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Recovery of Valuable Solvents from the Pharmaceutical Industry Wastewater

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The circular economy focuses on making the highest use of any molecule before being discarded. Compounds diluted in waste aqueous streams are usually eliminated instead of being recovered. When the separation process is not efficient enough, the energy consumed does not compensate the material recovered. The wastewater stream with diluted isopropanol and ethyl acetate from the pharmaceutical industry is an example of this situation, e.g., from the production of the antibiotic called ampicillin sodium. Pollution caused during ampicillin sodium production is due to the wastewater generated containing Ethyl Acetate (ETAC) and Isopropyl Alcohol (IPOH). In the literature, novel chemical processes have been proposed to recover these valuable compounds but require a third compound used as an extractive agent. Any third compound added to the mixture remains there and its presence in traces is unavoidable. The impurification of these solvents is a major issue for the pharmaceutical industry. In this study, a novel process is proposed that avoids the addition of an extractive agent. This type of wastewater has only 3 % of solvents and the ratio of isopropanol versus ethyl acetate in the feed is 5:1. Volatile solvents would be easily recovered from an ideal mixture; at least to reach a wastewater with 1 % solvents content. Unfortunately, there are four azeotropes present in the system studied and the separation is not straightforward. However, taking advantage of water / ethyl acetate immiscibility region and properly recycling and mixing process streams, then the mixture separation is possible employing only three distillation columns and a decanter. The process has been rigorously simulated and its feasibility proven. The environmental impact of the various alternatives proposed has been assessed using Waste Reduction Algorithm Software V.1.0 (WAR). Ethyl acetate and isopropanol can be separated from water without extracting agents, possibility proven using residue curve maps. The study shows that diluted wastewater streams are a suitable source of chemicals.

1. Introduction

Ampicillin sodium is a semi-synthetic antibiotic widely used in daily life because of its broad antibacterial spectrum, low toxicity, high efficiency, and low price, favouring the market prospects (Peizhe et al. 2020). Pollution caused during ampicillin sodium production is due to the wastewater generated containing Ethyl Acetate (ETAC) and Isopropyl Alcohol (IPOH). Xingyi et al. (2021) suggest that separating these compounds and their recirculation reduces pollution and production costs. Because of its ease of operation and control, distillation is the most common unit for separating liquid mixtures. The distillation process is now responsible for approximately 95 % of all liquid separations. Conventional distillation fails to produce rich phase volatility for systems with similar boiling points and azeotropes despite these benefits. As a result, the separation if azeotropic systems is not straightforward.

The mixture of isopropanol, ethyl acetate and water form a ternary azeotrope. This fact causes the separation to be complicated if a high purity is needed when using conventional distillation, therefore the necessity to break this azeotrope. Hanwen et al. (2020) suggested the possibility to recover these compounds with the aid of extractive agents such as dimethyl sulfoxide (DMSO) or ethylene glycol (EG). But because ETAC and IPOH are used in the pharmaceutical industry, it is crucial to work without any additional compounds to avoid their traces

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in the final pharmaceutical products. This study focuses on taking advantage of the existence of an immiscibility region that allows separation to occur without using extracting agents. The limitation of the previous research is due to the assumption that this separation cannot be performed without adding a third compound to the mixture. Infinite/Infinite analysis is used to propose novel feasible processes and DSE method to check their efficiency. In this way, a novel process, without using any extractive agent is proposed and it could compete with the process proposed in the literature.

1.1 Feasibility analysis

Compounds physical properties list contained in the system are shown in Table 1. The three main compounds have a similar boiling point, which implies that an azeotropic distillation is required. Because the azeotrope cannot be broken by distillation, enhanced distillation methods are required. As far as extractive distillation is concerned, it is not an appropriate method because adding a third compound to the mixture leaves traces. Residue curve maps (RCM) are useful to propose alternative processes to break up the azeotrope without requiring extracting agents. Exploiting the immiscibility zone of ETAC and water, different viable processes are suggested in Results section. The RCM of the three compounds is shown in Figure 1. There are three differentiated distillation regions. Temperature marks indicate where each azeotrope is located and its temperature.

