

Comparative Analysis of Bio-based Azelaic Acid Synthesis Methods and Techno-Economic Evaluation of Theoretical Process Design

Ariq D. Raharjanto

Supervisors:

Prof. H. J. Heeres Dr. P. J. Deuss Dr. C. W. Lahive

Faculty of Science and Engineering Department of Chemical Engineering University of Groningen

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Disclaimer

This BSc thesis has been carried out during the COVID-19 global pandemic (spring-summer 2020). In order to comply with all the learning goals specified for the BSc final project in Chemical Engineering at the University of Groningen, (some of) the results presented in this thesis were not experimentally obtained but provided by the main supervisor based on previous unpublished data and personal experience, or obtained from published literature. The source of data has also been specified explicitly or referenced wherever they appear in this text.

1 Abstract

Azelaic acid has been commercially produced for over 50 years for its uses as a plasticizer, lubricant, skincare treatment etc. It is currently industrially produced by oxidizing oleic acid with ozone to obtain the dicarboxylic acid, azelaic acid, and monocarboxylic acid, pelargonic acid. Over the past few years, alternative methods for synthesis of azelaic acid have been developed to overcome the large energy demands and form a greener process by using different chemicals and techniques. These methods were explored in this report and ranked according to appropriate Principles of Green Chemistry to determine an ideal method for designing a process for commercial production. Methods researched included both methods already used in industry and more novel approaches. The general approaches involved ozonolysis of oleic acid, catalytic oxidation and chemo-enzymatic approaches. The main factors that came into consideration were the safety and sustainability of the solvents used in each reaction, the human and environmental impacts of the reagents, use of catalysts and the highest yields of azelaic acid reported. It was found that a catalytic oxidation method described by V. Benessere [21], and further optimized by Z. Masyithah [23], that utilized H₂O₂ and H₂WO₄ catalyst to oxidize oleic acid without the use of solvents to obtain a yield of 91% for azelaic acid was the most ideal in terms of its overall "green" and production value.

A simple chemical plant was designed using the chosen method for an azelaic acid production capacity of 1000 tonnes/year. To achieve this, it was calculated that 174 kg/hr of technical grade oleic acid feedstock was required. This feedstock (73.5% oleic acid) was an important factor for the mass balances as the dicarboxylic acid produced in the reaction other than azelaic acid was malonic acid. In addition, as the feedstock did not contain an unsaturated fatty acid with a carbon chain greater than 18, no monocarboxylic acid produced was longer than 9 carbon atoms. A Techno-Economic Analysis was performed to examine the financial feasibility and determine the profitability of such a plant. The total investment costs were estimated to be just under 10 million euros and the production of azelaic acid was calculated to be approximately 9 euros per kilogram. With the price of azelaic acid currently valued at approximately 27.5 euros per kilogram, it was found that the maximum annual profit attained from this plant was roughly 17.5 million euros. Although it must be stated that many estimations were taken into consideration that resulted in the values described in the report and with this additional output of 1000 tonnes/year of AA, the market value of AA would surely decrease significantly.

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2 Introduction

As the world's fossil fuel reserves are depleting, attention is brought on to another natural resource: biomass. Biomass is now becoming the most important renewable feedstock for the chemical industry, specifically oils and fats derived from plants and animals, due to their worldwide availability and low prices. Generally, most oils contain unsaturated fatty acids, such as oleic acid (OA) and are mainly present in the form of free acids or ester derivatives of glycerol. [1] OA, also known as cis-9-octade-cenoic acid, is a monounsaturated fatty acid with an 18-carbon backbone. It is the most abundant fatty acid in the world, highly present in sunflower oil and palm oil. This particular renewable resource is commonly found in the south of France and Mediterranean countries. [2] Transformations done on OA include epoxidation, oxidative cleavage and hydroxylation. The products obtained from oxidative cleavage include pelargonic acid (PA), a 9-carbon monocarboxylic acid, and azelaic acid (AA), a 9-carbon dicarboxylic acid.

Azelaic acid has many uses that can be categorized into three separate areas: as a building block for the manufacture of polymers such as polyamides, polyesters and polyurethane, as skin treatment for acne and anti-inflammatory medicine in the pharmaceutical industry [3] and as an intermediate compound for the production of lubricants, adhesives, resins and fibers. AA is of particular interest due to its higher solubility in water and organic solvents in comparison to dicarboxylic acids in the C₄-C₁₂ range. This is advantageous in the formulation of high solids or solvent-free systems.[4] Industrially, AA is currently produced by ozonolysis of OA [5] where ozone is used to break the double bond of the carbon chain. This method has been used since 1953 [6]. However, the high temperatures of above 200°C and vacuum pressures that lead to large energy demands, the toxicity of ozone itself and the personnel safety risks attained has pushed the demand for safer and sustainable alternatives. [4]



Figure 1: Mechanism of OA ozonolysis

The purpose of the development of alternatives for the ozonolysis of OA into AA have been to improve the "greenness" of the process. A universal guide on a chemical process can be summarized by "The 12 Principles of Green Chemistry" developed by Paul Anastas and John Warner in 1998. [7] This guide describes aspects of chemistry that can lead to more sustainable and environmentally friendly chemical processes and products. Topics discussed include waste prevention/minimalization, solvent use, less hazardous chemical reagents/products, energy efficiency, renewable feedstock, etc.

The market for AA is mainly driven by the increasing demand for plastics and lubricants, accounting for over 70% of global azelaic acid utilization. In 2019, the global market of AA was approximately 130 million USD and is expected to grow at a rate of 7.7% over the next half decade, reaching an

estimated value of 210 million USD in 2024.[8] The current average price of technical grade AA is valued at 31 USD per kilogram, but can vary significantly depending on the location of production and export/import destination. [9] However, higher purities in polymer and cosmetic grade AA can greatly increase its price 2-3 times fold.

As shown in the upcoming sections, the different methods of AA synthesis will be discussed. Comparisons will be drawn about the classical approaches to AA synthesis with novel catalytic methodologies. These methods will then be ranked according to set criteria chosen from the Green Chemistry principles and its final yield of AA. The top-ranking method is then chosen to create a hypothetical process design using a chosen feedstock at an appropriate production scale to which will then be analyzed for its techno-economic potential.

