome, and the condensate runs into a collector on the side of the dome. A collection ridge at the end of the disk collects the film residue that is not vaporized. During the process, a continuous vacuum pump is operating to keep the system at low pressure.

Methanol Process

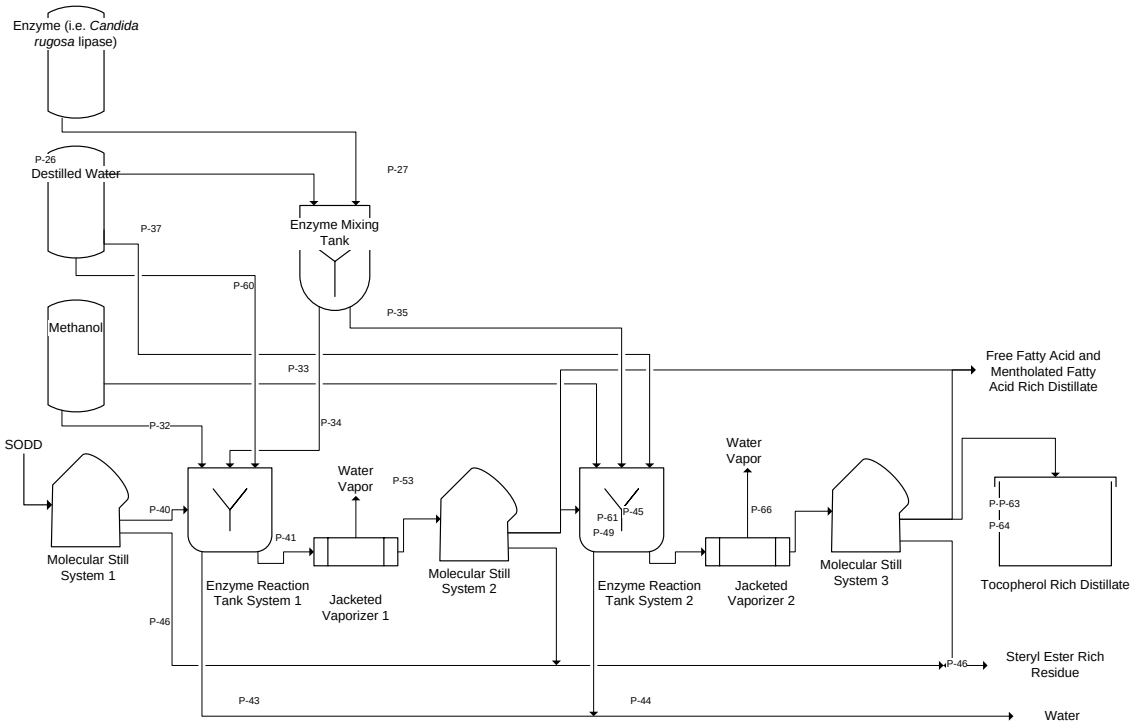


Figure 7. Process diagram for staged molecular distillation & enzyme reaction process with methanol

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Table 1. Stage descriptions for molecular distillation & enzyme reaction process with methanol

Stage	**Purpose**	**Collect**	**Remove**
Enzyme Mixing Tank	Dilute *Candida rugosa* lipase before adding to enzyme reactor	0.1g/mL solution of *Candida rugosa* lipase	N/A
Molecular Still System 1			
Still 1-1 (240°C, 0.02 mmHg)	Remove High boiling point substances (steryl esters, di-acylglycerols and tri-acylglycerols)	Distillate	Residue
Enzyme Reactor 1 (30°C)	Hydrolize acylglycerols, bond FFA and Sterols into steryl esters, bond FFA and methonal into FAME	Oil Layer	Water Layer
Vaporizer 1 (110°C)	Remove excess water from process solution	Process Solution	Water Vapor
Molecular Still System 2			
Still 2-1 (160°C, 0.2 mmHg)	Remove FFA and FAME from process solution	Residue	Distillate
Still 2-2 (240°C, 0.02 mmHg)	Concentrate Tocopherols in distillate	Distillate	Residue
Enzyme Reactor 2 (30°C)	Hydrolize acylglycerols, bond FFA and Sterols into steryl esters, bond FFA and methonal into FAME	Oil Layer	Water Layer
Vaporizer 2 (110°C)	Remove excess water from process solution	Process Solution	Water Vapor
Molecular Still System 3			
Still 3-1 (160°C & 175°C, 0.2 mmHg)	Remove FFA and FAME from process solution	Residue	Distillate
Still 3-2 (240°C, 0.02 mmHg)	Concentrate Tocopherols in distillate	Distillate	Residue

1. Initially a first stage molecular distillation is performed. This action is carried out in order to remove high boiling point substances, including steryl esters, tri-acylglycerols, and di-acylglycerols, from the raw SODD. The molecular distiller is operated at 240°C, 0.02 mmHg. The distillate goes to waste while the residue is passed onto the next step in the process.

2. The enzyme tank is loaded with a set amount of process material (molecularly distilled fraction). The tank is then loaded with *Candida rugosa* lipase at 200 U/g of process material. One unit (U) is the amount of enzyme required to liberate 1 μmol of fatty acid per minute. Water is also added to the reaction tank to a level where 20%wt of the mixture is water. This solution is then incubated and agitated. The mixture is incubated for 16 hours. Methanol is then added at 2 moles of methanol per mole of FFA in the mixture. This mixture is then incubated for an additional 6 hours in order to esterify FFAs in the reactor creating FAMEs. The water layer in the reactor is then drained out to waste and the oil layer is passed onto a vaporizer.
3. In the vaporizer, excess water is then boiled away from the oil layer to below 100 ppm and passed onto the next molecular distiller. This is monitored by a density sensor.
4. A second system of molecular distillers is used to remove FFAs and FAMEs from the process mixture. The 1st distiller is operated at 160°C and 0.2 mmHg. The distillate goes to waste and the residue is passed on to the 2nd distiller. This 2nd distiller in series operates at 240°C, 0.02 mmHg. This residue goes to waste and the distillate is passed onto the next step.
5. The second series of enzyme tanks are operated in the same fashion as the first enzyme reactors. The mixture is incubated for 16 hours. An amount of methanol is then added at 2 moles of methanol per mole of FFA in the mixture. This mixture is then incubated for an additional 6 hours to esterify FFAs in the reactor

creating FAMEs as before in the first reactors. The water layer in the reactor is then drained out and the oil layer is passed onto a vaporizer.

6. The second vaporizer has the same function as the first vaporizer in which water is reduced to 100 ppm in the oil layer coming off of the reactors which is monitored by a density sensor.
7. The final molecular distillers remove two fractions that are FFA and FAME rich to leave a tocoperol rich (75%wt) distillate and a steryl ester rich resin. A series of two stills are used, with the 1st still using two heat profiles. The 1st molecular still operates at 160°C and 175°C with 0.2 mmHg of pressure. The distillates go to waste and the residue is passed on to 2nd distiller. The 2nd molecular distiller operates at 240°C and 0.02 mmHg. The residue is passed to waste.
8. The exit distillate flow is ether collected for sale, passed on to a secondary process or both.

Non-Methanol Process

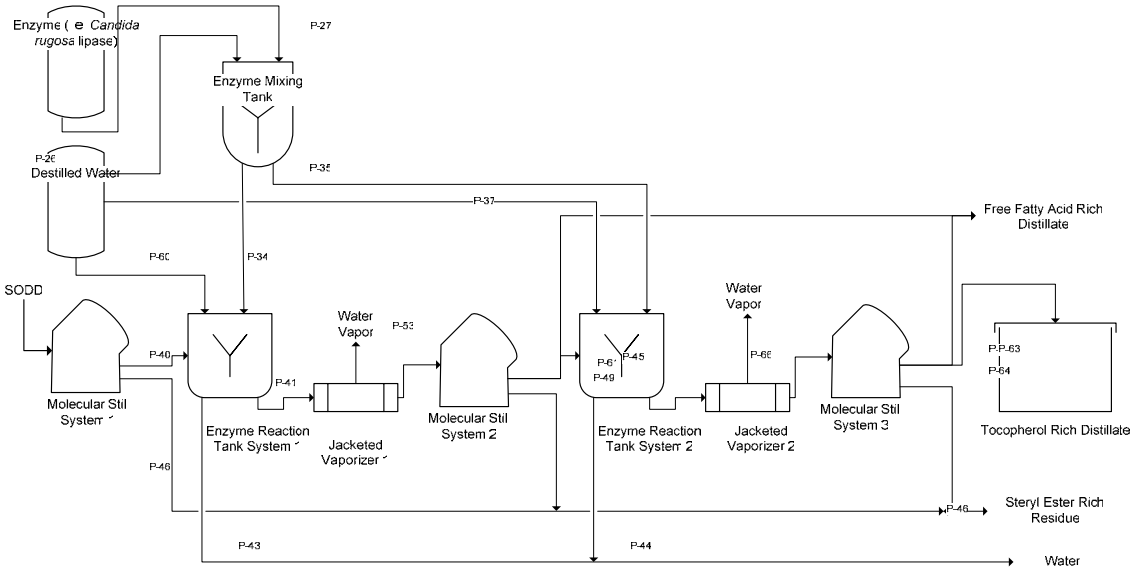


Figure 8. Staged molecular distillation & enzyme reaction process w/o methanol.

Table 2. Stage descriptions for molecular distillation & enzyme reaction process w/o methanol

Stage	**Purpose**	**Collect**	**Remove**
Enzyme Mixing Tank	Dilute *Candida rugosa* lipase before adding to enzyme reactor	0.1g/mL solution of *Candida rugosa* lipase	N/A
Molecular Still System 1			
Still 1-1 (250°C, 0.2 mmHg)	Remove High boiling point substances (steryl esters, di-acylglycerols and tri-acylglycerols)	Distillate	Residue
Enzyme Reactor 1 (35°C)	Hydrolize acylglycerols, bond FFA and Sterols into steryl esters	Oil Layer	Water Layer
Vaporizer 1 (110°C)	Remove excess water from process solution	Process Solution	Water Vapor
Molecular Still System 2			
Still 2-1 (250°C, 0.2 mmHg)	Remove FFAs from process solution	Distillate	Residue
Enzyme Reactor 2 (35°C)	Hydrolize acylglycerols, bond FFA and Sterols into steryl esters	Oil Layer	Water Layer
Vaporizer 2 (110°C)	Remove excess water from process solution	Process Solution	Water Vapor
Molecular Still System 3			
Still 3-1 (160°C & 200°C, 0.2 mmHg)	Remove FFA from process solution	Residue	Distillate
Still 3-2 (230°C, 0.04 mmHg)	Concentrate Tocopherols in distillate	Distillate	Residue

1. Initially a first stage molecular distillation is performed. This action is carried out in order to remove high boiling point substances, including steryl esters, tri-acylglycerols, and di-acylglycerols, from the raw SODD. The distiller is operated at 250°C and 0.2 mmHg. The distillate goes to waste while the residue is passed onto the next step in the process.
2. The enzyme tank is loaded with a set amount of process material (molecularly distilled fraction). The tank is then loaded with *Candida rugosa* lipase at 200 U/g of process material. One unit (U) is the amount of enzyme required to liberate 1

μmol of fatty acid per minute. Water is also added to the reaction tank to a level where 20%wt of the mixture is water. This solution is then incubated and agitated. The mixture is incubated for 24 hours at 35 °C. The water layer in the reactor is then drained out and the oil layer is passed onto a vaporizer.