Table 1: Physical properties of compounds at 1 atmosphere

Compound	Boling point (K)	Critical point (K)	Molar mass (g/mol)
Water	373.2	647.1	18.01
ETAC	350.2	530.0	88.11
IPOH	355.6	508.7	60.06

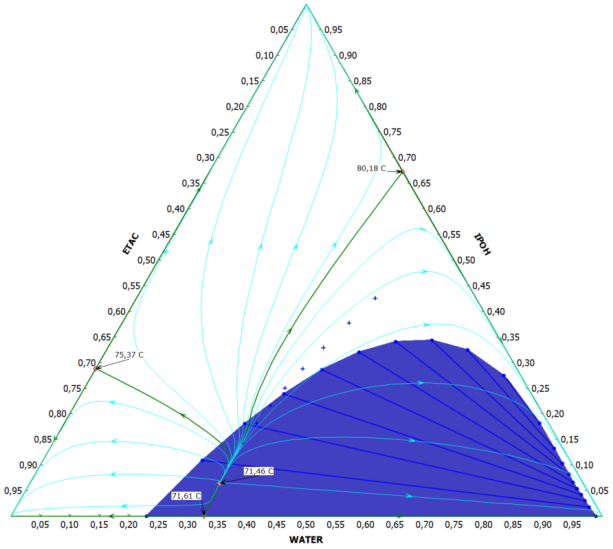

Figure 1: Residue curve map at atmospheric pressure

Four azeotropes are present at atmospheric pressure: one ternary and three binaries. The ternary azeotropic composition is sensitive to pressure but does not disappear from the system. Therefore, for sake of operational simplicity, atmospheric pressure is assumed. Table 2 provides the azeotropes characteristics of the system.

Table 2: Azeotropes at atmospheric pressure.

Temperature (K)	Phase split	Classification	Components	Water	ETAC	IPOH
353.33	Homogeneous	Saddle	2	0.327	-	0.673
348.33	Homogeneous	Saddle	2	-	0.288	0.712
344.76	Heterogeneous	Saddle	2	0.327	0.673	-
344.61	Heterogeneous	Unstable node	3	0.321	0.314	0.065

2. Method

The methodology consists of several steps: proposal of feasible processes, screening according to their efficiency and final screening according to their environmental impact (Figure 2). Infinite/Infinite analysis is widely used to propose feasible novel processes requiring only basic thermodynamic data, visualized using the residue curve maps. Furthermore, when applying the Distillation Sequence Efficiency (DSE) method, an efficiency of each process proposed can be assessed. However, DSE based on ∞/∞ analysis implies infinite investment (infinite number of stages) and operating costs (infinite reflux flow rate). Therefore, Plesu et al. (2015) proposed a DSE equation, where the distillation columns are hypothesized to be Carnot engines. The DSE equation calculates the overall efficiency of a distillation sequence (Eq(1)).

$$DSE = \sum_{i} \frac{W_i}{F_c} \cdot \prod_{C} \eta_{ic} \tag{1}$$

where W_i is the stream "i" depending on the feed, F_c the flow of crude feed and η_{ic} is the Carnot efficiency of the column. Carnot efficiency can be calculated by using Eq(2), with the corresponding bottom and distillate temperatures.

$$\eta_{ic} = \frac{T_B - T_D}{T_B} \tag{2}$$

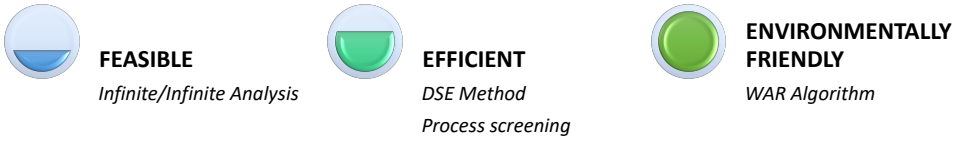

Figure 2: Methodology procedure

The distillate and bottom temperatures are obtained from a shortcut simulation with SEPs (Aspen, 2021). Based on the ternary system of Zhang et al. (2020), who conducted thermodynamic experiments and proposed the NRTL thermodynamic model. The environmental impact of the various alternatives proposed has been assessed using Waste Reduction Algorithm Software V.1.0 (WAR, 2021). This software can be used to calculate various environmental impact parameters such as global warming or aquatic toxicity, among others. The environmental effect of different sources of fuel will be analysed. Environmental parameters are obtained with flow rates and mass composition of the compounds of the inlets and outlets of the system.

