



Solvent Regeneration in Complex Mixture Using Pervaporation

Morgane Le Hir, Adrien Magne, Thomas Clair, Emilie Carretier, Philippe Moulin

► To cite this version:

Morgane Le Hir, Adrien Magne, Thomas Clair, Emilie Carretier, Philippe Moulin. Solvent Regeneration in Complex Mixture Using Pervaporation. *Organic Process Research and Development*, 2021, 25 (3), pp.469-485. 10.1021/acs.oprd.0c00442 . hal-03597582

HAL Id: hal-03597582

<https://hal.science/hal-03597582>

Submitted on 4 Mar 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Solvent Regeneration in Complex Mixture Using Pervaporation

Morgane Le Hir,* Adrien Magne, Thomas Clair, Emilie Carretier, and Philippe Moulin

ABSTRACT: This study aims to demonstrate the efficiency of dichloromethane (DCM) regeneration from a methanolic effluent by a combination of distillation and membrane pervaporation process. The presence of an azeotrope (MeOH/DCM/water) makes the regeneration of DCM via distillation alone impossible. A process simulation using ProSim software was carried out in order to evaluate the behavior of the azeotropic mixture. Two secondary treatments aiming to purify the DCM contained in the azeotrope were investigated. The first is the washing of the azeotrope with water. ProSim software was used to target the optimal conditions for washing before the experimental test. Residual water was recovered in the organic phase, meaning that the quality specifications for DCM were not reached. The second process studied for DCM purification was a pervaporation step. The feasibility of this had been proven at laboratory scale. The recovered DCM had the quality of a new solvent, and the whole process (distillation + pervaporation) reached a global DCM regeneration yield of 71.8% before optimization. This yield was limited by the distillation of methylal (also called dimethoxymethane) present in the methanolic effluent at the end of the distillation of the azeotrope, a compound retained by the pervaporation membrane. The pervaporation was performed on a hydrophilic Hybsi membrane letting methanol and water pass through and retaining the DCM (membrane surface = 0.15 m²). Optimization and scaling up were then carried out with a semi-industrial pervaporation pilot (membrane surface = 1.05 m²) which enabled the industrial scale-up. In order to facilitate the steering of the process and to ensure continuous and efficient monitoring of the regeneration operation, online monitoring by near-infrared probe (NIR) had been implemented allowing the composition of the mixture to be determined with an accuracy of $\pm 0.05\%$ on each compound. Finally, an assessment had been conducted of the regeneration pathways for methanol recovery at the bottom of the distillation column, for maximizing the regeneration of methanolic effluents by separating heavy compounds and methylal from methanol.

KEYWORDS: *solvents regeneration, azeotrope, distillation, pervaporation, NIR*

1. INTRODUCTION

Solvents are defined as a set of various chemicals whose essential characteristics are high solubilizing power and high volatility. These characteristics make them essential in the chemical and pharmaceutical industries, as in many industrial sectors, justifying a worldwide production of solvents other than water in 2012 of 28 million tons. Since the 90s, the use of solvents has been continuously discussed due to new constraints applied in terms of risk prevention but also in relation to the establishment of stricter regulations in terms of environmental protection. Thus, the total consumption of new solvents in France has gone down by 8.5% in ten years¹ (600,000 t·year⁻¹ in the 90s vs 550,000 t·year⁻¹ in the 2000s), with a corresponding move toward less dangerous or harmful solvents. Oxygenated solvents (alcohols, esters, ketones, ethers, glycol ethers) and hydrocarbons (petroleum and aromatic solvents) have been found to be preferable to halogenated solvents (chlorinated, fluorinated, brominated), which present high toxicities for humans and the environment^{1,2} as shown in Figure 1.

Dichloromethane (DCM), which is a volatile halogenated organic compound, is mainly used in Europe industrially as an extraction or synthesis solvent in the pharmaceutical industry.³ DCM is insoluble in water and miscible with most organic solvents. Its volatile characteristic and its ability to dissolve

many organic compounds make DCM an ideal solvent for many chemical processes. However, DCM is toxic, and it is classified as carcinogenic, mutagenic, and reprotoxic. Potential substitutes exist, but they are often dedicated to a specific use and appear to be frequently more expensive than DCM.³ Likewise, methanol is extensively used in the pharmaceutical industry due to its capacity to dissolve a larger number of plastics and mineral salts than ethanol and for its high reaction capacity. Just as for DCM, the toxicity of methanol is proven.⁴ In order to limit toxic solvent consumption, a great deal of research effort has been channeled in recent years into direct chemical syntheses for seeking greener solvents.^{5–8} With regard to the pharmaceutical industry, it can be difficult to replace some solvents with less toxic compounds without impacting the molecule or the chemistry of the process. This explains why the pharmaceutical industry is still using a high quantity and variety of organic solvents or volatile organic compounds (VOCs), although it does try to limit their

