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Optimization Through Simulation of a LLE Process

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Sponsoring Agency: Sunovion Pharmaceuticals, Marlborough, MA

Submitted to

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Abstract

Our project team developed and tested an Aspen Plus simulation for a liquid-liquid extraction (LLE) process to determine its viability for predicting experimental results. The simulation predictions were experimentally verified at laboratory scale for three different extraction scenarios. Having confirmed the adequacy of the Aspen model, a LLE methodology was developed to demonstrate how to separate and purify organic compounds. The simulation can now be used to predict the optimal operating conditions to reduce overall operational costs.

Acknowledgements

Nomenclature

LLE – Liquid-liquid extraction

API – Active Pharmaceutical Ingredient

UNIQUAC – Universal Quasichemical

UNIFAC – UNIQUAC Functional-group Activity Coefficients

NRTL – Non Random Two Liquid

MTBE – Methyl-tert-butylether

γ_i – Activity coefficient of component i

γ_i^R – Residual activity coefficient of component i

γ_i^C – Combinational activity coefficient of component i

G – Gibbs free energy

G^M – Gibbs free energy of mixing

G^{id} – Sum of ideal Gibbs free energy

G^E – Excess Gibbs free energy

x_i – Molar composition of component i

R – Ideal gas constant

T – Temperature

H – Enthalpy

S – Entropy

n_{i_a} – Number of moles of element i in compound a

m_i – Mass of compound i

Extraction – a chemical separation process

Wash – an individual step in a liquid-liquid extraction process

Simulation – modeling of a chemical process using software

Software – computer programs, such as DynoChem and Aspen

Aspen Plus – a comprehensive chemical process modeling system

DynoChem – an excel based software used to model chemical processes

Sponsor – Sunovion Pharmaceuticals

Free base – the compound being extracted in our LLE process, $C_9H_{13}NOS$

Triflate salt – any salt compound containing a triflate group, CF_3SO_3H

Organic phase – a liquid phase in an LLE that contains an organic solvent and its solutes

Aqueous phase – a liquid phase in an LLE that contains water and its solutes

Executive Summary

Our team was tasked by our sponsor to determine whether the batch processing of a liquid-liquid extraction (LLE) system can be modeled by process simulations. In order to complete this task, we simulated a LLE process in Aspen Plus v8.2 and DynoChem and analyzed different scenarios through simulations in order to optimize the LLE process for a pharmaceutical system. To ensure that the process was feasible, we performed experiments based on the proposed separation conditions predicted by the simulations. The experiments tested the validity of the simulations to determine if either could be used to optimize the process. Optimizing the process on a laboratory scale should allow for significant savings on the commercial scale. Finally, to ensure our results have an impact, a methodology was created from the most successful results so that the best method and simulation can be repeated for several processes.

Background

In the pharmaceutical industry processes are first tested on the laboratory scale before scaling up to a commercial process. The optimization of processes on a laboratory scale could translate into large operational cost savings on the commercial scale. The purpose of this project was to investigate whether software simulations can be implemented to effectively model a process on the laboratory scale. Our sponsor provided us with a liquid-liquid extraction process to be evaluated. In this process a salt split reaction was initiated using 2M KOH to remove the desired free base from triflate salt. Once the reaction came to completion, methyl-tert-butyl ether (MTBE) was added to the reaction mixture to separate the free base from the potassium triflate and water. As a part of this project, the LLE process was evaluated using two different software: DynoChem and Aspen Plus v8.2.

DynoChem is an Excel based software program used widely in the pharmaceutical industry to assist with process design and scale-up. Aspen Plus is commonly used in a variety of industries because of its ability to model both small and large scale processes. The student license versions of both these software simulators were available to us in order to model the LLE process. Before the simulations of the LLE process were developed, the free base's thermodynamic and transport properties needed to be estimated using the National Institute of Standards and Technologies ThermoData Engine (NIST TDE) program that was built into Aspen Plus v8.2. Using the estimated properties of the free base, the LLE process was solved by minimizing the Gibb's free energy of the system. When the Gibb's free energy is minimized, the system is said to be at equilibrium and the compositions of the organic and aqueous phase can be determined.

Methodology

The goal of our project was to use simulations to optimize the liquid-liquid extraction process given to us by our sponsor. In order to meet this goal, we developed three main objectives:

1. Minimize the amount of MTBE and find the optimal number of washes needed to complete the extraction
2. Maximize the recovery of the free base
3. Compare the Aspen simulation predictions to experimental results

Before any experiments and simulations were carried out, a material balance was completed. Given the reaction shown below in Equation 1, the total amount of free base created from the reaction needed to be determined.

$$C_9H_{14}NOS^+ \cdot CF_3SO_3^- + KOH \rightarrow \underbrace{C_9H_{13}NOS}_{Organic\ Phase} + \underbrace{K^+CF_3SO_3^- + H_2O}_{Aqueous\ Phase} \quad (1)$$
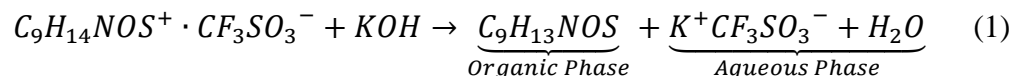
As seen in the reaction above, the free base ($C_9H_{13}NOS$) should prefer the organic phase. The potassium triflate (KCF_3SO_3) should prefer the aqueous phase. All experiments and simulations were completed at a small scale, which started with 10 grams of triflate salt of the free base and 20 grams of 2M KOH. Combining these contents facilitated the reaction and yielded 5.5 grams of free base.

Once the material balance was completed, the simulations in Aspen Plus could be developed and tested. A flow sheet was developed for each of the different extraction scenarios: the base case (three wash system), two wash system, and a four wash system. Once the simulations were developed, a sensitivity analysis was performed in Aspen to find the optimal amount of MTBE for each of the extraction scenarios. The sensitivity analysis gave possible solutions, some of which were tested in the laboratory.

A laboratory scale experiment was set up to confirm whether the Aspen predictions were accurate. The first step in the experiment was the salt split reaction, which yielded the free base. Once the reaction was complete, MTBE was added to the solution to extract out the free base. The contents were added to a separatory funnel, where the solution settled into two liquid phases. The bottom or aqueous phase, was removed and set aside for the next wash. The top or organic phase, was put into a round bottom flask, which was attached to a rotary evaporator. The rotary evaporator was used to evaporate off the MTBE and any residual water, leaving the free base. After the experiments were complete, the material balance was analyzed and compared with Aspen predictions.

Results

We investigated the capabilities of both simulation software, DynoChem and Aspen, to model a liquid-liquid extraction process. The investigation was completed by comparing our simulated results with that of a published paper. The results showed that Aspen could accurately model an LLE process, while DynoChem could not model it without advanced knowledge of the code. The next step was to determine if Aspen could model our specific LLE process. An Aspen simulation was completed using the base case numbers given to us by our sponsor. This simulation predicted a total percent recovery of 98% free base. This value was close to the 99% recovery that our sponsor reported, leading to the conclusion that Aspen could model our process. Once this was determined, we used Aspen to optimize the amount of MTBE used for a

three wash system (base case), a two wash, and four wash system at the laboratory scale. The sensitivity analyses run on each of the extraction scenarios produced the results seen in Figure 1.
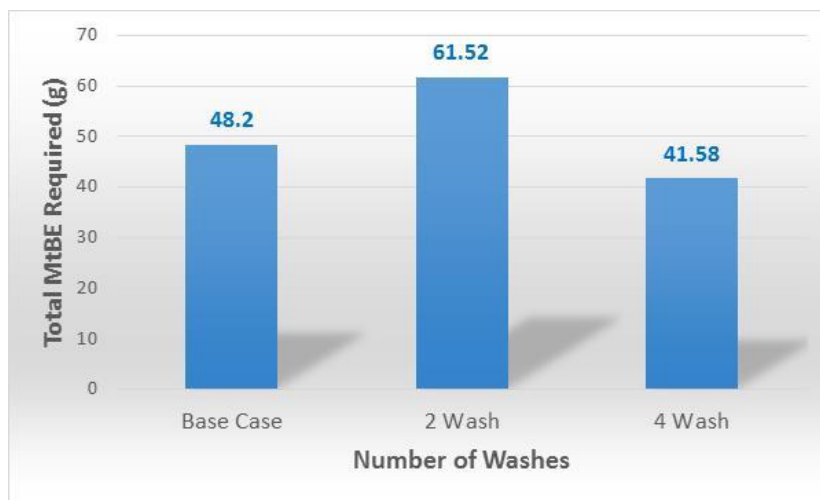
Figure 1: Optimal overall usage of MTBE in each extraction scenario

Once the optimal parameters for the three extraction scenarios were determined, they were tested in the lab to determine their validity. Table 1 shows our Aspen simulated predictions compared to our experimental results.

Table 1: Experimental results compared to the Aspen predictions for all three extraction scenarios

Wash Number	Free Base Recovered (g)								
	Base Case			2 Washes			4 Washes		
	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference
1	4.09	4.43	8 %	5.22	4.76	9 %	2.49	3.63	37 %
2	1.28	0.87	38 %	0.25	0.59	83 %	2.79	1.26	75 %
3	0.18	0.20	9 %	NA			0.30	0.32	6 %
4	NA						0.18	0.14	26 %
Total	5.55	5.50	0.8 %	5.47	5.35	2 %	5.77	5.35	8 %

All of the totaled experimental results were within 10% of the Aspen predictions leading us to conclude that Aspen could accurately model and optimize the process.

Final Conclusions and Recommendations

From our results, there were three main conclusions drawn.

1. DynoChem cannot simulate this LLE process since there is no functionality in DynoChem to predict novel compounds' physical properties such as the free base we extracted. However, DynoChem may be able to predict different conditions once the distribution coefficient is known.

2. The Aspen Plus simulation predictions were within 10% of experimental results for the total amount of free base extracted. However, individual runs were not always simulated well, which could be attributed to not fully extracting the free base expected in the first wash or experimental error in the laboratory. Since no simulation is expected to be perfect and there is always a possibility of experimental error, Aspen Plus was concluded to be an adequate way to simulate the overall liquid-liquid extraction process.
3. Using standardized values provided to us by our sponsor, we came up with estimated values for operational times: Base Case was 8.5 hours, 2 Wash was 6.25 hours, and 4 Wash was 10.75. Therefore, it was concluded that the 2 Wash extraction scenario would take 26.5% less time than the base case. However, operational costs would have to be determined to conclude which extraction would be the most cost efficient.

Based on the conclusions and results of this project, four main recommendations have been developed for future projects.

1. Run the same experiments performed in this report at a larger scale. The larger scale tests could reduce the impact of some of the experimental error and result in Aspen predictions closer in value to experimental results for individual washes. We recommend running tests on a 50 gram scale and then scaling up further to a 100 gram scale.
2. Run the same experiments performed in this report using different solvents. Solvents such as anisole, toluene, trans-1,2-dichloroethylene, and dichloromethane could possibly extract the free base more efficiently than MTBE.
3. Run the experiments using different parameters. Using different molarities of KOH, using different bases, and raising the system temperature could result in more efficient operating conditions.
4. Though DynoChem could not be used for this report, this software might be useful for evaluating possible outcomes if experimentally determined partition coefficients can be added to the database. Therefore, we recommend for future work that the use of user supplied partition coefficients be investigated in Dynochem.

In summary, Aspen Plus can adequately predict experimental results, which indicates that the simulation can help predict optimal operating conditions and lower operational costs.

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Introduction

The pharmaceutical industry frequently uses batch processing to convert raw materials into their final products (Majozi, 2010). As part of batch processing, companies form process development groups with the purpose of making the drug substance or the active pharmaceutical ingredient (API). These developmental groups specialize in sequencing the reactions and separations to produce the desired API (Basu, 1998). In order to design the process that produces an API, an understanding of the physical and chemical properties is required. Chemists and engineers use physical and chemical properties to try to optimize the recovery of the product through separation from the by-products while minimizing the operational handling and waste. "Despite the change of economic emphasis, batch process design is poorly served with design tools and methodologies when compared with continuous processing" (Basu, 1998). As a major contributor in the pharmaceutical industry, our sponsor has its own process development group investigating the optimization of batch processes.

Recently, companies have begun to explore the possibility of optimizing batch processes through process modeling. Studies have shown that the pharmaceutical industry as a whole wastes over fifty billion dollars a year (News, 2012). In the pharmaceutical industry each process would ideally use the perfect amount of raw materials and produce no waste; however, no process is one hundred percent efficient. Therefore, pharmaceutical companies must allocate money for handling waste. Companies can reduce waste costs through reduction of waste production by improving the efficiency of individual process steps. For instance, when performing liquid-liquid extraction (LLE), one large extraction is less efficient than several small extractions (Chem Courses, 2012). In this process step waste is produced in the form of excess solvent. Process modelling can "predict the interactions of chemical and physical rates as a function of operating conditions, scale, and equipment" (Hoffmann, 2014); therefore, process models can help reduce wastes and operational costs. These models would have to be straightforward, tested in a lab scenario, and clearly described and communicated in a methodology in order to successfully optimize practices within a company. Optimizing practices such as LLE can save time and money through recovering more product and producing less waste.

Our sponsor does not have a simulation designed to optimize a batch LLE process. The simulation would require having the capacity to model lab scale as well as commercial scale processes. Also, when testing the simulation at lab scale, optimizing LLE processes includes finding the best solvent to use as well as maintaining a minimum use of solvent to reduce waste. For example, if a system uses excess solvent, more waste is generated; however, if the optimal solvent quantity, which can be found through a simulation, is used for that same system, waste production can be reduced. At many companies solvent usage is being prioritized higher in hopes of optimizing systems to lower operational costs. Specifically, our sponsor wants to tests whether their LLE process can be improved through simulation.

Aspen Plus and DynoChem are two chemical process simulators that can be used to model pharmaceutical processes. Aspen Plus is a process modeling tool that can be used for the optimization of pharmaceutical industries. Aspen Plus is typically used to design and improve processes within industries (Aspentech, 2014). This simulator is actively used in industry and can be implemented to help improve the liquid-liquid extraction process and find the optimal solvent usage. In addition to Aspen Plus, DynoChem is another simulator used in the pharmaceutical industry. Though DynoChem is a newer simulator than Aspen Plus, it has already been adopted by several pharmaceutical companies and has the potential to optimize a process (Hoffman, 2014). Neither Aspen Plus nor DynoChem has been tested by our sponsor.

Our team was tasked by our sponsor to determine whether the batch processing of a LLE system can be modeled by process simulations. In order to complete this task, we simulated a LLE process in Aspen Plus and DynoChem and completed different scenarios through simulations in order to optimize the LLE process for a pharmaceutical system. To ensure that the process was feasible, we performed experiments based on the proposed separation conditions predicted by the simulations. The experiments tested the validity of the simulations to determine if Aspen could be used to optimize the process. Optimizing the process on a laboratory scale would allow for significant savings on the commercial scale. Finally, to ensure our results have an impact, a methodology was created from the most successful results so that the best method and simulation can be repeated for several processes.

Background

  The following section describes the research completed in order to understand all aspects of the task presented to us.

Overall Purpose of the Project

  The purpose of this project was to demonstrate the value of simulations when looking to optimize a process. Our sponsor provided a liquid-liquid extraction (LLE) process for us to evaluate the accuracy of model predictions. The commercial process starts at the lab scale as seen in Figure 2 (Carbogen, 2008); therefore, in order to stream line optimization, the laboratory scale was the focus of the project.
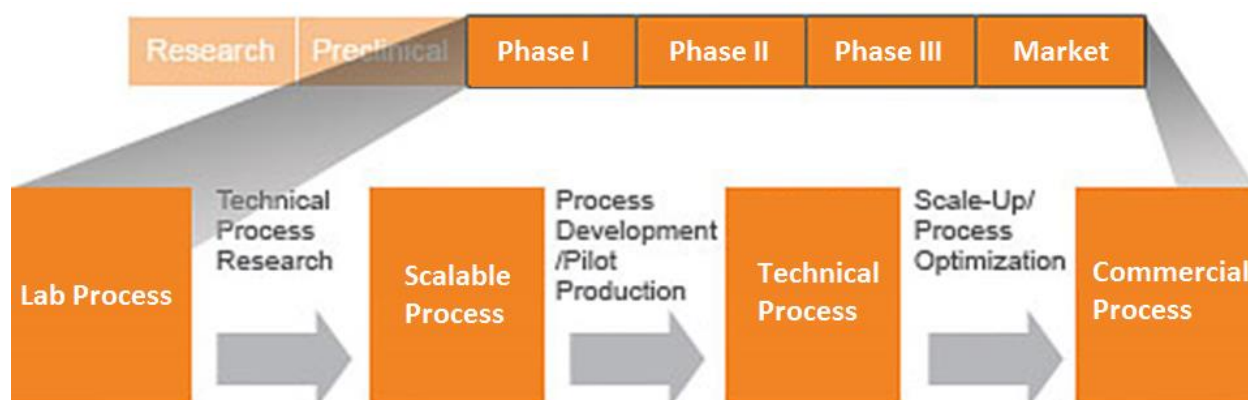
Figure 2: Drug development process for the pharmaceutical industry

  Throughout the drug development process including the one shown above, there are opportunities to optimize before reaching the commercial level. Optimization of processes on the laboratory scale could translate into large operational costs savings during the commercial process. The LLE process given to us by our sponsor was developed in their lab; however, the parameters of the experiments were not evaluated for optimal conditions. One evaluation method that can provide optimal conditions is the use of simulation software. As part of this project, we assessed the capabilities of two simulation software: Aspen Plus and DynoChem.

  Process simulation software are capable of performing a variety of tasks. Such tasks include modeling the chosen LLE process, performing energy and material balances, estimating the size of the equipment, and estimating the cycle time. Process simulation software can also be used to calculate utility usage and perform cost analyses. Completing studies on a process through computer simulations allows the process to be changed without having to consider safety and equipment restrictions. Therefore, the critical parameters can be changed in order to evaluate their impact on production and operational costs (Papavasileiou, Koulouris, Siletti, & Petrides, 2007). Creating a simulation on the laboratory scale would also help when the process is being transitioned to the larger scale. Batch sizes in the simulation can be adjusted accordingly and the simulation can be run to predict the outcome on a larger scale.

  The most valuable capability of simulation software evaluated in this project was the optimization tools. A sensitivity analysis is one of the tools available to the chemical industry to

assist with optimization. General process simulations result in a single outcome based on the inputted parameters; however, a sensitivity analysis results in multiple solutions by determining how a change in the independent variable impacts the dependent variable. These analyses examine the sensitivity of the process model to changes in the inputs or independent variables (Taylor, 2013). Optimal solutions can be determined when there is a target value for the dependent variable. The feasibility of each solution can be analyzed further when operational costs are considered (Seferlis & Hrymak, 1996). The process presented to us by our sponsor was simulated using software capabilities including the sensitivity analysis.

Process to be evaluated

The LLE process was performed in the lab as well as through simulation to determine whether the simulation had the capabilities needed to accurately predict experimental outcomes. The specifics of the LLE process, as described in this section, focused on the initial reaction followed by a liquid-liquid extraction. The reaction separated the free base from the triflate salt then the liquid-liquid extraction removed the free base from water and potassium triflate.

Salt Split Reaction

The first step in our process was the salt split reaction. Salt splitting is a unit operation in which a salt of a compound is separated through a deprotonation reaction resulting in free base of the salt. Industrially, salt splitting is performed using membranes (Genders, 1995); however, in order to simulate the process in a lab environment a simple beaker and a base can be used to carry out a salt split reaction.

For the specific process in this report, the salt split removes the triflate functional group (CF_3SO_3H) from the free base ($C_9H_{13}NOS$). The salt split reaction was promoted by 2M KOH. To ensure that all of the triflate salt compound was successfully split, excess 2M KOH was used. The salt split reaction equation can be seen in Equation 2.

$$C_9H_{13}NOSH^+ \cdot CF_3SO_3^- + KOH \rightarrow C_9H_{13}NOS + K^+CF_3SO_3^- + H_2O + KOH \quad (2)$$
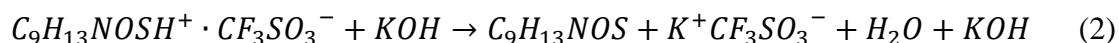
The resulting solution of the reaction contained the free base, potassium triflate salt, water, and excess KOH. This solution was then used in the next step of the process: liquid-liquid extraction.

Liquid-Liquid Extraction

The second step of the process under evaluation was liquid-liquid extraction. Liquid-liquid extraction (LLE) is a separation technique where a solvent is used to remove desired products from a liquid phase by transferring the product into a second liquid phase (Wankat, 2007). Once the solvent is added, the solution is mixed thoroughly to promote the mass transfer of the product into the desired phase (Wankat, 2007). Then, the mixture is given adequate time to settle to reach equilibrium, or rather the static condition in which no changes occur in the macroscopic properties of a system with time (Smith, Van Ness, & Abbot, 2005). In our case equilibrium was reached when the two phases (aqueous phase and organic phase) had a definitive interface and all mass transfer between the two phases had stopped. In order for the LLE process to be successful, the product that is being extracted must have a higher solubility in the solvent than in the aqueous phase. The solubility in the second liquid phase is considered the driving force in an LLE process (Wankat, 2007). The overall effectiveness of an LLE process

depends on several factors: the selectivity of the solvent for the product, the capacity of the solvent to dissolve the product, the density of the solvent compared to the aqueous phase, the chemical reactivity and stability of the solvent, and the overall cost of the solvent (Treybal, 1963). The effectiveness of an LLE process can also be determined by the way in which it is carried out. For example, a LLE process can be performed as single stage, countercurrent cascades, and cross-flow cascades (Wankat, 2007). For this project, our sponsor provided the guidelines for a multistage LLE process.

  A multistage LLE process has the capability to vary multiple parameters such as number of washes and solvent usage. In a multistage LLE process the aqueous phase from the initial LLE wash is saved so that the aqueous phase is used in the second wash to extract remaining product. This would be repeated for as many washes as necessary in order to extract as much product as was produced in the initial salt split reaction. The aqueous phase of our system contained water, free base, trace amounts of the solvent, and the potassium triflate salt. Due to their extremely high affinity for water, we assumed that potassium triflate salt and KOH were only in the aqueous phase; therefore, our organic phase would only contain the free base, solvent, and trace amounts of water. In the outline of the LLE process given to us, MTBE was used as the solvent of choice. The LLE process was evaluated on two main criteria: the number of washes and the amount of solvent used.

Software

  The liquid-liquid extraction process was modeled using two different software: DynoChem and Aspen Plus. Aspen Plus is commonly used in the chemical engineering industry to simulate both small and large scale processes. DynoChem is used in the pharmaceutical industry to optimize and assist with scale-up design. Both of these software were evaluated to see whether the simulation could accurately predict experimental results for a liquid-liquid extraction process on a laboratory scale.