3. Proposal from the literature

Hanwen et al. (2020) researched a possible sequence for separating the ternary azeotrope mixture of ethyl acetate, isopropyl alcohol, and water. The main goal is to acquire the above compounds with the highest purity possible. The crude feed with a flow rate of 20 t/h contains a large amount of water, i.e., 90 %, and a prefractionation column is required to eliminate most of it. The distillate collected from this prefractionation column is separated into pure compounds using extractive distillations due to the azeotropes present. DMSO is used as extractive agent with a flow rate of 10 t/h. The DMSO flowrate bifurcates to two extractive distillation columns: in the first, the ethyl acetate is recovered and in the second the isopropanol. DMSO is separated from water in a third column. The process is operated at vacuum: prefractionation column at 0.25 atm, first extractive distillation column at 0.4 atm, second extractive distillation column at 0.15 atm and the third extractive distillation column at 0.12 atm.

After performing the mass balances and SEPs simulation, the Carnot efficiencies of each column are calculated according to Eq(2) and are shown in Table 3. The DSE is determined by using all the required information. Eq(3) contains the expression for calculating DSE for this particular configuration (Bonet et al, 2017). Applying this equation, a DSE value of 0.954 is obtained, which indicates that the system proposed in the literature has already a high energy efficiency.

Table 3: Literature distillation columns efficiencies.

Column	T_B (K)	T_D (K)	η
T1	372.8	349.8	0.062
T2	377.9	350.0	0.074
T3	443.9	354.9	0.201
T4	463.4	371.8	0.198

$$DSE = \frac{B_1 + D_2 \cdot \eta_1 \cdot \eta_2 + D_3 \cdot \eta_1 \cdot \eta_3 + D_4 \cdot \eta_1 \cdot \eta_4}{F_C} \quad (3)$$

4. Results and discussion

In this paper, 3 alternatives to the Hanwen et al. (2020) sequence have been proposed using RCMs information. Figure 3 shows the RCM and the scheme of the first alternative, which consists in one decanter and three distillation columns. The decanter, the primary process in this setup, is directly connected to the crude feed. The decanter is provided by the D3, Rec, and D1 streams in addition to feed and generates two streams: aqueous and organic streams.