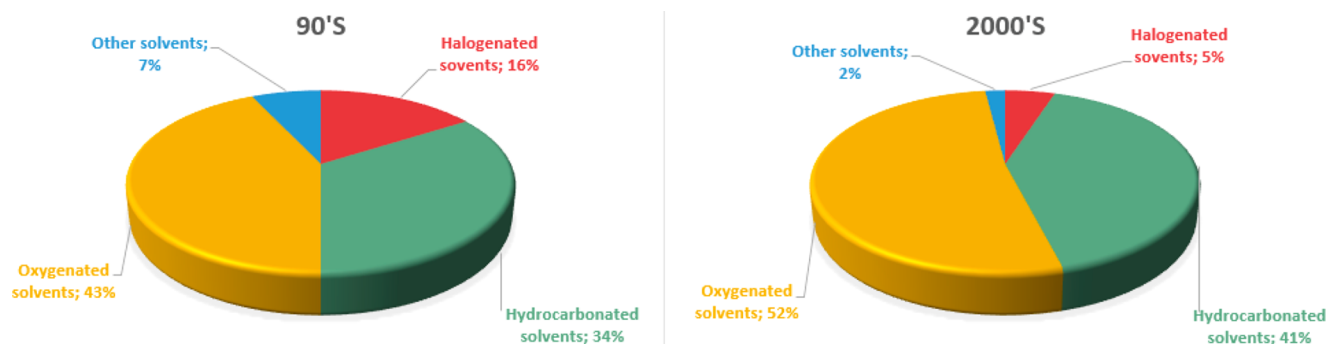


Figure 1. Solvent consumption in France during the 90s and 2000s¹

discharge and aims to develop their regeneration.⁹ The use of these organic solvents in making pharmaceutical products inevitably leads to a discharge of used solvents in complex mixtures with other solvents and/or heavy chemical compounds and byproducts. Thus, the effluents of pharmaceutical processes present some treatment issues due to the possible azeotropic mixtures formed, to the fact that the bacteria in the conventional activated sludge process are not able to convert all the substances into their nutrition, and to the fact that biological treatment is generally not authorized.^{10,11} Thus, it is necessary to implement strategies in order to minimize the generated waste and/or to consider solutions for the reuse and recycling of effluents, and it is important to note that, in the pharmaceutical industry, the targeted recycled solvents must meet very high quality requirements for reuse. Both these objectives demonstrate that solvent regeneration is a strategic issue in the pharmaceutical industry. Indeed, reuse and recycling represent a major challenge from the environmental and economic points of view, when it comes to limiting the management and destruction costs. Moreover, the very large tonnages (≈ 28 Mt/year) of solvents used by industries worldwide have led to the implementation of stricter monitoring requirements—registration, evaluation, authorization, and restriction of chemicals (REACH)—in order to improve the protection of human health and environmental performance while maintaining competitiveness.¹² These new regulations also aim to reinforce innovation in the European chemical industry. Various types of solvent recovery systems are proposed, such as distillation, liquid–liquid extraction, chemical extraction, absorption systems, film evaporation, crystallization, or membrane separation.^{8,13} As shown by Seyler et al.,⁹ only a few treatment processes are used on a large scale, such as incineration or distillation for solvent recovery. Waste solvents management is strongly influenced by such boundary conditions as costs, logistics, legislation and guidelines, storage capacity, safety considerations, and the existing technologies on the production site. Moreover, the complexity of the mixture to be treated significantly affects the regeneration feasibility and implementation. As mentioned previously, pharmaceutical effluents often have a more complex composition (azeotropic mixtures, presence of byproducts, salts, heavy compounds, etc.), meaning that treatment needs to be conceived with a combination of several processes. For example, Pandey et al.¹⁴ developed a solvent regeneration process with a system integrating different liquid–vapor separation units such as dehydration column, agitated thin film evaporator, and vacuum-distillation column. Nemeth et al.¹⁵ present their study on the use of two distillation columns

in order to regenerate solvent with high purity and productivity. As mentioned by Tóth et al.,¹⁰ the main physical–chemical treatment method used for pharmaceutical wastewater is distillation. This enables the organic impurities to be extracted, the pollutants to be concentrated at the bottom, and the distilled material to be reused, for generally reasonable investment costs. The main drawbacks are the difficulty to separate solvents with similar boiling points and the impossibility to separate compounds from azeotropic mixtures. The use of a separation process not based on boiling temperature, such as pervaporation, allows these limitations to be overcome or a distillation step to be completed. Pervaporation is a process that splits liquid mixtures by partially vaporizing them through a dense membrane. The separation is based on the solubility and diffusivity differences of various compounds passing through the membrane. The use of hydrophilic membranes allowing the dehydration of solvents, mainly alcohols, has been studied extensively.^{16–21} Slater et al.²² studied the integration of a pervaporation membrane with a constant-volume distillation process in order to limit solvent consumption. In this study, an oncology drug is in solution in a tetrahydrofuran (THF)/water mixture. During the synthesis, the water content has to be reduced by distillation but the THF–water mixture has an azeotrope at 95.7% THF (at standard temperature and pressure). In order to limit THF consumption, a pervaporation step on poly(vinyl alcohol) (PVA) composite membranes has been added to purify the distilled azeotrope and to reuse the dehydrated THF in the synthesis of the active pharmaceutical ingredient (API). The purification of pharmaceutical solvents by pervaporation through hybrid silica membranes has been studied by La Rocca et al.²³ They studied dehydration and purification of solvents from binary or multisolute mixtures composed of water, acetone, MeOH, DCM, methyl ethyl ketone (MEK), and/or toluene. Results showed that increasing the temperature could improve process efficiency. The separation of components is also greatly impacted by the composition of the feed mixture. The adding of a component may lead to a drop in purification of the solvent in question. These observations imply that the more the mixture treated by pervaporation is simplified, the more efficient and rapid its purification will be. With this objective in mind, in addition to the separation of an azeotropic mixture not based on boiling point, a combination of distillation and pervaporation may be envisaged to increase the pervaporation step efficiency. Several studies detail the optimization of azeotropic distillation through its combination with a pervaporation process. The use of hybrid distillation/pervaporation systems allows technological barriers to be

overcome, by simplifying the separation of a nonideal mixture²⁴ and improving the purity in the top and/or bottom products during distillation,^{25,26} all with real economic benefits.²⁷