3 Literature Overview

3.1 Ozone-based Approaches

The current industrial method for azelaic acid production is via ozonolysis of oleic acid in two steps as shown in Figure 1. Ozone is dangerous because of its instability and needs to be formed in-situ as its storage is undesirable. The world's largest AA supplier is Emery Oleochemicals who has been producing AA for over 60 years.[6] Their patent describes the first step by running oxygen through an ozone generator and fed to a reactor with OA at a temperature less than 45°C in counter-current flow. The products are then treated in counter-current with oxygen (2% ozone) for further oxidation. The highest AA yields were obtained when the operating temperature of the second oxidation step was just below 100°C. The PA and AA were purified by vacuum distillation and extracted in hot water to achieve a maximum AA yield of 78%. Niegowski [10] managed to obtain AA yields ranging between 80-93% from pure oleic acid using an inert solvent at a 1:1 ratio with OA. This invention revolved around obtaining AA from a mixture of oxidized acids by esterifying them to increase the AA ester yields before recovering it by fractional distillation. However, the theories explaining this increase are still unproven.

As ozonolysis to obtain AA is done in two steps, different strategies were developed to optimize either step. G. Izumi [11] performed the first step in glacial acetic acid until absorption of ozone became difficult. The optimum conditions for the second step were found to be at 95°C for 2 hours but a low yield of 45-47% was obtained. R. Ackman et. al [12] obtained high AA yields of up to 95% when methanol was the reaction solvent. Instead of using ozone for the oxidative work up in the second step, hydrogen peroxide was used. This indicated a more efficient pathway by using hydrogen peroxide as the oxidant as well as a lower percentage of other acids in the final product. In a more recent study, semicarbazide hydrochloride was used by G. Ishmuratov [13] to treat the oxidized products after ozonolysis was performed in an acetic acid-dichloromethane mixture and obtained yields of 75% PA and 74% AA. This study was used to identify intermediate compounds of AA formation.

An important step that can heavily change the final yield of a desired product is the separation and purification step. H. Oehlschlaeger [14] suggested using ozone during the purification steps of AA. Prepurified AA was treated once more with ozone after hot water extraction and obtained a higher purity of 90% AA. D. Gaige [15] describes an invention in which the AA is pre-purified by distillation to remove oxidised products before being sent to a dual contactor extraction vessel. The extractor utilizes an aqueous phase entering from the top and a water-immiscible phase entering from the bottom. A final purity of 92% weight purity of AA after recovery from the aqueous phase.

Some concerns from using an ozonolysis method is the process mass intensity of solvents and the safety risks that arose. A novel method of ozonolysis to solve this was reported by A. Kadhum without the use of solvents.[16] The reaction was done in a Bach bubbling reactor at 150°C for 2 h and obtained a yield of 20%. Despite a very low yield, this presents the possibility of ozonolysis processes without the safety

concerns or use of solvents and catalysts. Another invention that helps reduce toxicity concerns is patented by B. Gutsche [17]. This invention successfully conducts the ozonolysis of OA in a structured microreactor, giving the advantages of improved heat and material exchange and lower quantities of secondary products, simplifying cleaning and waste air treatment. A method of catalyzed oxidation of oleic acid via ozonolysis was reported by S. Radiman [18] where nanosized tungsten (IV) oxide was used. The catalyst showed a selectivity for AA of 54% and yield of 52%. The nanoscale catalyst was found to be more selective than commercial tungsten (IV) oxide nanopowder. E. Moran [19] describes an invention in which the ozone used for the process was generated from carbon dioxide instead. The CO_2 is fed to an ozone generator and passed through oleic acid for 1262 minutes. The final AA yield was measured to be 73.18%.



Figure 2: Summary of ozone-based approaches

3.2 Non-ozone-based Approaches



Figure 3: Main reaction pathways for OA cleavage into AA and PA [4]

Chemically catalysed oxidative cleavage reactions can be categorized into the number of steps required to synthesize AA. Pathway A involves direct cleavage of OA into AA and PA using strong oxidants such as sodium hypochlorite and peracetic acid in the presence of ruthenium catalysts.[4] Pathway B uses epoxidation and/or diol formation before oxidative cleavage typically using catalysed H_2O_2 . Pathway C, on the other hand, utilizes metathesis followed by cleavage whereas pathway D has a ketocarboxylic acid intermediate before cleavage. The metathesis of pathways C and D were conducted using O_2 or H_2O_2 oxidants and Grubbs catalysts and metals catalysts such as ruthenium and rhenium, resulting in low yields of 40% and conversion of less than 45%.[20][4] Cleavage reactions done without any catalyst were found to be unsuitable for industrial applications as used oxidants have low product

selectivity [4] and will not be discussed in detail. These pathways were not explored further in this report due to these reasons.

V. Benessere [21] describes using pathways A and B to obtain AA from OA. The first is oxidising OA to 9,10-dihydroxystearic acid (DSA) and then oxidatively cleaving with sodium hypochlorite while the second is direct cleavage of OA using a chemocatalytic system consisting H_2O_2 and H_2WO_4 at 100°C. The first method is useful with its milder conditions but resulted in an AA yield no higher than 51% whereas the second method reached an unexpected yield of 91%.

An invention describing the two-step method was patented in 2005 by G. Junjun [22] where tungstic acid was used to catalyse the oxidation with hydrogen peroxide in 2-propanol to form DSA and hydrogen peroxide in acetate was catalysed with sulfuric acid in the 2^{nd} step. AA yields of 50-76% were achieved. Z. Masyithah [23] followed up on the second method by identifying three variables to determine the optimum conditions of the reaction. The variables were substrate/oxidant mole ratio (OA/H₂O₂), percent catalyst (wH₂WO₄/wOA) and reaction temperature. Results showed that conversion values of up to 99% were achieved when the substrate/mole ratio was 1:8, 3:100 percent catalyst and a reaction temperature of 70°C. The use of peroxide is considered highly eco-friendly as water is the main by-product.