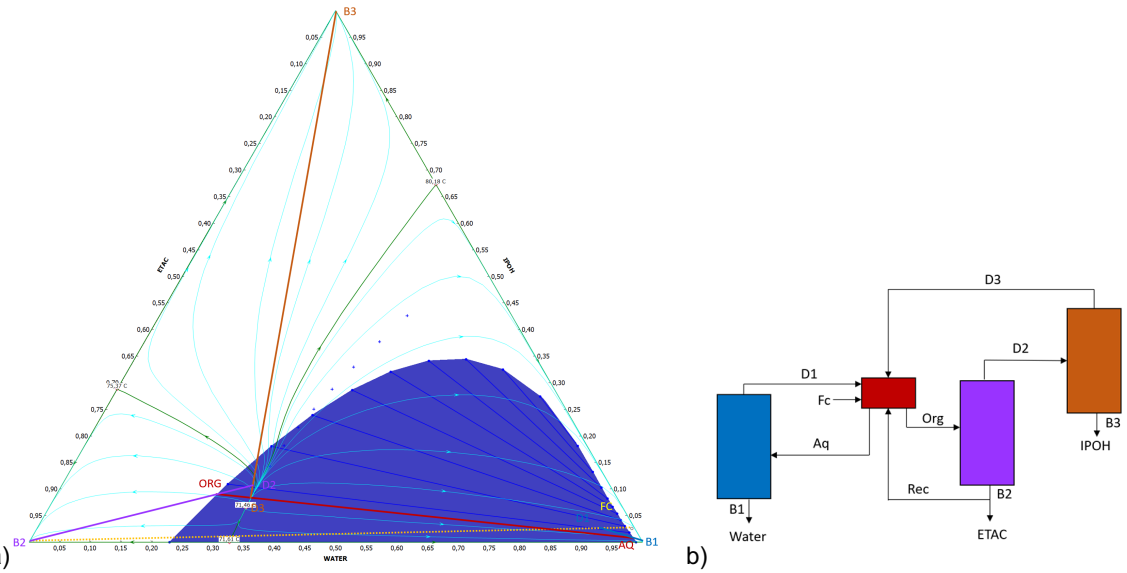

Figure 3: 3a: Alternative 1 residue curve map proposal and 3b: scheme of Alternative 1.

First, Aq feeds column 1 directly. On one hand, pure water is separated (from the bottom) in this column, and a mixture of water and IPOH is recirculated to the decanter (from the distillate). The organic stream, on either side, feeds column 2. ETAC is collected at the bottom in this column. The B2 stream splits into two streams, one of which goes back to the decanter, and the other gets pure ETAC. Column 3 is fed with a mixture of water and IPOH obtained from the distillate. Pure IPOH is obtained in column 3 and a ternary azeotropic composition is recirculated to the decanter. Once the RCM has been performed, and the feasibility of the process has been verified, a rigorous simulation is carried out. Figure 4 shows the RCM and the scheme of the second alternative. The ternary azeotropic composition corresponds to the distillate in column 2. At the same time, the composition of the binary azeotrope formed by water – isopropyl alcohol is roughly the same. As the binary azeotrope cannot be eliminated directly, column 4 (straight green line) must be used to achieve pure IPOH. This column distillate is combined with crude feed to feed column 1. Figure 5 shows the RCM and the scheme of the third alternative. The system consists of 3 distillation columns, which provide the pure compounds, and 1 decanter. The feed of the column consists of crude feed mixed with the aqueous stream. Pure water is obtained from the bottom of the column and a ternary mixture from the distillate. The IPOH is obtained in column 2 that it is fed with a mix of the distillate 1 and a fraction of organic stream and with the distillate 3. Pure ETAC is collected at Column 3 bottom. All the efficiencies and the necessary number of equipments are summarized in Table 6.

As a result, in terms of efficiency and necessary equipment numbers, Alternative 3 is the most appealing option in the second position after the literature process. The feasibility of all three alternatives has been verified using rigorous simulations, i.e. RADFRAC distillation columns.