DynoChem

  DynoChem is simulation software developed by Scale-up Systems for the purpose of optimization and scale up of chemical processes, specifically in the pharmaceutical industry. DynoChem is currently used by nine out of the top ten pharmaceutical companies (DynoChem Resources, 2014). These companies use DynoChem to scale up and optimize processes developed on the laboratory scale.

  Aside from the built-in physical properties for commonly used solvents, DynoChem also has different utilities and models that complete process calculations based on the user defined inputs. There are 160 pre-defined template models of common organic synthesis reactions and work up steps. The models include a variety of chemical processes such as solvent exchange, extraction, crystallization, filtration, distillation, and more. Experimental data can be used to generate temperature and pressure time-dependent profiles that can be used for optimization and other variables of interest. DynoChem also has various utilities which can complete calculations to find the operating conditions, mixing times, and solubility predictions (DynoChem Resources, 2014). For this project, DynoChem was used to try to evaluate the LLE process given to us by our sponsor.

Aspen Plus v8.2

Aspen Plus is a comprehensive modeling software that is used to simulate and optimize chemical processes. Aspen has a variety of programs that can be used to model specific processes including pharmaceuticals, polymer production, biofuel, and batch systems. The program chosen to model our system was the student edition of Aspen Plus v8.2. This software has an extensive property database of solid, liquids, and gases that is able to model both simple and rigorous processes. These processes can be modeled either on a laboratory or industrial scale. Also, Aspen Plus has the ability to estimate property parameters of user defined compounds not found in its property database using various group contribution methods (Aspen Technology Inc, 2014).

Modeling the LLE process

In the specific LLE process under consideration, the free base's properties needed to be estimated using Aspen Plus. The National Institute of Standards and Technology ThermoData Engine (NIST TDE) was used to estimate these missing thermodynamic properties (NIST, NIST Standard Reference Database 103b, 2014). The NIST TDE was first integrated into Aspen Plus v2006.5 in 2009 (AspenTech, 2009). The NIST TDE is a comprehensive software program that is built into Aspen that uses published experimental data, predicted values based off of structure, and user supplied data if any (NIST, ThermoData Engine). When first implemented into Aspen Plus v2006.5, the database only contained properties of pure components; however, in Aspen Plus v8.2 the database contains both pure and binary component properties. The current database contains thermodynamic and transport properties for over 21,000 pure components, 42,500 binary mixtures, 11,500 ternary mixtures, and 6,000 chemical reactions (NIST, NIST Standard Reference Database 103b, 2014). Using these databanks of properties, the NIST TDE is able to estimate enthalpies, equilibrium constants, and Gibbs free energies based off of different group contribution methods.

Aspen Plus v8.2 has the capabilities of modeling binary interactions between components using a variety of different models including UNIQUAC, Wilson, NRTL, Joback, and UNIFAC. For our process the UNIFAC (UNIQUAC Functional-group Activity Coefficients) group contribution method was chosen to model the LLE process. The UNIFAC model is an expansion of the UNIQUAC (Universal QuasiChemical) model, which models phase equilibria of two component systems. The UNIQUAC models these two component systems by accounting for compositions of each component as well as intermolecular forces (Prausnitz, 1998). UNIFAC is an expansion on the UNIQUAC model by breaking down molecules into smaller functional groups. These smaller functional groups allow for more accurate modeling of the interactions between molecules. By modeling these interactions, UNIFAC is able to estimate the activity coefficient of the components in a mixture. The activity coefficient is the measure of the non-ideality behavior of a component in a mixture. Equation 3 is the UNIFAC gamma activity coefficient model equation where γ_i is the activity coefficient of the ith component.

$$ln(\gamma_i) = ln(\gamma_i^C) + ln(\gamma_i^R) \tag{3}$$

In Equation 3 the activity coefficient is a function of two terms; the combinational (γ^C) and the residual (γ^R) activity coefficients. The combinational term accounts for the different

functional groups areas and volumes while the residual term accounts for the energy interaction between functional groups (Fredenslund, Jones, & Prausnitz, 1975).These activity coefficients were used to calculate the Gibbs free energy of the system in order to determine the equilibrium concentrations. The Gibbs free energy is calculated using the functionality of the decanter blocks in Aspen Plus.

The process under evaluation was a laboratory scale, batch liquid-liquid extraction containing multiple washes; therefore, in order to model this process, the decanter block was chosen to simulate one extraction wash in the overall process. The decanter block is a separation unit available in Aspen Plus that is capable of modeling LLE. This particular block allows for a sufficient residence time for the multiple liquids to separate into two phases. This eliminates the need for the user defined inputs for the mixing and settling time.

The LLE process was simulated using one feed stream to the decanter block and two exiting product streams (one for each phase) as seen in Figure 3.
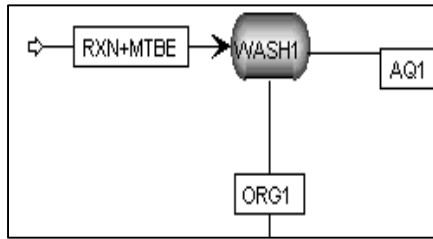
Figure 3: Decanter Block as seen in Aspen Plus flowsheet

The decanter block solved the phase equilibrium between the exiting streams by minimizing the Gibbs free energy. When Gibbs free energy of a system is minimized at a constant temperature and pressure, the system is said to have reached equilibrium (Olaya, 2013). Gibbs free energy is defined in Equation 4 where (T) is the temperature, (H) is the enthalpy, and (S) is the entropy.

$$G = H - TS \tag{4}$$

When mixing occurs in a process such as LLE, the entropy of the solution rises. The Gibbs free energy of the mixture can be evaluated as the sum of the ideal Gibbs free energy (G^{id}) and the excess Gibbs free energy (G^E) seen in Equation 5.

$$\frac{G}{RT} = \frac{G^{id}}{RT} + \frac{G^E}{RT} \tag{5}$$

For liquid systems, the ideal Gibbs free energy can be calculated by using the molar composition of each component (x_i), the ideal gas constant (R), and the temperature of the system (T). Equation 6 below shows the how the ideal Gibbs free energy can be calculated for liquid systems.

$$\frac{G^{id}}{RT} = \frac{1}{RT}\sum_i x_i G_i + \sum_i x_i \ln(x_i)$$

$$\tag{6}$$

The excess Gibbs free energy is the non-ideality correction to the Gibbs free energy of mixing. This non-ideality correction can be modeled using various correlations. However, UNIFAC, the chosen model for our process, calculates the activity coefficient (γ_i) for each component in the mixture. Using the UNIFAC activity coefficient, the Gibbs free energy coefficient can be calculated using Equation 7.

$$\frac{G^E}{RT} = \sum x_i \ln(\gamma_i) \tag{7}$$

Using the equations above, Aspen simultaneously solves for the compositions of the components of the mixture that yields the minimal Gibbs free energy. These compositions are the exiting compositions of the decanter block.

Laboratory Safety

Before any experiments were completed in the lab, safety considerations were researched. Safety concerns and procedures were considered for both the equipment and chemicals used in the experiments.

Experimental Safety

There are several different safety measures that had to be taken into account for these laboratory experiments. The first involved working with a rotary evaporator. All of the seals on the rotary evaporator had to be checked, since a leak could have drawn air into the apparatus which could cause a violent implosion (Simmler, 1995). Furthermore, since the rotary evaporator contained rotating parts, precautions needed to be taken such as no contact with the rotating parts, tying long hair back, no exposed jewelry such as necklaces and bracelets, and no loose clothing worn.

Other safety measures should be taken when dealing with the reaction. The reaction should be performed in a controlled environment and in small quantities so that there are no run away reactions. All components should be carefully weighed out. Furthermore, a hood in the unit operations lab was used to vent the reaction and provide further containment in case there was a spill. Safety goggles, gloves, and a lab coat should be worn at all times in order to avoid direct skin contact with the solvent and the triflate salt. All Material Safety Data Sheets (MSDS) were acquired for MTBE and KOH, so that the proper disposal methods and wash methods were known. These MSDS's can be found in Appendix G.

In order to ensure that our materials are not contaminated, each piece of equipment was cleaned out after each run. The round bottom flask attached to the rotary evaporator was cleaned after reweighing the free base. First, the free base was removed and kept in a disposable vial. Then, the round bottom flask was cleaned out in order to ensure that there was no left over free base when the next run is being performed. The collection flask attached to the condenser was emptied of any solvent before the next run, so that the run was not contaminated.

Solvent Safety

Prior to using MTBE in the lab, safety considerations were researched such as the hazards, health concerns, and information on personal protective equipment and storage.

Hazards

MTBE is a highly flammable liquid. Its boiling point is 55°C. The upper flammability limit of MTBE is 15.1% and the lower flammability limit is 2.5%. It can ignite in the presence of open flames and sparks. Oxidizing agents should be avoided since MTBE may react with those agents. If a fire were to start, a dry chemical powder fire extinguisher should be used for small fires. Alcohol foam should be used to extinguish larger fires. When MTBE is combusted, it may produce carbon monoxide, carbon dioxide, and acrid fumes. Incomplete combustion may result in the production of more toxic gases (Methy tert-butyl ether MSDS, 2013).

Health Concerns

MTBE is hazardous when it comes into contact with the skin and eyes. Contact with the eyes will result in redness, watering, and itching. Contact lenses should not be worn when working with MTBE. If MTBE comes into contact with the eyes, an eye wash station should be used to rinse the eyes for 15 minutes and medical attention should be sought. Contact with the skin will result in itching, scaling, reddening, and blistering. If MTBE comes into contact with the skin, water should be used to rinse the affected area. Contaminated clothing should be washed before it is worn again. If MTBE is inhaled at low concentrations, nose and throat irritation may occur. If liquid enters the lung through aspiration, chemical pneumonia, severe lung damage, respiratory failure, and death may occur (Methy tert-butyl ether MSDS, 2013).

Personal Protective Equipment and Storage

When MTBE is used in laboratories, it is important to have proper ventilation to keep the concentration of MTBE below its limits. Experiments using MTBE should be conducted in a hood. Personal protective equipment should be worn when working with MTBE. Gloves and safety googles should be worn. A lab coat should be worn to avoid contact with the skin and clothing. MTBE should be stored away from heat, ignition sources and strong oxidizing agents. It should be stored tightly in a closed container in a cool and well-ventilated place. Non-sparking tools should be used when handling MTBE (Methy tert-butyl ether MSDS, 2013).

Peroxide Safety

Before MTBE is used for distillation or evaporation experiments, the material should be tested for the presence of peroxides. Ethers that form peroxides should not be evaporated to dryness, because distillation and evaporation will result in the concentration of the peroxides. Peroxide strips were used to test the concentration of peroxides in MTBE. If 0 to 30 mg/L of peroxides are present, then all lab work with the solvent is acceptable. This includes vacuum distillation and evaporation to dryness. If greater than 30mg/L but less than 100mg/L of peroxides is present, the lab work is allowed. However, experiments including vacuum distillation and evaporation to dryness are not allowed. If the solution contains greater than 100 mg/L of peroxides, the solution should be treated as hazardous and the bottle should be isolated immediately (Sarpong, 2013).

Methodology

The overall purpose of the project was to test whether the two simulation software could accurately model an LLE process. The simulation software used in this project were Aspen Plus and DynoChem as described in the preceding background section. Process models were developed and then tested by comparing the predictions to laboratory experiments. If the simulations were able to model the process, the optimal parameters of the LLE could be predicted. This section describes the set up for the simulations as well as the laboratory experiments.

Initial Software Evaluation

Prior to developing the simulation for the liquid-liquid extraction (LLE) process given to us by our sponsor in Aspen Plus and DynoChem, an initial software evaluation was performed. A research paper that studied the liquid-liquid extraction of a ternary system, similar to our system, was used. The ternary system was composed of acetic acid, water, and MTBE. This study was completed to understand how acetic acid could be recovered from aqueous solutions produced from chemical and fermentation processes (Miao, Zhang, Wang, & He, 2007). This research paper provided experimental data, binary interaction parameters, and ternary diagrams. The data was inputted into Aspen Plus and DynoChem with the intention of replicating the results found in the paper. The purpose of this exercise was to determine whether DynoChem or Aspen Plus could model a process similar to the process given to us by our sponsor.

Aspen Plus

Aspen Plus had the capability of not only generating ternary diagrams but also solving for the binary interaction parameters. Therefore, Aspen was used to regenerate binary interaction parameters and ternary diagrams from experimental data provided in the research paper. The paper provided experimental data for the ternary system of water (1), acetic acid (2), and MTBE (3) at various temperatures. The data for 293.15K from LLE of the water-acetic acid- MTBE system can be seen in Figure 4 below.

solvent-rich phase			water-rich phase		
w_1	w_2	w_3	w_1'	w_2'	w_3'
$T = 293.15$ K					
0.0122	0.0000	0.9878	0.9509	0.0000	0.0491
0.0261	0.0502	0.9237	0.8998	0.0496	0.0506
0.0407	0.1102	0.8491	0.8323	0.1132	0.0545
0.0744	0.1720	0.7536	0.7796	0.1609	0.0595
0.1068	0.2381	0.6551	0.7236	0.2039	0.0725
0.1604	0.2744	0.5652	0.6386	0.2639	0.0975
0.2517	0.3282	0.4201	0.5242	0.3104	0.1654
0.2939	0.3311	0.3750	0.4724	0.3184	0.2092
0.3333	0.3328	0.3339	0.4459	0.3220	0.2321

Figure 4: Experimental Mass Fractions of water (w1), acetic acid (w2), and MTBE (w3) at 293.15K (Miao et al.)

Using the data provided above, Aspen data regression analysis was able to compute the binary interaction parameters for this ternary system. A data set was created in Aspen for the paper's experimental data, which can be seen in Figure 5.

Figure 5: Aspen Data Set-1 for Water, Acetic Acid, and MTBE mixture

With the data set created, a data regression analysis was performed on the data to solve for the binary interaction parameters. Binary interaction parameters for UNIQUAC and NRTL were generated and compared to values provided in the paper. The Aspen input screen for the data regression can be seen in Figure 6.

Figure 6: Aspen data regression input screen for UNIQUAC binary interaction parameters

The initial guess and the range of values were provided by the paper and were the same for each data regression. The element number was defined as 2 since the binary interaction parameters are temperature dependent.

DynoChem

Similar to the exercise completed in Aspen Plus, the MTBE, water, and acetic acid system was also studied in DynoChem. Ternary diagrams were generated from the VLLE utility found in the DynoChem resources. Unlike Aspen Plus, DynoChem needed the binary interaction parameters as an input in order to generate the ternary diagram. Experimental data from the

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research paper was used to generate the ternary diagrams. Figure 7 below shows where binary interaction parameters (BIPs) were inputted into DynoChem.

Figure 7: Binary interaction parameter input table in DynoChem

The binary interaction parameters are represented in DynoChem as G12 and G21. The non-randomness coefficient is represented in DynoChem by alpha12. In order to input the experimental data from the paper into DynoChem, new rows had to be added for each of the components. DynoChem was able to recognize each of the components and assign them an ID. Values for the BIPs and the non-randomness coefficient were inputted into the spreadsheet based on the data provided in the paper. Table 2 below shows the experimental data used for the binary interaction parameters.

Table 2: Binary interaction parameters for water, MTBE and acetic acid system at 293.15 K (Miao et al.)

	G12	G21
Water + Acetic Acid	1492.22	-263.87
Water + MTBE	1108.52	602.07
Acetic Acid + MTBE	430.82	500.16

In order to generate the ternary diagram, DynoChem required inputs such as the composition of the feed, the temperature, and the thermodynamic model. Figure 8 shows the input screen in DynoChem.

Figure 8: Ternary diagram inputs spreadsheet in DynoChem

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The three components were selected in the excel file from the list. The temperature was specified to be 20°C (293.15K) and the feed was kept at the default values. The thermodynamic model chosen was NRTL to be consistent with what was shown in the paper. The ternary diagrams generated in DynoChem were compared to those found in the research paper.

Material Balance

Prior to completing the simulations and experiments on the LLE process, the total amount of free base created in the reaction needed to be determined. The reaction in our experiment can be seen in Equation 8.

$$\underbrace{C_9H_{14}NOS^+ \cdot CF_3SO_3^-}_{triflate\ salt\ of\ the\ free\ base} + KOH \rightarrow \underbrace{C_9H_{13}NOS}_{Organic\ Phase} + \underbrace{K^+CF_3SO_3^- + H_2O + KOH}_{Aqueous\ Phase} \qquad (8)$$
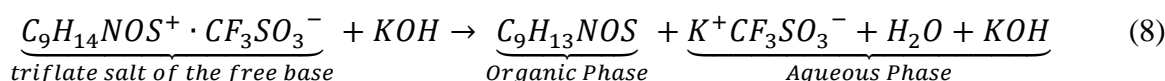
The free base ($C_9H_{13}NOS$) was assumed to be in the organic phase for each extraction. The potassium triflate (KCF_3SO_3) and KOH were assumed to only be present in the aqueous phase. Our tests were run with an initial target value of 10g of triflate salt and 20g of 2M KOH; therefore, the example below was completed using these numbers. The first step was to determine how much KOH was used in the reaction, and then convert the mass of triflate salt and KOH into moles. This was done by dividing each component's mass by its respective molar mass. An example can be seen below in Equations 9 and 10 for triflate salt and KOH respectively.

$$\text{Triflate salt: } 10g \div 333.35 \frac{g}{mol} = 0.030mol \qquad (9)$$

$$\text{KOH: } 2.018g \div 56.11 \frac{g}{mol} = 0.036mol \qquad (10)$$

Having calculated the moles of each initial component, mole balances were completed. Looking back at the reaction equation (8), it was determined through a nitrogen mole balance that all moles of nitrogen present in the triflate salt were converted into the free base. A fluorine mole balance shows that all moles of fluorine present in the triflate salt were converted into potassium triflate. Therefore, there were 0.03 moles of both free base and potassium triflate produced in the reaction. A potassium mole balance was also completed to determine how much KOH was used in excess for the reaction. The mole balance can be seen in Equation 11.

$$n_{K_{KOH}} = n_{K_{PotassiumTriflate}} + n_{K_{KOHExcess}} \qquad (11)$$

With the moles of initial KOH and potassium triflate, the moles of excess KOH were calculated. In this example there were 0.06 moles of KOH in excess.

The final step was to do a hydrogen mole balance to determine the amount of water formed in the reaction. The hydrogen mole balance can be seen in Equation 12.

$$14 * n_{H_{TriflateSalt}} + n_{H_{KOH}} = 13 * n_{H_{FreeBase}} + n_{H_{KOHExcess}} + 2 * n_{H_{Water}} \qquad (12)$$

The only unknown in the equation above was the moles of hydrogen in the water. Solving for this unknown, we found 0.030 moles of water were formed. All of the moles were then converted to masses, to determine the mass balance of the entire reaction. The total mass of initial components was 30g. After completing the mole balances and converting, the products of the reaction were found to have a total mass of 30.03g. This helped prove that the mole balances were done correctly and were well within 1% of the actual values. The difference of 1% can be attributed to rounding errors in the molecular weights of each component. These calculations were completed for each run of our experiment and can be seen below in Tables 3 and 4.

Table 3: Material balances for the inlet of the reaction

INLET						
Run	Mass of SEP-363492.Triflate (g)	SEP-363492.Triflate (mol)	KOH (g)	KOH (mol)	KOH Water (g)	Total (g)
1	10.008	0.03	2.443	0.044	21.774	34.225
2	10.137	0.03	1.964	0.035	17.5	29.601
3	9.844	0.03	2.046	0.036	18.235	30.125
4	9.94	0.03	1.973	0.035	17.588	29.501
5	9.909	0.03	1.995	0.036	17.784	29.688
6	9.915	0.03	2.009	0.036	17.904	29.828
7	9.958	0.03	1.946	0.035	17.344	29.248
8	9.954	0.03	1.99	0.035	17.734	29.678
9	10.07	0.03	2.007	0.036	17.892	29.969
10	50.172	0.151	9.788	0.174	87.234	147.194

Table 4: Material balance for outlet of reaction

OUTLET											
Run	SEP-363492 (mol)	Potassium Triflate (mol)	Water (mol)	KOH (mol)	KOH Water (g)	SEP-363492 (g)	Potassium Triflate (g)	Water (g)	KOH (g)	Total (g)	Discrepancy (g)
1	0.030	0.030	0.030	0.014	21.774	5.502	5.680	0.541	0.759	34.255	0.031
2	0.030	0.030	0.030	0.005	17.500	5.573	5.754	0.548	0.257	29.632	0.031
3	0.030	0.030	0.030	0.007	18.235	5.412	5.587	0.532	0.389	30.155	0.030
4	0.030	0.030	0.030	0.005	17.588	5.465	5.642	0.537	0.300	29.531	0.030
5	0.030	0.030	0.030	0.006	17.784	5.448	5.624	0.535	0.327	29.718	0.030
6	0.030	0.030	0.030	0.006	17.904	5.451	5.627	0.536	0.340	29.858	0.030
7	0.030	0.030	0.030	0.005	17.344	5.475	5.652	0.538	0.270	29.278	0.030
8	0.030	0.030	0.030	0.006	17.734	5.472	5.649	0.538	0.314	29.708	0.030
9	0.030	0.030	0.030	0.006	17.892	5.536	5.715	0.544	0.312	29.999	0.031
10	0.151	0.151	0.151	0.024	87.234	27.584	28.476	2.711	1.343	147.348	0.154

Simulations

Due to time and resource restrictions, we were not able to use DynoChem to model the given liquid-liquid extraction process. Having an unknown molecule with no information of the physical properties made it difficult to input into DynoChem. Once the properties, specifically the partition coefficient, are determined experimentally, DynoChem may be able to model the LLE process. Since the goal of our project was to use computer simulations to predict experimental results, we decided to move forward with the project and no longer use DynoChem.

Aspen Plus version 8.2 Set Up

Limitations of Aspen

Due to the limitations of the UNIFAC groups, the triflate salt could not be efficiently modeled in Aspen. The triflate salt could not be modeled because there were multiple bond groups that could not be inputted into Aspen. Therefore, the reaction step of the process could not be modeled. Under the assumption that 100% of the triflate salt was converted into free base, the Aspen simulation started with post-reaction solution (free base, MTBE, and water).