Not only were new oxidants explored, different catalytic systems were developed as well. A recent study by A. Ello [24] used catalysts made from organo-modified molybdenum trioxide with H₂O₂. The CTAB-capped molybdenum (1:3 molar ratio) gave AA yields of 83% and 68% yields of pelargonic acid. Various other catalysts were also reported for oxidising OA to AA. A. Godard [2] focused on the oxidative scission of OA and proposed the use of a peroxo-tungsten complex Q_3 {PO₄[WO(O₂)₂]₄} as phase-transfer catalyst and several different quaternary ammonium salts as catalysts. It was found that $[C_5H_5N(n-C_{16}H_{33})]_3$ {PO₄[WO(O₂)₂]₄} gave the highest catalytic activity. The process was then optimized and high yields of AA and PA of above 80% were obtained. Xiukai Li [25] reported using hydrogen peroxide with commercial tungsten (IV) oxide and added sodium stannate as a hydrogen peroxide stabiliser. It was discovered that the sodium stannate notably increased product yields and could possibly be recycled with the tungsten oxide catalyst. Isolated yields of up to 89% and 65% were reported for AA and PA respectively. V. Benessere followed up on his previous work and used high-oleic acid triglycerides in a catalytic system based on hydrogen peroxide/tungstic acid [26]. A comparison of the biomass sources with oleic acid triglycerides olive oil, fresh sunflower oil, exhausted sunflower oil and rapeseed oil was reported and found that, under optimized conditions, olive oil produced the highest AA yield of 71%. This result shows this process is competitive in terms of yields with those reported using simpler feedstock.

3.3 Chemo-enzymatic Approaches

Chemo-enzymatic usage is a relatively new study using chemically catalysed enzymes for cleaving oleic acid into AA. M. Takeuchi [27] used laccase-catalysed oxidative cleavage of fatty acids and found that after 8 hours, 0.58mM of sebacic acid was produced from 1.6 mM of α KetoA with a conversion rate of 35% (mol/mol). E. Brenna [28] managed to produce AA in high chemical purity but with a low yield of 44% by using hydrogen peroxide with Novoenzyme 435. It was found that the issues when using chemo-enzymatic methods are that the reaction conditions must be where the enzymes are most active. Temperatures cannot be higher than 50°C, H₂O₂ must be 1% w/w diluted in the final solution and the reactions time cannot exceed 6 hours. It can be seen that while a chemo-enzymatic route is highly valued as a green process, the yields obtained are not competitive enough to be adapted for commercial production.

4 Comparison Matrix

Based off of the literature overview regarding the multiple pathways of azelaic acid synthesis from biomass, a rank comparison matrix was constructed with set criteria. Though each principle has its own importance, only a few Principles of Green Chemistry were chosen for this comparison, namely: Safer Solvents and Auxiliaries, Inherently Safer Chemistry for Accident Prevention, and Catalysis. A principle that was not used in this report but considered of high importance is the Prevention principle. This principle takes into consideration the total weight of all the chemicals used and produced during the process. It can be measured by calculating the E-factor, the weight of the waste versus the weight of the product, or by calculating the process mass intensity, a total sum of the chemical substances used and discarded to obtain the desired product. [7] For H_2O_2 reactions, they have a theoretical atom economy of 82.7% whereas the remaining 17.3% is the water byproduct. [23] This indicates a very eco-friendly reaction. Ozonolysis reactions are estimated to much lower due to the dilute ozone in oxygen streams. However, many of the literature discussed in the previous section had data gaps in the precise amount of chemicals used or produced in their respective reports. These data gaps were different in each paper such as the specific weight of AA obtained, the amount of drying agent used, extraction solvent used etc. To calculate with such data gaps would create an unreliable criterion to rank the AA synthesis methods. If the lack of data did not occur, the prevention principle would play an important role in the rank matrix but was still of concern when looking at the process overall.

The rank matrix uses three color codes: red, yellow and green which correspond to a scale of 1-10 with 10 being the highest. The red indicates a very low value of 4< for the specific category while yellow shows moderate values between 4 and 8 and green means high values of over 8. It is vital to mention that although some chemicals were assigned with the same color, it does not mean they are of the same value. In the instance of water and acetate both being categorized as relatively safe and coded green, the irritant properties of acetate should not be ignored.

Principle number 5: Safer solvents and Auxiliaries discusses the use of solvents in chemical processes and states that the best-case scenario is to minimize the use of solvents or, if possible, not use them at all as research claims that over 50% of the mass of standard chemical processes are solvents. Not to mention that solvents facilitate the most of the energy consumption and safety risks.[7] Therefore, processes in the rank matrix that do not use any reaction solvents are given an automatic score of 10. When solvents were used, either in the reaction or as separation agents, their overall health hazard to humans and environmental impact were evaluated under the Safety column and their Sustainability aspect was ranked based on the waste category and life cycle analysis. These qualities were taken from analyses previously done by T. Welton [30] and C. Alder [31] and implemented in the rank matrix. These analyses considered similar factors for their assessments and where a difference was found, an average value was taken. Acetic acid was a popular reaction solvent to use. Its high life cycle value but low value in the waste category gave it a middle value for its Sustainability aspect while its irritant and flammable properties awarded its Safety with a middle value as well. A reaction solvent with a high sustainability value given is tert-butanol. It also has a high life cycle value appointed to it but its lower boiling point makes it easier to recycle, hence the green color. In the patent described by C. Goebel [6], PA was used because of its production as a byproduct and served to also decrease the viscosity of the OA and is later easily recycled by distillation. Hazards such as toxicity, flammability, and irritation were taken into consideration for the Safety column.

Alternatives for the use of ozone are developing due to its hazardous properties to humans. Acute exposure could lead to fluid accumulation in the lungs, headaches and irritation to skin and eyes. Chronic exposure may lead to chronic breathing disorders, including asthma. In the case of leaking to the surrounding environment, ozone can severely affect plant life and ozone discharge in a water solution is harmful to aquatic life. Hydrogen peroxide, on the other hand, decomposes into water and oxygen and is therefore not a threat to the environment. However, it is a corrosive chemical that can cause serious

damage to eyes and severe burns to human skin. It has been classified as a moderate threat to human safety. These were the two main oxidants identified in literature for cleaving the OA double bond. In terms of safety risks to humans using these substances, they are both hazardous. Nonetheless, hydrogen peroxide's non-threatening environmental impact ranks it higher than ozone overall.