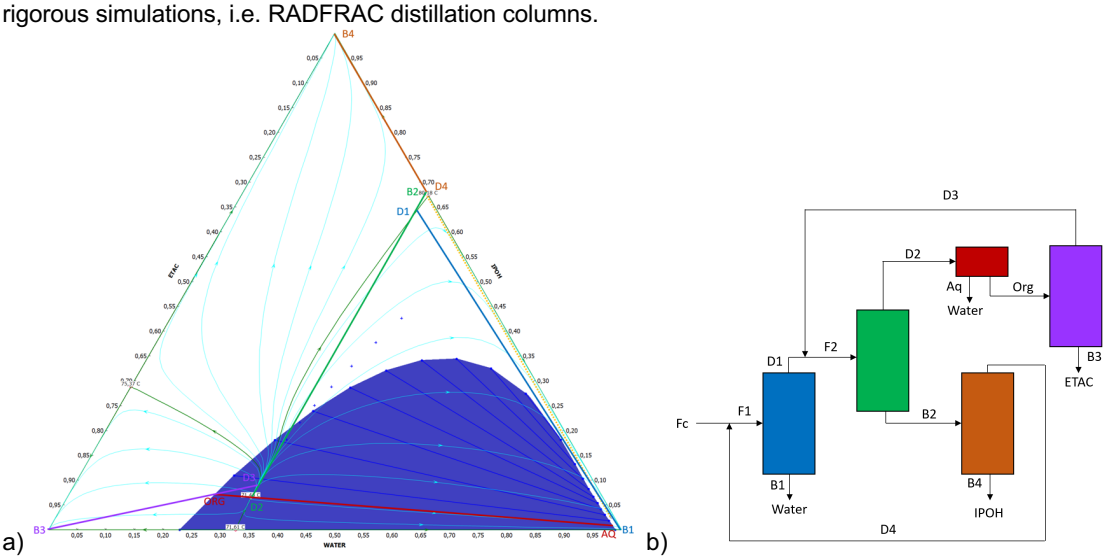

Figure 4: 4a: Alternative 2 residue curve map proposal and 4b: scheme of Alternative 2

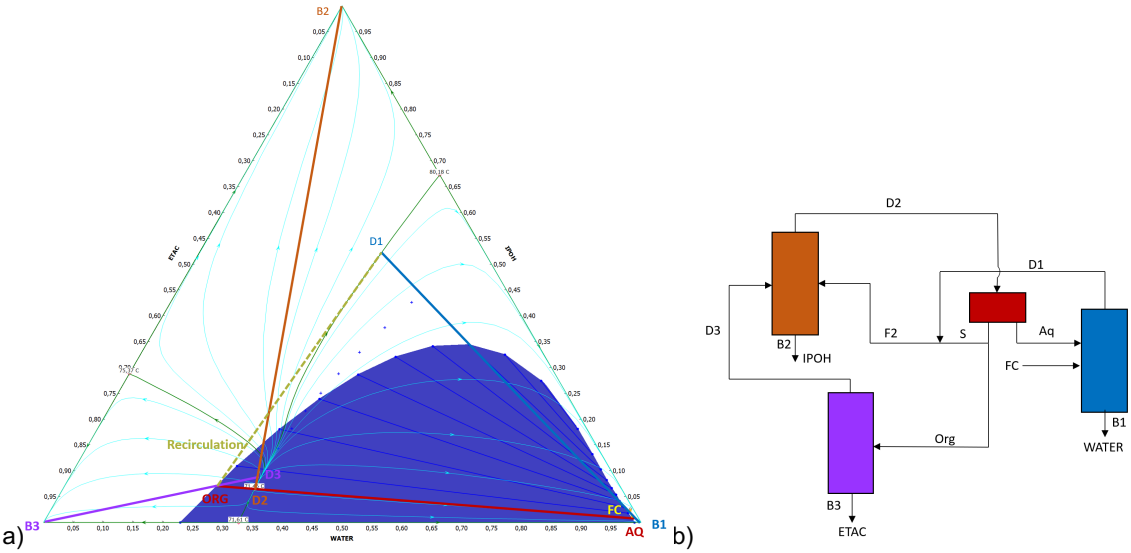

Figure 5: 5a: Alternative 3 residue curve map proposal and 5b: scheme of Alternative 3

Table 6: Summary of process characteristics

Process	DSE	Extractor agent	Number of columns	Number of decanters
Literature	0.954	DMSO/EG	4	0
Alternative 1	0.179	Not required	3	1
Alternative 2	-0.292	Not required	4	1
Alternative 3	0.929	Not required	3	1

Although the processes are not optimized, a first insight of the energy consumption and environmental impact is obtained. The energy consumption of all three alternatives is around 200, 300 and 15 MW respectively. The results obtained applying the WAR algorithm highlight that most of the environmental impact of the process is due to their Acidification Potential and in a lower measure by the Global Warming Potential and Aquatic Toxicity Potential. The Potential Environmental Impacts using gas as fuel for each alternative in PEI/h are respectively

792, 1,270 and 79. Therefore, the third alternative has clearly a lower energy consumption and environmental impact and therefore it is selected for further optimization of the process. The number of distillation units of the proposed process is lower than of the process proposed in the literature, i.e. 3 instead of 4, but the energy consumption is around 15 MW, which is much higher than the optimized 8 MW of the efficient process proposed in the literature by Hanwen et al. (2020). However, the novel process has the advantage that no extracting agents are used, which is significant since these compounds will be reused in the pharmaceutical industry.