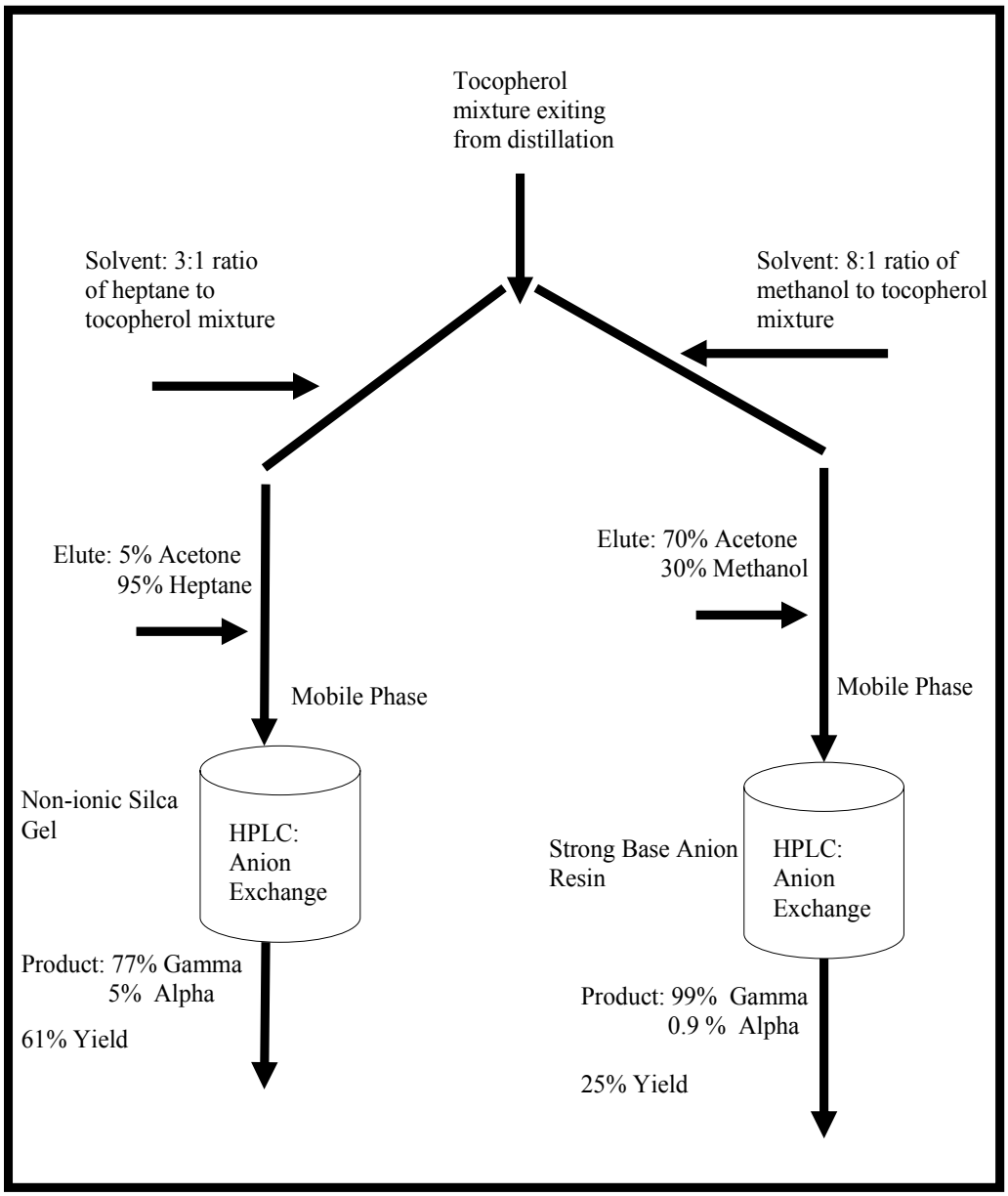
3. In the vaporizer, excess water is boiled away from the oil layer to below 100 ppm and passed onto the next molecular distiller. This is monitored by a density sensor.
4. A second system of molecular distillers is used to remove FFAs from the process mixture. The distiller is operated at 250°C and 0.2 mmHg. This residue goes to waste and the distillate is passed onto the next step.
5. The second series of enzyme tanks are operated in the same fashion as the first enzyme reactors. The mixture is incubated for 24 hours at 35 °C. The water layer in the reactor is drained out and the oil layer is passed onto a vaporizer.
6. The second vaporizer has the same function as the first vaporizer in which water is reduced to 100 ppm in the oil layer coming off of the reactors which is monitored by a density sensor.
7. The final molecular distiller removes two fractions that are FFA rich to leave a tocoperol rich (65%wt) distillate and a steryl ester rich resin. A series of two distillers are used, with the first distiller using two heat profiless. The 1st molecular distiller operates at 160°C and 200°C with 0.2 mmHg of pressure. The distillates go to waste and the residue is passed on to 2nd distiller. The 2nd molecular distiller operates at 230°C and 0.04 mmHg. The residue is passed to waste.

8. The exit distillate flow is ether collected for sale, passed on to a secondary process or both.

Chromatography

High performance liquid chromatography, HPLC, is used for the separation of α-tocopherol from γ-tocopherol. As discussed by Shizumasa[13], tocopherol homologues exhibit different acidities in weakly self-dissociating solvents (i.e. methanol and acetone). The self-dissociating solvents have a tendency to release protons in a slight degree. Basic anion exchange resins and non-ionic exchange resins are used in the chromatography to exploit these chemical differences. As shown in Figure 9, most of the tocopherol mixtures are combined with a non-polar solvent and passed through the column with non-ionic exchange resin. The remainder of the tocopherol mixtures are combined with a polar solvent and passed through a strong base anion resin. The non-ionic exchange resin is used to produce a product comprised of mostly γ-tocopherol, 77%, and small amounts of α-tocopherol, 5%. The strong base anion resin is used to achieve a product with 99% γ-tocopherol. A total of 1,315 HPLC columns are needed to process the plant's full capacity, 24,750 kg/day tocopherol mixture. Running at full capacity, the HPLC columns are able to produce 15,100 kg of γ-δ-tocopherol per day.

Figure 9. Chromatography Flow Diagram



Producing γ-δ-tocopherol Products

To produce a product that is comprised of mostly γ-tocopherol and small amounts of α-tocopherol, a non-ionic absorbent resin is used. The non-ionic silica based resins

separate the tocopherols based on polarity of the solvent and adsorption of the tocopherol oil onto the resin. The mobile phase is created by dissolving the tocopherol mixture in a long chain alkane, heptane, in a 3:1 ratio. A HPLC column is slurry packed in heptane. The resin is flushed with 10 bed volumes of HPLC grade heptane to ensure all traces of water have been removed. Thirty-three liters of the mobile phase is loaded into the column. This load contains 11 kilograms of tocopherols. The mobile phase is then eluted by a seven stage process. First three hundred and twenty-nine liters of pure heptane is eluted through the column. This stage removes a high percentage of α-tocopherol. Next, a series of 165 liter mixtures of 95% heptane and 5% acetone are eluted comprising of stages 2-5. These stages remove a high percentage of γ-tocopherol. This is due to the addition of the ketone acetone. The acetone modifies the polarity to suit desorption of γ-tocopherol. Stage 6 is eluted with 329 liters of a 70% acetone and 30% heptane mixture. The large amount of acetone is conducive to desorption of δ-tocopherol. The final stage,

Figure 10. Loading for Non-ionic Resin

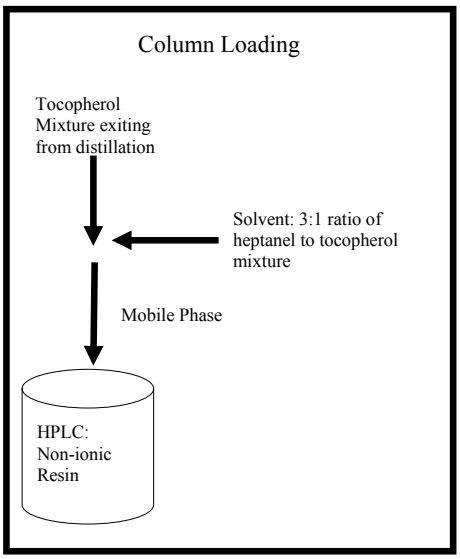
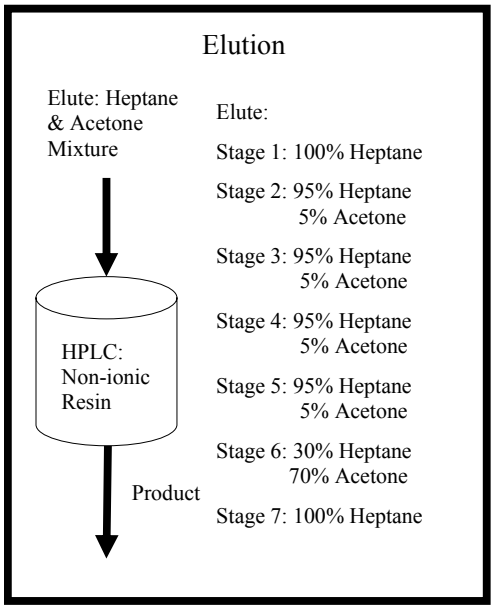


Figure 11. Elution for Non-ionic Resin



stage 7, cleans the column leaving it ready for another run by eluting 329 liters of pure heptane. Stage 3 has the highest yield and the largest percentage of γ-tocopherol, therefore, it is collected as the γ-δ-tocopherol-rich stream. The overall percentages and yields of each step are shown in the table below.

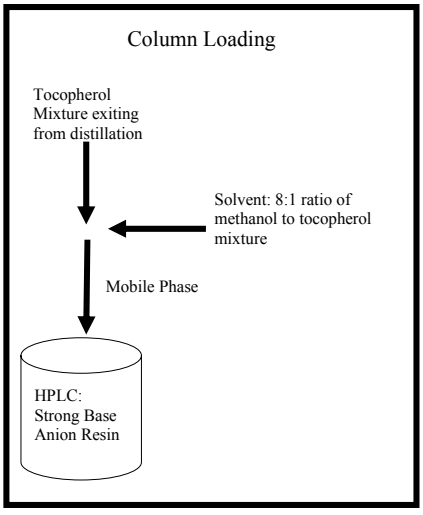
Table 3: Chromatography Data for γ-δ-tocopherol Product

Gamma-delta Rich Product				
	Alpha	Gamma	Delta	Yield
Stage 1	76.41%	19.48%	4.12%	8.12%
Stage 2	0.00%	0.00%	0.00%	0.00%
Stage 3	5.29%	77.21%	17.50%	61.71%
Stage 4	0.50%	27.78%	71.72%	12.49%
Stage 5	1.00%	12.32%	86.67%	5.14%
Stage 6	8.00%	22.00%	70.00%	4.60%
Stage 7	-	-	-	-

Producing 99% γ-tocopherol Product

To produce a product that is over 99% gamma-tocopherol, a strong basic anion exchange resin is used. It is important to use the strong anion resins in OH form due to little adsorption when the resin is in Cl or other forms. Using non-polar solvents, such as alkanes, on a strong basic anion exchange, does not separate the tocopherols. The mobile phase is created by dissolving the tocopherol mixture in a polar solvent, methanol, in an 8:1 ratio. A HPLC column is slurry packed in water. The resin is flushed with 7 bed volumes of deionized

Figure 12. Loading for Strong Base Resin



water to remove all contaminants. Since most resins are sold in the Cl form, the resin is converted to OH form by passing 7 bed volumes of 4% sodium hydroxide. The resin is again washed with deionized water until the washing solution becomes neutral. Once the column is prepared, 58.5 liters of the mobile phase containing 7 kg of tocopherols is loaded. The mobile phase is then eluted by an eight stage process. Stages 1-6 are eluted with 146 liters each of a 95% methanol and 5% acetone mixture. The addition of the ketone, acetone, modifies the polarity to suit desorption of γ-tocopherol. After 6 stages, the percentage δ-tocopherol is significantly reduced. Stage 7 consists passing a 146 liter mixture containing only 30% methanol and 70% acetone. This stage reduces the percentage of α-tocopherol to nearly 1%. The final stage, stage 8, cleans the resin by eluting 146 liters of pure methanol through the column. The exiting composition of the final stage contains 99% γ-tocopherol with a 25% yield. The compositions of each stage are tabulated below.

Figure 13. Elution Steps w/ Strong Base Resin

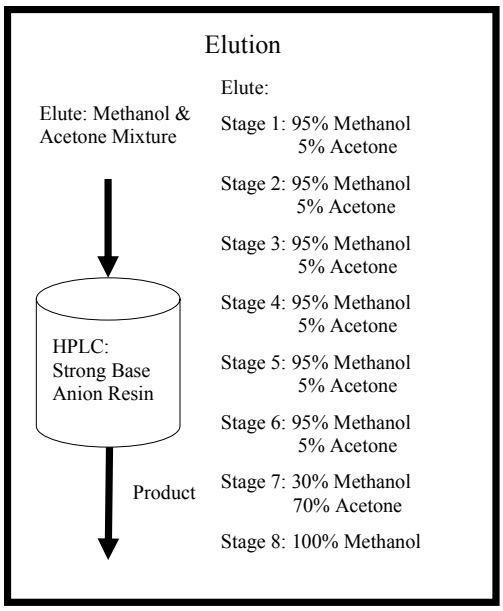


Table 4. Chromatography Data for γ- tocopherol Product

Gamma Rich Product				
	Alpha	Gamma	Delta	Yield
Stage 1	97.63%	2.07%	0.30%	7.82%
Stage 2	0.00%	0.00%	0.00%	0.00%
Stage 3	58.93%	41.07%	0.00%	4.29%
Stage 4	28.93%	70.94%	0.12%	4.73%
Stage 5	14.07%	85.81%	0.11%	5.86%
Stage 6	6.18%	93.75%	0.07%	6.66%
Stage 7	1.92%	97.89%	0.18%	30.89%
Stage 8	0.91%	99.03%	0.06%	25.43%

Chromatography Plant Sizing

To determine the size of the chromatography plant, information provided by U.S. patent 6,867,308 was used. In this patent, small scale chromatography was used to separate the tocopherol homologues. The superficial velocity of the small scale chromatography was estimated to be 36 cm/hour. According to Harrison[15], this value is assumed to be a standard velocity for small scale chromatography. Using the estimated velocity and the column diameter, 2.54 cm, the flowrate for the small scale column producing the γ-δ-tocopherol mixture is calculated by the following equation[15]:

$$Flowrate = \pi * \frac{InnerDiame\ ter^2}{4} * \sup erficialve\ locity = \pi * \frac{2.54^2}{4} * 36cm/h = 182.3cm^3/h = 3ml/\min$$

To scale the chromatography column the following equation is used:

$$\frac{Flowrate_1}{Volume_1} = \frac{Flowrate_2}{Volume_2}$$

Using this equation, a scale up factor is created by using a ratio of the flowrates: Q_2/Q_1. Waters Corporation has a large scale HPLC column with a maximum flowrate of 2 liters/min, therefore, the scale up factor becomes: 2,000/3 = 658. The scale up factor is

then multiplied to all volumes of the small scale process. These values are shown in the table below.