In this work, the treatment of an industrial effluent from the pharmaceutical industry has been studied. The aim is to recover and reuse solvents to limit the environmental impacts and global production/treatment costs. The effluent considered is principally composed of MeOH, DCM, water, and methylal. Interactions between these compounds are numerous and form a complex azeotropic mixture.^{28–31} Thus, the distillation of this flux leads to the recovering of an azeotrope at the distillate. The regeneration of the DCM by a single distillation step is therefore impossible. First, a process simulation approach using ProSim software³² was carried out in order to evaluate the feasibility of the regeneration with regard to the operating conditions applied during the distillation (pressure, reflux rate, number of theoretical stages, etc.). Two secondary treatments aimed at purifying the DCM were investigated. The first is the washing of the azeotrope with water. The use of ProSim software limited the number of laboratory tests by quickly targeting the optimal conditions for washing. The second process studied for the DCM purification was a pervaporation step on a hydrophilic Hybisi membrane. During this purification, water and methanol pass through the membrane while the DCM is retained and concentrated. First, feasibility was proven at a laboratory scale on one multichannel membrane (membrane area = 0.15 m²). Then, a scale-up and operating condition was applied on a semi-industrial pilot (membrane area = 1.05 m²) with synthetic mixtures. Once the operating conditions had been determined, a global purification of the industrial effluent (about 100 L treated) was conducted in the laboratory by combination of continuous distillation and pervaporation of the azeotrope collected at the distillate. The flux recovered at the bottom of the column during continuous distillation was collected and is the subject of an assessment for the regeneration pathways of methanol recovery presented at the end of this paper. In order to facilitate the steering of the process and to ensure continuous and efficient monitoring of the regeneration operation, online monitoring by near-infrared probe (NIR) was implemented. For this, a calibration step was carried out in the laboratory in order to determine the composition of the mixture with an accuracy of $\pm 0.05\%$ on each compound. This calibration could be carried out precisely thanks to the use of an automated installation with LabVIEW, for multiplying the measurement points.

2. MATERIALS AND METHODS

2.1. Industrial Effluent to Be Treated and Quality to Be Attained. The industrial effluent to be treated was a chemical synthesis effluent composed of MeOH, DCM, water, methylal, and a few heavy compounds. The average composition and the characterization tools used are presented in Table 1.

In order to be reused, the regenerated DCM had to meet some quality specifications as presented in Table 2. Gas chromatography was performed on the 6890 Series GC System (Agilent Technologies). The GC was fitted with an Rtx-1301 column (Restek), 30 m \times 0.53 mm ID \times 3 μ m containing 6% cyanopropylphenyl–94% dimethyl polysiloxane. Quantification of different solvents was determined by internal calibration using dioxane as internal standard. Water content

Table 1. Composition of Effluent to Be Treated

	Industrial effluent	Quantification method
MeOH % w/w	42.7%	Gas chromatography (GC) with dioxane as internal standard
DCM % w/w	39.2%	Gas chromatography with dioxane as internal standard
Methylal % w/w	2.8%	Gas chromatography with dioxane as internal standard
Water % w/w	2.6%	Karl Fischer (KF)
Nonvolatile residues	12.7%	Dry extract in a rotavapor
Heavy compounds*		
*Possible presence—Compound not quantified.		

Table 2. DCM Quality Specifications

Identification (GC)	Conforms
Appearance	Clear liquid
Coloration	Degree 7 maximum*
Water % w/v, KF	0.05 maximum
Residue on evaporation % w/v	0.1 maximum
Other impurity % w/v	0.1 maximum
Assay %, GC	99.8 minimum
Refractive Index	Between 1.423 and 1.425

*European Pharmacopoeia Anal. Methods 2.2.2 Degree of coloration of liquids.

measurements were performed on a DL38 Volumetric Karl Fischer Titrator (Mettler Toledo) using Hydranal Working Medium K and Hydranal Composite 5K as reagents.

To confirm the good quality of the DCM, the regenerated solvent will be used in a chemical synthesis at lab scale and the quality of the drug substance will be controlled.

2.2. Online Analysis of Flow Composition. Online analysis by near infrared (NIR) was developed in the laboratory to monitor the solvent mixtures continuously and in real-time. The calibration was conducted in a 3 L stirred reactor equipped with an NIR probe containing initially only DCM (solvent A). A pump monitored by the LabVIEW process regulated the addition of solvent B (pure solvent or solvent mixture). The NIR measurement was performed by spectrophotometry after each addition of solvent B. The spectral area(s) relevant for a compound was (were) fixed progressively to obtain good correlation between spectra variation and composition and to be sure that there were no spectral zone superpositions for the different solvents. Then, a relation between NIR spectra and mixture composition was determined with a mathematical model application illustrating the spectral variation. The data was processed on OPUS 7.5 software (Bruker). Thus, it was possible to determine the composition of the mixture in real time. Calibrations were taken from binary, ternary, and quaternary mixtures with the four compounds (DCM, MeOH, water, methylal) at different temperatures. In order to obtain the composition of the mixture with the highest possible accuracy, two OPUS models were generated from 93% to 100% DCM, which is enough to monitor the azeotrope composition and DCM purification. The first showed an MeOH content from 6%w/w to 0.2% and the second from 0.2% to 0.07%. The root mean square error of cross validation (RMSECV) value was optimized in order to be as low as possible, to ensure high accuracy in measuring the last traces of MeOH. For the second MeOH model (0.2% to 0.007%), the RMSECV is 0.00547.