UNIFAC Group Contribution Method

The liquid-liquid extraction process under consideration was modeled in Aspen Plus v8.2. In order to simulate the extraction process, a UNIFAC property method was chosen to model the separation behavior of each component. Since the free base was not in the Aspen property database, a user defined property model was created for the free base. The structure of the free base was inputted into the property definition table, which allows the user to draw a molecular structure. We used this feature to calculate the number and type of atoms in the molecule as well as the bonds between these atoms. The structure of the free base inputted into Aspen Plus can be seen in Figure 9.
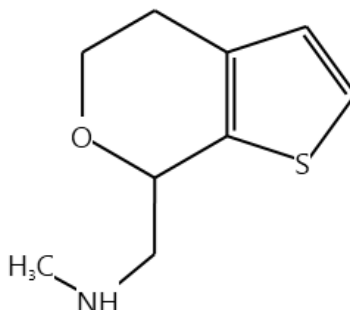
Figure 9: The structure of the free base

In order to achieve accurate property estimations, UNIFAC group contributions were inputted into the property definition table. To find the group contribution id numbers, the structure of the free base was compared to known UNIFAC property groups found in the Aspen database manual (Aspen Plus User Guide, nd). Figure 10 shows which groups were selected from the Aspen property database user manual as well as the UNIFAC group and subgroup numbers.
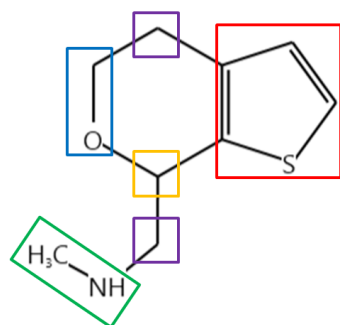
Number of Occurrences	Main Group Number	Sub Group Number	Symbol	Aspen ID
2	1	2	CH$_2$	1010
1	3	1	CH	1005
1	27	13	-O-C- (ring)	1600
1	31	15	CH$_3$NH	1710
1	108	50	C$_4$H$_2$S	3760

Figure 10: Free base with UNIFAC groups and subgroup numbers

The thermodynamic and transport properties based on these UNIFAC group contribution parameters were estimated using the NIST (National Institute of Standards and Technology) ThermoData Engine (TDE). This is a built-in software that Aspen uses to predict a compound's properties based off of published experimental data, molecular structure with corresponding state correlations, and any user supplied data. Below in Figure 11 are the property estimations for the free base using the NIST TDE data evaluation.

	Name	Description	Value	Units	Uncertainty
▶	OMEGA	Pitzer acentric factor	0.60398		0
	ZC	Critical compressibility factor	0.263		0.263
	VC	Critical volume	0.4762	cum/kmol	-0.0343
	PC	Critical pressure	3568527.9	N/sqm	3568527.9
	TC	Critical temperature	778	K	48.9
	DNLEXSAT	TDE expansion for liquid molar density	+	kg/cum	
	DHVLTDEW	TDE Watson equation for heat of vaporization	+	J/kmol	
	CPIALEE	TDE Aly-Lee ideal gas Cp	+	J/kmol-K	
	MW	Molecular weight	183.27		0
	TB	Normal boiling point	550.5	K	84.1
	DELTA	Solubility parameter @ 25 C	23393.1	(J/cum)**.5	23393.1
	SG	Specific gravity	1.309		0.113
	VLSTD	API standard liquid molar volume	0.1402	cum/kmol	0.0122

Figure 11: The NIST TDE property estimate results for the free base

Setting Up the Flow Sheet

With the properties of all the components of the system defined, the main flow sheet of the simulation was set up. To model each extraction wash, a decanter block was used, which models a single wash separation process for multiple liquid phases. The decanter block simplifies the extraction process by allowing for proper residence time so that both liquid phases fully separate. This simplification automates the mixing and settling times so that user inputted data is not needed.

Our sponsor gave us data on a liquid-liquid extraction step in an API production process, which was considered the base case. The base case was used in this section to explain how the Aspen required inputs were defined. In the base case 0.03 moles or 5.498 g of the free base

exited the salt split reaction step and entered the LLE step. In the LLE step the free base was removed from the aqueous phase by the addition of MTBE in three extraction washes. In Aspen three decanter blocks were used to model each wash where the exiting aqueous stream was fed into the next decanter block along with additional MTBE. The Aspen flow sheet of the base case can be seen in Figure 12.
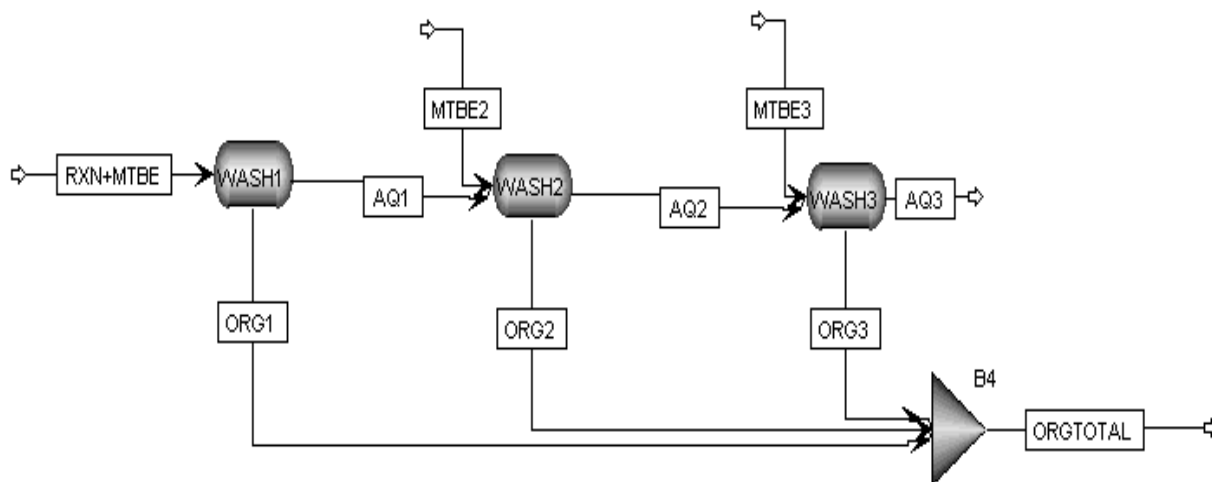
Figure 12: Aspen main flow sheet for base case (3 wash system)

The operating conditions of the feed for each decanter block needed to be specified. Since operating conditions were not specified, the temperature and pressure feed conditions were assumed to be atmospheric. The feed (RXN + MTBE) for the first decanter block consists of 17 g of water, 5.498 g of free base, and 22.2 g of MTBE. The second and third decanter blocks' feeds (MTBE2 and MTBE3) only consisted of pure MTBE, 15 and 11 grams respectively. In each decanter block a second liquid phase needed to be specified. In our process the second liquid phase was the organic phase, which consisted of MTBE and free base. The actual separation process modeled by the decanter block was solved by minimizing the Gibbs free energy resulting in two exiting streams, one aqueous and one organic stream. The organic exiting streams (ORG1, ORG2, and ORG3) from each extraction wash were saved and mixed together to give the total organic stream (ORGTOTAL), which will be processed further downstream. Our sponsor had a target recovery of 98%, or rather 5.44 g of free base to be extracted.

Sensitivity Analysis

In an extraction process, as the number of washes increases, the amount of solvent required to recover a product decreases. However, as the number of washes increase so does the operational costs of the process. These two variables, the number of washes and the amount of solvent required, were varied to give the minimal amount of operational cost and solvent used while still recovering 98% of the free base. In a single wash system the amount of solvent required is too large to be efficient. On the other hand, the five wash process would have too high of an operational cost to be efficient. Due to these factors, the number of washes that were under consideration for the process was two, three, and four washes.

To calculate the amount of solvent needed for the target recovery of 98% in the three different extraction scenarios, a sensitivity analysis was used. In a sensitivity analysis a single dependent variable can be calculated based off manipulated (independent) variables. In this specific process the dependent variable that was calculated was the total outlet flow (ORGTOTAL in Figure 12) of the free base. The manipulated variables were the solvent feed streams (RXN +MTBE, MTBE2, and MTBE3) to each of the decanter blocks. To input a specific sensitivity analysis the manipulated variables need to be defined first. A screen shot of the Aspen input menu for a two wash process can be seen in Figure 13.
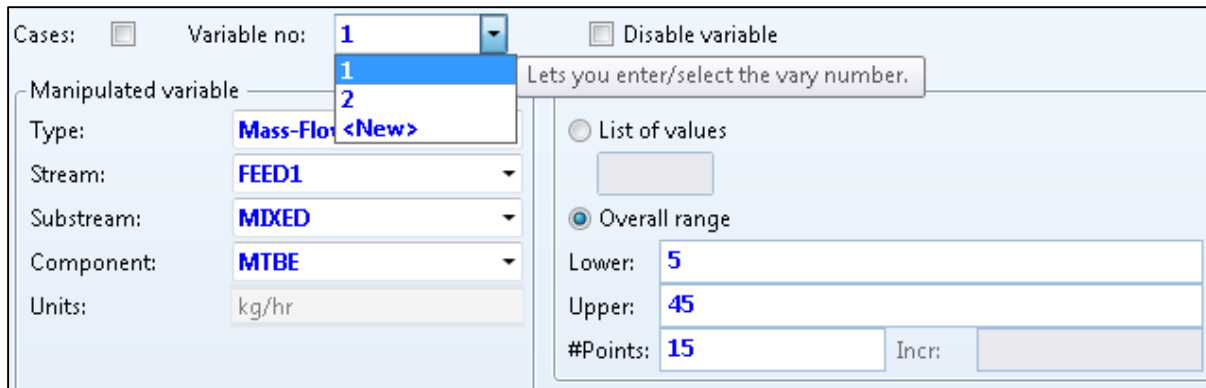
Figure 13: Aspen sensitivity analysis inputs

The MTBE mass flow rate of each feed stream was first defined for each variable number. Then, the range was selected for the manipulated variables. This range was defined by lower and upper boundary limits. Next, since the range of the values was so large, the number of points was chosen to be 15. With all manipulated variables inputted, the total free base outlet flow rate (dependent variable) was defined, which can be seen in Figure 14.
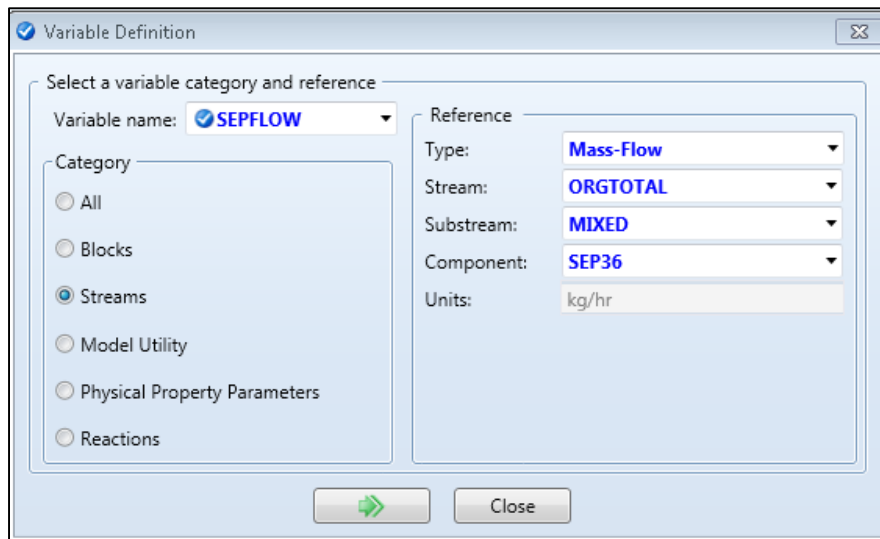
Figure 14: Aspen input screen for sensitivity analysis dependent variable

As seen in the figure above, the free base mass outlet flow was selected as the organic total stream (refer back to Figure 12, ORGTOTAL). With both the manipulated and dependent variables defined, the sensitivity analysis could finally be solved. The sensitivity analysis generates a list of solutions composed of various combinations of the manipulated variables, which can be seen in Figure 15.

	Row/Case	Status	VARY 1 FEED1 MIXED MTBE MAS SFLOW KG/HR	VARY 2 FEED2 MIXED MTBE MAS SFLOW KG/HR	VARY 3 FEED3 MIXED MTBE MAS SFLOW KG/HR	SEP FLOW OUT KG/HR
▸	1	OK	0.019	0.013	0.009	0.0053804
▸	2	OK	0.019	0.013	0.00933333	0.00538357
▸	3	OK	0.019	0.013	0.00966667	0.0053866
▸	4	OK	0.019	0.013	0.01	0.0053895
▸	5	OK	0.019	0.013	0.0103333	0.00539227
▸	6	OK	0.019	0.013	0.0106667	0.00539494
▸	7	OK	0.019	0.013	0.011	0.00539749
▸	8	OK	0.019	0.0136667	0.009	0.00538586
▸	9	OK	0.019	0.0136667	0.00933333	0.0053889
▸	10	OK	0.019	0.0136667	0.00966667	0.0053918
▸	11	OK	0.019	0.0136667	0.01	0.00539457

Figure 15: Aspen sensitivity results for a three wash process

The list of solutions provided both valid and extraneous extractions results. The outlying extractions either involved too little or too great amount of solvent in which no phase splitting occurred. These solutions were not considered in determining the optimal conditions. Of the valid solutions from the sensitivity analysis, only the solutions that extracted 98% of the free base (the base case value) or greater were considered to be optimal.

Experimental Procedure

Equipment

The rotary evaporator was the main piece of laboratory equipment used to conduct the experiments. The main components of the rotary evaporator are a round bottom flask, a heat bath, a condenser, and a vacuum system. The round bottom flask was used to hold the organic phase mixture, containing the solvent and the product. This piece was attached with a clip to a rotary drive, which rotated the flask. When the flask was rotated, a thin layer of solvent formed on the side of the flask allowing the solvent to evaporate quicker. A heat bath was filled with water and heated to a set temperature of 50 degrees Celsius. The vacuum hoses were attached to the condenser. This vacuum system lowered the air pressure of the system so that the solvent evaporated at a lower temperature, reducing the amount of heat required. As the solvent evaporated, it traveled up the axial into a condenser unit. The condenser unit was filled with dry

ice, causing the solvent to condense onto the glass siding of the condenser. The resulting liquid solvent then dripped down into a collection flask.

Components

  There are several important materials involved in the laboratory experiments. The first material was potassium hydroxide. This compound was used in the initial reaction in order to break down the triflate salt into the free base and potassium triflate. The free base extracted in this experiment was $C_9H_{13}NOS$. The solvent that was tested was MTBE. The solvent was tested multiple times, at different masses, to test the hypothetical values generated from our simulation sensitivity analysis.

Salt Split Reaction

  Before the salt split reaction could be initiated, a solution of 2M KOH needed to be made using KOH flakes. 0.9802 liters of water was added and mixed with 132 grams of KOH flakes to produce a 2M KOH solution. Appropriate amounts of triflate salt and 2M KOH were then measured out (10 grams and 20 grams, respectively). The contents were added to a 100mL beaker and mixed in order to trigger the salt split reaction. A magnetic stir plate was used to thoroughly mix the contents for five minutes. To ensure a complete reaction, the pH value of the final solution was measured. If the pH was over one unit greater than the given pKa value (9.5), the given reaction was considered complete.

Extraction

  Once the reaction was complete, the appropriate amount of MTBE for the first wash was measured and added to the reaction solution. The solution was mixed using a magnetic stir plate for five minutes at a constant speed. Once the solution was well mixed, it was added to a separatory funnel in order to complete the extraction of the organic phase. Once the two phases had reached equilibrium after five minutes of settling, the aqueous phase (bottom) was drained from the separatory funnel into a 100mL flask and set aside for the next wash. The two phases can be seen in Figure 16 where the top phase is the organic phase and the bottom phase is the aqueous phase.

Figure 16: Organic and Aqueous phases in the separatory funnel

Next, a 100mL round bottom flask was weighed. The remaining organic phase in the separatory funnel was drained into the round bottom flask and attached to the rotary evaporator. Once the solvent was evaporated from the organic phase, the vacuum was turned off. The round bottom flask was removed from the rotary evaporator and massed out. This determined the amount of free base extracted. This process was repeated for each subsequent wash by adding more MTBE to the saved aqueous phase. The amount of MTBE used in each wash for each extraction scenario can be seen in Table 5.

Table 5: Amount of MTBE used per wash per extraction

	MTBE Used		
	Base Case	*2-Wash*	*4-Wash*
Wash 1 (g)	22.2	37.125	13.365
Wash 2 (g)	15	24.395	13.365
Wash 3 (g)	11	NA	7.425
Wash 4 (g)	NA		7.425
Total (g)	**48.2**	**61.52**	**41.58**

Results

Having researched simulations that could be used, the models were tested for validity. Once the simulations were verified for functionality, laboratory experiments were performed to validate the theorized extraction results. This section describes the results predicted by the simulations as well as the results seen in lab scale experiments. Furthermore, an operational time analysis was completed on the extraction scenarios.

Initial Simulation Evaluation

The two software simulators (Aspen Plus v8.2 and DynoChem) were chosen to model the LLE process. First, these simulators were tested to see if they had the capability of predicting interaction parameters and generating ternary diagrams.

Aspen Plus

The results of the Aspen Plus generated binary interaction parameters for UNIQUAC and NRTL compared to the theoretical numbers found in the research paper can be found in the Tables 6 and 7 below.

Table 6: Generated UNIQUAC binary interaction parameters results compared to Miao et al. data at 293.15K

UNIQUAC		Theoretical (paper)		Aspen Generated	
Component i	Component j	A_{ij}/K	A_{ji}/K	A_{ij}/K	A_{ji}/K
Water	Acetic Acid	209.75	-216.58	208.879	-181.725
Water	MTBE	-51.33	-601.09	-51.032	-616.736
Acetic Acid	MTBE	299.95	-439.01	306.038	-428.777

Table 7: Generated NRTL binary interaction parameters results compared to Miao et al. data at 293.15K

NRTL		Theoretical (paper)		Aspen Generated	
Component i	Component j	A_{ij}/K	A_{ji}/K	A_{ij}/K	A_{ji}/K
Water	Acetic Acid	1492.22	-263.87	664.044	-278.844
Water	MTBE	1108.52	602.07	1133.26	624.647
Acetic Acid	MTBE	430.82	500.16	-0.7672	-28.3765

Comparing the binary interaction parameters from the paper to Aspen, it was observed that the UNIQUAC interaction parameters generated by Aspen closely matched those from the paper. The NRTL parameters generated for the acetic acid and MTBE were the only results not matching the theoretical values. This may be due to multiple solutions when solving for the parameters. Using both the UNIQUAC and NRTL binary interaction parameters, ternary diagrams were generated and compared to the ones provided in the paper. The ternary diagrams generated from the binary interaction parameters in the tables above can be seen in Figure 17. Since the NRTL and UNIQUAC ternary diagrams generated by Aspen were exactly the same, only the UNIQUAC ternary diagram is displayed below.
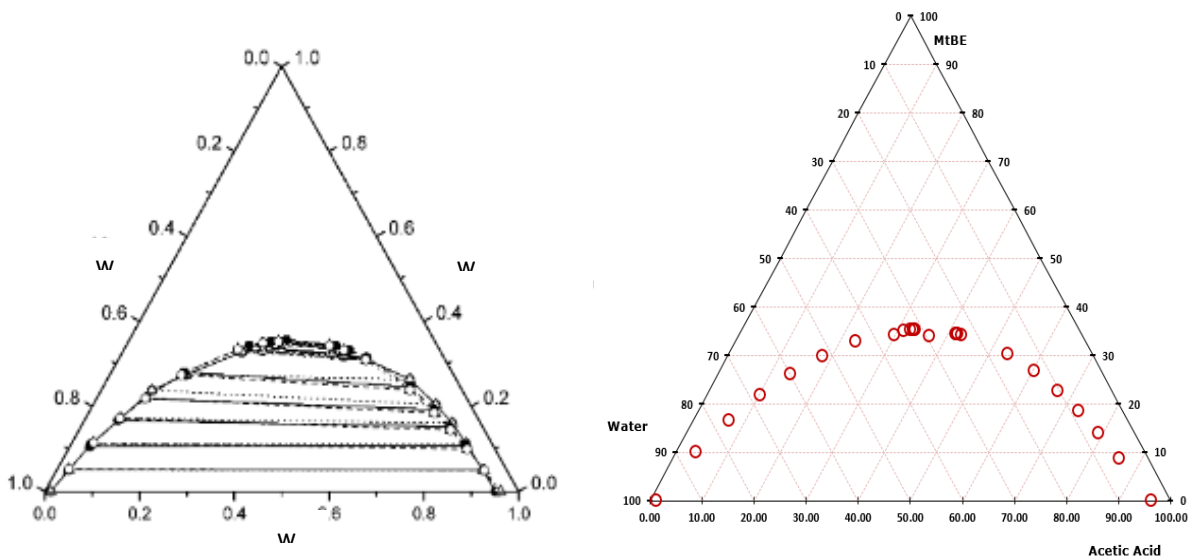
Figure 17: Theoretical (left) and Aspen generated (right) ternary diagrams of water, MTBE, and Acetic Acid system at 293.15K

Both the UNIQUAC and NRTL ternary diagrams generated by Aspen for the water, MTBE, and acetic acid system closely matched the diagrams given in the paper. Since UNIQUAC gave more accurate binary parameters, this property model was chosen over NRTL to simulate our process. From the results of the binary interaction parameters and the generation of consistent ternary diagrams, Aspen was determined to be capable of performing the simulations required for the laboratory experiments.

DynoChem

DynoChem was not found to have a model or utility that had the ability to regress UNIFAC or NRTL parameters from experimental data. Therefore, the UNIFAC and NRTL parameters provided in the paper were used to replicate the ternary diagrams. The outputs given by DynoChem were a table of results which contains the compositions of the liquid phases as well as a ternary diagram. The ternary diagram generated from DynoChem is compared the paper in Figure 18 below.
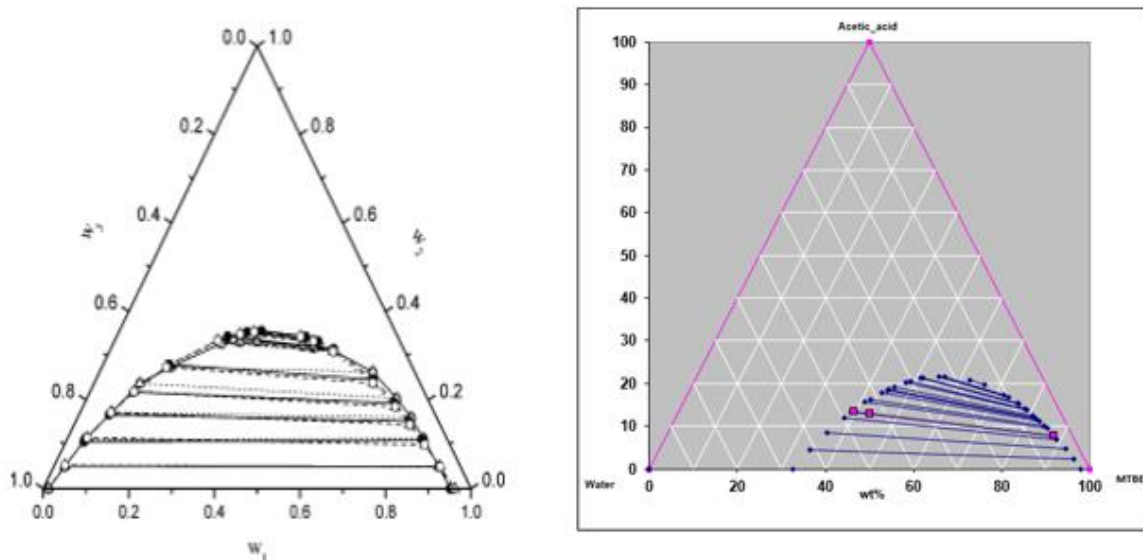
Figure 18: Theoretical (left) and DynoChem generated (right) ternary diagrams of water, MTBE, and Acetic Acid system at 293.15K

After comparing the two ternary diagrams, DynoChem was not replicating the ternary diagrams given in the research paper. Different values of the non-randomness coefficient for the NRTL parameters were tried in order to generate similar results to the paper. However, no value for the non-randomness parameter (the alpha value needed in the input) was found to give the ternary diagram from the study. We concluded that DynoChem may not work as well as Aspen to model a LLE process such as the one given to us by our sponsor. To confirm this, we contacted the representatives at DynoChem. At this time without advanced knowledge of the coding, this software could not be used to simulate the process given by our sponsor.