The use of catalysts in any chemical process is considered 'greener' based on the Principles of Green Chemistry. By increasing the efficiency of a chemical reaction, the minimization of waste is achieved. This is why this principle was chosen as an appropriate criterion for synthesis method comparison. All processes that did not use a catalyst were given an automatic score of 1. The ranking of the various catalysts was dependent on their safety for humans and the environment and their efficiency for recycling. Sulfuric acid is well-known as a corrosive substance and can cause very severe burns. It is also highly toxic to aquatic and terrestrial life at low concentrations. Tungstic acid is widely used as observed in the rank matrix. It has the advantage of being safe to humans as tungsten is a naturally occurring metal, is easily separated by aqueous extraction and filtration and can be recycled up to 6 times.[32] Molybdenum catalysts was found to be able to be recycled up to 4 times but the CTAB is classified as a hazardous chemical, lowering the MO-CTAB catalyst's safety value. The quaternary ammonium salt catalysts described by A. Godard lacks in the recyclability aspect due to its reported recovery value of only 35 mol%.[2] At the same time, no hazardous properties have been investigated for these catalysts. Tungsten (IV) oxide is also categorized as a low-risk substance for humans but has an even higher recyclability value of 7 times with minimal weight and efficiency loss. However, the price of tungsten (IV) oxide is significantly higher than tungstic acid.

As the goal of this project is for assessing AA synthesis methods for commercial production, yields lower than 70% was decided as the cut-off value. Any process that does not merit a yield higher than that was deemed inadequate for scaling up. It can be observed that the use of ozone as the oxidant generally leads to lower yields of AA compared to using hydrogen peroxide. The highest achieved yield was recorded by R. Ackman [12] when ozone formed DSA and hydrogen peroxide was utilized for the oxidative work-up. Papers such as [18], [29], and [25] did not indicate any separation or purification steps for their products, leading to an assumption that the yields reported are higher than the actual yields if any purification steps were conducted. This also brought down the overall process described by X. Li [25] because, despite having very high yields, purification steps were unknown.

Overall, the process in which the highest values (most green in their respective row) was [21] that used no-solvent, hydrogen peroxide as the oxidant, tungstic acid as the catalyst and reached a 91% AA yield. Special credit is given to R. Ackman [12] who obtained the highest AA yield of 95% by incorporating both ozone and hydrogen peroxide in the methodology and achieved low weight percentages of other dicarboxylic acid. However, this process has a higher overall process mass intensity compared to V. Benessere's process. [21]

	Reaction	n Solvent	Stoichiomet	tric Reagent	Catalyst us	sed (if any)	Separatio	Yield	
Criteria	Sustainability	Safety	Safety	Environmental Impact	Safety	Recyclability	Sustainability	Safety	
[6]	Pelargonic acid*	Pelargonic acid*	Ozone	Ozone	-	-	water	water	78%
			Ozone	Ozone			wator	wator	
[10]	Inert solvent	Inert solvent	Dimethyl sulfite Dimethyl sulfite		-	-	organic solvent organic solvent		93%
			Water	Water			Ű		
			Ozone	Ozone			Acetone	Acetone	
[11]	Acetic acid	Acetic acid	Methanol	Methanol	-	-	Petroleum ether	Petroleum ether	45-47%
							water	water	
[16]	-	-	Ozone	Ozone	-	-	n-hexane	n-hexane	20%
[18]	-	-	Ozone	Ozone	Tungsten (IV) Oxide	Tungsten (IV) Oxide	did not purify	did not purify	38-53%*
	Formic Acid	Formic Acid	Ozone	Ozone			Acetone	Acetone	
[12]					-	-	Water	Water	95%
	Methanol	Methanol	H2O2	H2O2			Toluene	Toluene	
	Acetic acid	Acetic acid	Ozone	Ozone			CHCI3	CHCI3	
[13]	Disbloromothono	Dichloromothano	Semicarbazide	Semicarbazide	-	-	Water	Water	74%
	Dichloromethane	Dichloromethane	hydrochloride	hydrochloride			Na2SO4	Na2SO4	
[19]	Acetic acid	Acetic acid	Ozone*	Ozone*	-	-	did not purify	did not purify	73%*
[22]	2-propanol	2-propanol			Sulfuric acid	Sulfuric acid	Ethyl acetate	Ethyl acetate	
	Acetate Acetate		H2O2	H2O2	H2WO4	H2WO4	Water	Water	50-76%
	Water	Water			112.001				
	-						Ethyl acetate	Ethyl acetate	
[21]			-	-	H2O2	H2O2	H2WO4	H2WO4	Water
							Na2SO4	Na2SO4	
[26]	-	-	H2O2	H2O2	H2WO4	H2WO4	Ethyl acetate	Ethyl acetate	71%
	tert-Butanol	tert-Butanol	H2O2	H2O2			Ethanol	Ethanol	
[24]	tert-butanoi	tert-butanoi	11202	11202	MO-CTAB	MO-CTAB	Water	Water	70-83%
	Methanol	Methanol	Boron trifluoride	Boron trifluoride		ino crab	Petroleum ether	Petroleum ether	10 00/8
							Na2SO4	Na2SO4	
[2]	-	-	H2O2	H2O2	Q3{PO4[WO(O2)2]4} as a phase-transfer catalyst/co-oxidant	Q3{PO4[WO(O2)2]4} as a phase-transfer catalyst/co-oxidant	Ethyl acetate	Ethyl acetate	81%
			HCI	HCI	[C5H5N(n-C16H33)]3 {PO4[WO(O2)2]4}	[C5H5N(n-C16H33)]3 {PO4[WO(O2)2]4}	Na2SO4	Na2SO4	
[23]	-	-	H2O2	H2O2	H2WO4	H2WO4	Ethyl acetate	Ethyl acetate	unknown*
			11202	11202			Na2504	Na2SU4	
[25]	-	-	Sodium Stannate	Sodium Stannate	Tungsten (IV) Oxide	Tungsten (IV) Oxide	unknown	unknown	89%*
			Sourdin Stannate	Souldin Stanlate					
Legen <4 4 <x<8 8<x<1< td=""><td>d 3 0</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></x<1<></x<8 	d 3 0								

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8 <x<10< td=""><td></td></x<10<>	
N/A	

Figure 4: Rank comparison matrix of different literature describing azelaic acid synthesis from oleic acid

5 Process Design

5.1 Block Diagram



Figure 5: Block diagram of chosen method

Based on the process chosen from the previous section, the synthesis of azelaic acid was conducted in 3 steps: the oxidation reaction, ethyl acetate extraction and organic layer removal. As described in the literature, the reaction can be done in a one-pot method when adding the oleic acid to the tungstic acid in 60% hydrogen peroxide. The reaction mixture was then extracted with hot ethyl acetate where excess H_2O_2 and the tungstic acid catalyst were separated into the aqueous layer while the organic oxidized products were transferred to the ethyl acetate organic layer. The reaction was done at 70°C to maximize reaction rate but not at a temperature high enough to decompose H_2O_2 . The block diagram for this process can be seen in Figure 5.