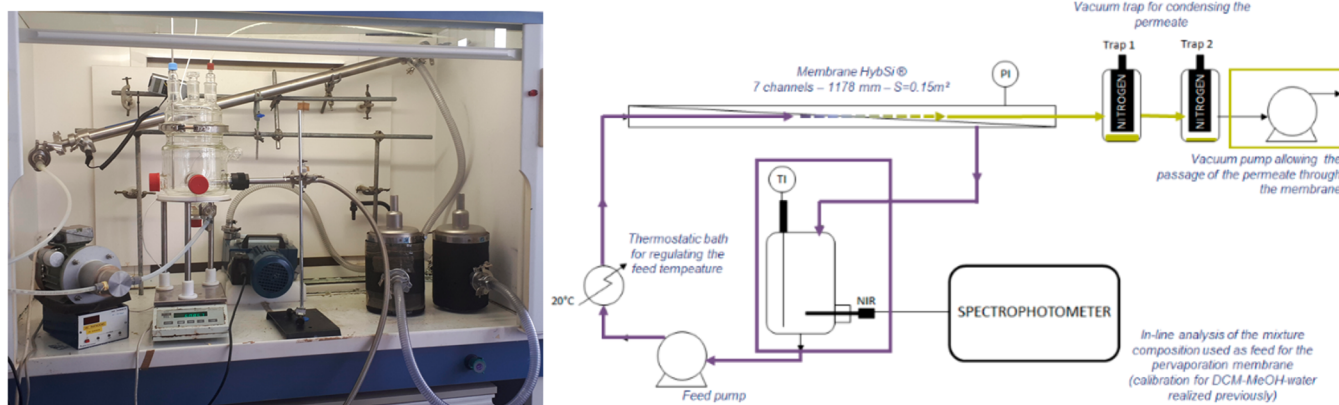


Figure 2. Lab-scale installation to determine the feasibility of DCM purification by pervaporation.

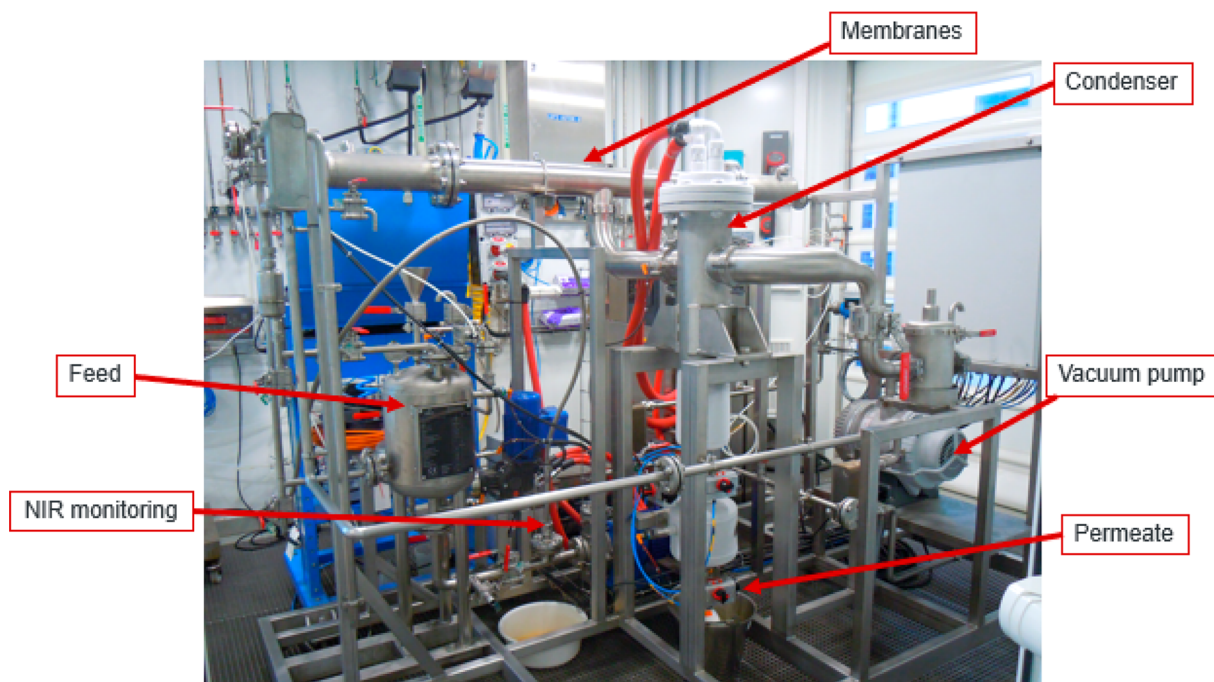


Figure 3. Semipilot installation used for pervaporation of the azeotrope.

2.3. Simulation and Optimization. Simulations made using ProSimPlus software were used initially to evaluate the thermodynamic behavior of the industrial effluent and its distillation. Once the first simulations had been performed, experimental runs were conducted in order to validate the thermodynamic model applied for the simulations. When the experimental results concurred with the simulated results, the optimization step was conducted through simulation. The optimum was then validated via experimental confirmation.

2.4. Distillation. After a simulation step with ProSim, experimentation was performed at the lab. The lab was equipped with a distillation column of 20 theoretical trays. It was automated and driven by LabVIEW and could be run in batch or in continuous mode. In order to validate the thermodynamic model applied in ProSim simulation, batch distillation was conducted using reconstituted fluxes. Once the behavior was validated, distillation with real industrial effluents was conducted before developing toward continuous distillation.

2.5. Water Wash. Initially, ProSim simulations were made to evaluate the influence of the operating temperature and the influence of the ratio of the azeotrope mass/water mass on the recovered DCM quality and yield. The model used for these simulations was the modified UNIFAC (Dortmund) 1993 model which faithfully transcribed the experimental data concerning batch distillation conducted at lab scale. The influence of the temperature and $m_{\text{azeo}}/m_{\text{water}}$ ratio on the DCM purity and yield obtained was evaluated. Once the optimum conditions were determined by the simulation results, experiments on the azeotrope water wash were carried out in a 500 mL thermoregulated reactor. Water with different pH was tested to perform extraction of MeOH from the azeotrope and recover purified DCM.