Table 5. Scale Up Volumes

Scale Up Volumes To Produce Gamma-delta Mixture			
Load:	32,909 ml		
	10,970 grams		
	Acetone (ml)	Heptane (ml)	Total (ml)
Stage 1	0	329,088	329,088
Stage 2	8,227	156,317	164,544
Stage 3	8,227	156,317	164,544
Stage 4	8,227	156,317	164,544
Stage 5	8,227	156,317	164,544
Stage 6	230,361	98,726	329,088
Stage 7	0	329,088	329,088
Totals	263,270	1,382,168	1,645,439

Table 6. Run Times For Scale Up Volumes

Run Time For Scale Up Volumes To Produce Gamma-delta Mixture				
Run time:	Load	16.45439 min		
	Elute	658.1754 min		
	Clean	164.5439 min		
Total		839.1737 min -->	13.98623 hours	

With a flowrate of 2 liters/min, each chromatography batch run will take approximately 14 hours. Therefore 18.8 kg/day of tocopherol mixture is processed per column. To process the maximum capacity of 24,750 kg/day of tocopherol mixture per day 1,315 columns are required. The same method was applied to the 99% γ-tocopherol product where the scale up factor was found to be 293. However, to produce 1,000 kg per year of γ-tocopherol only 6,666 kg of the tocopherol mixture needs to be processed. To process the 6,666 kg per year, only 1 column is needed.

Distillation of Chromatography Products

The product streams coming from the chromatography columns were produced by eluting with various solvents. These solvents include acetone, heptane, and methanol. In order to sell the tocopherol mixture these solvents must be removed. The boiling points of these solvents vary from 55^{o}C to 100^{o}C at 760 mmHg. That is a significant difference from the boiling points of the tocopherol homologues which boil between the temperatures of 200^{o}C and 220^{o}C at 1 mmHg. Utilizing this difference, the product streams are sent through a distillation column where the solvents are evaporated and recycled for repeated use in the chromatography process. After evaporating the solvents, the tocopherols are purified and ready for commercial use.

Economic Analysis

Plant Design Selection

Production Rates Considered

Numerous parameters were considered when selecting the plant designs. The tocopherol processing facility could be designed to produce solely α-rich tocopherol, as shown in Figure 14, both α and δ-γ-rich tocopherol, as shown in Figure 15, only α and 99.9% pure γ tocopherol, Figure 16, or a combination of all three products, Figure 17.

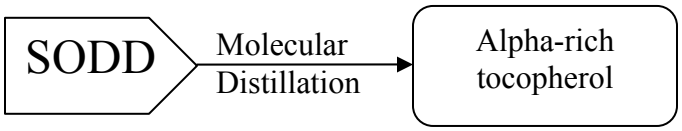


Figure 14: Production of α-rich tocopherol

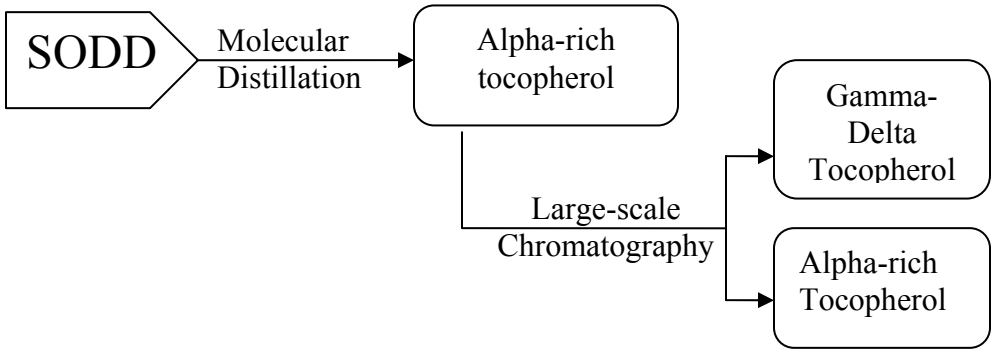


Figure 15: Production of Gamma-Delta Tocopherol with Alpha-rich Byproduct

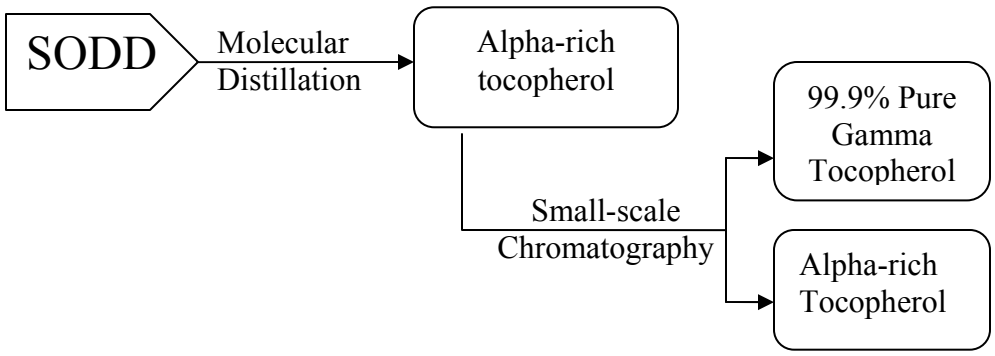


Figure 16: Production of 99.9% Pure Gamma Tocopherol with Alpha-rich Byproduct

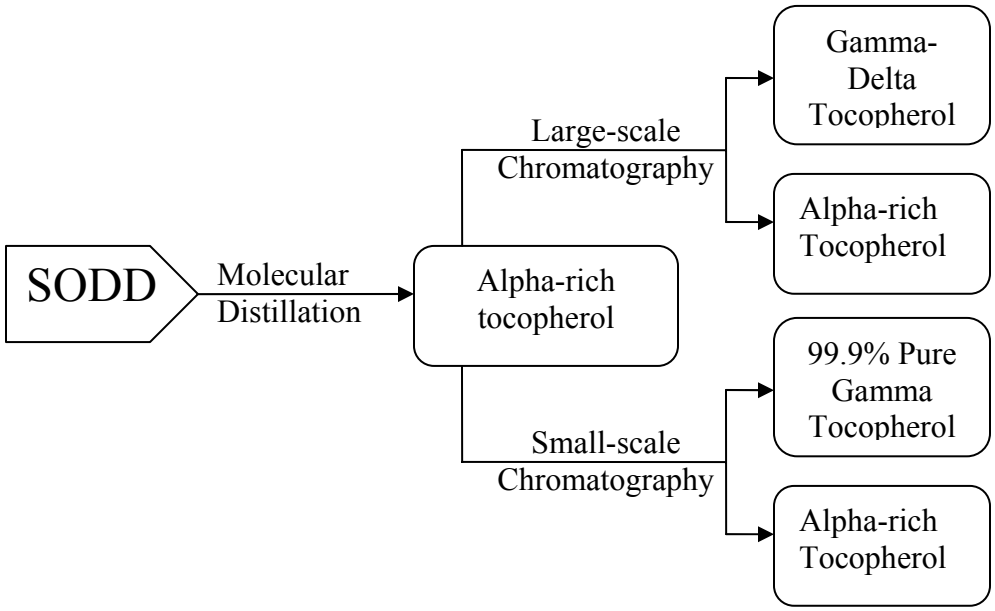


Figure 17: Production of Pure Gamma, Gamma-Delta, and Alpha-rich Tocopherols

The sales of α-tocopherol mixtures over the past several years have been declining rapidly, (Appendix C), presumably due to the association between α-tocopherol and heart disease. In addition, the sales prices of γ-δ and pure γ-tocopherol, $350/kg and $100,000/kg respectively, are significantly higher than the sales price of α-rich

tocopherol, $44/kg. For these reasons, and due to the fact that producing δ-γ and γ-tocopherol yields an α-rich byproduct, all of the tocopherol mixture produced by enzymatic distillation was processed to produce either δ-γ or pure γ-tocopherol. Pure γ-tocopherol is used primarily in research, and its market is relatively small. For this reason, the amount of pure γ-tocopherol produced for all designs was limited to 1,000kg/yr or less. Five plant designs were considered for the process. Designs 1 through 4 produce 1, 10, 100, and 1,000kg of pure γ-tocopherol per year, respectively. In order to determine whether the additional capital and operating costs required to produce pure γ-tocopherol were worth the additional revenue, a control model, Design 5, produces only γ-δ-tocopherol and an α-rich byproduct. The total production rates for all designs are shown in Table 7. The life spans for all five plants were assumed to be 10 years, based on the average life span of industrial chromatography columns.

Table 7. Product Rates

	Production Rates (kg/yr)			
Design Scheme	Pure Gamma	Gamma-Delta	Alpha-Rich	Sterol Esters
1	1	5510585	3523164	90337500
2	10	5510563	3523177	90337500
3	100	5510344	3523307	90337500
4	1000	5508148	3524603	90337500
5	0	5510588	3523163	90337500

Use of Methanol for Distillation

Both methanol and water may be used for distillation of SODD. However, using methanol for distillation results in a significantly higher concentration of the tocopherol product stream (75% tocopherols), than is obtained when water is used for distillation (60% tocopherols). The remainder of the product stream is comprised primarily of sterol

esters and free fatty acids. Processing streams containing high concentrations of free fatty acids and sterol esters can damage chromatography equipment. In addition, processing streams with low tocopherol concentrations necessitates increasing the number of columns in order to attain the same amount of tocopherol product that would be produced by processing a stream with a high tocopherol concentration. For these reasons, methanol was used for distillation in all 5 design schemes.

Product Prices

The estimated product sales prices for the next ten years are listed in Table 8. The sales price of α-tocopherol, currently $44/kg, is expected to decrease over the next 10 years, due to its association with an increased risk of heart disease. For this reason, a 10% decrease in sale price per year was assumed. Because γ-δ-tocopherol may be used as a substitute for α-rich tocopherol, demand is expected to increase over the next 5 years, driving prices up. However, as more production facilities shift their focus toward producing γ-d-tocopherols, supply will increase, and competition will drive the price down. Based on these assumptions, the sales price of γ-d-tocopherol was predicted to increase by 5% per year for the first five years, then decrease at a rate of 10% per year for the remaining 5 years. The market for pure γ-tocopherol, which is relatively small, may expands slightly, but various facilities are currently competing for the available market share, and increasing production capacity would be relatively simple for established companies. Therefore, competition among suppliers should result in a decrease in sales price, and a price decrease of 10% per year was assumed. The sales price of a mixture of sterol esters and free fatty acids is currently $0.10/kg. Because this price is relatively

small, it was assumed to be constant over the next ten years. All calculations involving sales prices assume a 50% standard deviation.

Table 8. Product Sales Prices

	Product Sales Prices			
Year	α-rich mixture	γ-δ-tocopherol	Pure γ-tocopherol	Sterol Esters
1	$44	$350	$ 100,000	$0.10
2	$40	$368	$ 90,000	$0.10
3	$36	$386	$ 81,000	$0.10
4	$32	$405	$ 72,900	$0.10
5	$29	$425	$ 65,610	$0.10
6	$26	$382	$ 59,049	$0.10
7	$23	$364	$ 53,144	$0.10
8	$21	$346	$ 47,830	$0.10
9	$19	$328	$ 43,047	$0.10
10	$17	$312	$ 38,742	$0.10

Net Present Worth and Return on Investment

The net present worth for all five designs are shown in Table 9, below:

Table 9.

Design	kg/yr Pure γ-tocopherol	NPW (Billions)
1	1	$928,163,987
2	10	$930,839,273
3	100	$957,592,140
4	1000	$1,225,120,803
5	0	$930,424,966

As evidenced, the highest net present worth was obtained by producing the highest amount of pure γ-tocopherol. The net present worth increased as production of γ-tocopherol increased, with one exception: The net present worth for Design 1 (1kg/yr γ-tocopherol) was lower than the net present worth for Design 5 (0 kg/yr γ-tocopherol). The amount of revenue generated annually by selling 1 kg/yr was not significant enough to

make up for the additional capital investment required for the γ-tocopherol chromatography process.

The annual return on investment for each Design is shown in Table 10. The return on investment is consistently highest for Design 4 (1000 kg/yr), and consistently lowest for Designs 1 and 5. The return on investment for the first year is the most accurate, as the prices are based on current market prices, whereas the sales prices for years 2 through 10 are based on estimates.