Modification were done to Figure 5 to include recycling of catalysts and solvents. The aqueous layer from the ethyl extraction was sent to a peroxide decomposer which decomposes the excess hydrogen peroxide at 90°C into water and oxygen and the catalyst could be recovered by hot filtration to be reused in the reactor. It was considered using a cationic exchange resin for catalyst precipitation as described by W. Francis [33]. The reaction mixture could be passed through a bed of DOWEX-50 and 82.7% of initial tungstic acid could be precipitated. However, the use of the peroxide decomposer was favored for its simplicity and had no indication that the catalyst recovered cannot be higher that 82.7%. The water by-product was then discarded. It could potentially be reused in the water extraction steps. However, it is unknown if it can be used directly or requires further purification. The ethyl acetate from the organic layer was then evaporated at 90°C. It was assumed that none of the mixed oxidized products are loss due to ethyl acetate's boiling point which is much lower (77°C) that of the oxidized products (>140°C). The ethyl acetate is then condensed for reuse.



Figure 6: Block diagram of designed AA synthesis method

From stream 4 onwards, it was decided to use a different method than described by V. Benessere [9]. In this study, the product was recovered by drying the organic layers after the hot ethyl extraction with anhydrous sodium sulfate. In industry, this technique is not economically beneficial. Therefore, inspiration was taken from ozonolysis patents [6],[14] and [15] which describe purification techniques of azelaic acid on an industrial scale. Two distillation columns and a hot water extraction step was implemented. The mixed oxidized products in stream 4 were distilled at 230°C at 25 mmHg in the 1st still to remove monobasic acids with boiling points lower than that of AA such as the other main by-product pelargonic acid and lower carbon chain monocarboxylic acids. This stream of pelargonic acid could potentially be sent to a purification plant to increase the pelargonic acid purity, increasing its value and can be commercially sold.

The remaining compounds from the 1st still in stream 5 were then distilled once more at an even lower pressure of 4 mmHg and at 270°C. Here, azelaic acid, along with compounds with similar boiling points, were vaporized, leaving a residue consisting of non-volatile compounds.

The volatile components produced from the 2^{nd} distillation column were condensed and brought back to atmospheric pressure to be extracted with hot water at 95°C. Here, the components were separated based on their solubility in H₂O. AA and water-soluble acids were dissolved by the water while saturated fatty acids with longer chains were left behind due to their very low water solubility. With the desired product, azelaic acid, in the aqueous phase, the water is then evaporated to be recycled and the product left is approximately 76% azelaic acid. According to [14], further purification could be done by recrystallization of azelaic acid to achieve purities of 92%. However, the targeted applications of the AA produced in this project do not require such high purity but is a viable option to consider.

5.2 Mass Balances

Firstly, the feedstock oleic acid was chosen as technical grade oleic acid that is produced commercially. The composition of the OA used was taken from a patent [14] and is shown in Table 1.

Monounsaturated Fatty Acids							
Oleic Acid	73.5 %						
Palmitoleic Acid	6.0 %						
Myristoleic Acid	1.5 %						
Polyunsaturated Fatty Acids							
Linoleic Acid	8.0 %						
Linolenic Acid	1.0 %						
Saturated Fatty Acids	5						
Myristic Acid	3.0 %						
Palmitic Acid	5.0 %						
Margaric Acid	1.0 %						
Stearic Acid	1.0 %						

Table 1: Technical grade oleic acid feedstock composition

In the reactor, hydrogen peroxide reacts with the carbon-carbon double bond of unsaturated fatty acids to form diols which is further oxidized into carboxylic acids. The composition of the mixed oxidized products leaving the reactor was determined by assuming all the double bonds of the fatty acids were successfully cleaved into their respective shorter carboxylic acids. The fatty acids and their corresponding oxidized products can be observed in Figure 7.



Figure 7: Feedstock composition and their corresponding oxidized products

As the production of AA is several thousand tons per year, a production capacity of 1000 tons per year was chosen for this plant. To start off, operation hours of 8000 hours a year was taken to provide adequate time for cleaning and maintenance of the plant. The minimum required flow of azelaic acid product to reach the production target was then calculated to be 125 kg/hr. With the assumption that the oxidation reaction goes to completion and that all double bonds were broken, the amounts of each oxidized product was calculated according to their unsaturated fatty acid reactant. All mono and dicarboxylic acids were assumed to have 100% yield except for the main products, azelaic acid and pelargonic acid. These yields were taken from the results reported by V. Benessere [21] of 91% and 69% respectively. The remaining percentages of 9% and 31% were placed under an additional component labeled "Unknown".

Using an OA feedstock flow rate 174 kg/hr, 285.85 kg/hr of H_2O_2 and 1.58 kg/hr flow rate of H_2WO_4 was determined using the 1:8 OA/ H_2O_2 molar ratio and 100:1 molar ratio of OA/ H_2WO_4 described by V. Benessere [21]. The mass balances and composition across all streams can be found in Appendix A. It was assumed that H_2O_2 was fully consumed in the reactor as little to no remaining hydrogen peroxide was reported by V. Benessere [21] and Z. Masyithah [23]. With this amount of hydrogen peroxide, the water by-product could be calculated as each mol of H_2O_2 provides 1 mol of water, resulting in 89.75 kg/hr of water. By calculating the moles of AA and PA and multiplying them with their respective yields, 96.12 kg/hr of AA and 49.43 kg/hr of PA was formed.