2.6. Pervaporation. Lab Scale. To perform lab-scale experimentation and determine the feasibility of DCM purification by pervaporation, the installation presented in Figure 2 was implemented. A 3 L reactor was used to load the feed. In this reactor, a NIR probe continuously tracked the evolution of the feed composition and a temperature

Table 3. Binary Interaction Parameters Used for Prosim Simulations

Formulation : $g_{ij} - g_{jj} = C_{ij}0 + C_{ij}T(T - 273.15)$, $a_{ij} = a_{ij}0 + a_{ij}T(T - 273.15)$

Component	Component	Cij0	Cji0	aij0	CijT	CjiT	aijT
DCM	METHYLAL	-702.2	177.7	0.2	1.5	-1.5	0
DCM	MEOH	2362.9	-476.6	0.2	-9.0	2.3	0
DCM	WATER	1949.8	2022.8	0.2	-6.3	4.0	0
DCM	HEAVY*	-63.8	17.3	0.2	-1.8	1.9	0
METHYLAL	MEOH	994.3	-193.2	0.2	-1.2	1.3	0
METHYLAL	WATER	-359.2	1176.0	0.2	-3.4	7.2	0
METHYLAL	HEAVY*	1081.9	-672.5	0.2	-3.7	1.3	0
MEOH	WATER	78.3	66.7	0.2	-5.0	10.7	0
MEOH	HEAVY*	307.2	1394.9	0.2	9.1	-10.9	0
WATER	HEAVY*	5082.0	1790.4	0.2	6.7	-6.5	0

Not provided

Provided

Imported

Estimated

measurement was made. A feed pump (no control of feed flow) was used to send the feed to a thermostatic bath in which the temperature was set at 20 °C to maintain a constant temperature throughout the test. After passing through the thermostatic bath, the feed was sent into the pervaporation membrane (membrane HybSi—7 channels—membrane area = 0.15 m²). The flux that did not pass through the membrane, the retentate, returned to the feed reactor. On the other side of the membrane, a vacuum pump enabled the passage of the permeate through the membrane (pressure ≈ 1.8 mbar). During this passage through the membrane, due to the imposed vacuum, the flow underwent a phase change and turned into vapor. In order to collect the permeate, two vacuum traps regularly filled with nitrogen were used to condense the vapors. Before starting the azeotrope pervaporation, the installation was tested for leaks and a vacuum test was carried out.

Semipilot Scale. To perform semipilot scale experiments for optimizing the operating conditions and projecting onto an industrial scale, a semipilot plant was rented from Orelis—Alsys Group (Salindres, France). The pilot is presented in Figure 3, and its operation is the same as the lab-scale installation, except that the permeate was this time condensed by a condenser with the temperature set to −50 °C. A liquid nitrogen trap provided additional safety condensation upstream of the vacuum pump. Seven membranes could be placed in the module, offering a membrane area of 1.05 m². The feed tank was thermostated, and the temperature could be set from 10 to 120 °C. A nitrogen gas feed enabled work under pressure on the feed side, and the vacuum pump could set a pressure of about 50 mbar on the permeate side. The NIR probe was installed in the feed loop for monitoring the DCM purification throughout the pervaporation process. The permeate was collected by fraction for the duration of the experiment by means of vacuum isolation. The permeate flux was not measured during the pervaporation experiment; however, the NIR analysis of feed composition over the period allowed determination of an average flux for each component in the course of the pervaporation experiments, defined by eq 1:

$$J_x = \frac{m_x}{t_x \cdot A} \quad (1)$$

where J_x is the mass flux of component x (g·min^{−1}·m^{−2}), m_x is the mass of the component x passed through the pervaporation membrane during the purification experiment (g), t_x is the time required for the removal of m_x (min), and A is the membrane area (m²).

Before starting the azeotrope pervaporation, the installation was tested for leaks. A membrane integrity test (with a standard mixture of water/n-butanol) and a vacuum test were carried out. The pressure drop in the module containing the membranes was measured, and varied from 0.1 to 0.2 bar as a function of the circulation flow, which varied between 640 L·h^{−1} and 1170 L·h^{−1}.

Hydrophilic Membrane. The membranes used during this study were hydrophilic hybrid silica membranes (HybSi),³³ purchased from CTI—Alsys Group (Salindres, France). Their structures were composed of several layers of different oxides (Al₂O₃, TiO₂, ZrO₂) and a selective layer of zirconia-doped hybrid silica. The membranes were 7-channel tubular membranes and measured 1.178 m long for an active area of 0.15 m² each.

Separation Factor. The separation factor, denoted $\alpha_{i,j}$, is defined as the mass fraction ratio of the component i (the most permeable to the membrane) compared to the component j in the permeate relative to the mass fraction ratio of the component i compared to the component j in the feed.^{34,35}

Equation 2 shows the relation defining the separation factor:

$$\alpha_{i,j} = \frac{w_i^P / w_j^P}{w_i^F / w_j^F} \quad (2)$$

where $\alpha_{i,j}$ is the separation factor, w_i^P and w_j^F are the mass fractions of the most permeable component respectively in the permeate and in the feed, and w_j^P and w_i^F are the mass fraction of the other component, in the permeate and in the feed, respectively.