Aspen Simulations

The student version of Aspen Plus v8.2 was used to simulate the LLE process. The base case was first simulated using the values given to us by our sponsor. Once Aspen was proven to be able to simulate the base case, different process scenarios were simulated that varied the amount of MTBE and the number of washes.

Base Case

The three wash system provided by our sponsor, also known as the base case of the liquid-liquid extraction (LLE), was modeled in Aspen Plus. Due to the limitations of the UNIFAC group contribution parameters, the salt split reaction step could not be modeled effectively in Aspen. Therefore, 100% of the triflate salt was assumed to convert to the free base, which was the desired product. With 100% conversion 6.736 kg of the salt resulted in the isolation of 3.703 kg of the free base. The residual water in the reaction mixture was assumed to be the water present in the 2M KOH solution that was added during the salt split step (11.451 kg of water). The amount of MTBE solvent used in each individual wash step in the base case can be seen in Table 8.

Table 8: Base case values of MTBE used in the extraction process

	MTBE Used		
	Mass (kg)	**Moles**	**Volume (L)**
Wash 1	14.95	169.63	20.20
Wash 2	10.10	114.62	13.65
Wash 3	7.41	84.05	10.01
Total	**32.47**	**368.30**	**43.85**

The simulations were carried out at atmospheric conditions for both the feed streams and the decanter blocks. The simulation was completed with no errors, and the results for the compositions of the final organic and aqueous phases can be seen in Table 9 below. A 98% percent recovery of the free base was desired for the exiting organic stream.

Table 9: Aspen generated results of the composition of the final phases

	Organic Stream		Aqueous Stream	
	Mass (kg)	**Moles**	**Mass (kg)**	**Moles**
Free Base	3.655	19.943	0.048	0.262
MTBE	9.930	112.649	0.102	1.157
Water	5.754	319.312	5.792	321.421

As seen in the table, the Aspen simulation predicted a total recovery of 3.655 kg of free base. This resulted in a 98% recovery of the free base. This simulation shows that Aspen is capable of

modeling a LLE process accurately and now could potentially be used further to optimize this process.

Having proven that the Aspen simulation can successfully simulate the desired model, we then scaled down the base case to a laboratory scale. Wanting to achieve the same product recovery of greater than 98% (which we found in the initial tests), we ran the Aspen simulation using scaled down numbers of the base case (10 grams of triflate salt of the free base). Table 10 shows the material balance of the laboratory scale salt split reaction as well as the MTBE required for each wash.

Table 10: Initial Parameters inputted to Aspen and resulting values

	Material	**(g)**
Inlet	Triflate Salt	10
	2M KOH	20
Outlet	Free Base	5.498
	Potassium Triflate	5.676
Extraction	MTBE – Wash 1	22.2
	MTBE – Wash 2	15
	MTBE – Wash 3	11

Using the material balance values, Aspen predicted the free base recovery was 5.427 grams, which resulted in a recovery of greater than 98%. Therefore, we concluded that Aspen successfully models the laboratory scale as well as the commercial scale. These numbers were later used in our laboratory experiments.

Sensitivity Analysis

Since the base case was successfully simulated, we wanted to determine if the amount of MTBE could be reduced while providing the same product recovery. Setting our target value as greater than 98% product recovery, a sensitivity analysis was used to optimize the total amount of MTBE used in the process. This analysis generated a list of possible solutions, which can be seen in Table 11.

Table 11: Aspen sensitivity analysis results

Row #	Status	MTBE Flow Rate (g)				Free Base Extraction	
		Wash 1	Wash 2	Wash 3	Total (g/hr)	Recovered (g/hr)	% recovered
3341	Error	45	39.3	33.6	118	5.5	100
451	Poor	10.7	5	5	20.7	4.9	90
931	OK	16.4	10.7	5	32.1	5.3	96
2491	Good	36.4	7.9	5	49.3	5.4	98
640	Best	24	13	11	48	5.4	98
1453	Base	22.2	15	11	48.2	5.4	98

As seen in the table above, multiple solutions were generated that needed to be filtered to find the optimal MTBE usage. The first row of the sensitivity analysis generated an error, which was due to excess MTBE used in the process. As a result of the excess MTBE in the system, all of the free base was extracted by the second wash. Therefore, no phase separation occurred in the third wash, which resulted in an error in Aspen. The other possible solutions that had to be filtered were feasible solutions; however, these solutions extracted less than the 98% target recovery or used more MTBE than the base case. After sorting through the solutions from the sensitivity analysis, it was determined that the optimal MTBE usage was 48 grams (Best) This value was compared back to the base case (Base) and found that the optimal case only used 0.2 grams less MTBE. Therefore, moving forward with the laboratory experiments the base case was used since it was very close to optimal.

Once the base case was determined to be close to optimal, the number of washes was varied to see the effect on MTBE usage. When the number of washes is greater than four the operational costs usually outweigh the savings from the reduction in solvent usage. For this reason, we chose to study the MTBE usage in single to four wash processes. A sensitivity analysis was performed on each of these extraction scenarios to determine the solvent usage, which can be seen in Figure 19.
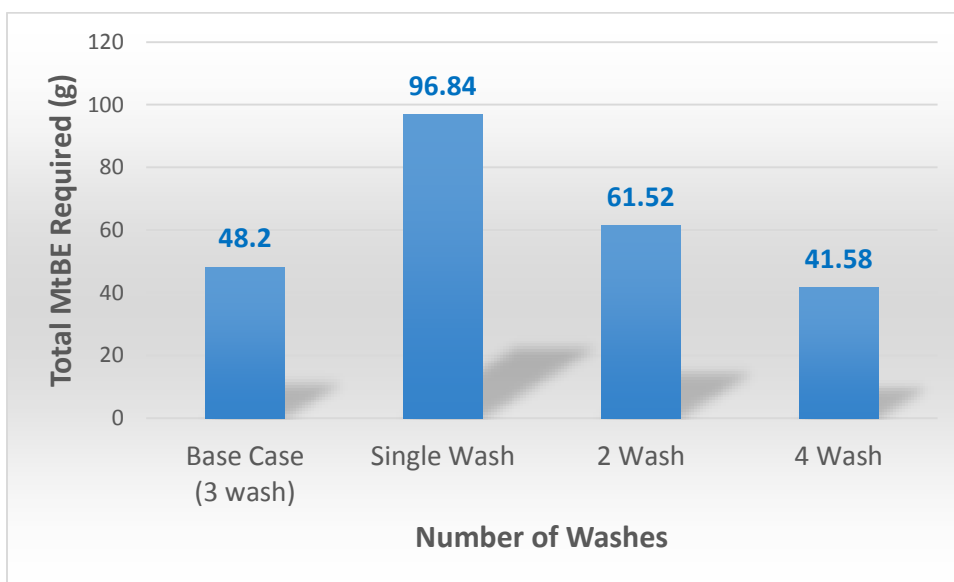
Figure 19: Laboratory scale sensitivity analysis results

As expected when the number of washes increases the amount of MTBE required decreases. The single stage extraction requires twice as much MTBE compared back to the base case. This large increase in MTBE usage would require larger equipment and operational cost to accommodate the extra MTBE used in the system. Therefore, the single stage extraction was not considered for the laboratory experiments since it would not be economically feasible when run on a commercial scale. Based on the sensitivity analysis, the laboratory experiments used the following extraction scenarios: base case (3 wash), 2 wash, and 4 wash. The amount of MTBE required for each individual wash for three different extraction scenarios can be seen in Figure 20.
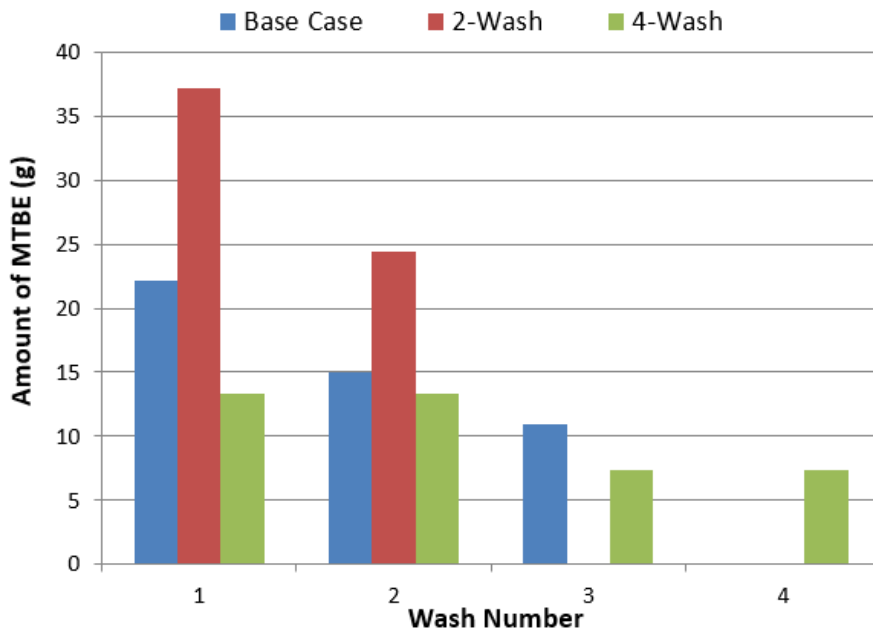
Figure 20: The MTBE usage in each extraction scenario

Using the values of MTBE seen above, the product recovery for each wash and overall recovery were then simulated in Aspen. The Aspen predicted values of the free base recovered for each of the different extraction scenarios can be seen in Table 12.

Table 12: Aspen predicted free base recovery for each extraction scenario

	Free Base Recovery		
	Base Case	*2 Wash*	*4 Wash*
Wash 1 (g)	4.397	4.836	3.799
Wash 2 (g)	0.839	0.592	1.199
Wash 3 (g)	0.191	NA	0.280
Wash 4 (g)	NA		0.141
Total (g)	**5.427**	**5.428**	**5.419**

The data generated from the Aspen sensitivity analysis for each of the different extraction scenarios were used as predictions for laboratory experiments. All three of these extraction scenarios were replicated in the lab.

Lab Scale Experimental Results

Having predicted the theoretical values in Aspen, laboratory experiments were run to validate the Aspen predicted values. The experiments were run under the same conditions as the base case, two wash extraction, and four wash extraction simulations. The amount of free base

extracted in the lab from each wash was compared with the amount predicted by Aspen and the percent differences were calculated.

Base Case

The base case was run experimentally with the same initial values as inputted into Aspen. The results for the base case experiment, which consisted of three wash steps, can be seen in Table 13.

Table 13: Product recovered for each individual wash for base case experiment

Run	Wash 1			Wash 2			Wash 3			Total		
	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference
1	5.239	4.039	25.9	0.522	0.986	61.5	0.204	0.301	38.5	5.965	5.326	11.3
2	4.088	4.434	8.1	1.277	0.869	38.1	0.183	0.200	8.9	5.549	5.503	0.8
3	4.078	4.300	5.3	1.288	0.878	37.9	0.187	0.212	12.7	5.553	5.390	3.0

The results in this table indicate that Aspen was accurate when simulating the extraction scenarios as a whole but was not very accurate when predicting individual washes. Specifically, Aspen did a poor job simulating the second wash for each run of the experiment completed. The total free base extracted in each wash was very close to the values simulated in Aspen. The only run which exceeded a 10% difference was the first run completed, which can be attributed to human error since it was a trial run.

2 Wash System

The two wash extraction was run experimentally with the same initial values as inputted into Aspen. The results for the two wash experiment can be seen in Table 14.

Table 14: Product recovered for the two wash experiment

Run	Wash 1			Wash 2			Total		
	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference
1	5.205	4.708	10	0.284	0.603	72	5.489	5.311	3.3
2	5.221	4.760	9.2	0.246	0.594	82.8	5.467	5.354	2.1
3	5.295	4.845	8.9	0.231	0.596	88.3	5.526	5.441	1.5

The experimental results confirm that Aspen simulated the two wash extraction experiments within 5% for the overall free base extracted. However, similar to the base case results, the second wash results varied greatly from the Aspen predictions. We attributed this large percent difference to the small scale of the experiment as well as not all of the free base being extracted from the aqueous phase in the first wash.

4 Wash System

The four wash extraction was run experimentally with the same initial values as inputted into Aspen. The results for the four wash experiment can be seen in Table 15.

Table 15: Product recovered for the four wash experiment

Run	Product Recovered (g)														
	Wash 1			Wash 2			Wash 3			Wash 4			Total		
	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference
1	2.661	3.670	31.900	2.787	1.257	75.664	0.411	0.314	26.754	0.158	0.133	16.784	6.016	5.375	11.260
2	2.494	3.629	37.069	2.792	1.263	75.437	0.302	0.320	5.963	0.182	0.140	26.200	5.769	5.351	7.516
3	2.745	3.679	29.075	2.572	1.253	68.968	0.157	0.312	66.319	0.107	0.136	23.839	5.581	5.380	3.665

These results indicated that Aspen did not simulate the individual washes accurately. Only one wash in one of the experiments had a percent difference less than 15%. Even with larger discrepancies in the product recovered for each individual wash, the percent difference for the total amount of free base extracted in each run was still below 15%. Overall, Aspen accurately simulated the total free base recovered for the four wash experiments run in the lab, but was not as accurate at predicting each individual wash.

Summary Statement

One possible reason for the poor percent difference values for the individual washes could have been poor mixing or not long enough settling time. If either of these occurred then the system would not have reached equilibrium, resulting in less free base extracted in the first wash but more extracted in the second wash. This possibility could explain the large percent difference.

Overall Product Recovery

The percent of the product recovered for both the Aspen simulations and the experimental results were calculated for each extraction. Table 16 shows the percent recovered for each run of the three extraction scenarios tested in the lab as well as in Aspen.

Table 16: Overall percent recovered of free base for each extraction scenario

Run	Percent Product Recovered (%)					
	3 Wash		2 Wash		4 Wash	
	Actual	Aspen	Actual	Aspen	Actual	Aspen
1	108.4	96.8	101.4	98.1	110.1	98.4
2	99.6	98.7	100.3	98.2	105.9	98.2
3	101.4	98.5	99.8	98.3	102.0	98.3

As seen in the table, the percent of free base recovered for the majority of the experiments was greater than 100%, especially in the four wash extraction. This would suggest that we recovered more free base than what was originally in the system, which is not possible. One possible reason for recovery greater than 100% is that the free base recovered is not pure. To confirm this claim, a sample of extracted free base from the two wash extraction was tested for impurities by our sponsor to determine the cause of this discrepancy. An HPLC test and a Karl Fischer titration test were run on the extracted free base. Figure 21shows the HPLC results of the free base extracted from the third run of our two wash experiment.
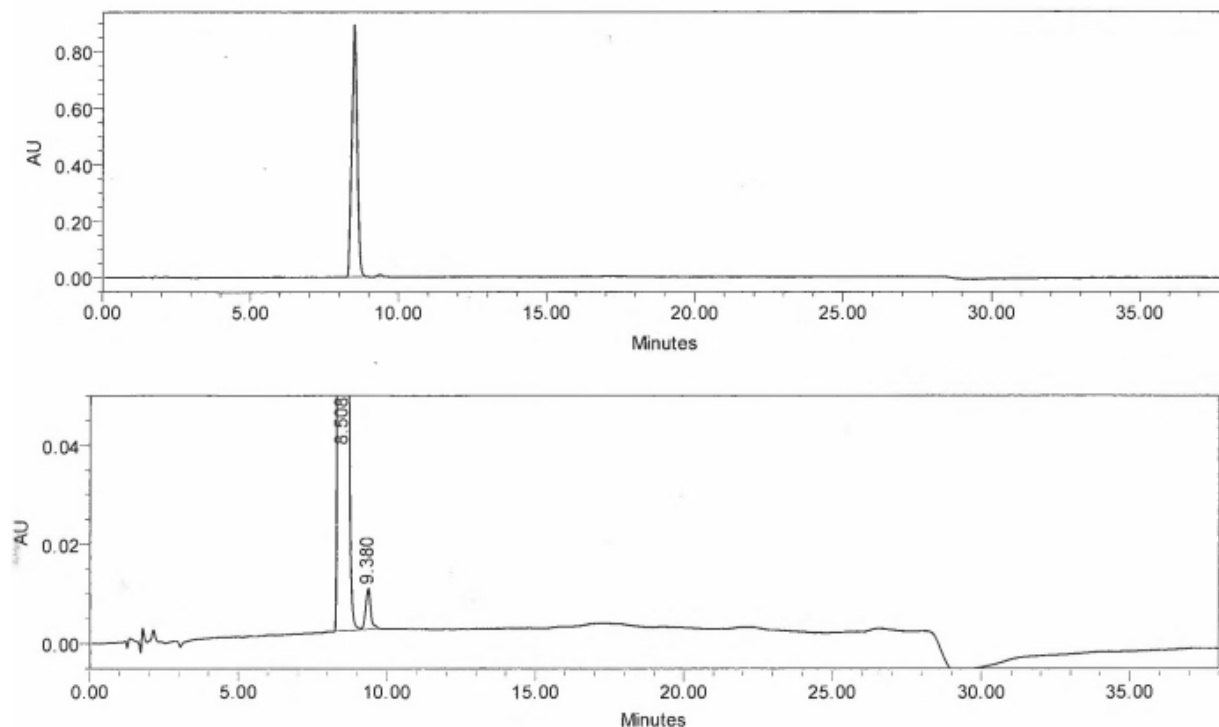
Figure 21: HPLC results of free base extracted from a two wash extraction

Figure 21 shows that the free base extracted had almost no impurities in it. However, the free base tested was from a two wash extraction that did not have over 100% recovery. Therefore, the discrepancies in our data from Table 14 for the two wash scenario were not due to any impurities visible on an HPLC test. The Karl Fischer titration test revealed that our free base contained an average of 0.74% water. Since the other tests were greater than 100%, these samples could have contained more water in the free base. Another possible explanation for the inconsistency in our recovery data could be an inorganic contamination that we have not been able to analyze. Finally, the discrepancy could also be due to the inaccuracy of the balance as well as weighing and human errors. In the end, it was most likely a combination of these three things that led to the yields of greater than 100%. However, only three results were well over 100%, so we have concluded that overall our experimental results were successful and led to accurate comparisons with the Aspen predictions.

Operational Time Analysis

A time analysis of the liquid-liquid extraction process was performed in order to look at the operations of the system. In order to perform the time analysis, we received standardized time estimates for our process, which can be seen in Table 17.

Scenario	Time (min)
Load Salt	30
Load 2M KOH	30
Load MTBE	30
Settling	30
Mixing	15
Separating	60
Inert	30

Using these values a time analysis could be calculated, which can be seen in Table 18. The time analysis values were compared to the base case.

Table 18: Time analysis results

	Base Case	2 Wash	4 Wash
Total Time (hr)	8.50	6.25	10.75
% Time Increase	-	-26.5%	+26.5%

As expected the two wash system required less time than the base case since less time was required for mixing, settling, and separating. Similarly the four wash process requires more time compared to the base case since an additional wash is present. The time analysis values are estimates since the time for each individual step can vary based on equipment and batch size. These time analysis values do not represent the operational costs of the different processes since the values do not include labor, utilities, and raw material costs. These additional costs need to be assessed to complete a full operational cost analysis.

Conclusions

Having finished the experiments and tested the simulations, there are several conclusions that have arisen. This section describes the conclusions drawn from this project.

DynoChem Simulation

Having talked to DynoChem representatives, we have concluded that DynoChem cannot simulate our liquid-liquid extraction (LLE) process since there is no functionality in DynoChem to predict novel compounds' physical properties such as the free base we worked with. Due to the unknown variables in the process, we were unable to use DynoChem for this project. However, DynoChem may be able to model the process once the distribution coefficient is found, which can be done in the lab during experiments. The distribution coefficient can be found by taking the ratio of the composition of the free base in the organic phase over the aqueous phase. The composition of the free base is calculated using a mass balance based on mass of the free base recovered from the rotary evaporator. Using the distribution coefficient, DynoChem could be used for evaluation once experimental work is completed.

Aspen Plus Simulation

As seen in our results and in Table 19, the expected results as predicted by Aspen Plus were within 10% of the experimental results.

Table 19: Aspen results compared to experimental results

Wash Number	Free Base Recovered (g)								
	Base Case			2 Washes			4 Washes		
	Actual	Aspen	% Difference	Actual	Aspen	% Difference	Actual	Aspen	% Difference
1	4.09	4.43	8 %	5.22	4.76	9 %	2.49	3.63	37 %
2	1.28	0.87	38 %	0.25	0.59	83 %	2.79	1.26	75 %
3	0.18	0.20	9 %	NA			0.30	0.32	6 %
4	NA						0.18	0.14	26 %
Total	5.55	5.50	0.8 %	5.47	5.35	2 %	5.77	5.35	8 %

As seen in the table above, Aspen Plus predicted the results within 10% for the total amount of free base extracted in the lab. However, individual runs were not always simulated well. A reason for Aspen Plus over predicting for certain runs could be that the first wash in the lab did not fully extract the amount of free base expected, and so in the second wash the excess free base was extracted resulting in the difference between lab results and simulation results. A reason for Aspen Plus under predicting the amount of free base extracted could be due to experimental error in the lab. For example, some free base that was measured after the rotary evaporator step could have not been fully dried resulting in excess water. The excess water could account for the discrepancy since the measured free base extracted would appear greater. Since no simulation is expected to be perfect and there is always a possibility of experimental error, Aspen results within ten percent of the experimental results led to the conclusion that Aspen Plus proved to be an adequate way to simulate the overall liquid-liquid extraction process.

Time Effectiveness

Working with our sponsor, we were able to come up with estimated time values for operational steps when extracting the free base. Table 20 below shows the estimated time values for extracting the free base at a commercial process scale.