Table 10. Return on Investment

	Return on Investment (Dollars per Dollar Invested)				
Year	Design 1 (1 kg/yr)	Design 2 (10 kg/yr)	Design 3 (100 kg/yr)	Design 4 (1000 kg/yr)	Design 5 (0 kg/yr)
1	$0.13	$0.13	$0.13	$0.15	$0.13
2	$0.15	$0.15	$0.15	$0.17	$0.15
3	$0.17	$0.17	$0.17	$0.19	$0.17
4	$0.19	$0.19	$0.19	$0.21	$0.19
5	$0.21	$0.21	$0.21	$0.23	$0.21
6	$0.16	$0.16	$0.16	$0.17	$0.16
7	$0.13	$0.13	$0.13	$0.15	$0.13
8	$0.11	$0.11	$0.11	$0.12	$0.11
9	$0.09	$0.09	$0.09	$0.10	$0.09
10	$0.06	$0.06	$0.07	$0.07	$0.06

Risk Analysis

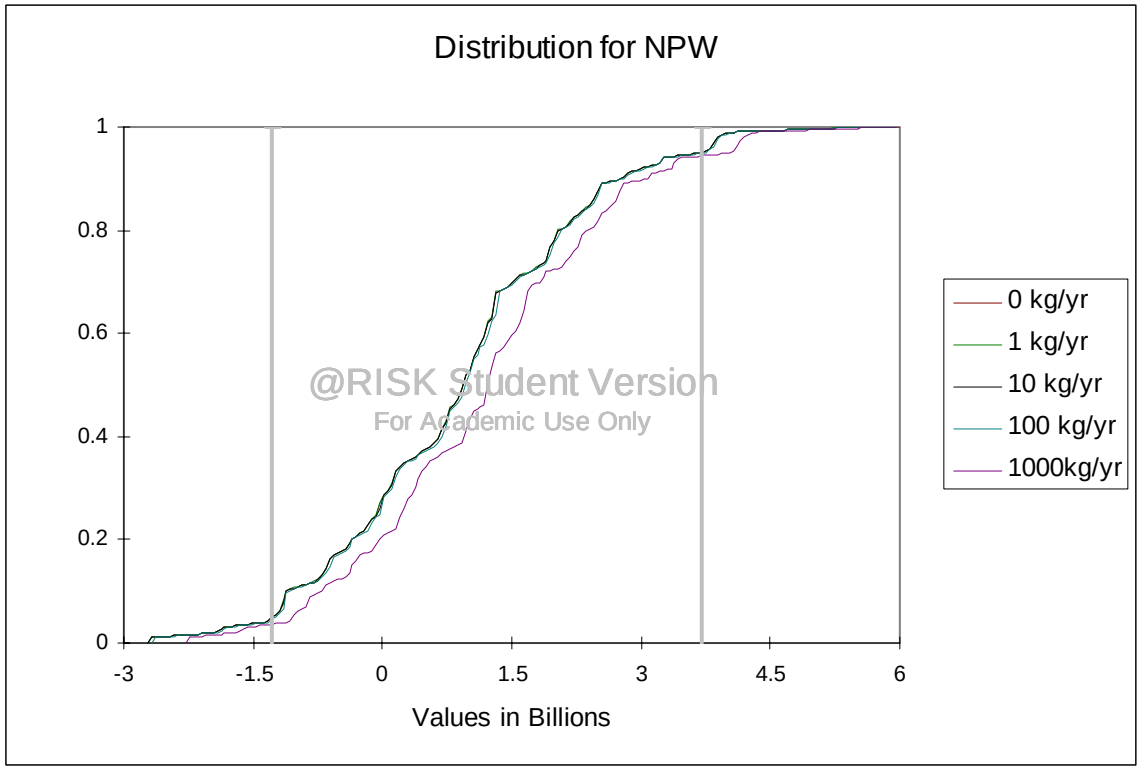
A risk analysis of the net present worth for each Design was performed using @Risk in Excel. The maximum, minimum, and mean net present worth for each design are depicted in Table 11. Design 4, which produced 1000kg/yr of g-tocopherol, had the highest value for the minimum, maximum, and mean net present worth. Design 1, which produced 1 kg γ-tocopherol per year, had the lowest minimum, maximum, and mean net present worth. With this exception, the net present worth increased as γ-tocopherol production increased.

Table 11. Net Present Worth

	NPW (in Billions)				
	Design 1 (1 kg/yr)	Design 2 (10 kg/yr)	Design 3 (100 kg/yr)	Design 4 (1000 kg/yr)	Design 5 (0 kg/yr)
Minimum	-$2.70	-$2.70	-$2.66	-$2.27	-$2.70
Mean	$0.93	$0.94	$0.96	$1.23	$0.94
Maximum	$5.53	$5.53	$5.55	$5.81	$5.53

Figure 18 depicts the risk curves for all five designs. As shown, the risks for Designs 1, 2, 3, and 5 are incredibly similar, while Design 4 has a higher probability to generate a profit than the other four designs.

Figure 18. Distribution for Net Present Worth



It is recommended that the γ-chromatography processes be built in addition to the γ-δ-chromatography process. Though it would be profitable to produce solely γ-δ-tocopherol, producing even minimal amounts of pure γ-tocopherol in addition to γ-δ-

tocopherol increases the overall profitability. In addition, profitability increases as the amount of γ-tocopherol produced increases.

GAMS Analysis

The price of pure γ-tocopherol is expected to fluctuate widely over the next several years, and accurately predicting future prices cannot be done with great certainty. Because prices are so uncertain, it is necessary to determine the maximum decrease in product cost that could be absorbed before γ-tocopherol production becomes less profitable than γ-δ-tocopherol production. GAMS modeling software was used to determine the minimum sales price of γ-tocopherol necessary for each system. For Design 1, which produces, 1 kg/yr of γ-tocopherol, the small-scale chromatography process is not profitable at current sales prices. Pure γ-tocopherol must be sold at $603,365.22/kg in order for this design to be profitable. However, Design 2, which produces 10 kg/yr of pure γ-tocopherol, can absorb a significant drop in the sale price of γ-tocopherol: The product could be sold at $60,398.62/kg, and the process would be as profitable as producing solely a γ-δ-mixture. Design 3 can accommodate an even larger price drop, falling to $6,245.96/kg, before producing only γ-δ-tocopherol becomes more profitable. Design 4, the 1000 kg/yr system, can absorb the highest price drop. The sales price of pure γ-tocopherol could drop to $830.70/kg before the process would be less profitable than producing only γ-δ-tocopherol.

Minimum Production for Profitability

Because not all of the pure γ-tocopherol producing designs were as profitable as Design 5, which produced no γ-tocopherol, calculations were performed using the Solver tool in Excel in order to determine the minimum production rate of γ-tocopherol. Assuming the depreciation rates, price fluctuations, and interest rates assumed for the net present worth calculations, 8.61kg/yr of pure γ-tocopherol must be produced in order for the small column chromatography to be as profitable as a system using only large scale chromatography.

FDA Regulations

Vitamins and other dietary supplements are regulated under different regulations than standard pharmaceuticals. The Dietary Supplement Health and Education Act of 1994 (DSHEA) states that dietary supplement manufacturer is responsible for ensuring the supplement is safe before it is marketed. The FDA is responsible for taking action against any unsafe dietary supplement product after it reaches the market. Post-marketing responsibilities include monitoring supplemental adverse reporting significant events, and providing information through labeling, claims, package inserts, and accompanying literature[1].

Proposed Improvements

Distillation

Immobilization of the *Candida rugosa* lipase could reduce the raw materials costs of the enzyme reactions. Microencapsulation in beads would be the best way to immobilize the lipase for use in the reactors, because they could be filtered out from the rest of the reaction mixture[16]. Currently polystyrene and chitosan are the most prevalent materials used to make enzyme immobilization beads[17]. With minimal loss of enzyme, the raw material costs for *Candida rugosa* lipase could be reduced from $18-38 million to $72-154 thousand per year. The cost to immobilize using Polystyrene beads[18] would be $216-$462 thousand per year and $112-$240 thousand per year for Chitosan beads[17]. Taking into account both the immobilization beads and lipase costs, this is a significant reduction in yearly costs.

Drawbacks to using immobilization would be longer incubation times in the reactors and/or and increases in the amount of enzyme needed in each batch. This is because diffusion effects through the beads control the interaction times between the lipase and the substrates in the reactor. Filters would need to be employed in order to remove the enzyme beads before the process media is passed on to the next production apparatus. More reactors and/or larger reactors and filters could lead to an increase in capitol investment costs.

Chromatography

All natural sources that contain tocopherol also contain free fatty acids that can interfere with the separation process. Reducing the concentration of these acids in tocopherol mixtures leads to more effective separation. In addition, FFAs cause fouling in chromatography columns. Therefore, using mixtures with low FFA concentrations causes less fouling and extends column life. The feed material must have a pH value less than 10. A pH of 1 would be ideal, but columns operate reasonably at a pH of 3 or less. It is important to test the exiting distillation stream to accurately gauge the effectiveness of the chromatography. The number of chromatography columns needed for this process is extremely high. This is could be a result of the estimated superficial velocity of the small scale process.

Alternative Processes

Affinity Chromatography

Affinity chromatography uses biomolecules that bind specifically to the target molecule to cause separation. Affinity chromatography typically uses ligands or antibodies to bind proteins. It would be possible to use an antibody or a protein whose substrate is α-tocopherol.

One protein that binds α-tocopherol over γ-tocopherol and δ-tocopherol is called α-tocopherol transfer protein. It can be separated from tissue or produced as a recombinant protein in *Escherichia coli*. The challenges of this approach would be attaching the protein to a support matrix and determining conditions for the initial elution of the tocopherol mixture, and the subsequent desorption of α-tocopherol from the solid

phase. The conditions would have to be gentle enough not to denature the proteins. The column lifetime would be a critical factor in determining the economic viability of the column. Once the solid phase and elution conditions were designed, isotherms and permeability would have to be determined experimentally. Then, scale-up calculations could be performed. This process is based upon the assumption that δ-tocopherol does not interfere with γ-tocopherol and has no detrimental health effects, so removing the δ homologue would not be necessary.

Bioprocessing

One possible method for producing various tocopherol mixtures is bioprocessing. To produce tocopherols using biosynthesis, the biological pathway that produces tocopherols in plants must studied and mapped. From this information, the necessary steps, ingredients, and environments conducive to tocopherol production could be determined. These parameters could then be applied to a genetically manipulated bacterium that would produce tocopherols. Through experiments, conditions could be altered to produce the tocopherol homologue desired. Through extensive research, this process could prove to be an economically efficient approach to produce tocopherol homologues.

Genetic Engineering

Genetically engineered foods are produced from crops whose genetic makeup has been altered through a process known as gene splicing, to give the plant a desirable trait. In most cases this approach has been used to make plants resistant to common diseases

and to become more productive. However, soybeans and other tocopherol producing vegetables can be altered to produce a specific tocopherol. This is an in-depth process that requires research into the biological pathway of tocopherols. The benefit of this process is that once the plant produces a specific tocopherol homologues, for example γ-tocopherol, no further tocopherol separation steps are required. These separation processes are extremely costly; therefore, a genetically engineered plant such as soybeans would be an economically viable option.

Appendices

Appendix A – Key Terms

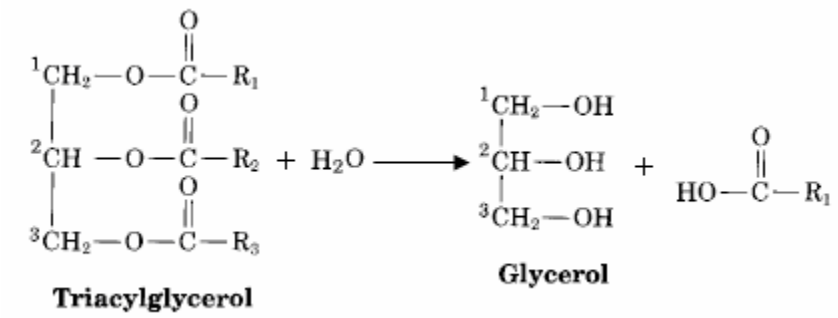
Candida rugosa – an enzyme most normally used to hydrolize acylglycerols. It is also has the ability to bond organic acids and alcohols to make esters.

Ester - Any of a class of organic compounds corresponding to the inorganic salts and formed from an organic acid and an alcohol.

Glycerol - A syrupy, sweet, colorless or yellowish liquid, C3H8O3, obtained from fats and oils as a byproduct of saponification and used as a solvent, an antifreeze, a plasticizer, and a sweetener and in the manufacture of dynamite, cosmetics, liquid soaps, inks, and lubricants.

Hydrolysis - Decomposition of a chemical compound by reaction with water, such as the dissociation of a dissolved salt or the catalytic conversion of starch to glucose.

Hydrolysis



Where R_1, R_2, and R_3 are fatty acid residues.

Isocratic - same solvent strength

Lipid - Any of a group of organic compounds, including the fats, oils, waxes, sterols, and triglycerides that are insoluble in water but soluble in nonpolar organic solvents, are oily

to the touch, and together with carbohydrates and proteins constitute the principal structural material of living cells.

Lipophilic - Having an affinity for, tending to combine with, or capable of dissolving in lipids

Reverse phase chromatography – During regular chromatography the media (solvent or buffer) is not polar and the gel is polar. While in reverse phase the media is polar and the gel is not polar.

Sterol - Any of a group of solid, cyclic, unsaturated alcohols, with a complex structure that includes four carbon rings; cholesterol is an example. Steroids are derived from sterols.

Triglyceride - A naturally occurring ester of three fatty acids and glycerol that is the chief constituent of fats and oils.