The separation factor varies during the pervaporation experiment due to the modification of feed composition over the course of the purification. The pervaporation experiment was stopped once the DCM feeding of the pervaporation (the retentate) reached the quality specification (~99.9%). At this

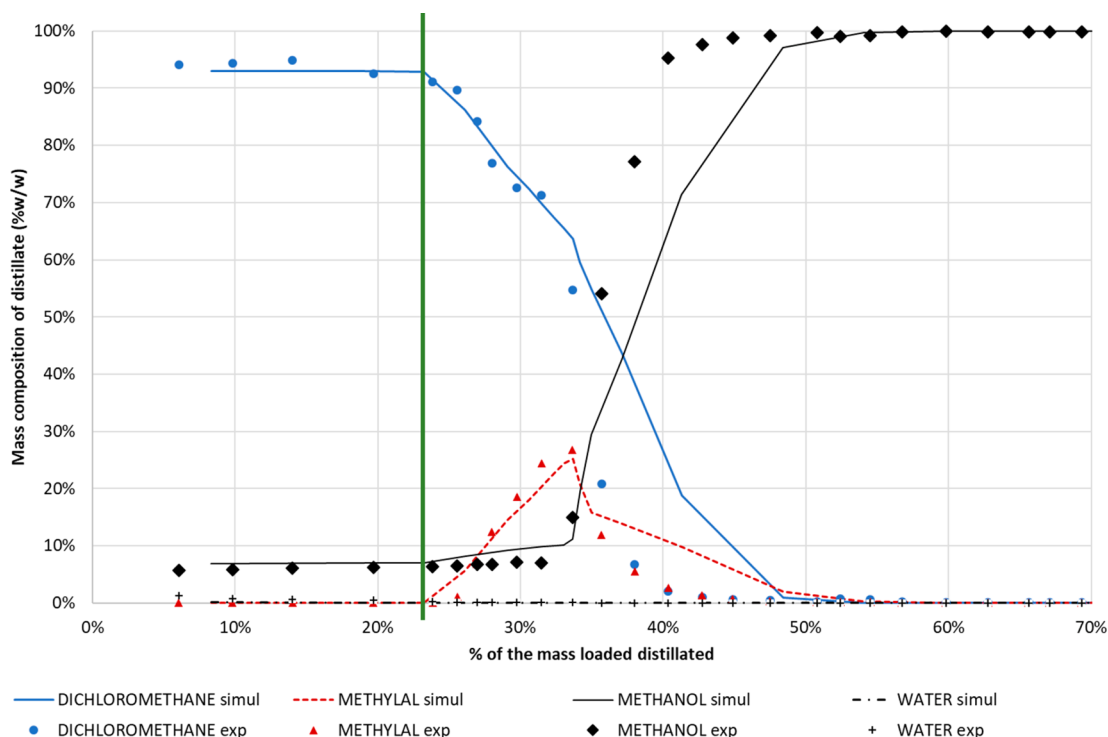


Figure 4. Comparison of simulated and experimental batch distillation—distillate composition over the distillation.

Table 4. Simulation and Experimental Data Considered for Batch Distillation

		Simulation on BatchColumn		Experimentation
Column characteristics	Number of theoretical trays	20	20	
	Reflux ratio	2	2 (distillate valve: 2s open/4s closed)	
	Heating	Constant amount of heat supplied to the boiler	Constant ΔT between the load at the boiler and the double envelope - maintained to 10 °C	
Initial flux composition	% DCM (w/w)	30%	30%	
	% MeOH (w/w)	55%	55%	
	% methylal (w/w)	2.5%	2.5%	
	% water (w/w)	12.5%	12.5%	
Distillation data	Mass loaded at the boiler (g)	5000	5000	
	Distillate (recovered in several fractions over the distillation time)	-	3900	
	Boiler at the end of the distillation	-	875	
	Global mass balance	-	4.5%*	

*Distillation conducted for 5 h; solvent volatility may explain the mass balance.

final time, separation factors $\alpha_{\text{MeOH,DCM}}$, $\alpha_{\text{Water,DCM}}$ and $\alpha_{\text{Water,MeOH}}$ were calculated.

3. DISTILLATION OF THE AZEOTROPE

3.1. Thermodynamic Models, Simulations, and Experimentation. ProSim simulations of batch distillation at atmospheric pressure taking into account the solvent composition of the industrial effluent were carried out. With the aid of ProSim support, different thermodynamic models were tested involving different binary interaction parameters between DCM–MeOH–water–methylal. Results of these simulations show a ternary DCM 93.6%/MeOH 5.7%/water 0.7% (w/w) with a boiling point at 36.8 °C under atmospheric pressure. This mixture presents other binary or ternary azeotropes such as

DCM 92.9%/MeOH 7.1% (w/w);
DCM 98.5%/water 1.5% (w/w);
MeOH 4.1%/methylal 95.9% (w/w);

DCM 32.2%/MeOH 10.5%/methylal 57.3% (w/w); with very close boiling points in the range 36.8 to 41 °C under atmospheric pressure (NRTL model modified with the aid of ProSim support). The Binary interaction parameters used are presented in Table 3. All these simulations show the thermodynamic equilibrium complexity of the effluent to be treated.