Table 20: Estimated operational times of the LLE process (standardized values per RJP)

Scenario	Time (min)
Load Salt	30
Load 2M KOH	30
Load MTBE	30
Settling	30
Mixing	15
Separating	60
Inert	30

Based on the estimated operational times, the total time of the LLE process was calculated for each extraction scenario as seen in Table 21.

Table 21: Total time of LLE Process

	Base Case	2 Wash	4 Wash
Total Time (hr)	8.50	6.25	10.75
% Time Increase	-	-26.5%	+26.5%

As seen in the table above, the base case was concluded to take 8.5 hours, while the 2 wash would take 6.25 hours and the 4 wash would take 10.75 hours. Based on these times, it can be seen in the table that the 2 wash system would take 26.5% less time than the base case (3 wash system) whereas the 4 wash would take more time than the base case. Based on the time analysis, the 2 wash extraction was concluded to be the most time efficient extraction. However, these times can vary based on batch size or the equipment sized. Furthermore, the time estimates shown here do not represent operational costs of each extraction system. The operational costs would have to be determined to conclude which extraction would be the most cost efficient.

Recommendations

Based on the conclusions and the results of this project, recommendations have been developed in order to continue the investigation of the best way to simulate the liquid-liquid extraction (LLE) process.

Larger Lab Scale Tests

Our first recommendation is to run the same experiments performed in this report at a larger scale. As described above, one of the reasons we could have had a discrepancy in free base recovery between experiments and Aspen could be that there was experimental or human error in some of the experiments. At the small scale we ran, a small error has a greater impact on the mass balance, which could affect our results. We believe that if the experiments are scaled-up, some of the experimental error could be reduced. Reduced experimental error could lead to more accurate results between what is predicted in Aspen and what is observed in the lab for the individual washes. We did one scaled-up run based off one scaled-up simulation to test this recommendation in the lab. The results from our scaled-up run can be seen in Table 22.

Table 22: Scaled-up Laboratory Experiment

Triflate Salt	2M KOH	MTBE needed	Expected Free Base Recovery	Actual Free Base Recovery	%Recovered
50 g	97 g	241 g	27.5 g	29.6g	107%

As seen in the table above, we scaled up our three wash extraction from 10g triflate salt of the free base to 50g triflate salt. Using the same material balance sheet that we had created for our other experiments, we reacted the fifty grams triflate salt with 97 grams 2M KOH and then added MTBE to each wash, totaling 241 grams of MTBE for the extraction. After mixing the MTBE in for 10 minutes (instead of the usual five minutes at the 10 gram scale), we put the solution into a separatory funnel and let the contents settle for another ten minutes. We then removed the aqueous phase and gathered the organic phase to put onto the rotary evaporator in the same fashion as with the ten gram scale. After having evaporated off the MTBE, we found that we extracted 29.6 grams of free base which was just over 2 grams more than the 27.5 grams of free base predicted by Aspen. From this scaled up version, we were able to conclude that our experiments were consistent since we still recovered over 100 percent. However, since we were using a scaled up version, there could have been water still present in the free base. To prevent this, we recommend putting the recovered free base in a vacuum oven overnight to ensure all excess water is removed from the free base. We further recommend more scaled up experiments be run, first with 50 grams of trifalte salt, similar to our scaled up three wash experiment. After doing the scaled up 50 gram experiments, we recommend continuing the scale up to 100 grams in order to validate the theory that experimental results are closer to Aspen Plus predictions for individual washes at larger scales.

Different Solvents

Our next recommendation is to run the same experiments performed in this project under the same conditions but with different solvents. MTBE was used as a solvent during this project

because that was the solvent that our sponsor uses. However, after doing research on different solvents (as described in Appendix B), we found a number of solvents that may extract the free base more efficiently than MTBE. These solvents include anisole, trans-1,2-dichloroethylene, and dichloromethane. After having found possible alternatives to MTBE, we ran the simulation with the different solvents in order to see if they would work for the LLE process described. The results of the simulation can be seen in Figure 22.
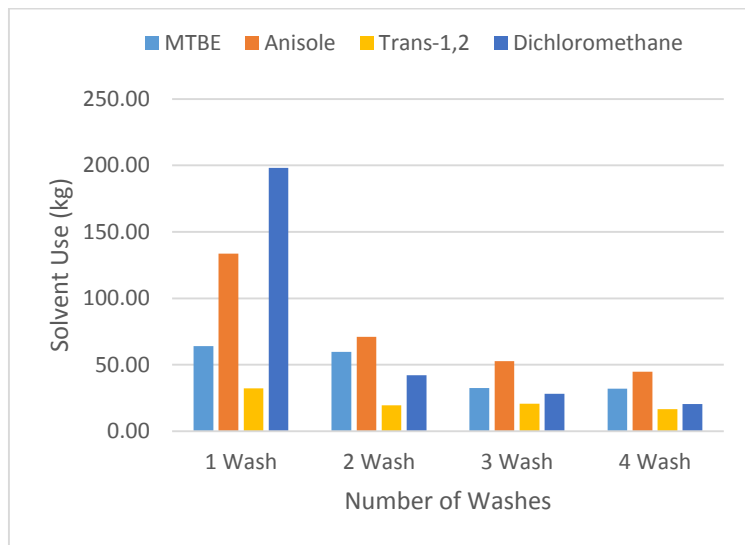
Figure 22: Optimal Solvent Usage of alternative solvents

In the figure above, the simulation was set up so that the amount of solvent needed to extract 98% of the free base was found. For each of the extraction scenarios, trans-1,2-dichloroethylene extracted 98% using the least amount of solvent. However, trans-1,2-dichloroethylene would be a safety concern in our lab; therefore, the next best option would be dichloromethane.

Though anisole and trans-1,2-dicholoroethylene are not widely used in industry due to their toxicity levels and reactivity, dichloromethane is a common solvent used in the pharmaceutical industry. Therefore, we recommend running experiments with dichloromethane first and comparing the results to those presented in this report to determine whether using dichloromethane can further optimize the LLE process. After testing dichloromethane, other solvents such as toluene should be tested. Toluene, however, is temperature sensitive and would perform better at higher temperatures.

Different Experimental Parameters

Our next recommendation is to run the experiments using different parameters. The first parameter change would be testing different molarities of the base used. We recommend initiating the reaction with different molarities of KOH. For example, possible molarities that can be tested are 1M KOH and 4M KOH. 1M KOH could be tested to see if lower molarities are efficient. If lower molarities are adequate, their use could reduce raw material used. 4M KOH could be tested to see if higher molarities reduce the excess water in the organic phase. The two

tests can then be compared to the results in this report to determine whether higher or lower molarities are optimal.

Next, we recommend experimenting with different bases other than KOH. Similar to the MTBE solvent selection, the KOH base was chosen for this project because it was the same base that the company uses. However, we recommend testing a weak base versus a strong base, such as sodium hydroxide, to see if the strength of the bases affects the overall reaction. However, it is important to note that the bases tested must be inorganic so that they remain in the aqueous phase during the extraction process. The different bases should also be tested at different molarities to ensure that the most efficient solution is being used. With these recommendations, the process that was proven to accurately be simulated in Aspen can now be tested to further optimize the LLE process.

Our final experimental parameter recommendation would be to test the temperature of the system. We generally ran the experiments at atmospheric conditions (25 degrees Celsius). However, testing to see if higher temperatures affect the experiments could help with the optimization of the process. For example, if higher temperatures are tested, toluene could then be used as a solvent. Also, other solvents that are temperature sensitive could be evaluated for optimization.

DynoChem

Though DynoChem could not be used for this report, the simulation could be used to evaluate possible outcomes after the experimental work is completed. Certain parameters needed for DynoChem to run could be found in the lab during the experimental process. Therefore, we recommend for future work that the distribution coefficient be determined as part of the process analysis. The distribution coefficient could then be inputted into DynoChem and then the process model could be run to simulate the extraction process.

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Appendices

Appendix A: Sample Calculations

Assuming 10g of initial triflate salt and 20g of 2M KOH, which contains 2.018g of KOH:

$$C_9H_{14}NOS \cdot CF_3SO_3 + KOH \rightarrow C_9H_{13}NOS + KCF_3SO_3 + H_2O$$
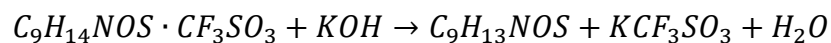
First known masses are converted to moles:

$$\text{Triflate salt: } 10g \div 333.35\frac{g}{mol} = 0.030mol = n_{i_{TriflateSalt}}$$

$$\text{KOH: } 2.018g \div 56.11\frac{g}{mol} = 0.036mol = n_{i_{KOH}}$$

Then mole balances for each element are calculated:

$$n_{N_{TriflateSalt}} = n_{N_{FreeBase}}$$

$$n_{N_{FreeBase}} = 0.030mol$$

$$3 * n_{F_{TriflateSalt}} = 3 * n_{F_{PotassiumTriflate}}$$

$$n_{F_{PotassiumTriflate}} = 0.030mol$$

$$n_{K_{KOH}} = n_{K_{PotassiumTriflate}} + n_{K_{KOHExcess}}$$

$$0.036mol = 0.030mol + n_{K_{KOHExcess}}$$

$$n_{K_{KOHExcess}} = 0.006mol$$

$$14 * n_{H_{TriflateSalt}} + n_{H_{KOH}} = 13 * n_{H_{FreeBase}} + n_{H_{KOHExcess}} + 2 * n_{H_{Water}}$$

$$14 * 0.030mol + 0.036mol = 13 * 0.03mol + 0.006mol + 2 * n_{H_{Water}}$$

$$n_{H_{Water}} = 0.030mol$$

Moles are converted back into grams:

$$\text{Triflate salt: } 0.030mol * 333.35\frac{g}{mol} = 10g$$

$$\text{KOH: } 0.036mol * 56.11\frac{g}{mol} = 2.018g$$

$$\text{KOH Excess: } 0.006mol * 56.11\frac{g}{mol} = 0.337g$$

$$\text{Free Base: } 0.030mol * 183.27\frac{g}{mol} = 5.498g$$

$$\text{Potassium Triflate: } 0.030mol * 189.2\frac{g}{mol} = 5.676g$$

$$\text{Water: } 0.030mol * 18.01\frac{g}{mol} = 0.540g$$

$$\text{Water from original } 2M\ KOH = 17.982g$$

Finally complete a mass balance over the reaction:

$$m_{Triflate\ Salt} + m_{KOH} + m_{KOHwater}$$
$$= m_{FreeBase} + m_{PotassiumTriflate} + m_{ExcessKOH} + m_{water} + m_{KOHwater}$$

$$10g + 2.018g + 17.982g = 5.498g + 5.676g + 0.337g + 0.540g + 17.982g$$

$$30g \cong 30.033g$$

Percent Recovery of the Free Base for the Base Case Aspen Simulation:

$$\%Recovery = \frac{m_{FreeBaseExtracted}}{m_{TotalFreeBase}} * 100\%$$

$$\%Recovery = \frac{5.4g}{5.498g} * 100\% = 98.2\%$$

Percent Difference between experimental results and Aspen predictions of the total free base extracted for the first run of the two wash system:

$$\%Difference = \frac{|m_{Theoretical} - m_{Experimental}|}{\dfrac{(m_{Theoretical} + m_{Experimental})}{2}} * 100\%$$

$$\%Difference = \frac{|5.311g - 5.489g|}{\dfrac{5.311g + 5.489g}{2}} * 100\% = 3.297\%$$

Appendix B: Solvent Selection

One of the optimization parameters for the liquid liquid extraction process that was considered when completing the project was the solvent used. A list of acceptable solvents for the pharmaceutical industry taken from the ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) website was used as a starting place. The list was narrowed down to include solvents that would work with the process given. Some of the necessary properties the solvent needed to have was to be a class 2, 3 or 4 solvent, immiscible in water, a boiling point close to MTBE, and meet some of the safety standards.

ICH Ratings

All of the solvents on the class 1 list were eliminated because of their toxicity and their harmful environmental effects. Class 4 solvents are acceptable for pharmaceutical use, however, there was no adequate toxicological data for these solvents. These solvents were not considered for the given process. Class 2 and 3 solvents were acceptable to use in the manufacturing of drug substances, so all of the solvents on this list were looked at. Class 2 solvents are acceptable for the manufacturing of drug substances or drug products, but their use should be limited because they are toxic. Class 3 solvents are less toxic and are less of a risk to human health.

Miscibility with water

For the given process, in order to extract the product, the solvent needed to be immiscible in water. All of the solvents that were miscible in water were eliminated. Some of the solvents were showed some miscibility with water. Since the base case solvent, MTBE, was partially miscible with water, solvents that showed some miscibility with water were also considered. However if a solvent was partially miscible and did not meet other required properties, then it was eliminated.

Boiling Point

One of the other properties the solvent needed to have was lower boiling point. In the steps following the extraction, the solvent will be distilled off. In order to ensure that similar equipment can be used in the steps following the extraction, the boiling point of the solvent was to be close to that of MTBE. Solvents will very high boiling points were eliminated.

Safety Considerations

Safety was also considered when looking at solvents. Since experiments were to be run in the lab, some safety criteria had to be met in order for the solvent to be considered. Health hazards, fire hazards, the flash point and exposure limits were looked at for each of the solvents. The National Fire Protection Association (NFPA) Hazard Rating system was looked at when identifying safety concerns with each of the solvents. Solvents with a class 3 health hazard were eliminated. A rating of 3 for a health hazard identifies the chemical as highly to extremely toxic. The flammability of a solvent show how susceptible the chemical is to ignite or burn. This rating is related to the material's flash point or ignition temperature. A rating of 2 identifies the material as having a flash point between 200°F and 100°F. A rating of 3 identifies the solvent as having a flash point between 100°F and 73°F. Class 4 flammability ratings will have a flash point below 73°F. MTBE did have a very low flash point, but since it was the base case solvent it was not eliminated. However when looking at other options, solvents with low flash points were no longer considered.

The exposure limit was also considered when looking at the safety of the list. High exposure limits were desirable, so solvents with high exposure limits were still considered. Some exposure limits

were not available because they did not pose a significant risk when exposed or because there wasn't data to give a limit. Those solvents were considered as long as it met the other criteria.

Ranking the solvents

In the end, the solvents that were considered acceptable for the process were Tetralin, Isobutyl acetate, Anisole, MTBE, toluene, dichloromethane and trans-1,2-dichloroethene. These solvents best met the physical property and safety criteria. Below is the list of solvents and the safety and physical property data.

Solvent	ICH Rating	Boiling Point (°C)	Health Rating	Fire Rating	Exposure Limit (ppm)
MTBE	Class 3	55.2	Class 2	Class 3	N/A
Tetralin	Class 2	208	Class 0	Class 2	N/A
Isobutyl Acetate	Class 3	118	Class 2	Class 3	200
Anisole	Class 3	154	Class 1	Class 2	N/A
Trans-1,2-Dichloroethene	Class 2	48.5	Class 2	Class 3	200
Dichloromethane	Class 2	40	Class 2	Class 0	N/A
Toluene	Class 2	110.6	Class 2	Class 3	300

Initial Solvent Selection

Different solvents can be used for the process, which could result in different recoveries and operational costs. In order to optimize the liquid-liquid extraction process, different solvents were considered. These solvents included tetralin, anisole, trans-1,2,-Dichloroethlyene, toluene, dichloromethane, and isobutyl acetate. Each of these solvents were simulated in the base case scenario to determine if any of the other solvents were more effective than MTBE in removing SEP-363492 from the aqueous phase.

Each wash of the base case required different amounts of solvent to be used. The first wash required 169.63 moles, and the second and third wash required 114.62 moles and 84.05 moles of MTBE, respectively. The total number of moles of MTBE needed for the base case was 368.3. When running the simulation with other solvents, the number of moles used for each wash was kept constant. The percent recovery of the free base when other solvents were used was compared to the base case. A chart of the percent recoveries of the various solvents can be seen in Figure 23.
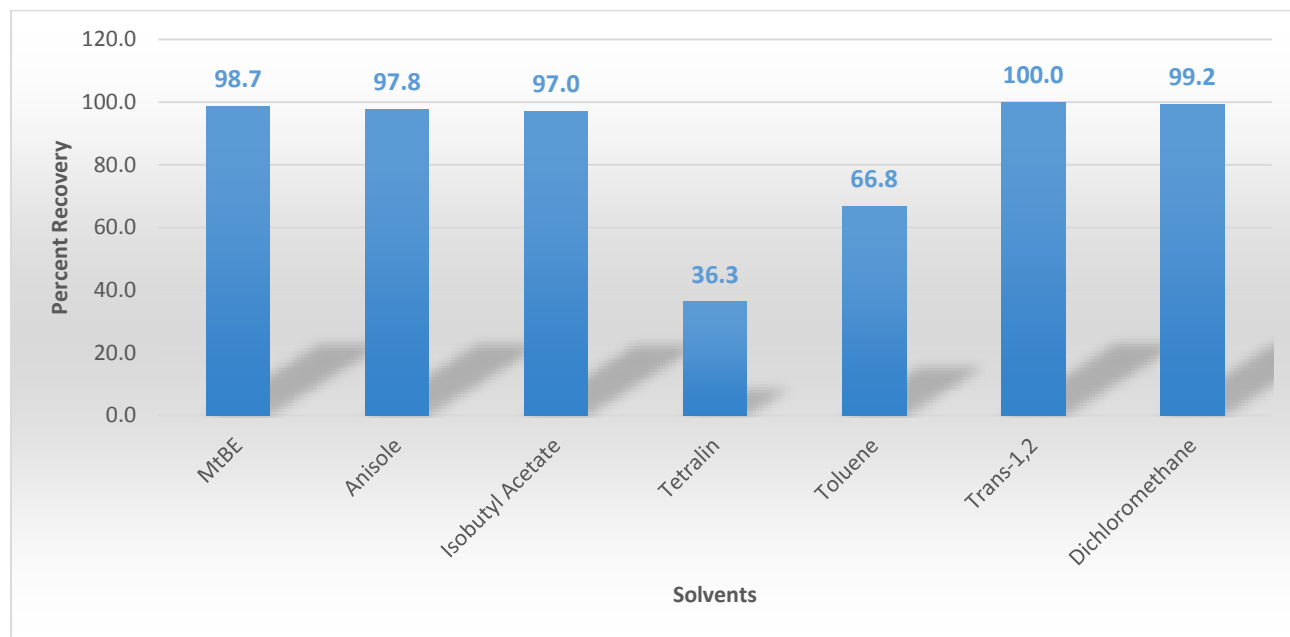
Figure 23: Comparison of the Aspen simulation's percent recoveries of the seven different solvents

Trans-1,2-dichloroehlyene had a recovery of 100% which was greater than all the other solvents. Since the percent of recovery was 100%, an excess amount of trans-1,2-dichloroehlyene was in the system and that allowed SEP-363492 to be fully recovered. The actual amount of trans-1,2-dichloroehlyene needed was much lower than the 368.304 moles that was used in the simulations. Anisole, dichloromethane, and isobutyl acetate were the only other solvents to compare well against MtBE with percent recoveries of 97.8%, 99.2%, and 97.0% respectively. Toluene and tetralin require too much solvent usage in this system to be both efficient and economical. Therefore, toluene and tetralin were eliminated from further consideration. Based on the percent recoveries for the base case, the solvents that were chosen

for the optimization simulations were MtBE, anisole, isobutyl acetate, dichloromethane, and trans-1,2-dichloroehlyene.

The optimization process in Aspen helped determine the number of stages and the amount of solvent required. As the amount of stages increase the amount of solvent usage decreases. Single stage to four stage washes were considered. For systems using more than four stages, the operational costs of running an additional wash will outweigh the cost of the solvent saved. The following sections will discuss the optimization of the solvent usage compared back to the base case scenario using MTBE.

Single Stage Optimization

The five solvents that were determined to have similar recoveries compared to MTBE in the base case were simulated for a single stage extraction. In a single stage extraction a design specification was used to achieve a 98% recovery of the free base. The results of the design specifications for each of the different solvents can be seen in the figure below.
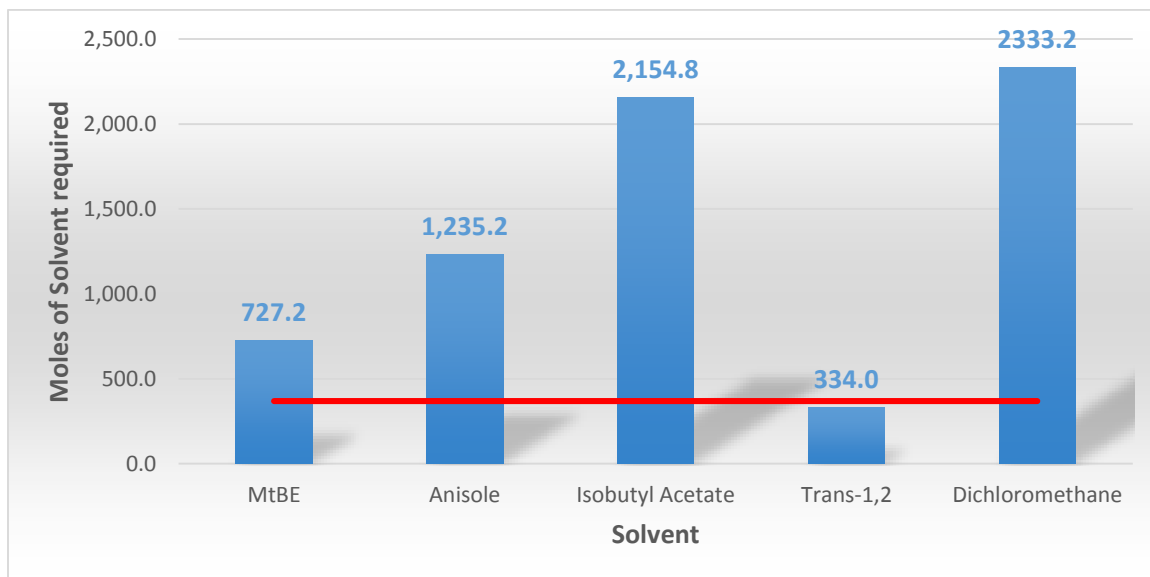
Figure 24: Minimum solvent moles required to achieve 98.7% recovery of SEP-363492

The red horizontal line (y=368.3moles) indicates the amount of moles originally used in the base case extraction process. From the figure it can be clearly seen that a significant amount of additional solvent is required for the same recovery as in a three stage process. The exception is trans-1,2-dichloroethlyene, because in the base case an excess of trans-1,2-dichloroethylene was added in the extraction process.