Following the reactor, the oxidized products were extracted with hot ethyl acetate. It was assumed that no organic compounds were lost at this stage and that the water by-product and tungstic acid were fully in the aqueous phase. The amount of ethyl acetate used was determined by using the solubility of PA in ethyl acetate at 20°C, 250 g/L. [34] This value was assumed to be the solubility of the entire mixture as no other value of solubility in ethyl acetate was found for any of the oxidized products. It helped provide a value on the highest possible amount of ethyl acetate needed for extraction, where in reality it would be much lower. This was important for the financial analysis in the next section. It was calculated that the maximum amount of ethyl acetate that could be used was 855.54 kg/hr. During ethyl acetate recovery, for financial calculation purposes, a value of 95% recovery was chosen with 5% assumed to be unrecyclable.

After removal of ethyl acetate, the mixed oxidized products were distilled at 25 mmHg and 230°C with PA being the light key. To determine an accurate estimation of the distillate fraction, the distillation

column was modelled in Aspen Plus V.8.6 as seen in Appendix B. The column specifications inputted were estimated based off the fact that approximately 40% of the feedstock mass-wise was distilled out as written by C. Goebel [6]. 8 trays were used and a reflux ratio of 1.2 was chosen based on that the low energy cost optimum reflux ratio is 1.3 and high energy costs is 1.1.[35] The model was simulated and was found that 99% of PA, heptanoic acid, hexanoic acid, pentanoic acid and propanoic acid was removed in the first distillation column while 6.5% of malonic acid was removed. As these values were obtained using estimated column specifications, a value of 90% separation for the compounds mentioned before except malonic acid were used in the mass balance. This was to ensure a more similar product composition to commercial AA. As the "Unknown" is unidentifiable and its properties unknown, it was assumed that it consisted of lower carbon length diacids and unreacted oleic acid. Therefore, it was assumed that 10% of the "Unknown" was lost in this step.

The second distillation column serves to remove non-volatile components from the volatile compounds such as fatty acids with a much longer chain. According to C. Goebel [6], this non-volatile residue amounted to 7% of the initial oleic acid feed. Unfortunately, with the composition of the OA used, no mono or dicarboxylic acids are obtainable from oxidation. Therefore, it was decided to take 40% of the "unknown" component to be residue. This residue amounted to approximately 6.5% of the OA feed used.

The volatile compounds were condensed back to liquid and extracted with hot water. Since an exact amount of water required to separate this could not be modeled in Aspen Plus, a mass ratio of OA to water used was taken from C. Goebel's patent [6] of 1:8. Once again, a value of 90% of separation of long chain fatty acids such as myristic acid, palmitic acid, margaric acid, and stearic acid was taken despite being water-insoluble, but to better fit commercial AA composition that could not be achieved with the chosen feedstock. Since the "Unknown" component may have unreacted oleic acid, 10% of the remaining mass was considered insoluble in water. The shorter chain carboxylic acids were assumed to be fully soluble in water so no AA was lost. The water is then evaporated with 95% recovery as it is assumed that 5% of the water is contaminated and cannot be recycled. The final AA product's composition can be seen in Table 2.

Component	Mass flow (kg/hr)	%
Azelaic acid	96.12	76.57
Pelargonic acid	4.94	3.94
Malonic acid	6.05	4.82
Heptanoic acid	0.53	0.43
Hexanoic acid	0.58	0.46
Pentanoic acid	0.12	0.09
Propanoic acid	0.05	0.04
Myristic acid	0.52	0.42
Palmitic acid	0.87	0.69
Margaric acid	0.17	0.14
Stearic acid	0.17	0.14
Unknown	15.41	12.28
Total	125.54	

Table 2: Composition of final azelaic acid product

The final azelaic acid purity in the final product is considered similar to commercially produced AA EMEROX 1110[®] which is 79% with 19% other dicarboxylic acids and 2% monocarboxylic acid. The dicarboxylic composition difference can be explained by the oleic acid feedstock in which only azelaic

acid and malonic acid could be produced. Using different feedstocks of oleic acid could provide greater knowledge regarding the separation of the carboxylic acids and obtain different final AA compositions.

6 Techno-Economic Analysis

The Techno-Economic Analysis (TEA) is a tool used in research and commercial project development that serves to assesses the economic feasibility of a process. It combines engineering aspects such as design and process modeling with economic evaluation. [36] Capital costs estimations are reported in this section to evaluate the profitability of the theoretical process designed in this report. The capital cost was calculated by adding the fixed capital investment with the working capital. The fixed capital investment consists of the inside battery limits (ISBL) investments, infrastructure modifications also known as offsite, engineering and construction costs and contingency charges. [37] The ISBL costs include all processing equipment, installation labor, construction etc. Meanwhile, the offsite costs include additions to the site's infrastructure such as power generation, laboratories etc. Engineering costs mainly cover contractor charges and other engineering services and heavily dependent on duration of client- contractor and their relationship. Contingency, on the other hand, are estimated extra costs added to the project budget to address risks during project development such as labor disputes, changes in material prices and other unexpected problems. The working capital can be described as costs related to maintaining material inventories, and cash on hand and is required for the duration of plant operation.

To calculate the ISBL, the costs of the purchased equipment are summed up and multiplied with an installation Lang Factor of 3.63 for mixed fluids-solids processing plant. Equipment costs were obtained via estimation from typical prices or using Equation 7.9 described by Towler. [37].

$$C_e = a + b S^n$$
 Eq. 7.9

Where C_e is the purchased equipment cost, a and b are cost constants, S is the sizing parameter and n is the exponent of the specific equipment. The pricing of the equipment can be seen in Table 3.

Equipment	Price
Main Reactor	€ 150,000.00
EtOAc Extractor	€ 200,000.00
Peroxide decomposer	€ 100,000.00
EtOAc Evaporator	€ 100,000.00
Still 1	€ 120,000.00
Still 2	€ 120,000.00
Water Extractor	€ 200,000.00
Water Evaporator	€ 100,000.00
Utilities (HeatXs & pumps)	€ 90,000.00
Total	€ 1,180,000.00

Table 3: Purchased equipment costs

The remaining capital costs was calculated based on the total equipment costs. Offsite costs are typically between 20-50% of the ISBL cost. [37] Therefore a value of 40% of the ISBL cost were used for the offsite costs. A general consensus for engineering costs is that it is 30% of the sum of the ISBL and offsite costs for smaller projects. A minimum contingency charge of 10% of the ISBL and offsite sum is required. This increases up to 50% the more novel the technology is.[37] Since AA synthesis is a well-established process but the usage hydrogen peroxide for OA oxidation has not been explored at a large scale, a value of 20% were applied. The working capital was then calculated as 10% of the fixed capital costs. The total investment costs are reported in Table 4.