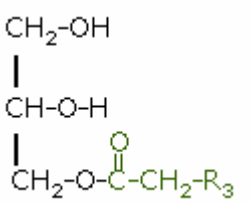
Appendix B- Chemical properties

Acylglycerols

Acylglycerol is a molecule of glycerol that has had one or more of the hydroxyl groups replaced with a fatty acid residues. They are formed during a dehydration reaction between glycerol and fatty acids. In biological systems, this reaction is catalyzed by a lipase.

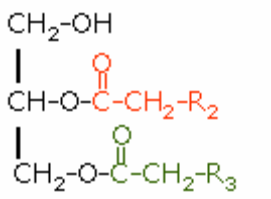
>>> The R groups in the following structures are the carbon tails of fatty acid residues<<<<

Mono-acylglycerols



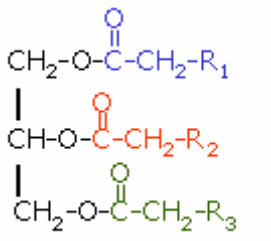
http://www.med.uiuc.edu/m1/biochemistry/TA%20reviews/sam/FAmetabolism.htm

Di-acylglycerols



http://www.med.uiuc.edu/m1/biochemistry/TA%20reviews/sam/FAmetabolism.htm

Tri-acylglycerols



http://www.med.uiuc.edu/m1/biochemistry/TA%20reviews/sam/FAmetabolism.htm

Free Fatty Acids (FFA)

Lauric Acid

$HO_2C-(CH_2)_{10}-Me$

Structure

Formula: C12 H24 O2

Properties

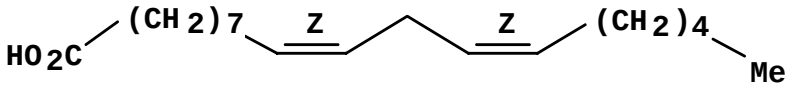
Calculated		
Property	**Value**	**Condition**
Bioconc. Factor	3900	pH 1
Bioconc. Factor	3350	pH 4
Bioconc. Factor	23.8	pH 7
Bioconc. Factor	2.67	pH 8
Bioconc. Factor	1	pH 10
Boiling Point	296.1±3.0 °C	Press: 760 Torr
Enthalpy of Vap.	56.59±3.0 kJ/mol	
Flash Point	134.1±21.4 °C	
H acceptors	2	
H donors	1	
Koc	12900	pH 1
Koc	11100	pH 4
Koc	78.9	pH 7
Koc	8.86	pH 8
Koc	1.11	pH 10
logD	5.03	pH 1
logD	4.96	pH 4
logD	2.81	pH 7
logD	1.86	pH 8
logD	0.96	pH 10
logP	5.028±0.185	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Slightly Soluble	pH 8
Molar Solubility	Soluble	pH 10
Molecular Weight	200.32	
pKa	4.78±0.20	Most Acidic
Vapor Pressure	6.61E-4 Torr	Temp: 25 °C

Experimental		
Property	**Value**	**Condition**
Boiling Point	223 °C	Press: 100 Torr
Boiling Point	167-168 °C	Press: 8 Torr
Boiling Point	160-165 °C	Press: 20 Torr

Boiling Point	145 °C	Press: 0.37 Torr
Boiling Point	95-100 °C	Press: 0.2 Torr
Melting Point	56-57 °C	
Melting Point	45 °C	
Melting Point	44.5-44.8 °C	
Melting Point	44-45 °C	
Melting Point	44 °C	
Melting Point	43.0-43.5 °C	
Melting Point	42-44 °C	
Melting Point	41-43 °C	
Melting Point	41-43 °C	
Melting Point	41-43 °C	
Melting Point	40-42 °C	

Linoleic Acid

Structure



Formula: C18 H32 O2

Properties

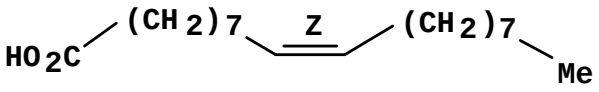
	Calculated	
Property	**Value**	**Condition**
Bioconc. Factor	1.68E5	pH 1
Bioconc. Factor	1.44E5	pH 4
Bioconc. Factor	1020	pH 7
Bioconc. Factor	114	pH 8
Bioconc. Factor	14.4	pH 10
Boiling Point	360.6±0.0 °C	Press: 760 Torr
Enthalpy of Vap.	66.60±6.0 kJ/mol	
Flash Point	273.0±25.9 °C	
H acceptors	2	
H donors	1	
Koc	1.91E5	pH 1
Koc	1.64E5	pH 4
Koc	1160	pH 7
Koc	130	pH 8
Koc	16.4	pH 10
logD	7.18	pH 1
logD	7.11	pH 4
logD	4.96	pH 7
logD	4.01	pH 8
logD	3.11	pH 10
logP	7.180±0.256	

Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	280.45	
pKa	4.78±0.20	Most Acidic
Vapor Pressure	3.54E-6 Torr	Temp: 25 °C

	Experimental	
Property	**Value**	**Condition**
Boiling Point	195-205 °C	Press: 1 Torr
Boiling Point	179-183 °C	Press: 0.8 Torr
Boiling Point	179-183 °C	Press: 0.8 Torr
Boiling Point	177 °C	Press: 0.5 Torr
Boiling Point	148.1-150.7 °C	Press: 0.21 Torr
Boiling Point	148.1-150.7 °C	Press: 0.21 Torr
Boiling Point	141-144 °C	Press: 0.17 Torr
Density	0.9122 g/cm3	Temp: 20 °C
Density	0.9016 g/cm3	Temp: 20 °C
Melting Point	-5.2-5 °C	Solv: ligroine (8032-32-4)
Melting Point	-5.4 °C	Solv: ligroine (8032-32-4)
Melting Point	-8.8-7.1 °C	
Refractive Index	1.4699	Temp: 20 °C

Oleic Acid

Structure



Formula: C18 H34 O2

Properties

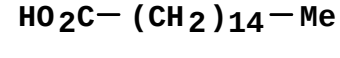
	Calculated	
Property	**Value**	**Condition**
Bioconc. Factor	4.16E5	pH 1
Bioconc. Factor	3.57E5	pH 4
Bioconc. Factor	2510	pH 7
Bioconc. Factor	283	pH 8
Bioconc. Factor	35.6	pH 10
Boiling Point	360.0±0.0 °C	Press: 760 Torr
Enthalpy of Vap.	66.53±6.0 kJ/mol	
Flash Point	270.1±25.9 °C	
H acceptors	2	
H donors	1	
Koc	3.66E5	pH 1
Koc	3.14E5	pH 4

Koc	2210	pH 7
Koc	249	pH 8
Koc	31.3	pH 10
logD	7.70	pH 1
logD	7.63	pH 4
logD	5.48	pH 7
logD	4.53	pH 8
logD	3.63	pH 10
logP	7.698±0.199	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	282.46	
pKa	4.78±0.20	Most Acidic
Vapor Pressure	3.70E-6 Torr	Temp: 25 °C

Property	**Experimental Value**	**Condition**
Boiling Point	230 °C	Press: 15 Torr
Boiling Point	213-216 °C	Press: 5 Torr
Boiling Point	210-212 °C	Press: 4 Torr
Boiling Point	205-210 °C	Press: 5 Torr
Boiling Point	204-206 °C	
Boiling Point	196-210 °C	Press: 2 Torr
Boiling Point	195-197 °C	Press: 2 Torr
Boiling Point	170-173 °C	Press: 0.25 Torr
Boiling Point	43-49 °C	Press: 100 Torr
Density	0.8871 g/cm3	Temp: 20 °C
Electric Resistivity	10-14 ohm*cm	
Melting Point	16 °C	
Melting Point	13.3 °C	
Melting Point	13 °C	
Melting Point	12 °C	

Palmitic Acid

Structure



Formula: C16 H32 O2

Properties

Property	**Calculated Value**	**Condition**

Bioconc. Factor	1.61E5	pH 1
Bioconc. Factor	1.38E5	pH 4
Bioconc. Factor	974	pH 7
Bioconc. Factor	109	pH 8
Bioconc. Factor	13.7	pH 10
Boiling Point	340.6±5.0 °C	Press: 760 Torr
Enthalpy of Vap.	61.66±3.0 kJ/mol	
Flash Point	154.1±22.4 °C	
H acceptors	2	
H donors	1	
Koc	1.85E5	pH 1
Koc	1.59E5	pH 4
Koc	1120	pH 7
Koc	126	pH 8
Koc	15.8	pH 10
logD	7.15	pH 1
logD	7.09	pH 4
logD	4.93	pH 7
logD	3.99	pH 8
logD	3.08	pH 10
logP	7.154±0.185	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	256.42	
pKa	4.78±0.20	Most Acidic
Vapor Pressure	3.28E-5 Torr	Temp: 25 °C

Property	**Experimental Value**	**Condition**
Boiling Point	352.3 °C	
Melting Point	64 °C	Solv: hexane (110-54-3) benzene (71-43-2)
Melting Point	63 °C	
Melting Point	62.5 °C	
Melting Point	62-63 °C	
Melting Point	61-64 °C	
Melting Point	61-63 °C	
Melting Point	60-62 °C	
Melting Point	60-62 °C	
Melting Point	60-62 °C	
Melting Point	60-62 °C	
Melting Point	60-62 °C	
Melting Point	60 °C	Solv: hexane (110-54-3)
Melting Point	59-60 °C	
Melting Point	59 °C	
Melting Point	57-62 °C	
Melting Point	51-53 °C	Solv: ethyl acetate (141-78-6)

Stearic Acid

Structure

Formula: C18 H36 O2

Properties

Calculated		
Property	**Value**	**Condition**
Bioconc. Factor	1.03E6	pH 1
Bioconc. Factor	8.84E5	pH 4
Bioconc. Factor	6250	pH 7
Bioconc. Factor	702	pH 8
Bioconc. Factor	88.2	pH 10
Boiling Point	359.4±5.0 °C	Press: 760 Torr
Enthalpy of Vap.	63.84±3.0 kJ/mol	
Flash Point	162.4±22.4 °C	
H acceptors	2	
H donors	1	
Koc	7.01E5	pH 1
Koc	6.01E5	pH 4
Koc	4250	pH 7
Koc	477	pH 8
Koc	60.0	pH 10
logD	8.21	pH 1
logD	8.15	pH 4
logD	6.00	pH 7
logD	5.05	pH 8
logD	4.15	pH 10
logP	8.216±0.186	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	284.48	
pKa	4.78±0.20	Most Acidic
Vapor Pressure	8.58E-6 Torr	Temp: 25 °C

Experimental		
Property	**Value**	**Condition**
Boiling Point	465 °C	
Boiling Point	376 °C	Press: 760 Torr
Boiling Point	232 °C	Press: 15 Torr
Density	0.96 g/cm3	
Electric Resistivity	10-14 ohm*cm	
Melting Point	71.5 °C	
Melting Point	70-73 °C	Solv: chloroform

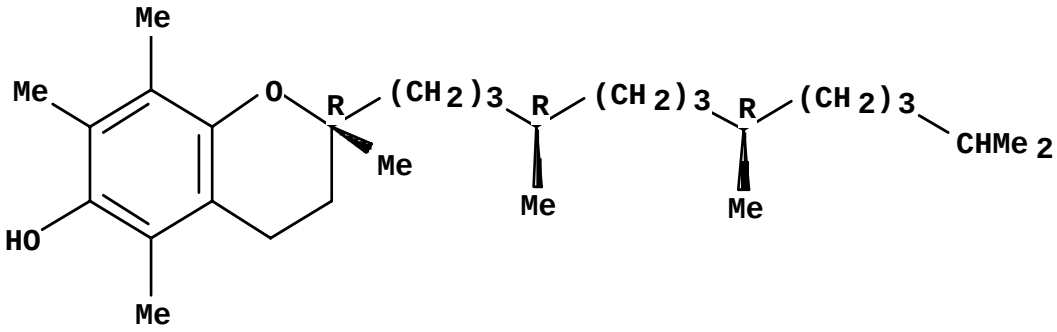
		(67-66-3) methanol (67-56-1)
Melting Point	69.9 °C	
Melting Point	69-70 °C	
Melting Point	69-70 °C	
Melting Point	69 °C	
Melting Point	69 °C	
Melting Point	68-70 °C	
Melting Point	68-70 °C	
Melting Point	68 °C	
Melting Point	66 °C (polymorph)	
Melting Point	65-69 °C	
Melting Point	65 °C	

Arquidic Acid

Tocopherols

Alpha Tocopherol

Structure



Formula: C29 H50 O2

Properties

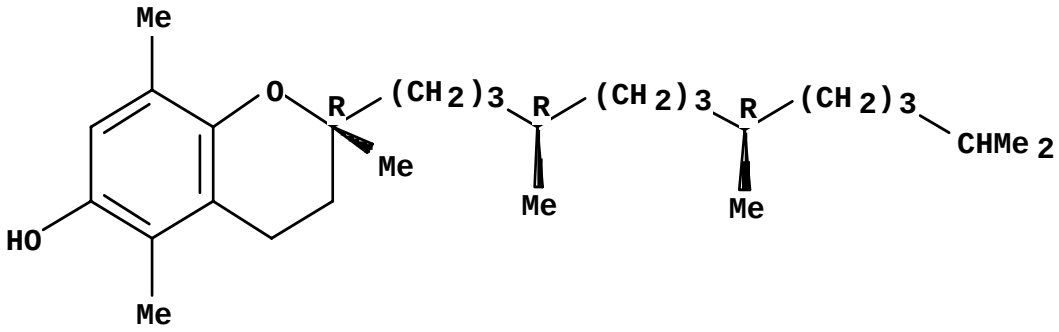
Property	Calculated Value	Condition
Bioconc. Factor	1.00E6	pH 1
Bioconc. Factor	1.00E6	pH 4
Bioconc. Factor	1.00E6	pH 7
Bioconc. Factor	1.00E6	pH 8
Bioconc. Factor	1.00E6	pH 10
Boiling Point	529.5±35.0 °C	Press: 760 Torr
Enthalpy of Vap.	83.48±3.0 kJ/mol	
Flash Point	210.2±36.3 °C	