Two Stage Optimization

The two wash process was tested next which required a sensitivity analysis in order to find the optimal solvent usage. The sensitivity analysis varied both the inlet solvent feed streams in order to solve for the total exiting free base. The solutions to the sensitivity analysis were filtered and the desired percent recovery was set as 98.9% (3.662kg). This percent recovery

allowed for an easy comparison between all the solvents since the Trans-1,2 solutions did not extract less than 98.9% recovery. The optimal solvent usage for each different solvent usage can be seen in the figure below. The red line represents the amount of moles used in the base case.
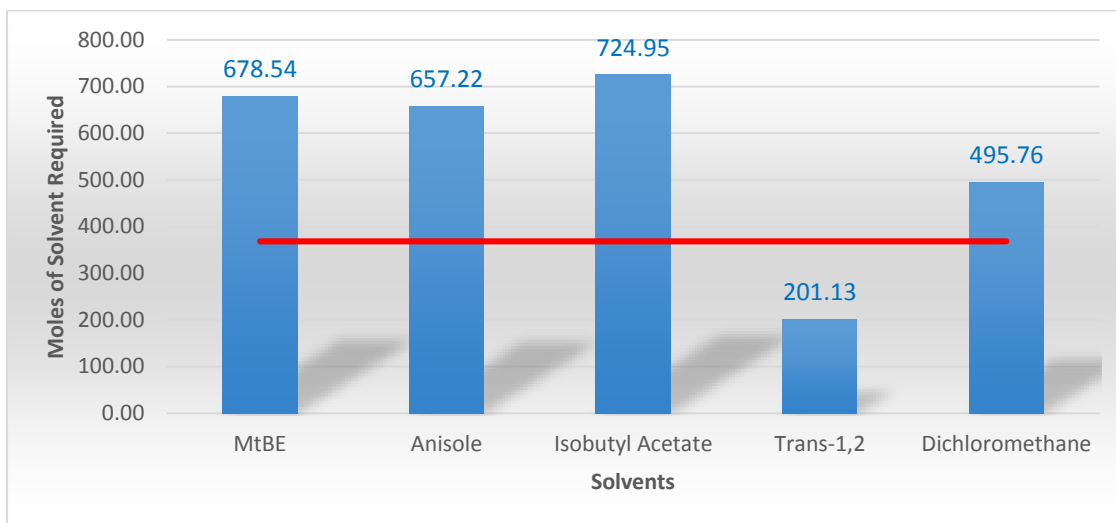
Figure 25: Aspen simulations of optimal solvent usage in moles for the extraction process

Similarly to the single stage process, the amount of solvent required is still greater than that of the base case except for trans-1,2-dichloroethylene. When comparing the single stage wash to the two stage wash, dichloromethane became a more optimal solvent for the two stage process. This may have to do with the dichloromethane's capacity to dissolve the free base being low. By introducing multiple washes which adds pure solvent back into the system allows for the dichloromethane dissolve more of the free base than if it was already saturated with the free base. A summary of how much individual solvent was added in each step can be found in the table below.

Table 23: Aspen predicted solvent usage in each wash of the two stage extraction process

	Wash 1 (kg)	Wash 2 (kg)
MtBE	22.14	22.14
Anisole	38.93	32.14
Isobutyl Acetate	52.63	31.58
Trans-1,2	14.57	4.93
Dichloromethane	21.05	21.05

Three Stage Optimization

Just as in the two stage wash a sensitivity analysis was used to optimize the base case (3 wash) system. All five solvents under consideration were run in the sensitivity analysis and the results can be seen in figure below. To compare all the solvent usage equally a recovery of 98.9% was chosen as the desired recovery just as in the single and two stage process.
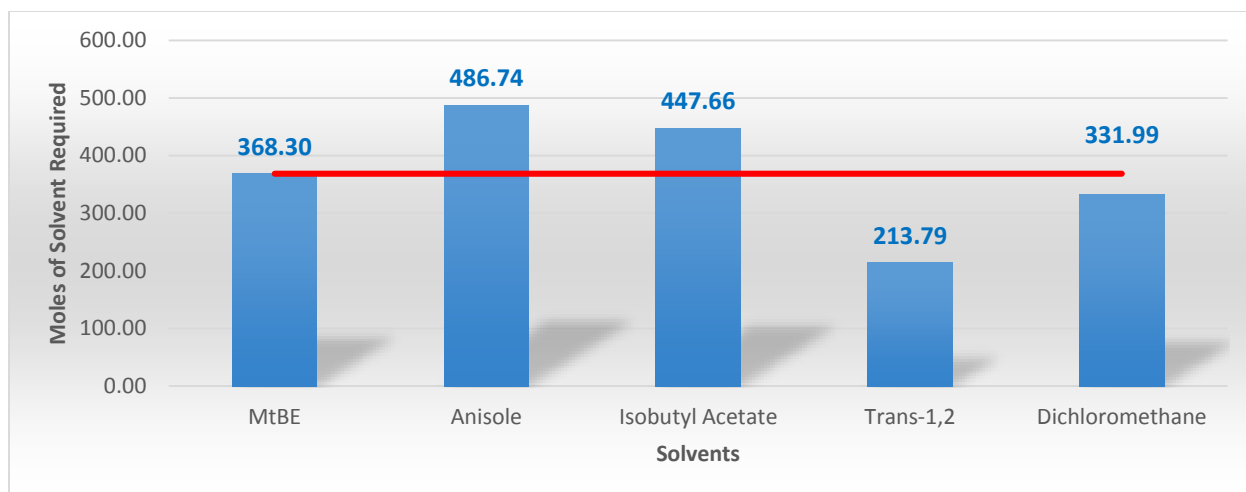
Figure 26: Aspen generated optimal solvent usage in a three stage extraction process

The red horizontal line just as in the single and the two wash processes represents the base case value of moles used. All the solvent except anisole were under the base case value. Both trans-1,2 and dichloromethane showed significant improvement with values under the base case value. The value of MtBE is slightly less than the base case, which implies the process that was run by our sponsor was run at close to optimal conditions already in terms of MtBE use. The distribution of each solvent in the different stages can be seen in the table below.

Table 24: Individual wash solvent use for a three wash process

	Wash 1 (kg)	Wash 2 (kg)	Wash 3 (kg)	Total (kg)
MtBE	14.95	10.10	7.41	32.47
Anisole	25.82	18.73	8.09	52.64
Isobutyl Acetate	22.00	18.50	11.50	52.00
Trans-1,2	11.64	4.55	4.55	20.73
Dichloromethane	10.53	10.53	7.14	28.20

Four Stage Optimization

Similarly the four stage optimization used a sensitivity analysis for each of the different solvents under consideration. Again the desired percent recovery was set at 98.9% (the same as the 2 and 3 stage) and the results can be seen in the figure below.
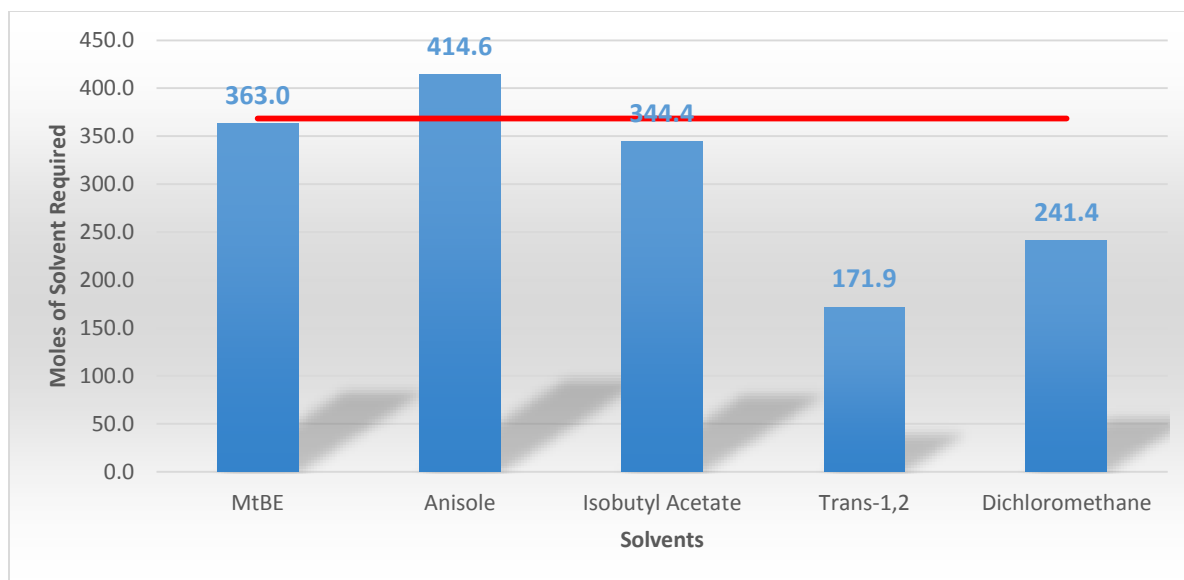
Figure 27: Sensitivity analysis results for a four stage process

The red horizontal line just as in the single and the two wash processes represents the base case value of moles used. All the solvent except anisole were under the base case value. Both trans-1,2 and dichloromethane showed significant improvement with values with solvent required over 100 moles under the base case value. The value of MtBE is slightly less than the base case, which implies the process has come close to the minimum amount of MTBE required to extract 98% of the free base. If the number of washes were increased again the amount of MTBE is expected to show little improvement again. The distribution of each solvent in the different stages can be seen in the table below.

Table 25: Solvent usage for each individual wash step

	Wash 1 (kg)	Wash 2 (kg)	Wash 3 (kg)	Wash 4 (kg)	Total (kg)
MtBE	13.00	9.00	9.00	1.00	32.00
Anisole	9.17	9.17	9.17	17.33	44.83
Isobutyl Acetate	10.00	10.00	10.00	10.00	40.00
Trans-1,2	13.67	1.00	1.00	1.00	16.67
Dichloromethane	6.50	6.50	4.67	2.83	20.50

Summary

Having completed all the sensitivity analysis for each solvent for all the different wash scenarios, the results were plotted on the same graph for easy comparison. The results for all the sensitivity analyses can be seen in the figure below.
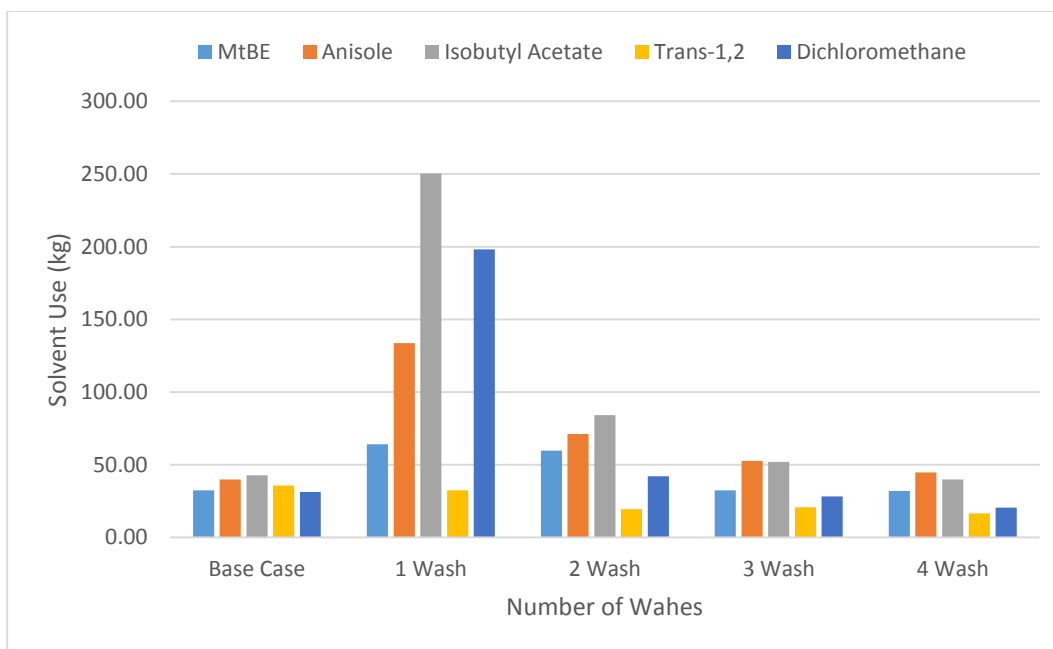
Figure 28: Optimal solvent usage for multiple solvents

As it was expected the single wash scenario required the most solvent and the four wash required the least. Dichloromethane was the second worst performer in the single wash system but ended up being the second best performer by the four wash. This probably has to due to the capacity to dissolve the free base is low so the addition of the pure dichloromethane in multiple washes greatly increases the efficiency. Also it can be seen that the amount of solvent save between the three wash and the four wash systems was not that significant. This could mean that if the number of wash steps were to continue to increase the solvent required for the extraction would start to level off. Finally the trans-1,2 shows significant reduction in solvent required in the single wash system compared to the other solvents used. With this result it may be possible to run a single wash process without having to use larger equipment, which would make this economically feasible. All these simulations results should be tested in the lab to confirm the simulation predictions.

Appendix C: Laboratory Procedures

Rotary Evaporator

In order to start up the Rotary Evaporator, the following procedure is executed:

1. Pour the mixture of solvent and free base into a round bottom flask. Ensure that the round bottom flask is no more than half full with the mixture.
2. Use a clip to attach the round bottom flask to the rotary drive.
3. Attach the vacuum hose to the top of the apparatus.
4. Add dry ice to the condenser of the rotary evaporator.
5. Close the pressure valve.

6. Attach the collection flask so that the solvent can be recovered after it condenses.
7. Turn on the vacuum pump. Do not turn off the vacuum. Do not open the pressure valve.
8. Heat the water bath to approximately 50°C.
9. Use the control panel to lower the flask such that it barely touches the water.
10. Use the control panel to start rotating the solution. A thin layer of solvent should form on the side of the flask.
11. Allow the sample to rotate the necessary amount of time to evaporate off the solvent.

After the solvent has been evaporated off and only the free base is left in the round bottom flask, the following shutdown procedure will be executed:

1. Use the control panel to stop the rotation.
2. Use the control panel to raise the flask out of the water.
3. Turn off the vacuum pump.
4. Open the pressure valve.
5. Clean out the remaining dry ice.
6. Do not remove the mixture until pressure has been restored to the chamber.

Salt Split Reaction and separation of phases

Materials: 2M KOH, triflate salt of the free base

Solvent: MTBE

Equipment needed: 100mL beaker, 2-50mL graduate cylinder, 50mL flask, 50mL round bottom flask, separator funnel, scale, ring stand, magnetic stir plate, and magnetic bar

The procedure below will be used to complete the experiment:

1. Clean all glassware to be used in the lab.
2. Mass out 10 grams of triflate salt of the free base and place it into a 100mL beaker.
3. Place the 100mL beaker onto a magnetic stir plate.
4. Mass out 20 grams of 2M KOH in a 50mL graduated cylinder.
5. Mix the 2M KOH and free base to start the salt split reaction using a magnetic bar.
6. Mass out needed amount of the solvent in a graduate cylinder (50mL).
7. Add the solvent to the salt split reaction and mix using a magnetic stir plate.
8. Transfer the solution of MTBE and the salt split reaction to a separatory funnel, which will be used to separate the aqueous phase from the organic phase.
9. Gently shake the funnel and place it on the ring stand.
10. Once equilibrium between the two phases is obtained, drain the aqueous layer (bottom) into a 50mL flask.
11. Weigh the 50mL round bottom flask which will be used to hold the organic phase.
12. Drain the organic layer (top) into a round bottom flask, which will be attached the rotary evaporator.

Determining the operating pressure for each solvent
1. Place the solvent into the round bottom flask and clamp to the rotary evaporator.
2. Fill the rotary evaporator bath with water.
3. Fill the condenser with dry ice.
4. Check to ensure the vent on the rotary evaporator is open and then turn on the vacuum of the rotary evaporator.
5. Slowly close the vent on the rotary evaporator.
6. Lower the round bottom flask into the bath.
7. Turn on the heating element and then spin.
8. Adjust the pressure on the vacuum pump to the lowest possible pressure setting.
9. Slowly raise the pressure a few mmHg and wait ten minutes.
10. Continue raising the pressure and waiting until the solvent evaporates off.
11. Once the solvent is evaporated, record the temperature at which this occurs.
12. Spin and temperature are turned off and the rotary evaporator is lifted out of the bath.

13. The vent is opened and the vacuum is turned off.
14. The device is turned off.

Isolating the Product

1. Record the mass of organic phase recovered from the reaction.
2. Mass out the rotary evaporator's round bottom flask and collection flask.
3. Place the recovered organic phase into the round bottom flask.
4. Connect the other round bottom flask to the condenser to collect the solvent.
5. Fill the rotary evaporator bath with water.
6. Turn on the rotary evaporator.
7. Fill the condenser of the rotary evaporator with dry ice.
8. Check to ensure the vent on the rotary evaporator is open and then turn on the vacuum of the rotary evaporator.
9. Clamp the round bottom flask filled with the organic phase to the rotary evaporator.
10. Slowly close the vent on the rotary evaporator without pulling up any of the solvent.
11. Lower the rotary evaporator into the water bath.
12. Turn on the heating element and rotate the flask.
13. Turn off the spin and lift the rotary evaporator out of the water bath.
14. Once the solvent has been evaporated off, turn off the vacuum and open the vent.
15. Remove the round bottom flask carefully and weight it to determine the mass of the free base.
16. Remove the collection flask and weigh it to determine the amount of solvent removed from the organic phase.
17. Turn off the heating element and then turn off the rotary evaporator.

Appendix D: Methodology Flow Sheet Handout

**Optimization of a General Process Through Simulation
Using Aspen Plus v. 8.2**

Input chemical components for the given process to be simulated.

If a component has unknown chemical properties, use Aspen to estimate the properties by creating a user-defined compound.

If components have known properties, search the Aspen database and select the components.

If experimental data for the unknown component is available, set up a data regression analysis to estimate desired properties.

If no experimental data is available, enter the chemical structure into the Aspen property definition table and calculate the number of atoms and bonds.

Select the a group contribution method. Then find and input the corresponding groups and Aspen ID numbers for the compound.

Use the NIST TDE to estimate the thermodynamic and transport properties of the compound.

If any necessary properties still remain unknown, set up a specific property estimation for the property needed.

With all components identified, select the property method that would successfully model the process (UNIQUAC, NRTL, WILSON, ect.)

Develop a flowsheet for the given process.

Evaluate the model to determine if the simulation accurately predicts the process.

After confirming an accurate model, determine the independent and dependent variables.

Using these variables, develop a sensitivity analysis to create a table of results for a large combination of independent variables.

Insert the newly created table into Excel. Using the sorting function of Excel, find the optimal values for the process.

Assess the validity of the optimal values by completing lab scale experiments.

Appendix E: Material Balance

		INLET					
Run	Mass of SEP-363492.Triflate (g)	SEP-363492.Triflate (mol)	KOH (g)	KOH (mol)	KOH Water (g)	Total (g)
1	10.008	0.030	2.443	0.044	21.774	34.225
2	10.137	0.030	1.964	0.035	17.500	29.601
3	9.844	0.030	2.046	0.036	18.235	30.125
4	9.940	0.030	1.973	0.035	17.588	29.501
5	9.909	0.030	1.995	0.036	17.784	29.688
6	9.915	0.030	2.009	0.036	17.904	29.828
7	9.958	0.030	1.946	0.035	17.344	29.248
8	9.954	0.030	1.990	0.035	17.734	29.678
9	10.070	0.030	2.007	0.036	17.892	29.969
10	50.112	0.150	9.788	0.174	87.234	147.134

OUTLET										
SEP-363492 (mol)	Potassium Triflate (mol)	Water (mol)	KOH (mol)	KOH Water (g)	SEP-363492 (g)	Potassium Triflate (g)	Water (g)	KOH (g)	Total (g)	Discrepancy (g)
0.030	0.030	0.030	0.014	21.774	5.502	5.680	0.541	0.759	34.255	0.031
0.030	0.030	0.030	0.005	17.500	5.573	5.754	0.548	0.257	29.632	0.031
0.030	0.030	0.030	0.007	18.235	5.412	5.587	0.532	0.389	30.155	0.030
0.030	0.030	0.030	0.005	17.588	5.465	5.642	0.537	0.300	29.531	0.030
0.030	0.030	0.030	0.006	17.784	5.448	5.624	0.535	0.327	29.718	0.030
0.030	0.030	0.030	0.006	17.904	5.451	5.627	0.536	0.340	29.858	0.030
0.030	0.030	0.030	0.005	17.344	5.475	5.652	0.538	0.270	29.278	0.030
0.030	0.030	0.030	0.006	17.734	5.472	5.649	0.538	0.314	29.708	0.030
0.030	0.030	0.030	0.006	17.892	5.536	5.715	0.544	0.312	29.999	0.031
0.150	0.150	0.150	0.024	87.234	27.551	28.442	2.707	1.353	147.287	0.153

KOH Calculation Sheet

2M Solution (L)	KOH Flakes (g)	KOH Needed (g)	KOH in Flakes (g)	Total Volume of Solution (L)	Water to Add (L)	Water in Flakes (g)	KOH Molar Mass (g/mol)	KOH in Flakes (mol)	Water in Flakes (L)	KOH Needed (mol)	Volume of KOH (mL)
1.000	132.000	112.200	112.200	1.055	0.980	19.800	56.100	2.000	0.020	2.000	54.892

Wt% KOH
10.088

2M Solution Used (g)	KOH Used (g)
24.217	2.443
19.464	1.964
20.281	2.046
19.561	1.973
19.779	1.995
19.913	2.009
19.290	1.946
19.724	1.990
19.899	2.007
97.022	9.788

Appendix F: Raw Data

MTBE Evaporation Test

	With Cover				Without Cover			
10mL of Each KOH and MtBE added to a beaker and stirred for 5mins then let to sit for 5mins in the Sepatory funnel with the glass stopper on. The mass of the mixture was taken before and after each individual steps								
	Initial	After Mix	After Sep	(grams)	Intial	After Mix	Affter Sep	(grams)
Total	67.2853	67.0809	66.1887		68.2602	66.0156	65.2752	
Intial beaker	49.625	-	49.7333		49.6354		49.6223	
Mass of MTBE +KOH	17.6603	17.4559	16.4554		18.6248	16.3802	15.6529	
Product Loss		-0.2044	-1.0005			-2.2446	-0.7273	
Observations								
The watch glass does not completely cover the the beaker due the beaker having a lip. The covering of the beaker during the mixing step prevented almost a 2 gram loss of the MtBE+KOH mixture.The Sepatory funnel was covered for both runs by placing the glass stopper on top. The potassium triflate (a solid) which was not present in these runs may contribute more to mass loss across the system since it is easier to leave a solid residue behind commpared to a liquid.								