ISBL	€ 4,283,400.00
Off-site	€ 1,713,360.00
Design & Engineering	€ 1,799,028.00
Contingency	€ 1,199,352.00
Fixed Capital Cost	€ 8,995,140.00
Fixed Capital Cost Working Capital	€ 8,995,140.00 € 899,514.00
Fixed Capital Cost Working Capital Total Investment Cost	€ 8,995,140.00 € 899,514.00 € 9,894,654.00

Table 4: Capital cost results

The prices of the chemicals used were then calculated for the 8000 hours of operation. Recycling and replenishing solvents and the catalyst was taken into account. It is important to note that prices of each chemical are a fair estimate but can vary depending on the most up to date prices and supplier. The OA feedstock and hydrogen peroxide are consumed so their total prices were considering the full 8000 operational hours. Since 95% of the ethyl acetate and water were assumed to be recycled, the mass flow of the remaining 5% was used calculate to price of adding in new solvent. However, as solvents are not infinitely reusable, it was decided that after 100 passes, the solvent would be replenished with new solvent. The prices for replenishing water and ethyl acetate were calculated according to this assumption. It is important to note that the mass flow of ethyl acetate was based of the solubility of pelargonic acid, meaning it is most likely that the mass flow reported is much higher than practical. It was used to provide an overestimate of the process costs. The price of tungstic acid was calculated by considering the fact that tungstic acid could be recycled up to 6 times. As it can be seen in Table 5, a major contributor of the material cost is the high valued OA feedstock.

Material	Flow (kg/hr)	Price (€/kg)	Total Price (€/year)
OA Feedstock	174	2.5	3,480,000.00
H_2O_2	285.85	0.95	2,172,460.00
Recyclable Material	Lost Mass Flow (kg/hr)	Price (€/kg)	Total Price (€/year)
Ethyl acetate	42.78	0.93	318,283.20
Water	69.6	1.2	668,160.00
Replenishable Material	New Material Mass (kg)	Price (€/kg)	Total Price (€/year)
Ethyl acetate	812.76	0.93	60,469.34
Water	1322.4	1.2	126,950.40
H ₂ WO ₄	1.58	25	52,666.67
Total			€ 8,105,519.22

Table 5: Breakdown of material costs

To determine the profitability of the plant designed, it was decided for this plant to have a lifetime of 10 years. Subsequently, the total investment cost was divided by 10 years of operation and added with the material costs. Consequently, it was found that it requires approximately 9 euros to make 1 kilogram of technical grade azelaic acid. Another expenditure to consider is employee costs. Since a plant with a production capacity of 1000 tons per annum is considered small, a value of 1 million euros was chosen.

This may vary depending on the size of the company. With the price of AA found to be 27.5 euros per kilogram [9], it was found that a maximum profit of nearly 17.5 million euros per year could be achieved. It is imperative to say that as the world production of AA is only several thousand tonnes a year, this additional input of 1000 tonnes per year is quite a significant percentage increase. Therefore, the market price of AA will surely decrease.

Total Investment Cost	€ 989,465.40							
Material cost	€ 8,105,519.22							
Total cost	€ 9,094,984.62							
Cost per kg of AA	€ 9.09							
Market price of AA/kg	€ 27.50							
Sales Revenue	€ 27,500,000.00							
Employee cost	€ 1,000,000.00							
Sales Return	€ 18,405,015.38							
Profit	€ 17,405,015.38							
Table 6: Annual financial calculations								

Using a cruder feedstock, such as lard oil which is 49% oleic acid [38], may be significantly cheaper due to being a waste product of the meat industry. However, to reach the target production capacity, the feedstock flow rate would need to be increased to accommodate for the decrease in oleic acid inlet. As the price of such a feedstock is without certainty, two additional TEAs were done. One using an assumption that the price is two-thirds of the technical oleic acid due to its lower oleic acid content of one-third. Another one used a price of $\notin 0.2/kg$ from a brief online survey of suppliers. These additional TEAs can be seen in Appendix C.

7 Conclusion

Methods for producing azelaic acid were reviewed in this report and ranked according to certain criteria inspired from the Principles of Green Chemistry. Azelaic acid is currently industrially produced via ozonolysis of oleic acid at a scale of several thousand tonnes per year for over half a century. However, the toxicity of ozone and large energy demands attained from this process have driven researchers to develop new methods over the years. It was found that the use of hydrogen peroxide as an oxidant was another popular oxidant with yields competitive to ozone. Another aspect to H_2O_2 's appeal is that it is a benign oxidant as it breaks down into water and oxygen.

The methods reviewed were ranked using set criteria: the use solvents and their safety, the use of catalysts, the safety of all the chemicals used in the process to humans and the environment, and ultimately their yield. It was decided that a 70% yield was the cut-off, removing any processes that did not produce a high enough yield to be considered for upscaling. Based on the ranking matrix in Figure 4, it could be seen that the process described by V. Benessere [21] was the "greenest" compared to the other methods mentioned in this report. This process uses 8 molar ratios of hydrogen peroxide in no solvent to oxidize oleic acid in the presence of 1 mol% of tungstic acid. A high yield of 91% of azelaic acid and 69% of pelargonic acid was reported.

A plant was designed using this H_2O_2 and tungstic acid catalyzed system to produce 1000 tonnes of azelaic acid per year. It was found that to obtain this production capacity, a flow rate of 174 kg/hr of technical grade oleic acid is required. The final product was calculated with certain assumption to have a purity of 76% azelaic acid which is relatively close to the lowest grade of commercially produced azelaic acid which has 79%. From this, a TEA was conducted to determine the economic viability of the designed plant. Results showed that it takes approximately 9 euros to produce 1 kg of AA and the profit of such a plant would be 17.5 million euros a year. However, it must be recognized that the process designed used numerous assumptions and that these values obtained are heavily dependent on them.