H acceptors	2	
H donors	1	
Koc	1.00E7	pH 1
Koc	1.00E7	pH 4
Koc	1.00E7	pH 7
Koc	1.00E7	pH 8
Koc	1.00E7	pH 10
logD	11.86	pH 1
logD	11.86	pH 4
logD	11.86	pH 7
logD	11.86	pH 8
logD	11.84	pH 10
logP	11.862±0.268	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight		430.71
pKa	11.40±0.20	Most Acidic
Vapor Pressure	7.93E-12 Torr	Temp: 25 °C

Property	**Experimental Value**	**Condition**	**Note**
Optical Rotatory Power		-2.76 ° g/100mL Temp: 20 °C	Conc: 1.07

Beta-Tocopherol

Structure



Formula: C28 H48 O2

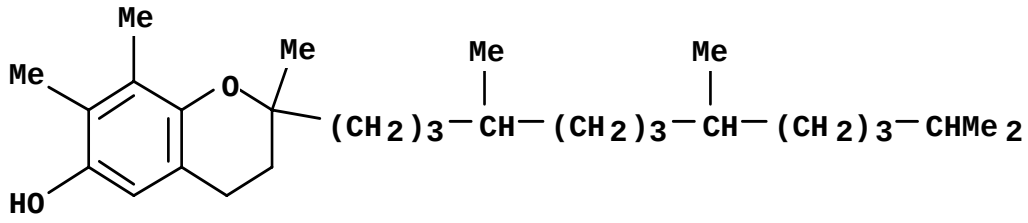
Properties

Property	**Calculated Value**	**Condition**
Bioconc. Factor	1.00E6	pH 1
Bioconc. Factor	1.00E6	pH 4

Bioconc. Factor	1.00E6	pH 7
Bioconc. Factor	1.00E6	pH 8
Bioconc. Factor	1.00E6	pH 10
Boiling Point	516.3±35.0 °C	Press: 760.0 Torr
Enthalpy of Vap.	81.81±3.0 kJ/mol	
Flash Point	204.7±36.3 °C	
H acceptors	2	
H donors	1	
Koc	1.00E7	pH 1
Koc	1.00E7	pH 4
Koc	1.00E7	pH 7
Koc	1.00E7	pH 8
Koc	1.00E7	pH 10
logD	11.40	pH 1
logD	11.40	pH 4
logD	11.40	pH 7
logD	11.40	pH 8
logD	11.36	pH 10
logP	11.402±0.266	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	416.68	
pKa	11.05±0.20	Most Acidic
Vapor Pressure	2.80E-11 Torr	Temp: 25.0 °C

Gamma Tocopherol

Structure



Formula: C28 H48 O2

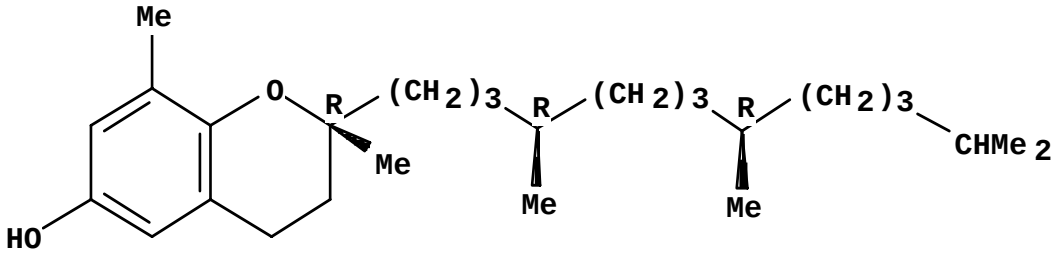
Properties

Property	Calculated Value	Condition	Note
Bioconc. Factor	1.00E6	pH 1	
Bioconc. Factor	1.00E6	pH 4	
Bioconc. Factor	1.00E6	pH 7	
Bioconc. Factor	1.00E6	pH 8	
Bioconc. Factor	1.00E6	pH 10	
Boiling Point	518.1±35.0 °C	Press: 760 Torr	

Enthalpy of Vap.	82.04±3.0 kJ/mol	
Flash Point	206.0±36.3 °C	
H acceptors	2	
H donors	1	
Koc	1.00E7	pH 1
Koc	1.00E7	pH 4
Koc	1.00E7	pH 7
Koc	1.00E7	pH 8
Koc	1.00E7	pH 10
logD	11.40	pH 1
logD	11.40	pH 4
logD	11.40	pH 7
logD	11.40	pH 8
logD	11.36	pH 10
logP	11.402±0.266	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	416.68	
pKa	11.05±0.20	Most Acidic
Vapor Pressure	2.35E-11 Torr	Temp: 25 °C

Delta Tocopherol

Structure



Formula: C27 H46 O2

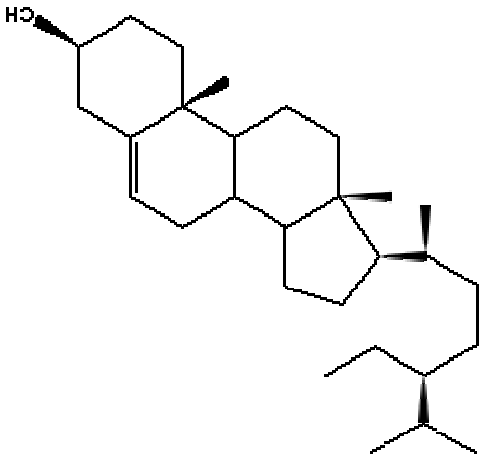
Properties

	Calculated	
Property	**Value**	**Condition Note**
Bioconc. Factor	1.00E6	pH 1
Bioconc. Factor	1.00E6	pH 4
Bioconc. Factor	1.00E6	pH 7
Bioconc. Factor	1.00E6	pH 8
Bioconc. Factor	1.00E6	pH 10
Boiling Point	504.3±35.0 °C	Press: 760 Torr
Enthalpy of Vap.	80.31±3.0 kJ/mol	

Flash Point	200.1±36.3 °C	
H acceptors	2	
H donors	1	
Koc	1.00E7	pH 1
Koc	1.00E7	pH 4
Koc	1.00E7	pH 7
Koc	1.00E7	pH 8
Koc	1.00E7	pH 10
logD	10.94	pH 1
logD	10.94	pH 4
logD	10.94	pH 7
logD	10.94	pH 8
logD	10.86	pH 10
logP	10.942±0.264	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	402.65	
pKa	10.70±0.20	Most Acidic
Vapor Pressure	8.54E-11 Torr	Temp: 25 °C

Sterols

Beta-Sitosterol



Product identification cas no. 83-46-5

Einecs no. 201-480-6
Formula C29H50O
Mol wt. 414.71

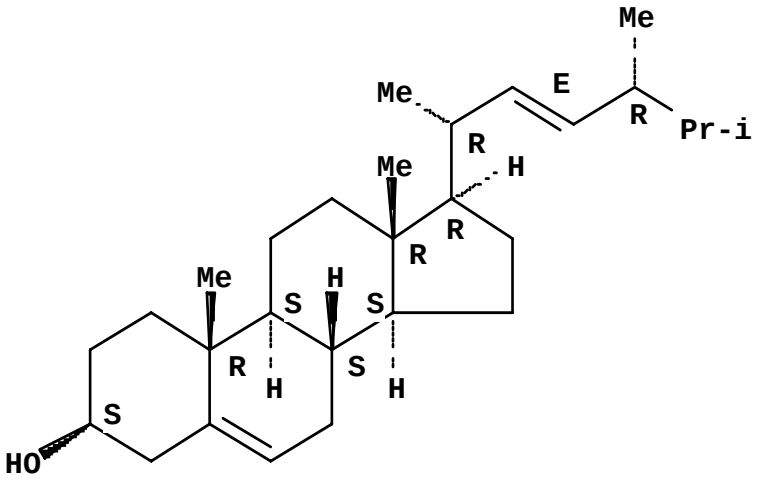
Synonyms stigmast-5-en-3beta-ol;

22,23-dihydro-stigmasterol; beta-sitosterin; angelicin; cinchol; cupreol; rhamnol;
(3beta)-stigmast-5-en-3-ol; alpha-dihydrofucosterol; quebrachol; 24alpha-ethylcholesterol; 5-cholesten-24beta-ethyl-3beta-ol; stigmast-5-en-3-ol;

Physical and chemical properties
Physical state white solid
Melting point 130 - 145 c
Solubility in water insoluble
Nfpa ratings health: 1; flammability: 0; reactivity: 0
Stability stable under normal conditions

Brassicasterol

Structure



Formula: C28 H46 O

Properties

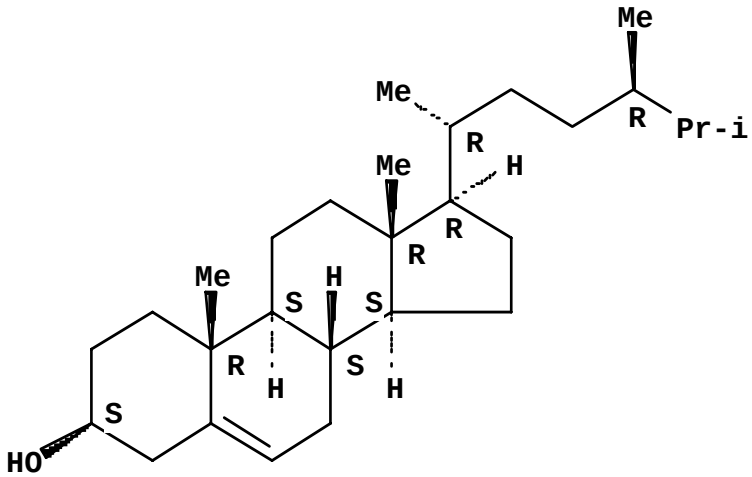
Property	Calculated Value	Condition
Bioconc. Factor	1.00E6	pH 1
Bioconc. Factor	1.00E6	pH 4
Bioconc. Factor	1.00E6	pH 7
Bioconc. Factor	1.00E6	pH 8
Bioconc. Factor	1.00E6	pH 10
Boiling Point	488.7±14.0 °C	Press: 760 Torr
Enthalpy of Vap.	86.96±6.0 kJ/mol	
Flash Point	213.4±22.2 °C	
H acceptors	1	
H donors	1	
Koc	4.38E6	pH 1
Koc	4.38E6	pH 4

Koc	4.38E6	pH 7
Koc	4.38E6	pH 8
Koc	4.38E6	pH 10
logD	9.68	pH 1
logD	9.68	pH 4
logD	9.68	pH 7
logD	9.68	pH 8
logD	9.68	pH 10
logP	9.679±0.296	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	398.66	
Vapor Pressure	1.34E-11 Torr	Temp: 25 °C

	Experimental	
Property	**Value**	**Condition**
Melting Point	184-186 °C	
Melting Point	150-151 °C	
Melting Point	149-151 °C	
Melting Point	145 °C	

Campesterol

Structure



Formula: C28 H48 O

Properties

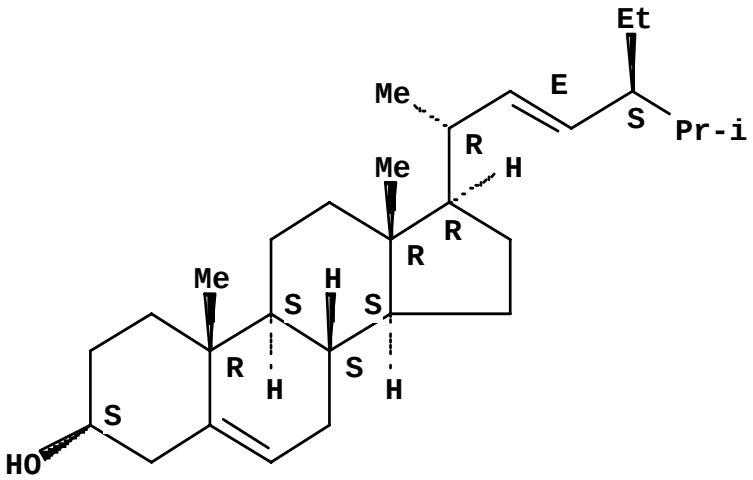
	Calculated	
Property	**Value**	**Condition**
Bioconc. Factor	1.00E6	pH 1