5. Conclusions

This study proves, using residue curve maps, that ethyl acetate and isopropanol can be separated from water without extracting agents. This is critical since these compounds will be used in the pharmaceutical industry where the presence of third compounds to the system is not desirable. Three alternatives have been assessed and alternative 3 showed the highest efficiency among the assessed alternatives, but a bit lower than the one proposed in the literature. Comparing the novel process with the literature, in both cases the crude feed is introduced in a first prefractionation column where most of the water present is eliminated by the column bottoms. The main difference is that the literature process uses extractive distillation columns with DMSO to recover the remaining compounds and the proposed process takes advantage of the phase split between water and ethyl acetate. In the literature, a distillation column is required to separate the water from the extractive agent and in the proposed process this column is not required; all the water is recycled and recovered at the prefractionation column bottoms.

Future studies include the optimization of the rigorously simulated process for an accurate comparison between the novel process and the process in the literature. However, the first results prove that the use of a third compound to separate the mixture is not required. Compared to the literature, this alternative is desirable as one distillation column is eliminated, the extracting agent is not necessary, and the efficiency is also maintained quite high. All this together can potentially reduce Total Annual Costs and more importantly, it removes the possibility of leaving possible traces in the separation of the compounds. Additionally, the novel process has clearly the lowest environmental impacts of all the proposals assessed.

Nomenclature

B – Bottom Stream Mole Flow, kmol/h
D – Distillate Stream Mole Flow, kmol/h
ETAC – Ethyl Acetate
F_c – Crude Feed, kmol/h
DMSO – Dimethyl Sulfoxide
DSE – Distillation Sequence Efficiency
IPOH – Isopropyl Alcohol
NRTL – No Random Two Liquids
RCM – Residue Curve Map
T_B – Bottom Temperature, K
T_D – Distillate Temperature, K
WAR – Waste Reduction Algorithm
η_{ic} – Carnot Efficiency

References

Aspen, 2021, <aspentech.com/en/products/engineering/aspen-plus> accessed 12.02.2022.

Bonet J., Parra-Paz A., Bonet Ruiz A.E., Plesu V., Iancu P., Llorens J., 2017, Distillation Sequence Efficiency (DSE) Applied to Trains of Columns with Recycle Streams, Computer Aided Chemical Engineering, 40, 751 – 756.

Hanwen G., Fangxu F., Guanrong S., Xiao–Hong W., 2020, Recovery of organic matter from pharmaceutical wastewater by energy – saving complex distillation column. Separation Science and Technology, 56, 1910 – 1932.

Peizhe C., Fei Z., Dong Y., Zhaoyuan M., Shuhua L., Xin L., Lei W., Zhaoyou Z., Yinglong W., Yixin M., Dongmei Xu, 2020, Energy-Saving Exploration of Mixed Solvent Extractive Distillation Combined with Thermal Coupling or Heat Pump Technology for the Separation of an Azeotrope Containing Low-Carbon Alcohol. Industrial & Engineering Chemistry Research, 59, 13204 – 13219.

Pleşu V., Bonet Ruiz A.E., Bonet J., Llorens J., Iancu P., 2015, Shortcut assessment of alternative distillation sequence schemes for process intensification, Computers & Chemical Engineering, 83, 58-71.

Xingyi L., Peizhe C., Fei Z., Yuanyuan S., Shuhua L., Dapeng M., Zhaoyou Z., Yixin M., Yinglong W., 2021, Sustainable wastewater treatment via PV-distillation hybrid process for the separation of ethyl acetate/isopropanol/water. Separation and Purification Technology, 257, 117 – 919.

WAR, 2021, <epa.gov/chemical-research/waste-reduction-algorithm-chemical-process-simulation-waste-reduction> accessed 14.05.2021.

Zhang Y., Xin X., Yang H., Gao J., Dongmei X., Zhang L., Wang Y., 2020, Separation of Azeotropic Mixture Isopropyl Alcohol and Ethyl Acetate: Vapor – Liquid Equilibrium Measurements and Interaction Exploration. Fluid Phase Equilibria, 507, 1 – 8.