PreReaction

Date	Intials	Experiment Number	Bottle of SEP-363492 (g)	Intial Reaction Beaker (g)	Empty SEP-363492 Tray (g)	SEP-363492.triflate in Tray (g)	Intial wieght of SEP-363492.triflate	Post SEP-363492 Tray (g)	Initial Weight of Graduated Cylinder (g)
2/20/2014	AJC	Initial	134.815	-	-	-	-	-	-
2/20/2014	AJC	1	124.576	111.219	2.1704	12.2426	10.0722	2.235	134.273
2/21/2014	TNS	2	114.587	111.346	2.1702	12.3313	10.1611	2.1941	134.453
2/24/2013	VAS	3	104.699	111.296	2.1839	12.2314	10.0475	2.3876	134.059
2/26/2014	AEM	4	94.6972	111.175	2.0798	12.1482	10.0684	2.2084	134.064
2/26/2104	TNS	5	84.6042	111.306	2.2269	12.2769	10.05	2.368	134.097
2/28/2104	TNS	6	74.5581	111.296	2.1273	12.1616	10.0343	2.2469	134.212
3/1/2014	VAS	7	64.4763	111.276	2.2341	12.2585	10.0244	2.3009	134.219
3/3/2014	AEM	8	54.4706	111.292	2.1831	12.254	10.0709	2.3002	134.057
3/5/2014	AJC	9	44.3193	111.3	2.224	12.3533	10.1293	2.2838	134.056
3/28/2014	AJC	10	91.599	218.531	2.233	52.405	50.172	2.293	134.318
			Bottle of SEP		empty tray	Significant amount of SEP left in tray,			
			104.699		2.228	we reweighed the bottle and the tray			
						after putting the remaing SEP back into			

KOH Graduated Cylinder (g)	Post KOH Graduated Cylinder (g)	2M KOH In Reaction (g)	SEP-363492.Triflate Residue (g)	SEP-363492.Triflate in Reaction (g)	pH reaction	Weight of beaker with reaction (g)	Residue Reaction Beaker (g)	Reaction (g)	New Beaker (g)	New Beaker with Reaction (g)	Reaction in new beaker (g)
-	-	-	-	-	-	-					0
158.6	134.383	24.217	0.0646	10.0076	13	145.197					0
153.744	134.28	19.464	0.0239	10.1372	13	140.651					0
154.543	134.262	20.281	0.2037	9.8438	14	141.232					0
153.643	134.082	19.561	0.1286	9.9398	13	140.411					0
154.047	134.268	19.779	0.1411	9.9089	14	140.872					0
154.175	134.262	19.913	0.1196	9.9147	14	140.921					0
153.625	134.335	19.29	0.0668	9.9576	14	140.371					0
154.09	134.366	19.724	0.1171	9.9538	14	140.875					0
154.119	134.22	19.899	0.0598	10.0695	14	141.147					0
231.316	134.294	97.022	0.06	50.112	14	364.83	219.794	145.036	167.41	312.285	144.875
					Theo	Act					
			167.41	312.285	34.2246	33.978	Possible causes could be: 1.) losing some KOH and SEP in mixing step if				
		0			29.6012	29.305	some splashes out 2.) Evaporation of KOH?? 3.) Losing some reaction				
					30.1248	29.936	mixture when removing stirring bar				
					29.5008	29.236					

Post Reaction – Wash 1

Date	Intials	Experiment Number	Initial Graduated Cylinder (g)	MTBE Graduated Cylinder (g)	Post MTBE Graduated Cylinder (g)	MTBE Used In First Extraction (g)	Intial Reaction Beaker (g)	Reaction Beaker with entire solution (g)	Beaker post seperation (g)	Solution Added to Sep Funnel (g)
2/20/2014	AJC	1	134.273	156.592	134.17	22.422	111.219	164.54	111.487	53.053
2/21/2014	TNS	2	134.227	156.491	134.161	22.33	111.346	160.835	111.58	49.255
2/24/2014	VAS	3	134.235	171.43	134.15	37.28	111.296	176.397	111.523	64.874
2/26/2014	AEM	4	134.07	147.537	134.02	13.517	111.175	152.998	111.456	41.542
2/26/2014	TNS	5	134.26	147.608	134.206	13.402	111.306	153.196	111.513	41.683
2/28/2014	TNS	6	134.262	171.427	134.177	37.25	111.296	177.341	111.44	65.901
3/1/2014	VAS	7	134.314	156.252	134.278	21.974	111.276	161.503	111.464	50.039
3/3/2014	AEM	8	134.348	147.875	134.197	13.678	111.292	153.627	111.55	42.077
3/5/2014	AJC	9	134.272	171.317	134.079	37.238	111.3	177.096	111.59	65.506
3/28/2014	AJC	10	233.52	344.237	233.602	110.635	167.41	422.92	167.453	255.467

Aqueous beaker empty (g)	Aqueous beaker with solution (g)	Aqueous Phase Collected in Wash 1	pH of aqueous phase	Rotary RBF Empty (g)	Rotary RBF with Organic Phase (g)	Organic Phase Collected (g)	Rotary RBF Post RotoVap (g)	SEP-363492 Recovered After 1st Wash	Water + MTBE in Orgo Phase (g)
49.627	77.1048	27.4778	---	75.975	100.095	24.12	81.268	5.293	18.827
49.6205	75.1035	25.483	---	75.9701	98.51	22.5399	80.0583	4.0882	18.4517
49.6211	73.4726	23.8515	14	75.9752	115.736	39.7608	81.1806	5.2054	34.5554
49.5658	78.4805	28.9147	14	75.8875	87.376	11.4885	78.5481	2.6606	8.8279
49.6205	79.195	29.5745	14	75.9826	85.3394	9.3568	78.4766	2.494	6.8628
49.6183	73.4023	23.784	14	75.9711	117.163	41.1919	81.1917	5.2206	35.9713
49.6102	75.0604	25.4502	14	75.9515	99.2358	23.2843	80.0293	4.0778	19.2065
49.6208	78.657	29.0362	14	75.9721	87.8734	11.9013	78.7169	2.7448	9.1565
49.6239	73.3071	23.6832	14	75.9693	116.364	40.3947	81.2643	5.295	35.0997
111.261	233.057	121.796	14	153.026	282.931	129.905	179.432	26.406	103.499

Post Reaction – Wash 2

Date	Intials	Experiment Number	Initial Graduated Cylinder (g)	MTBE Graduated Cylinder (g)	Post MTBE Graduated Cylinder (g)	MTBE Used In Second Extraction (g)	Wash Beaker Empty (g)	Beaker with Aqueous Solution (g)	Aqueous Solution Used in 2nd Wash (g)	Aqueous Collection beaker empty (g)	Aqueous collection beaker with Aqueous solution (g)
2/20/2014	AJC	1	134.273	149.610	134.759	14.851	49.627	76.852	27.225	49.685	75.580
2/21/2014	TNS	2	134.244	149.442	134.124	15.318	49.621	74.710	25.090	49.780	72.282
2/24/2014	TNS	3	134.111	158.876	134.176	24.700	49.764	73.233	23.469	49.620	72.346
2/26/2014	AEM	4	134.148	147.581	134.136	13.445	49.566	78.203	28.637	49.776	72.877
2/26/2014	TNS	4	134.164	147.477	134.186	13.291	49.621	78.965	29.345	49.758	72.786
2/28/2014	AEM	6	134.135	158.526	134.135	24.391	49.618	73.259	23.641	49.772	72.472
3/1/2014	AJC	7	134.206	149.346	134.176	15.170	49.610	74.725	25.115	49.744	72.175
3/3/2014	AEM	8	134.174	147.643	134.180	13.463	49.621	78.393	28.772	49.748	72.842
3/5/2014	AEM	9	134.049	158.447	134.035	24.412	49.624	72.930	23.306	49.744	72.319
3/28/2014	AJC	10	134.230	209.539	134.041	75.498	111.699	232.354	120.655	111.699	225.001

Aqeuous Phase Collected in 2nd Wash	pH	Aqueous Phase with MTBE Wash (g)	Total Solution for 2nd Wash (g)	Rotary RBF empty (g)	Rotary RBF with organic phase (g)	Organic Phase Collected (g)	Rotary RBF Post RotoVap (g)	SEP-363492 Extracted from 2nd Wash	Water + MTBE in Orgo Phase (g)	SEP-363492 Extracted (g)	SEP-363492 Created in Reaction (g)	Discrepancy (g)
25.895		91.943	42.258	75.936	90.413	14.477	76.458	0.522	13.955	5.815	5.502	0.313
22.502		88.613	38.833	76.048	91.338	15.290	77.325	1.277	14.013	5.366	5.586	-0.221
22.726		96.966	47.346	76.065	99.751	23.686	76.349	0.284	23.402	5.489	5.412	0.077
23.101	13	91.025	41.250	76.041	93.508	17.467	78.827	2.787	14.680	5.447	5.535	-0.088
23.028	14	91.163	41.405	76.032	93.798	17.766	78.752	2.720	15.046	5.214	5.448	-0.234
22.700	14	97.062	47.290	75.997	99.673	23.676	76.261	0.264	23.412	5.485	5.451	0.034
22.431	14	89.394	39.649	76.022	92.365	16.343	77.310	1.288	15.054	5.366	5.475	-0.109
23.094	14	91.292	41.544	76.031	93.622	17.591	78.603	2.572	15.019	5.317	5.472	-0.155
22.575	14	96.777	47.033	76.082	99.266	23.184	76.313	0.231	22.953	5.526	5.536	-0.010
113.302	14	303.748	192.049	153.101	223.268	70.167	156.267	3.166	67.001	29.572	27.489	2.083

Post Reaction – Wash 3

Date	Intials	Experiment Number	Initial Graduated Cylinder (g)	MTBE Graduated Cylinder (g)	Post MTBE Graduated Cylinder (g)	MTBE Used In Third Extraction (g)	Wash Beaker Empty (g)	Wash Beaker with Aqueous Solution (g)	Aqueous Solution Used in 3rd Wash (g)	Aqueous Collection beaker empty (g)	Aqueous collection beaker with Aqueous solution (g)
2/20/2014	AJC	1	133.924	145.181	133.885	11.296	49.676	75.458	25.782	49.684	75.056
2/21/2014	TNS	2	134.235	145.213	134.121	11.092	49.78	72.1672	22.3872	49.88	71.5309
2/24/2014	TNS	3	-	-	-	-	-	-	-	-	-
2/26/2014	AEM	4	134.121	141.702	134.114	7.588	49.5658	72.7105	23.1447	49.7271	71.816
2/26/2014	TNS	5	134.143	141.621	134.153	7.468	49.7579	72.616	22.8581	49.7942	73.5306
2/28/2014	AJC	6	-	-	-	-	-	-	-	-	-
3/1/2014	VAS	7	134.141	145.484	134.165	11.319	49.7443	71.8483	22.104	49.7929	71.1744
3/3/2014	TNS	8	134.06	141.515	134.055	7.46	49.7479	72.3379	22.59	49.7404	71.9268
3/5/2014	AEM	9	-	-	-	-	-	-	-	-	-
3/28/2014	VAS	10	134.012	189.294	134.003	55.291	111.699	225.001	113.302	111.632	223.287

Aqeuous Phase Collected in 3rd Wash	pH of Aqueous Phase	Aqueous Phase with MTBE Washes (g)	Total Solution for 3rd Wash (g)	Rotary RBF empty (g)	Rotary RBF with organic phase (g)	Organic Phase Collected (g)	Rotary RBF Post RotoVap (g)	Water + MTBE in Orgo Phase (g)	SEP-363492 Extracted from 3rd Wash	SEP-363492 Created in Reaction
25.372		86.289	36.605	75.901	85.483	9.582	76.105	9.378	0.204	5.502
21.6509		81.6335	31.7535	76.1016	85.3603	9.2587	76.2846	9.0757	0.183	5.586
-	-	-	-	-	-	-	-	-	0	5.412
22.0889	14	79.7594	30.0323	76.2054	83.6072	7.4018	76.6176	6.9896	0.4122	5.535
23.7364	14	79.9512	30.157	76.0203	81.4285	5.4082	76.3219	5.1066	0.3016	5.448
-	-	-	-	-	-	-	-	-	0	5.451
21.3815	14	82.3907	32.5978	75.9866	86.3962	10.4096	76.1733	10.2229	0.1867	5.475
22.1864	14	79.1826	29.4422	76.0823	82.5363	6.454	76.239	6.2973	0.1567	5.472
-	-	-	-	-	-	-	-	-	0	5.536
111.655	14	277.907	166.275	153.6	206.56	52.96	153.85	52.71	0.25	27.489

Total SEP-363492 Extracted (g)	Discepancy	Cumulative Error	Notes
5.815	-0.313	0.029	Interface was placed into RotoVap with Organic Phase which caused an inflated amount of supposed SEP-363492 extracted in the 1st wash. All other washes were done the correct way by keeping the interface in the aqueous phase. Waste Container had small pressure buildup - Contact Bob on potential causes. Use cold water for remaining ones or place dry ice into RotoVap at the last possible second to reduce condensation buildup. Figure out how to resolve our scale problem. Need to brainstorm ways to calculate mass balance if we can't keep our MTBE and Water seperate in our RotoVap.
5.366	0.221	0.029	Less KOH was used, so no "third phase" was seen. We added a third waste bottle for the SEP-363492/Acetone. Lowered the pressure of the vaccum to 550 from 750.
5.489	-0.077	0.029	
5.447	0.088	0.029	
5.214	0.234	0.029	
5.485	-0.034	0.029	
5.366	0.109	0.029	*Changed temperature of the water to 60 for the last wash to try and evaporate off the water
5.317	0.155	0.029	
5.526	0.010	0.029	
29.572	-2.083	0.029	

Post Reaction – Wash 4

Date	Intials	Experiment Number	Initial Graduated Cylinder (g)	MTBE Graduated Cylinder (g)	Post MTBE Graduated Cylinder (g)	MTBE Used In Third Extraction (g)	Wash Beaker Empty (g)	Wash Beaker with Aqueous Solution (g)	Aqueous Solution Used in 3rd Wash (g)	Aqueous Collection beaker empty (g)
2/20/2014	AJC	1	133.924	145.181	133.885	11.296	49.676	75.458	25.782	49.684
2/21/2014	TNS	2	-	-	-	-	-	-	-	-
2/24/2014	VAS	3	-	-	-	-	-	-	-	-
2/26/2014	AEM	4	134.108	141.473	134.109	7.364	49.7271	71.716	21.9889	49.7535
2/26/2014	TNS	5	134.124	141.54	134.17	7.37	49.7942	73.1313	23.3371	49.7443
2/28/2014	TNS	6	-	-	-	-	-	-	-	-
3/1/2014	VAS	7	-	-	-	-	-	-	-	-
3/3/2014	AEM	8	133.996	141.496	134.016	7.48	49.7404	71.6888	21.9484	49.7727
3/5/2014	AJC	9	-	-	-	-	-	-	-	-
3/28/2014	AJC	10	-	-	-	-	-	-	-	-

Aqueous collection beaker with Aqueous solution (g)	Aqeuous Phase Collected in 4th Wash	pH	Aqueous Phase with MTBE Washes (g)	Total Solution for 4th Wash (g)	Rotary RBF empty (g)	Rotary RBF with organic phase (g)	Organic Phase Collected (g)	Rotary RBF Post RotoVap (g)	Water + MTBE in Orgo Phase (g)
75.056	25.372		86.289	36.605	75.901	85.483	9.582	76.105	9.378
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
71.3112	21.5577	14	78.5135	28.76	76.0346	82.7107	6.6761	76.1922	6.5185
71.5275	21.7832	14	80.1223	30.378	76.0014	83.85	7.8486	76.1831	7.6669
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-
71.2903	21.5176	14	78.6255	28.8528	76.006	82.5022	6.4962	76.1134	6.3888
-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-

SEP-363492 Extracted from 4th Wash	SEP-363492 Created in Reaction	Total SEP-363492 Extracted (g)	Cumulative Error
0.204	5.502	5.6934	0.039
0	5.586	5.8593	0.039
0	5.412	5.5153	0.039
0.1576	5.535	5.6425	0.039
0.1817	5.448	5.7344	0.039
0	5.451	5.4739	0.039
0	5.475	5.5261	0.039
0.1074	5.472	29.9294	0.039
-	5.536	#VALUE!	0.039
-	27.489	#VALUE!	0.039

Notes
In the first wash, we discovered three phases. After trying to remix the solution together (in the sep funnel and then again with the magnetic stirrer) we could not get rid of the thrid phase. Therefore, we included it with the aqueous phase, which upon the second wash the third phase was gone. We hypothesize that the third phase was formed due to too little MTBE being in the first solution. We have noticed that there are water droplets in the RBF that do not evaporate off (which could be a reason why we keep creating mass); therefore, we have determined that we should evaporate the product to dryness to ensure that no water remains.
We had three phases, so we mixed it by hand in the sep funnel for approximately 45 seconds

Appendix G: Material Safety Data Sheets

This section contains the material data sheets that were reviewed for safety concerns before performing any laboratory experiments. The material data sheet for the free base was not available due to the novelty of the compound. Therefore, only the data sheets for potassium hydroxide and MTBE are included

KOH

Health	3
Fire	0
Reactivity	2
Personal Protection	J

Material Safety Data Sheet
Potassium hydroxide MSDS

Section 1: Chemical Product and Company Identification	
Product Name: Potassium hydroxide	**Contact Information:**
Catalog Codes: SLP4096, SLP3085, SLP4900, SLP2071	Sciencelab.com, Inc.
CAS#: 1310-58-3	14025 Smith Rd. Houston, Texas 77396
RTECS: TT2100000	US Sales: **1-800-901-7247** International Sales: **1-281-441-4400**
TSCA: TSCA 8(b) inventory: Potassium hydroxide	Order Online: ScienceLab.com
CI#: Not available.	**CHEMTREC (24HR Emergency Telephone), call:** 1-800-424-9300
Synonym:	
Chemical Name: Potassium Hydroxide	**International CHEMTREC, call:** 1-703-527-3887
Chemical Formula: KOH	**For non-emergency assistance, call:** 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Potassium hydroxide	1310-58-3	100

Toxicological Data on Ingredients: Potassium hydroxide: ORAL (LD50): Acute: 273 mg/kg [Rat].

Section 3: Hazards Identification

Potential Acute Health Effects:
Very hazardous in case of skin contact (corrosive, irritant), of eye contact (irritant, corrosive), of ingestion, of inhalation. The amount of tissue damage depends on length of contact. Eye contact can result in corneal damage or blindness. Skin contact can produce inflammation and blistering. Inhalation of dust will produce irritation to gastro-intestinal or respiratory tract, characterized by burning, sneezing and coughing. Severe over-exposure can produce lung damage, choking, unconsciousness or death. Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:
CARCINOGENIC EFFECTS: Not available. MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. The substance may be toxic to upper respiratory tract, skin, eyes. Repeated or prolonged exposure to the substance can produce target organs damage. Repeated exposure of the eyes to a low level of dust can produce eye irritation. Repeated skin exposure can produce local skin destruction, or dermatitis. Repeated inhalation of dust can produce varying degree of respiratory irritation or lung damage.

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Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Cold water may be used. Get medical attention immediately.

Skin Contact:
In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Cover the irritated skin with an emollient. Cold water may be used. Wash clothing before reuse. Thoroughly clean shoes before reuse. Get medical attention immediately.

Serious Skin Contact:
Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek immediate medical attention.

Inhalation:
If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention immediately.

Serious Inhalation:
Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. WARNING: It may be hazardous to the person providing aid to give mouth-to-mouth resuscitation when the inhaled material is toxic, infectious or corrosive. Seek immediate medical attention.

Ingestion:
Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately. Loosen tight clothing such as a collar, tie, belt or waistband.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Non-flammable.

Auto-Ignition Temperature: Not applicable.

Flash Points: Not applicable.

Flammable Limits: Not applicable.

Products of Combustion: Not available.

Fire Hazards in Presence of Various Substances: metals, acids

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of mechanical impact: Not available. Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions: Not applicable.

Special Remarks on Fire Hazards:
Violent reaction or ignition under appropriate conditions with acids, alcohols, p-bis(1,3-dibromoethyl) benzene, cyclopentadiene, germanium, hyponitrous acid, maleic anhydride, nitroalkanes, 2-nitrophenol, potassium peroxodisulfate, sugars, 2,2,3,3-tetrafluoropropanol, thorium dicarbide. Molten ortho -nitrophenol reacts violently with potassium hydroxide. When potassium hydroxide and tetrachloroethane are heated, a spontaneously flammable gas, chloroacetylene, is formed. When phosphorus is boiled in a solution of potassium hydroxide, phosphine gas is evolved which is spontaneously flammable. 1,2-Dichloroethylene and Potassium hydroxide reaction produces chloroacetylene which is spontaneously flammable in air. Potassium Persulfate and a little Potassium hydroxide and water will ignite. When wet, attacks metals such as aluminum, tin, lead, and zinc, producing flammable hydrogen gas.

Special Remarks on Explosion Hazards:

Potentially explosive reaction with bromoform + crown ethers, chlorine dioxide, nitrobenzene, nitromethane, nitrogen trichloride, peroxidized tetrahydrofuran, 2,4,6-trinitrotoluene. Reaction with ammonium hexachloroplatiate(2-) + heat forms heat sensitive explosive product. Potassium hydroxide will cause explosive decomposition of maleic anhydride. Detonation will occur when potassiuim hydroxide is mixed with n-methyl-nitroso urea and methylene chloride. Nitrogen trichloride explodes on contact with potassium hydroxide.

Section 6: Accidental Release Measures

Small Spill:
Use appropriate tools to put the spilled solid in a convenient waste disposal container. If necessary: Neutralize the residue with a dilute solution of acetic acid.

Large Spill:
Corrosive solid. Stop leak if without risk. Do not get water inside container. Do not touch spilled material. Use water spray to reduce vapors. Prevent entry into sewers, basements or confined areas; dike if needed. Call for assistance on disposal. Neutralize the residue with a dilute solution of acetic acid. Be careful that the product is not present at a concentration level above TLV. Check TLV on the MSDS and with local authorities.

Section 7: Handling and Storage

Precautions:
Keep container dry. Do not ingest. Do not breathe dust. Never add water to this product. In case of insufficient ventilation, wear suitable respiratory equipment. If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes. Keep away from incompatibles such as organic materials, metals, acids, moisture.

Storage: Keep container tightly closed. Keep container in a cool, well-ventilated area. Do not store above 23°C (73.4°F).

Section 8: Exposure Controls/Personal Protection

Engineering Controls:
Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.

Personal Protection:
Splash goggles. Synthetic apron. Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:
Splash goggles. Full suit. Vapor and dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits:
CEIL: 2 (mg/m3) from OSHA (PEL) [United States] CEIL: 2 (mg/m3) from ACGIH (TLV) [United States] Consult local authorities for acceptable exposure limits.

Section 9: Physical and Chemical Properties

Physical state and appearance: Solid. (Solid pellets.)

Odor: Odorless.

Taste: Not available.

Molecular Weight: 56.11 g/mole

Color: White.

pH (1% soln/water): 13 [Basic.]

Boiling Point: Decomposition temperature: 1384°C (2523.2°F)

Melting Point: 380°C (716°F)

Critical Temperature: Not available.

Specific Gravity: 2.044 (Water = 1)

Vapor Pressure: Not applicable.

Vapor Density: Not available.

Volatility: Not available.

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water.

Solubility:
Easily soluble in cold water, hot water. Insoluble in diethyl ether.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Incompatible materials, dust generation, exposure to moist air or water.