Bioconc. Factor	1.00E6	pH 4
Bioconc. Factor	1.00E6	pH 7
Bioconc. Factor	1.00E6	pH 8
Bioconc. Factor	1.00E6	pH 10
Boiling Point	489.5±14.0 °C	Press: 760 Torr
Enthalpy of Vap.	87.08±6.0 kJ/mol	
Flash Point	214.3±22.2 °C	
H acceptors	1	
H donors	1	
Koc	8.38E6	pH 1
Koc	8.38E6	pH 4
Koc	8.38E6	pH 7
Koc	8.38E6	pH 8
Koc	8.38E6	pH 10
logD	10.20	pH 1
logD	10.20	pH 4
logD	10.20	pH 7
logD	10.20	pH 8
logD	10.20	pH 10
logP	10.198±0.287	
Molar Solubility	Sparingly Soluble	pH 1
Molar Solubility	Sparingly Soluble	pH 4
Molar Solubility	Sparingly Soluble	pH 7
Molar Solubility	Sparingly Soluble	pH 8
Molar Solubility	Sparingly Soluble	pH 10
Molecular Weight	400.68	
Vapor Pressure	1.23E-11 Torr	Temp: 25 °C

Property	**Experimental Value**	**Condition**
Melting Point	158-159 °C	
Melting Point	158-159 °C	
Melting Point	157.5-158.0 °C	
Melting Point	155-156 °C	
Melting Point	155.0-155.5 °C	
Melting Point	152 °C	
Melting Point	140-141 °C	
Optical Rotatory Power		-33 °

Stigmasterol

Structure



Formula: C29 H48 O

Properties

Property	Calculated Value	Condition	Note	
Bioconc. Factor	1.00E6	pH 1	(1) ACD	
Bioconc. Factor	1.00E6	pH 4	(1) ACD	
Bioconc. Factor	1.00E6	pH 7	(1) ACD	
Bioconc. Factor	1.00E6	pH 8	(1) ACD	
Bioconc. Factor	1.00E6	pH 10	(1) ACD	
Boiling Point	501.1±19.0 °C	Press: 760 Torr	(1) ACD	
Enthalpy of Vap.	88.66±6.0 kJ/mol		(1) ACD	
Flash Point	219.4±24.7 °C		(1) ACD	
H acceptors	1		(1) ACD	
H donors	1		(1) ACD	
Koc	8.52E6	pH 1	(1) ACD	
Koc	8.52E6	pH 4	(1) ACD	
Koc	8.52E6	pH 7	(1) ACD	
Koc	8.52E6	pH 8	(1) ACD	
Koc	8.52E6	pH 10	(1) ACD	
logD	10.21	pH 1	(1) ACD	
logD	10.21	pH 4	(1) ACD	
logD	10.21	pH 7	(1) ACD	
logD	10.21	pH 8	(1) ACD	
logD	10.21	pH 10	(1) ACD	
logP	10.211±0.296		(1) ACD	
Molar Solubility	Sparingly Soluble	pH 1	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 4	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 7	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 8	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 10	(1) ACD	
Molecular Weight		412.69		(1) ACD
Vapor Pressure	3.84E-12 Torr	Temp: 25 °C	(1) ACD	

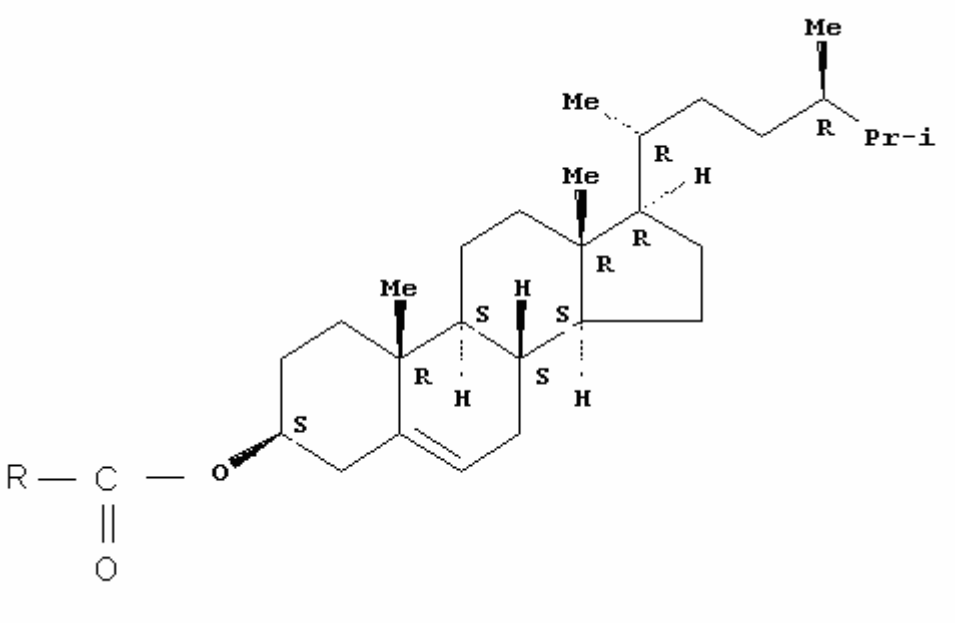
Experimental

Property	Value	Condition	Note
Melting Point	170-172 °C	Solv: acetone (67-64-1)	(2) CAS
Melting Point	170 °C		(3) CAS
Melting Point	170 °C		(4) CAS
Melting Point	169-171 °C	Solv: acetone (67-64-1)	(5) CAS
Melting Point	169-170 °C		(6) CAS
Melting Point	168.5 °C	Solv: methanol (67-56-1) ethyl ether (60-29-7)	(7) CAS
Melting Point	168-170 °C		(8) CAS
Melting Point	168-169 °C	Solv: methanol (67-56-1)	(9) CAS
Melting Point	168 °C	Solv: methanol (67-56-1) ethyl ether (60-29-7)	(7) CAS
Melting Point	168 °C		(10) CAS
Melting Point	167-169 °C	Solv: methanol (67-56-1)	(11) CAS
Melting Point	167-168 °C		(12) CAS
Melting Point	167 °C	Solv: methanol (67-56-1)	(13) CAS
Melting Point	166.5-168.0 °C		(14) CAS
Melting Point	166-168 °C		(15) CAS
Melting Point	165-170 °C		(16) CAS
Melting Point	165-167 °C		(17) CAS
Melting Point	165-166 °C		(18) CAS
Melting Point	164-166 °C		(19) CAS
Melting Point	164-166 °C		(20) CAS
Melting Point	163-165 °C		(21) CAS
Melting Point	162-164 °C		(22) CAS
Melting Point	155-156 °C		(23) CAS
Melting Point	153-154 °C		(24) CAS
Melting Point	141-142 °C		(25) CAS
Melting Point	138-140 °C		(26) CAS
Melting Point	136-138 °C		(27) CAS
Melting Point	136-138 °C	Solv: ethyl acetate (141-78-6)	(28) CAS
Melting Point	135-137 °C		(29) CAS
Melting Point	135-137 °C		(30) CAS
Melting Point	123-125 °C		(31) CAS
Optical Rotatory Power		-35 ° nm Temp: 24 °C	Wavlen: 589.3 (26) CAS
Optical Rotatory Power		-42 ° (67-66-3) Wavlen: 5800 nm Temp: 18 °C	Solv: chloroform (20) CAS
Optical Rotatory Power		-42.9 ° g/100mL Solv: chloroform	Conc: 1.2 (32) CAS

	(67-66-3) Wavlen: 589.3 nm Temp: 27 °C		
Optical Rotatory Power	-46 °	Conc: 0.1 g/100mL Solv: chloroform (67-66-3) Wavlen: 589.3 nm Temp: 20 °C	(33) CAS
Optical Rotatory Power	-50 °	Solv: chloroform (67-66-3) Wavlen: 589.3 nm	(9) CAS
Optical Rotatory Power	-50.5 °	Conc: 1 g/100mL Solv: chloroform (67-66-3) Wavlen: 589.3 nm Temp: 23 °C	(34) CAS
Optical Rotatory Power	-51 °	Conc: 0.90 g/100mL Solv: chloroform (67-66-3) Wavlen: 589.3 nm Temp: 25 °C	(2) CAS
Optical Rotatory Power	-52.3 °	Conc: 0.1 g/100mL Solv: chloroform (67-66-3) Wavlen: 589.3 nm Temp: 25 °C	(35) CAS
Optical Rotatory Power	-60.8 °	Conc: 1.23 g/100mL Solv: chloroform (67-66-3) Wavlen: 589.3 nm Temp: 25 °C	(36) CAS

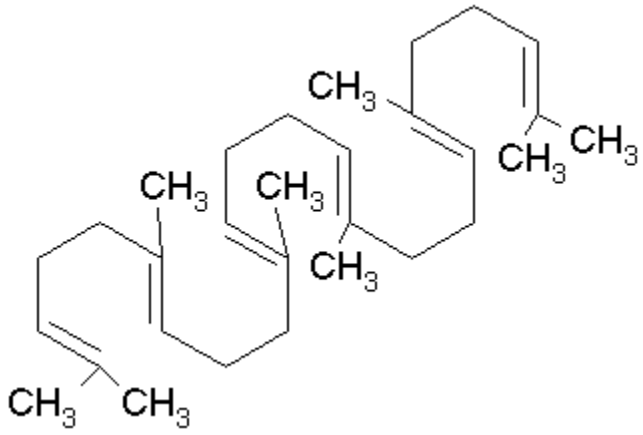
Steryl Esters (also called Sterol Esters)

Steryl esters are sterols that have reacted with fatty acids. The following structure is an example of a steryl ester. The sterol reacted is campesterol and the R group represent the hydrocarbon chain of a fatty acid residue.



Squalene

Structure



Formula: C30 H50

Properties

Property	Calculated Value	Condition	Note
Bioconc. Factor	1.00E6	pH 1	(1) ACD
Bioconc. Factor	1.00E6	pH 4	(1) ACD
Bioconc. Factor	1.00E6	pH 7	(1) ACD
Bioconc. Factor	1.00E6	pH 8	(1) ACD
Bioconc. Factor	1.00E6	pH 10	(1) ACD
Boiling Point	429.3±0.0 °C	Press: 760 Torr	(1) ACD
Enthalpy of Vap.	65.81±0.8 kJ/mol		(1) ACD
Flash Point	254.1±29.9 °C		(1) ACD

H acceptors	0		(1) ACD	
H donors	0		(1) ACD	
Koc	1.00E7	pH 1	(1) ACD	
Koc	1.00E7	pH 4	(1) ACD	
Koc	1.00E7	pH 7	(1) ACD	
Koc	1.00E7	pH 8	(1) ACD	
Koc	1.00E7	pH 10	(1) ACD	
logD	13.09	pH 1	(1) ACD	
logD	13.09	pH 4	(1) ACD	
logD	13.09	pH 7	(1) ACD	
logD	13.09	pH 8	(1) ACD	
logD	13.09	pH 10	(1) ACD	
logP	13.089±0.415		(1) ACD	
Molar Solubility	Sparingly Soluble	pH 1	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 4	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 7	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 8	(1) ACD	
Molar Solubility	Sparingly Soluble	pH 10	(1) ACD	
Molecular Weight		410.72		(1) ACD
Vapor Pressure	3.56E-7 Torr	Temp: 25 °C	(1) ACD	

Property	**Experimental Value**	**Condition**	**Note**	
Boiling Point	266-270 °C	Press: 0.2 Torr	(2) CAS	
Boiling Point	248-252 °C	Press: 4 Torr	(3) CAS	
Boiling Point	230-245 °C		(4) CAS	
Boiling Point	220 °C	Press: 0.2 Torr	(5) CAS	
Boiling Point	213 °C	Press: 1 Torr	(6) CAS	
Boiling Point	212-214 °C	Press: 10-14 Torr	(7) CAS	
Boiling Point	162 °C	Press: 0.01 Torr	(8) CAS	
Boiling Point	160 °C	Press: 0.001 Torr	(9) CAS	
Boiling Point	145-150 °C	Press: 0.001 Torr	(10) CAS	
Boiling Point	115 °C	Press: 0.02 Torr	(8) CAS	
Density	0.9391 g/cm3		(2) CAS	
Density	0.8076 g/cm3	Temp: 25 °C	(11) CAS	
Melting Point	-4.8-5.2 °C		(12) CAS	
Optical Rotatory Power		+64 ° g/100mL Solv: chloroform (67-66-3) Wavlen: 589.3 nm	Conc: 0.017	(13) CAS

Appendix C – Financial Calculations

Goals

Maximum Production

275,000	kg/day SODD processed
100,375,000	kg/yr SODD processed
24,750	kg/day tocopherol mixture (90% recovery)
9,033,750	kg/yr tocopherol mixture (90% recovery)
90337500	kg/yr sterol esters

Start-up Production, 33% Max Capacity

90750	kg/day SODD processed
33123750	kg/yr SODD processed
8167.5	kg/day tocopherol mixture (90% recovery)
2981137.5	kg/yr tocopherol mixture (90% recovery)
29811375	kg/yr sterol esters

Assumptions

BASF produces -->	20000000	kg/year tocopherol mixture		
	54794.52055	kg/day		
Of tocopherol mixture	70.00%	livestock feed		
	30.00%	dietary and comestics		
Initial production	33.00%	of max. capacity		
Plant operates	365	days a year		
			Tocopherol Composition	
SODD Composition:	10.00%	tocopherols	20.00%	alpha
	45.00%	esters	60.00%	gamma
	45.00%	sterols	20.00%	delta