The first simulation of batch distillation on a BatchColumn showed that, during the first part of distillation, the ternary DCM/MeOH/water is collected in the distillate. After that, the methylal is recovered in the distillate while the latter is exhausted in DCM and enriched in MeOH. The simulated composition of the distillate over the distillation run was compared to the distillate composition obtained by experimentation in a synthetic mixture (Figure 4). The flux loaded at the boiler and the operating conditions of distillation are presented in Table 4. In order not to obtain a completely empty boiler at the end of the batch distillation experiments,

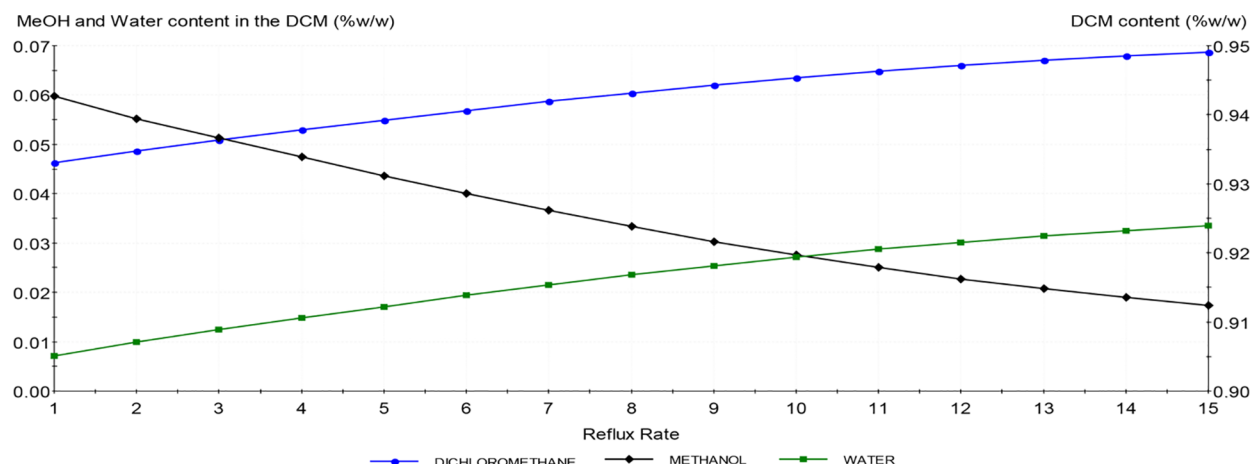


Figure 5. Impact of RR on distillate composition for continuous distillation simulation.

water was added to the solvent mixture. The water content was therefore higher than the water content of the industrial effluent considered.

Simulation and experimentation data show that after distillation of about 23% of the mass loaded into the boiler the azeotrope composition is modified: the methanol content in the distillate increases progressively while the DCM content suddenly falls when the methylal is vaporized and found in the distillate. The distillation yield with regard to DCM regeneration is limited by the recovering of methylal in the distillate (illustrated by the green line in Figure 4). In fact, it will be shown that methylal cannot be treated during the DCM purification step. Considering the distillation feed composition of 30% w/w DCM and distillate composition of 93.6% DCM, the first experimentation demonstrated that the DCM recovery yield during the distillation step was at least 71.8%. Results of simulations using BatchColumn showed that the thermodynamic model used reflected relatively accurately the behavior of the distilled mixture, even if simulations do not perfectly match the experimental data. Thus, this model could be used to optimize operating conditions for limiting solvent use in the lab.

3.2. Optimization. First simulation and experiment results showed that a DCM yield of 71.8% could be obtained before optimization. The impacts of reflux ratio, number of theoretical trays, batch or continuous mode, and feed position were investigated via use in simulation with BatchColumn and ProSimPlus.

Batch Optimization of Distillation. First of all, the impact of the theoretical trays number (TTN) was simulated with respect to a reflux ratio (RR) of 2 during the batch distillation. Batch distillation with only 5 theoretical trays did not enable separation of the methylal from the azeotrope. An increase in the theoretical trays led to a delay of the methylal recovery in the distillate reflecting a DCM yield increase. In the same way, the study of RR impact on DCM recovery yield for a considered TTN of 20 was conducted. An increase of the reflux ratio to 15 enabled a DCM recovery yield of about 90% to be reached (limit value whatever the conditions tested with ProSimPlus simulations). An experiment was conducted in the lab to evaluate the gap between simulation and experimentation. Experimentally, the DCM recovery yield obtained with a high RR of 15 was 85.9%, i.e., about 4% less than the simulation value (batch distillation conducted on 5 kg of synthetic mixture with the composition presented in Table 4/

RR = 15 (distillate valve 2s open/30s closed)/global mass balance = 4.95%).

Continuous Optimization of Distillation. Since continuous distillation was envisaged on an industrial scale, it was necessary to assess whether the behavior of the batch distillation would be maintained continuously. Simulations were performed on the ProSimPlus software. Globally, the thermodynamic model had been conserved so the composition of the distillation fluxes and DCM recovery rate were conserved too. However, the distillate composition announced by continuous simulations with ProSimPlus only seemed accurate for an RR inferior to 5, with the distillate composition varying from 93.45% DCM/5.75% MeOH/0.80% water (RR = 2) to 93.85% DCM/4.55% MeOH/1.60% water (RR = 5) for an initial flux composition similar to the one described in Table 4, and with a distillation column composed of 20 theoretical trays (Figure 5). For a higher RR, the MeOH composition in the distillate decreased significantly, something that was not observed in the experiments (only 1.50% MeOH in the distillate at RR = 15 according to ProSimPlus simulations, whereas the azeotrope composition was still found during the tests). Besides, with a reflux ratio of 1, simulations showed that methylal can be obtained in the distillate. Therefore, the distillation process had to use a minimum RR of 2.