Incompatibility with various substances:
Highly reactive with acids. Reactive with organic materials, metals, moisture.

Corrosivity:
Extremely corrosive in presence of aluminum, brass, and zinc. Slightly corrosive in presence of copper, of stainless steel(304). Non-corrosive in presence of stainless steel(316).

Special Remarks on Reactivity:
Hygroscopic (absorbs moisture from air). When dissolved in water or alcohol or when the solution is treated with acid, much heat is generated. Reacts violently with acids, halogens, halogenated hydrocarbons, maleic anhydride, organic anhydrides, isocyanates, alkylene oxides, epichlorhydrin, aldehydes, alcohols, gylcols, phenols, cresols, caprolactum solution. Also incompatible with nitro compounds (nitrobenzene, nitromethane, nitrogen trichloride), organic materials, acid anhydrides, acid chlorides, magnesium, peroxidized tetrahydrofuran, chlorine dioxide, maleic dicarbide, sugars. When wet attacks metals such as aluminum, tin, lead, and zinc.

Special Remarks on Corrosivity:
When wet, attacks metals such as aluminum, tin, lead, and zinc, producing flammable hydrogen gas. Severe corrosive effect on brass and bronze.

Polymerization: Will not occur.

Section 11: Toxicological Information

Routes of Entry: Absorbed through skin. Inhalation. Ingestion.

Toxicity to Animals: Acute oral toxicity (LD50): 273 mg/kg [Rat].

Chronic Effects on Humans:

MUTAGENIC EFFECTS: Mutagenic for mammalian somatic cells. May cause damage to the following organs: upper respiratory tract, skin, eyes.

Other Toxic Effects on Humans:
Extremely hazardous in case of inhalation (lung corrosive). Very hazardous in case of skin contact (corrosive, irritant), of eye contact (corrosive), of ingestion, .

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: May affect genetic material based on animal data.

Special Remarks on other Toxic Effects on Humans:
Acute Potential Health Effects: Skin: Causes severe skin irritation and burns. Eyes: Causes severe eye irritation and burns. May cause irreversible eye injury. Inhalation: Causes severe irritation and burns of the respiratory tract and mucous membranes. Irritation may lead to chemical pneumonitis Ingestion: Harmful if swallowed. May cause severe and permanent damage to the digestive tract. Causes severe irritation and burns of the gastrointestinal (digestive) tract with abdominal pain, vomiting and possible death. May cause perforation of the digestive tract. Chronic Potential Health Effects: Chronic contact with dilute solutions of potassium hydroxide can cause dermatitis. Inhalation can produce chronic productive cough, and shortness of breath.

Section 12: Ecological Information

Ecotoxicity: Ecotoxicity in water (LC50): 80 mg/l 24 hours [Mosquito Fish].

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are less toxic than the product itself.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:
Waste must be disposed of in accordance with federal, state and local environmental control regulations.

Section 14: Transport Information

DOT Classification: Class 8: Corrosive material

Identification: : Potassium hydroxide, solid UNNA: 1813 PG: II

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:
New York release reporting list: Potassium hydroxide Pennsylvania RTK: Potassium hydroxide Florida: Potassium hydroxide Minnesota: Potassium hydroxide Massachusetts RTK: Potassium hydroxide New Jersey: Potassium hydroxide California Director's List of Hazardous Substances: Potassium hydroxide TSCA 8(b) inventory: Potassium hydroxide CERCLA: Hazardous substances.: Potassium hydroxide: 1000 lbs. (453.6 kg)

Other Regulations:
OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200). EINECS: This product is on the European Inventory of Existing Commercial Chemical Substances.

Other Classifications:

WHMIS (Canada):
CLASS D-1B: Material causing immediate and serious toxic effects (TOXIC). CLASS E: Corrosive solid.

DSCL (EEC):

HMIS (U.S.A.):

    Health Hazard: 3

    Fire Hazard: 0

    Reactivity: 2

    Personal Protection: j

National Fire Protection Association (U.S.A.):

    Health: 3

    Flammability: 0

    Reactivity: 1

    Specific hazard:

Protective Equipment:
Gloves. Synthetic apron. Vapor and dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate. Splash goggles.
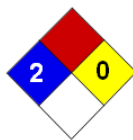
Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/10/2005 08:23 PM

Last Updated: 05/21/2013 12:00 PM

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ScienceLab.com
Chemicals & Laboratory Equipment

Health	2
Fire	3
Reactivity	0
Personal Protection	H

Material Safety Data Sheet
Methyl tert-butyl ether MSDS

Section 1: Chemical Product and Company Identification

Product Name: Methyl tert-butyl ether

Catalog Codes: SLM2152

CAS#: 1634-04-4

RTECS: KN5250000

TSCA: TSCA 8(b) inventory: Methyl tert-butyl ether

CI#: Not available.

Synonym:

Chemical Name: Methyl tert-Butyl Ether

Chemical Formula: C5-H12-O

Contact Information:

Sciencelab.com, Inc.
14025 Smith Rd.
Houston, Texas 77396

US Sales: 1-800-901-7247
International Sales: 1-281-441-4400

Order Online: ScienceLab.com

CHEMTREC (24HR Emergency Telephone), call:
1-800-424-9300

International CHEMTREC, call: 1-703-527-3887

For non-emergency assistance, call: 1-281-441-4400

Section 2: Composition and Information on Ingredients

Composition:

Name	CAS #	% by Weight
Methyl {tert-}butyl ether	1634-04-4	100

Toxicological Data on Ingredients: Methyl tert-butyl ether: ORAL (LD50): Acute: 4000 mg/kg [Rat]. 5960 mg/kg [Mouse]. VAPOR (LC50): Acute: 23576 ppm 4 hour(s) [Rat].

Section 3: Hazards Identification

Potential Acute Health Effects:
Extremely hazardous in case of eye contact (irritant), of ingestion. Very hazardous in case of skin contact (irritant), of inhalation. Hazardous in case of skin contact (permeator). Inflammation of the eye is characterized by redness, watering, and itching. Skin inflammation is characterized by itching, scaling, reddening, or, occasionally, blistering.

Potential Chronic Health Effects:
Extremely hazardous in case of eye contact (irritant), of ingestion. Very hazardous in case of skin contact (irritant), of inhalation. Hazardous in case of skin contact (permeator). CARCINOGENIC EFFECTS: Not available. MUTAGENIC EFFECTS: Not available. TERATOGENIC EFFECTS: Not available. DEVELOPMENTAL TOXICITY: Not available. The substance is toxic to lungs, the nervous system, mucous membranes. Repeated or prolonged exposure to the substance can produce target organs damage. Repeated or prolonged inhalation of vapors may lead to chronic respiratory irritation.

Section 4: First Aid Measures

Eye Contact:
Check for and remove any contact lenses. Immediately flush eyes with running water for at least 15 minutes, keeping eyelids open. Cold water may be used. Do not use an eye ointment. Seek medical attention.

Skin Contact:
After contact with skin, wash immediately with plenty of water. Gently and thoroughly wash the contaminated skin with running water and non-abrasive soap. Be particularly careful to clean folds, crevices, creases and groin. Cold water may be used. Cover the irritated skin with an emollient. If irritation persists, seek medical attention. Wash contaminated clothing before reusing.

Serious Skin Contact:
Wash with a disinfectant soap and cover the contaminated skin with an anti-bacterial cream. Seek medical attention.

Inhalation: Allow the victim to rest in a well ventilated area. Seek immediate medical attention.

Serious Inhalation:
Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek medical attention.

Ingestion:
Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.

Serious Ingestion: Not available.

Section 5: Fire and Explosion Data

Flammability of the Product: Flammable. **Auto-**

Ignition Temperature: 224°C (435.2°F) **Flash**

Points: CLOSED CUP: -28°C (-18.4°F).

Flammable Limits: LOWER: 2.5% UPPER: 15.1%

Products of Combustion: These products are carbon oxides (CO, CO2).

Fire Hazards in Presence of Various Substances: Flammable in presence of open flames and sparks.

Explosion Hazards in Presence of Various Substances:
Risks of explosion of the product in presence of mechanical impact: Not available. Risks of explosion of the product in presence of static discharge: Not available.

Fire Fighting Media and Instructions:
Flammable liquid, soluble or dispersed in water. SMALL FIRE: Use DRY chemical powder. LARGE FIRE: Use alcohol foam, water spray or fog.

Special Remarks on Fire Hazards: Not available.

Special Remarks on Explosion Hazards: Not available.

Section 6: Accidental Release Measures

Small Spill:
Dilute with water and mop up, or absorb with an inert dry material and place in an appropriate waste disposal container.

Large Spill:
Flammable liquid. Keep away from heat. Keep away from sources of ignition. Stop leak if without risk. Absorb with DRY earth, sand or other non-combustible material. Do not touch spilled material. Prevent entry into sewers, basements or confined areas; dike if needed. Eliminate all ignition sources.

Section 7: Handling and Storage

Precautions:
Keep away from heat. Keep away from sources of ignition. Ground all equipment containing material. Do not ingest. Do not breathe gas/fumes/ vapour/spray. In case of insufficient ventilation, wear suitable respiratory equipment If ingested, seek medical advice immediately and show the container or the label. Avoid contact with skin and eyes

Storage:
Flammable materials should be stored in a separate safety storage cabinet or room. Keep away from heat. Keep away from sources of ignition. Keep container tightly closed. Keep in a cool, well-ventilated place. Ground all equipment containing material. A refrigerated room would be preferable for materials with a flash point lower than 37.8°C (100°F).

Section 8: Exposure Controls/Personal Protection

Engineering Controls:
Provide exhaust ventilation or other engineering controls to keep the airborne concentrations of vapors below their respective threshold limit value. Ensure that eyewash stations and safety showers are proximal to the work-station location.

Personal Protection:
Splash goggles. Lab coat. Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.

Personal Protection in Case of a Large Spill:
Splash goggles. Full suit. Vapor respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Exposure Limits: Not available.

Section 9: Physical and Chemical Properties

Physical state and appearance: Liquid.

Odor: Characteristic. (Strong.)

Taste: Not available.

Molecular Weight: 88.15 g/mole

Color: Clear Colorless.

pH (1% soln/water): Not available.

Boiling Point: 55.2°C (131.4°F)

Melting Point: -109°C (-164.2°F)

Critical Temperature: Not available.

Specific Gravity: 0.7405 (Water = 1)

Vapor Pressure: 245 mm of Hg (@ 20°C)

Vapor Density: 3.1 (Air = 1)

Volatility: 100% (v/v).

Odor Threshold: Not available.

Water/Oil Dist. Coeff.: Not available.

Ionicity (in Water): Not available.

Dispersion Properties: See solubility in water, methanol, diethyl ether.

Solubility:

Soluble in methanol, diethyl ether. Partially soluble in cold water.

Section 10: Stability and Reactivity Data

Stability: The product is stable.

Instability Temperature: Not available.

Conditions of Instability: Not available.

Incompatibility with various substances: Not available.

Corrosivity: Non-corrosive in presence of glass.

Special Remarks on Reactivity: Not available.

Special Remarks on Corrosivity: Not available.

Polymerization: No.

Section 11: Toxicological Information

Routes of Entry: Dermal contact. Eye contact. Inhalation. Ingestion.

Toxicity to Animals:
WARNING: THE LC50 VALUES HEREUNDER ARE ESTIMATED ON THE BASIS OF A 4-HOUR EXPOSURE. Acute oral toxicity (LD50): 4000 mg/kg [Rat]. Acute toxicity of the vapor (LC50): 23576 ppm 4 hour(s) [Rat].

Chronic Effects on Humans: The substance is toxic to lungs, the nervous system, mucous membranes.

Other Toxic Effects on Humans:
Extremely hazardous in case of ingestion. Very hazardous in case of skin contact (irritant), of inhalation. Hazardous in case of skin contact (permeator).

Special Remarks on Toxicity to Animals: Not available.

Special Remarks on Chronic Effects on Humans: Not available.

Special Remarks on other Toxic Effects on Humans: Not available.

Section 12: Ecological Information

Ecotoxicity: Not available.

BOD5 and COD: Not available.

Products of Biodegradation:
Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.

Toxicity of the Products of Biodegradation: The products of degradation are more toxic.

Special Remarks on the Products of Biodegradation: Not available.

Section 13: Disposal Considerations

Waste Disposal:

Section 14: Transport Information

DOT Classification: Class 3: Flammable liquid.

Identification: : Methyl tert-butyl ether : UN2398 PG: II

Special Provisions for Transport: Not available.

Section 15: Other Regulatory Information

Federal and State Regulations:
Pennsylvania RTK: Methyl tert-butyl ether Massachusetts RTK: Methyl tert-butyl ether TSCA 8(b) inventory: Methyl tert-butyl ether SARA 313 toxic chemical notification and release reporting: Methyl tert-butyl ether CERCLA: Hazardous substances.: Methyl tert-butyl ether

Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications:

WHMIS (Canada):
CLASS B-2: Flammable liquid with a flash point lower than 37.8°C (100°F). CLASS D-2A: Material causing other toxic effects (VERY TOXIC).

DSCL (EEC):
R11- Highly flammable. R38- Irritating to skin. R41- Risk of serious damage to eyes.

HMIS (U.S.A.):

    Health Hazard: 2

    Fire Hazard: 3

    Reactivity: 0

    Personal Protection: h

National Fire Protection Association (U.S.A.):

    Health: 2

    Flammability: 3

    Reactivity: 0

    Specific hazard:

Protective Equipment:
Gloves. Lab coat. Vapor respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate. Splash goggles.

Section 16: Other Information

References: Not available.

Other Special Considerations: Not available.

Created: 10/10/2005 08:23 PM

Last Updated: 05/21/2013 12:00 PM

Appendix H: Aspen Input Files – Base Case

;Input Summary created by Aspen Plus Rel. 28.0 at 13:35:59 Tue Apr 22, 2014
;Directory \\filer\home\My_Documents\MQP\LabScaleSims\Sunovionprocedure_3
Filename \\filer\home\My_Documents\MQP\LabScaleSims\sunovionprocedure.inp

IN-UNITS MET

DEF-STREAMS CONVEN ALL

DATABANKS 'APV82 PURE28' / 'APV82 AQUEOUS' / 'APV82 SOLIDS' / &
    'APV82 INORGANIC' / NOASPENPCD

PROP-SOURCES 'APV82 PURE28' / 'APV82 AQUEOUS' / 'APV82 SOLIDS' &
    / 'APV82 INORGANIC'

COMPONENTS
    WATER H2O /
    MTBE C5H12O-D2 /
    SEP36 SEP-363492

FORMULA SEP36 SEP-363492

SOLVE
    RUN-MODE MODE=SIM

FLOWSHEET
    BLOCK WASH1 IN=FEED1 OUT=AQ1 ORG1
    BLOCK WASH2 IN=FEED2 AQ1 OUT=AQ2 ORG2
    BLOCK WASH3 IN=AQ2 FEED3 OUT=AQ3 ORG3
    BLOCK B1 IN=ORG1 ORG2 ORG3 OUT=ORGTOTAL

PROPERTIES UNIFAC
    PROPERTIES UNIF-LL

STRUCTURES
    STRUCTURES SEP36 O1 C2 S / C2 C3 S / C3 C4 S / C4 &
        C5 D / C5 C6 S / C6 O1 S / C4 C7 S / C7 C8 &
        D / C8 S9 S / C5 S9 S / C6 C10 S / C10 N11 S / &
        N11 C12 S
    UNIFAC SEP36 1010 2 / 1005 1 / 1600 1 / 1710 1 / &
        3760 1

PROP-DATA
    PROP-LIST ATOMNO / NOATOM
    PVAL SEP36 6 1 7 8 16 / 9. 13. 1. 1. 1.

ESTIMATE ALL

PROP-DATA PCES-1
  IN-UNITS MET
  PROP-LIST DHFORM / DGFORM / VB / RKTZRA
  PVAL SEP36 -5321.486577 / 48151.33276 / 153.1111980 / &
    .2344427150

PROP-DATA TDE-1
  IN-UNITS MET PRESSURE='N/sqm' TEMPERATURE=K DELTA-T=C &
    MOLE-VOLUME='cum/kmol' PDROP=bar INVERSE-PRES='1/bar'
  PROP-LIST OMEGA / ZC / VC / PC / TC / MW / TB / SG / &
    VLSTD
  PVAL SEP36 0.60398 / 0.263 / 0.4762 / 3568527.9 / 778 / &
    183.27 / 550.5 / 1.309 / .1402000000

;TDE Aly-Lee ideal gas Cp
; "Heat capacity (Ideal gas)"

PROP-DATA CPIALE-1
  IN-UNITS MET MOLE-HEAT-CA='J/kmol-K' PRESSURE=bar &
    TEMPERATURE=K DELTA-T=C PDROP=bar INVERSE-PRES='1/bar'
  PROP-LIST CPIALEE
  PVAL SEP36 85471.03 469447.8 -1120.756 256582.5 500.4814 &
    0 8.31447 200 1000

PROP-DATA CPIG-1
  IN-UNITS MET
  PROP-LIST CPIG
  PVAL SEP36 -10.74543804 .2424118659 -1.7108054E-4 &
    4.82946403E-8 0.0 0.0 280.0000000 1100.000000 &
    8.605426579 7.72030333E-3 1.500000000

;TDE Watson equation for heat of vaporization
; "Enthalpy of vaporization or sublimation (Liquid vs. Gas)"

PROP-DATA DHVLTD-1
  IN-UNITS MET PRESSURE=bar TEMPERATURE=K DELTA-T=C &
    MOLE-ENTHALP='J/kmol' PDROP=bar INVERSE-PRES='1/bar'
  PROP-LIST DHVLTDEW
  PVAL SEP36 18.4679 0.5461876 0.1617902 -0.2728796 778 4 &
    255 778

;TDE expansion for liquid molar density

; "Density (Liquid vs. Gas)"

PROP-DATA DNLEXS-1
   IN-UNITS MET PRESSURE=bar TEMPERATURE=K DELTA-T=C &
      MOLE-DENSITY='kmol/cum' PDROP=bar INVERSE-PRES='1/bar'
   PROP-LIST DNLEXSAT
   PVAL SEP36 2.100053 4.778674 1.464926 0.1756092 &
      -0.07657542 0 0 778 6 240 778

;ThermoML polynomials for liquid thermal conductivity
; "Thermal conductivity (Liquid vs. Gas)"

PROP-DATA KLTMLP-1
   IN-UNITS MET PRESSURE=bar TEMPERATURE=K &
      THERMAL-COND='Watt/m-K' DELTA-T=C PDROP=bar &
      INVERSE-PRES='1/bar'
   PROP-LIST KLTMLPO
   PVAL SEP36 0.2156676 -0.000222956 0.000000256662 &
      -2.877521E-10 4 200 700

;ThermoML polynomials for vapor thermal conductivity
; "Thermal conductivity (Gas)"

PROP-DATA KVTMLP-1
   IN-UNITS MET PRESSURE=bar TEMPERATURE=K &
      THERMAL-COND='Watt/m-K' DELTA-T=C PDROP=bar &
      INVERSE-PRES='1/bar'
   PROP-LIST KVTMLPO
   PVAL SEP36 -0.004558092 0.00001715581 0.0000000823644 &
      -3.56068E-11 4 560 1160

;PPDS9 equation for liquid viscosity
; "Viscosity (Liquid vs. Gas)"

PROP-DATA MULPPD-1
   IN-UNITS MET PRESSURE=bar TEMPERATURE=K VISCOSITY='N-sec/sqm' &
      DELTA-T=C PDROP=bar INVERSE-PRES='1/bar'
   PROP-LIST MULPPDS9
   PVAL SEP36 0.00002578544 1.971326 2.013121 925.5743 &
      -25.46359 296 770

;ThermoML polynomials for vapor viscosity

; "Viscosity (Gas)"

PROP-DATA MUVTML-1
    IN-UNITS MET PRESSURE=bar TEMPERATURE=K VISCOSITY='N-sec/sqm' &
        DELTA-T=C PDROP=bar INVERSE-PRES='1/bar'
    PROP-LIST MUVTMLPO
    PVAL SEP36 -0.000000796883 0.0000000238910 -1.501594E-12 &
        -6.475801E-16 4 560 1160

PROP-DATA SIGDIP-1
    IN-UNITS MET
    PROP-LIST SIGDIP
    PVAL SEP36 86.10518210 1.222222220 1.28658805E-9 &
        -1.4446487E-9 5.7385765E-10 550.5000000 762.4400000

;TDE Wagner 25 liquid vapor pressure
; "Vapor pressure (Liquid vs. Gas)"

PROP-DATA WAGN25-1
    IN-UNITS MET PRESSURE='N/sqm' TEMPERATURE=K DELTA-T=C &
        PDROP=bar INVERSE-PRES='1/bar'
    PROP-LIST WAGNER25
    PVAL SEP36 -9.252672 2.853329 -5.430383 -4.391381 15.08766 &
        778 240 778

PROP-SET PS-1 RHO UNITS='kg/cum' SUBSTREAM=MIXED COMPS=SEP36 &
        PHASE=L

STREAM FEED1
    SUBSTREAM MIXED TEMP=25. <C> PRES=1. FREE-WATER=NO NPHASE=1 &
        PHASE=L
    MASS-FLOW WATER 0.017 / MTBE 0.0222 / SEP36 0.005498

STREAM FEED2
    SUBSTREAM MIXED TEMP=25. <C> PRES=1.
    MASS-FLOW MTBE 0.015

STREAM FEED3
    SUBSTREAM MIXED TEMP=25. <C> PRES=1.
    MASS-FLOW MTBE 0.011

BLOCK B1 MIXER
    PARAM PRES=1. NPHASE=1 PHASE=L T-EST=25. <C>
    BLOCK-OPTION FREE-WATER=NO

BLOCK WASH1 DECANTER
  PARAM TEMP=25. <C> PRES=1. LL-METH=GIBBS L2-COMPS=SEP36 MTBE

BLOCK WASH2 DECANTER
  PARAM TEMP=25. <C> PRES=1. LL-METH=GIBBS L2-COMPS=MTBE SEP36 &
    L2-CUTOFF=0.3

BLOCK WASH3 DECANTER
  PARAM TEMP=25. <C> PRES=1. LL-METH=GIBBS L2-COMPS=MTBE SEP36 &
    L2-CUTOFF=0.3

EO-CONV-OPTI

STREAM-REPOR MOLEFLOW MASSFLOW STDVOLFLOW

PROPERTY-REP PCES NOPROP-DATA NODFMS

PROP-TABLE PURE-1 PROPS
  IN-UNITS MET TEMPERATURE=C
  MOLE-FLOW SEP36 1
  PROPERTIES UNIFAC FREE-WATER=STEAM-TA SOLU-WATER=3 &
    TRUE-COMPS=YES
  VARY TEMP
  RANGE LOWER=15. UPPER=40. NPOINT= 49
  VARY PRES
  RANGE LIST=1.000000000
  PARAM
  TABULATE PROPERTIES=PS-1