Variables

SODD Purchase Price ($/k	0.175
Column Price	500000

Chromatography Equipment Cost, Research Grade Gamma

for 1000	$500,000
for 100	$500,000
for 10	$500,000
for 1	$500,000

Product Sales Prices	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10
Sterol Esters	$0.10	$0.10	$0.10	$0.10	$0.10	$0.10	$0.10	$0.10	$0.10	$0.10
alpha-mixture	$44	$40	$36	$32	$29	$26	$23	$21	$19	$17
gamma-delta	$350	$368	$386	$405	$425	$382	$364	$346	$328	$312
research grade gamma	100000	90000	81000	72900	65610	59049	53144	47830	43047	38742

Equipment for Distillation

Unit	Size	Price	#	Total
Vaporizer 1	6.6	$14,639	1	$14,639
Vaporizer 2	2.8	$10,720	1	$10,720
Reactor 1	9.8	$41,669	28	$1,166,732
Reactor 2	3.9	$25,196	28	$705,488
Tank(water)	57	$28,002	1	$28,002
Tank(C.r.)	5.6	$30,698	1	$30,698
Tank(MeOH)	18.7	$18,331	1	$18,331
Tank(Product)	30.3	$22,522	1	$22,522
Tank(waste)	160	$35,305	1	$35,305
Tank(mixing)	0.05	$3,949	1	$3,949
M.D. 1	400	$300,000	2	$600,000
M.D. 2	2000	$900,000	4	$3,600,000
Total				$6,236,386

Molecular Distillers from --> Meyers
Vacuum
All other from Peter-Timmerhaus estimation

Equipment for Chromatography, G-D Mixture

Unit	Size	Price	#	Total
Varicol Chromatography Unit		$500,000	1315	$657,500,000
Distillation Tower		$40,000		$40,000
Total				$657,540,000

Chromatography Unit price from Procon
All other from Peter-Timmerhaus estimation

Equipment for Chromatography, Research Grade Gamma

Production Rate (kg/yr)	Price
1	$500,000
10	$500,000
100	$500,000
1000	$500,000

Materials for Distillation

Material	Amount				Material Cost		
	Per Year	Per Day	Per Hour	Unit	Unit Cost	Cost/day	Cost/year
Candia rugosa	$ 22,776,000	$ 62,400	$ 2,600	g	$1.66 /g	$103,584.00	$37,808,160.00
Methanol	$ 20,476.50	$ 56.10	$ 2.34	gal	$0.95 /gal	$53.30	$19,452.68
Methanol from CMR Candia rugosa www.sigma.com							

Materials for Chromatography, Gamma-Delta

Material	mL per kg Tocopherol Mixture	mL per kg Product	Unit Cost	Cost/kg Product
Heptane for Dissolution	3000	4918	$0.0003 $/mL	$1.57
Heptane for Elution	87000	142623	$0.0003 $/mL	$45.53
Acetone for Elution	87000	142623	$0.0010 $/mL	$143.64
			Cost per kg product	$190.75

Materials for Chromatography, Pure Gamma

Material	mL per kg Tocopherol Mixture	mL per kg Product	Unit Cost	Cost/kg Product
Methanol for Dissolution	8000	32000	$0.0003	$8.02
Acetone for Elution	20000	80000	$0.0010	$80.57
Methanol for Elution	140000	560000	$0.0003	$140.37
			Cost per kg product	$228.96

Labor for Distillation

Cost of Workers ($/hr)	Number of Workers/Shift	# of Shifts/day	Worker Cost per Day	Worker Cost per Year
$33.67	4	3	$3,232	$1,179,797

Labor for Chromatography, Both Systems

Cost of Workers ($/hr)	Number of Workers/Shift	# of Shifts/day	Worker Cost per Day	Worker Cost per Year
$33.67	30	3	$24,242	$8,848,476

Total Labor Cost for Plant

Total # of Workers	102
Total Cost	$10,028,273 /year
	$27,475 /day

Utilities for Distillation

	Amount			Units	Cost			
	Per year	Per Day	Per Hour			Per Year	Per Day	Per Hour
Water (Distilled)			25.206	m^3	0.85	187683.9	514.2024	21.4251
Steam			11644	/1000 kg	5.95	606908.6	1662.763	69.2818
Electricity			580	kWh	0.085	431868	1183.2	49.3

Utilities for Chromatography, G-D

	Usage per kg Product	Units	Cost	Cost per kg Product
Electricity	0.8	kWh	0.085	0.068

Utilities for Chromatography, Research Grade Delta

	Usage per kg Product	Units	Cost	Cost per kg Product
Electricity	0.4	kWh	0.085	0.034

Total Capital Investment for Distillation

Based on Peters-Timmerhaus

Direct Cost

Purchased Equipment		--	$6,236,386
Delivery		0.1	$623,639
Total Cost of Equipment			$6,860,025
Equipment Installation		0.39	$2,675,410
Controls		0.26	$1,783,606
Piping		0.31	$2,126,608
Electrical Systems		0.1	$686,002
Buildings		0.29	$1,989,407
Yard		0.12	$823,203
Service Facilities		0.55	$3,773,014
	Total direct cost		$20,717,274

Indirect Cost

Engineering		0.32	$2,195,208
Constuction		0.34	$2,332,408
Legal expenses		0.04	$274,401
Contractor's Fee		0.19	$1,303,405
Contingency		0.37	$2,538,209
	Total indirect Cost		$8,643,631
	Fixed Capital Investment		$29,360,905
	Working Capital	0.75	$5,145,018

Total Capital Investment	$34,505,924

Total Capital Investment for Chromatography

Based on Peters-Timmerhaus

Direct Cost

Purchased Equipment	--	$657,540,000
Delivery	0.1	$65,754,000
Total Cost of Equipment		$723,294,000
Equipment Installation	0.39	$282,084,660
Controls	0.26	$188,056,440
Piping	0.31	$224,221,140
Electrical Systems	0.1	$72,329,400
Buildings	0.29	$209,755,260
Yard	0.12	$86,795,280
Service Facilities	0.55	$397,811,700
Total direct cost		$2,184,347,880

Indirect Cost

Engineering	0.32	$231,454,080
Constuction	0.34	$245,919,960
Legal expenses	0.04	$28,931,760
Contractor's Fee	0.19	$137,425,860
Contingency	0.37	$267,618,780
Total indirect Cost		$911,350,440
Fixed Capital Investment		$3,095,698,320
Working Capital	0.75	$542,470,500

Total Capital Investment	$3,638,168,820

TCI, Research Grade Gamma, 1kg/yr

Based on Peters-Timmerhaus

Direct Cost

Purchased Equipment	--	$500,000
Delivery	0.1	$50,000
Total Cost of Equipment		$550,000
Equipment Installation	0.39	$214,500
Controls	0.26	$143,000
Piping	0.31	$170,500
Electrical Systems	0.1	$55,000
Buildings	0.29	$159,500
Yard	0.12	$66,000
Service Facilities	0.55	$302,500
Total direct cost		$1,661,000

Indirect Cost

Engineering	0.32	$176,000
Constuction	0.34	$187,000
Legal expenses	0.04	$22,000
Contractor's Fee	0.19	$104,500
Contingency	0.37	$203,500
Total indirect Cost		$693,000
Fixed Capital Investment		$2,354,000
Working Capital	0.75	$412,500

Total Capital Investment	$2,766,500

TCI, Research Grade Gamma, 10kg/yr

Based on Peters-Timmerhaus

Direct Cost

Purchased Equipment	--	$500,000
Delivery	0.1	$50,000
Total Cost of Equipment		$550,000
Equipment Installation	0.39	$214,500
Controls	0.26	$143,000
Piping	0.31	$170,500
Electrical Systems	0.1	$55,000
Buildings	0.29	$159,500
Yard	0.12	$66,000
Service Facilities	0.55	$302,500
Total direct cost		$1,661,000

Indirect Cost

Engineering	0.32	$176,000
Constuction	0.34	$187,000
Legal expenses	0.04	$22,000
Contractor's Fee	0.19	$104,500
Contingency	0.37	$203,500
Total indirect Cost		$693,000
Fixed Capital Investment		$2,354,000
Working Capital	0.75	$412,500

Total Capital Investment	$2,766,500

TCI, Research Grade Gamma, 100kg/yr

Based on Peters-Timmerhaus

Direct Cost

Purchased Equipment	--	$500,000
Delivery	0.1	$50,000
Total Cost of Equipment		$550,000
Equipment Installation	0.39	$214,500
Controls	0.26	$143,000
Piping	0.31	$170,500
Electrical Systems	0.1	$55,000
Buildings	0.29	$159,500
Yard	0.12	$66,000
Service Facilities	0.55	$302,500
Total direct cost		$1,661,000

Indirect Cost

Engineering	0.32	$176,000
Constuction	0.34	$187,000
Legal expenses	0.04	$22,000
Contractor's Fee	0.19	$104,500
Contingency	0.37	$203,500
Total indirect Cost		$693,000
Fixed Capital Investment		$2,354,000
Working Capital	0.75	$412,500

Total Capital Investment	$2,766,500

TCI, Research Grade Gamma, 1000kg/yr

Based on Peters-Timmerhaus

Direct Cost

Purchased Equipment	--	$500,000
Delivery	0.1	$50,000
Total Cost of Equipment		$550,000
Equipment Installation	0.39	$214,500
Controls	0.26	$143,000
Piping	0.31	$170,500
Electrical Systems	0.1	$55,000
Buildings	0.29	$159,500
Yard	0.12	$66,000
Service Facilities	0.55	$302,500
Total direct cost		$1,661,000

Indirect Cost

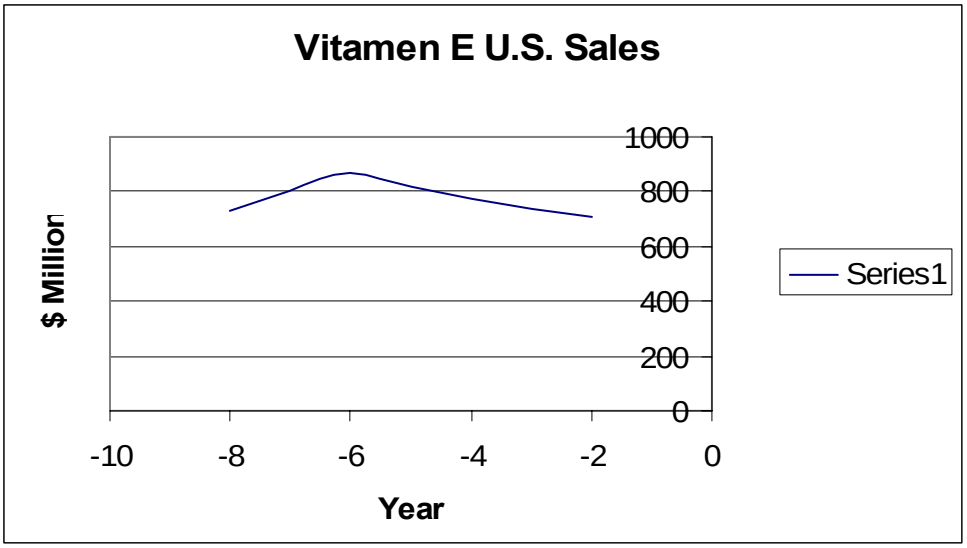
Engineering	0.32	$176,000
Constuction	0.34	$187,000
Legal expenses	0.04	$22,000
Contractor's Fee	0.19	$104,500
Contingency	0.37	$203,500
Total indirect Cost		$693,000
Fixed Capital Investment		$2,354,000
Working Capital	0.75	$412,500

Total Capital Investment	$2,766,500

Return on Investment (Dollars per Dollar Invested)					
Year	Design 1	Design 2	Design 3	Design 4	Design 5
1	$0.13	$0.13	$0.13	$0.15	$0.13
2	$0.15	$0.15	$0.15	$0.17	$0.15
3	$0.17	$0.17	$0.17	$0.19	$0.17
4	$0.19	$0.19	$0.19	$0.21	$0.19
5	$0.21	$0.21	$0.21	$0.23	$0.21
6	$0.16	$0.16	$0.16	$0.17	$0.16
7	$0.13	$0.13	$0.13	$0.15	$0.13
8	$0.11	$0.11	$0.11	$0.12	$0.11
9	$0.09	$0.09	$0.09	$0.10	$0.09
10	$0.06	$0.06	$0.07	$0.07	$0.06

Pure Gamma Production	NPW (Billions of Dollars)		
kg/yr	Minimum	Average	Maximum
0	-0.74	0.93	3.53
1	-0.75	0.92	3.53
10	-0.74	0.93	3.53
100	-0.72	0.95	3.56
1000	-0.46	1.22	3.83

Pure Gamma Production	NPW (Billions of Dollars)			Maximum Regret
kg/yr	Minimum	Average	Maximum	($)
0	0.28	0.29	0.30	0.30
1	0.29	0.30	0.30	0.30
10	0.28	0.29	0.30	0.30
100	0.26	0.27	0.27	0.27
1000	0.00	0.00	0.00	0.00



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