Certain significant issues regarding the selection procedure arose such as no catalyst usage in a process resulted in an immediate value of 1. Although usage of catalysts is considered greener, if processes can proceed without the use of catalysts, it does not mean they are poor reactions. Another critical point is the assignment of a 70% yield cut-off value. While it is fair to say higher yields are better, the overall process conditions to obtain such a high yield must be considered. This includes reaction time, temperature and pressures of the processes and the energy efficiency. A suggestion would be to perform an energy balance to see the overall energy demand of such a plant as the designed plant is half-inspired from ozonolysis processes which have high energy demand. Therefore, it cannot be claimed that this process has lower energy demands but has a lower process mass intensity than classical AA synthesis methodologies. Another suggestion for future similar projects would be to compile as many different AA synthesis approaches as possible without consideration for yield, conversion, reagents etc. to broaden the variety of methodologies for comparison in the rank matrix. This mistake can be seen in Figure 4 which narrowed down and essentially divides the approaches into only ozone-based and H_2O_2 -based.

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9 Appendix

9.1 Appendix A

Stream	kg/hr	Oleic	Linoleic	Palmitic	Stearic	Linolenic	Myristic	Myristoleic	Palmitolei	Margaric					
1	174.00	127.89	13.92	8.70	1.74	1.74	5.22	2.61	10.44	1.74				H2O2 (60%)	H2WO4
		Azelaic	Pelargonic	Malonic	Heptanoid	Hexanoic	Pentanoic	Propanoic	Palmitic	Stearic	Myristic	Margaric	unknown		
2	306.26	96.12	49.43	6.47	5.34	5.77	1.18	0.46	8.70	1.74	5.22	1.74	31.71	-	1.58
3	1,069.42	96.12	49.43	6.47	5.34	5.77	1.18	0.46	8.70	1.74	5.22	1.74	31.71	-	-
4	213.88	96.12	49.43	6.47	5.34	5.77	1.18	0.46	8.70	1.74	5.22	1.74	31.71	-	-
5	154.33	96.12	4.94	6.05	0.53	0.58	0.12	0.05	8.70	1.74	5.22	1.74	28.54	-	-
6	142.91	96.12	4.94	6.05	0.53	0.58	0.12	0.05	8.70	1.74	5.22	1.74	17.13	-	-
7	1,517.54	96.12	4.94	6.05	0.53	0.58	0.12	0.05	0.87	0.17	0.52	0.17	15.41	-	-
8	125.54	96.12	4.94	6.05	0.53	0.58	0.12	0.05	0.87	0.17	0.52	0.17	15.41	-	-
9	285.85	-	-	-	-	-	-	-	-	-	-	-	-	285.85	-
10	855.54	ETHYL AC	ETATE	-	-	-	-	-	-	-	-	-	-	-	-
11	92.37	-	-	-	-	-	-	-	-	-	-	-	-	-	1.58
12	90.80	WATER BYPRO	DUCT +cat	-	-	-	-	-	-	-	-	-	-	-	0.00
13	1.58	CATALYST REC	CYCLED	-	-	-	-	-	-	-	-	-	-	-	1.58
14	812.76	ETHYL AC	ETATE	-	-	-	-	-	-	-	-	-	-	-	-
15	59.55	-	44.49	0.42	4.81	5.19	1.06	0.42	-	-	-	-	3.17	-	-
16	11.42	-	-	-	-	-	-	-	-	-	-	-	11.42	-	-
17	1,392.00	WATER	-	-	-	-	-	-	-	-	-	-	-	-	-
18	17.37	-	-	-	-	-	-	-	7.83	1.57	4.70	1.57	1.71	-	-
19	1,322.40	WATER	-	-	-	-	-	-	-	-	-	-	-	-	-
20	0.00	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Appendix B 9.2



Appendix C 9.3

Material	Flow (kg/hr)	Price (€/kg)	Total Price (€/year)]	
OA Feedstock	200	1.65	€ 2,640,000.00	T-t-Linux transformer	6 000 465 40
H2O2	285.85	0.95	€ 2,172,460.00	I otal Investment Cost	€ 989,465.40
	Lost Mass Flow			Material cost	€ 7,265,519.22
Recyclable	(kg/hr)	Price (€/kg)	Total Price (€/year)	Total cost	€ 8,254,984.62
EtOAc	42.78	0.93	€ 318,283.20	Cost per kg of AA	€ 8.25
Water	69.6	1.2	€ 668,160.00	1	
	Now Matorial		,	Market price of AA/kg	€ 27.50
Replenishables	Mass (kg)	Price (€/kg)	Total Price (€/year)	Sales Revenue	€ 27,500,000.00
FLOA -	141035 (Kg)	0.03	6 60 460 24	Employee cost	€ 1,000,000.00
EtUAc	812.76	0.93	€ 60,469.34	Sales Return	€ 19.245.015.38
Water	1322.4	1.2	€ 126,950.40	Profit	£ 18 2/15 015 38
H2WO4	1.58	25	€ 52,666.67		0 10,2-10,010.00
Total			€ 7,265,519.22		

Material	Flow (kg/hr)	Price (€/kg)	Total	Price (€/year)			
OA Feedstock	200	0.2		€ 320,000.00	T-t-Line to a transfer	c	000 465 40
H2O2	285.85	0.95		€ 2,172,460.00	I otal investment Cost	£	989,465.40
	Lost Mass Flow				Material cost	ŧ	4,945,519.22
Recyclable	(kg/hr)	Price (€/kg)	Total	Price (€/year)	Total cost	€	5,934,984.62
E+0.4.0	(Kg/11) 40.70	0.02		£ 210 202 20	Cost per kg of AA	€	5.93
LIUAL	42.70	0.93		£ 310,203.20			
Water	69.6	1.2	ŧ	668,160.00		6	27.50
	New Material			a	Iviarket price of AA/kg	£	27.50
Replenishables	Mass (kg)	Price (€/kg)	Total Price (€/year)		Sales Revenue	€	27,500,000.00
E+OA-	012.70	0.03	£	60.460.24	Employee cost	€	1,000,000.00
ELUAC	812.70	0.95	ŧ	00,409.34	Sales Return	£	21 565 015 38
Water	1322.4	1.2	€	126,950.40	sales neturn	-	21,505,015.50
H2WO4	1.58	25	€	52,666.67	Profit	ŧ	20,565,015.38
Total				€ 4,945,519.22			