The impact of the feed position was evaluated for a column with 20 theoretical trays. Simulation results concluded that the composition of the distillate (tray 1) stays the same for a feed position between tray 15 to 10, when the RR is inferior to 5. For a feed position on tray 5, simulation showed that methylal appeared in the distillate until a reflux ratio of 12. Thus, this feed position was not sufficiently satisfactory for the process. Finally, the maximum DCM yield was studied via a variation of distillate flow with a constant feed flow of $2.72 \text{ kg}\cdot\text{h}^{-1}$ ($0.83 \text{ kg}_{(\text{DCM})}\cdot\text{h}^{-1}$). The simulation results showed that a maximum distillate flux of $0.8 \text{ kg}\cdot\text{h}^{-1}$ could be obtained before there was an increase in methylal and a decrease in the azeotrope quality. With an azeotrope composed of 94% DCM, this meant that the DCM distillate flux could be around $0.75 \text{ kg}_{(\text{DCM})}\cdot\text{h}^{-1}$. Therefore, a DCM yield of about 90% for distillation was possible according to the simulations. This value is the same as the value announced for batch simulations or as expected from batch experiments.

3.3. Experimental Continuous Distillation. *Distillation of Industrial Effluent.* For carrying out the laboratory tests, the same distillation column was used (TTN = 20) with a reflux

Continuous distillation

Industrial effluent
22.4 kg treated for 7h41

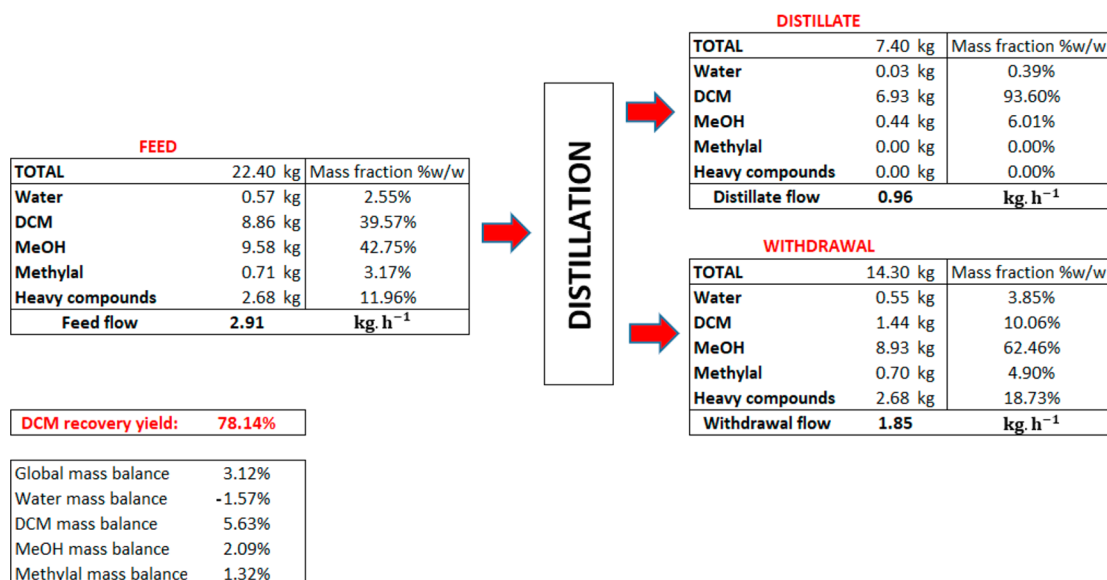


Figure 6. Global vision of continuous distillation performed on industrial effluent.

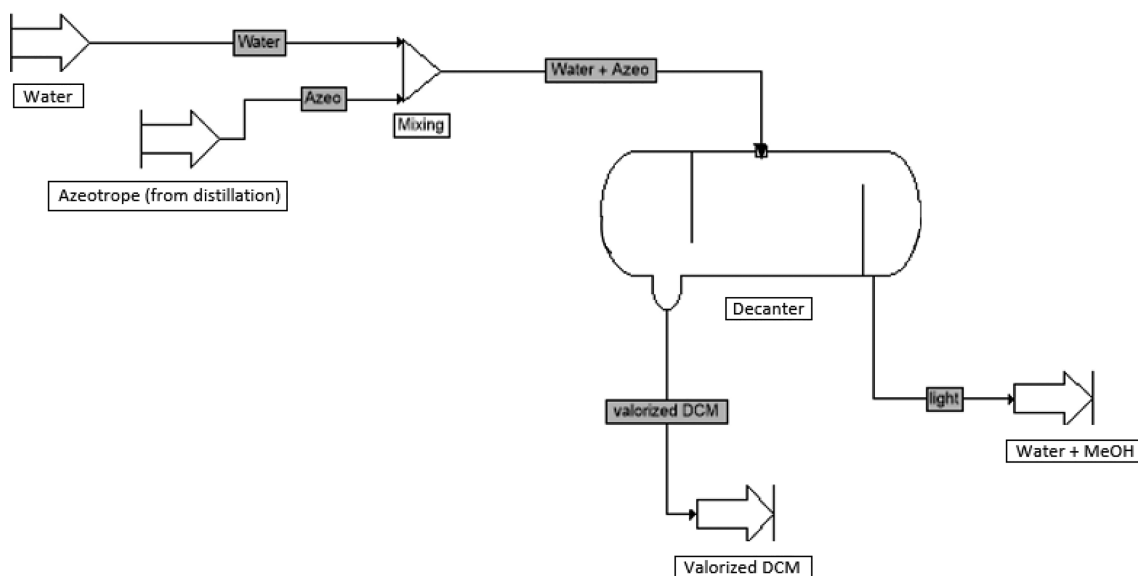


Figure 7. ProSim simulation of azeotrope water wash followed by decantation.

ratio of 2. The feed was attached to plate 15 in order to have enough trays above the feed to separate the azeotrope from the methylal. Continuous distillations were performed on synthetic solvent mixtures. Distillation was conducted for a day, and more than 22 kg of feed were treated. About 7.4 kg of distillate composed of azeotrope (93.6% DCM, 6.0% MeOH, and 0.4% water) was recovered, i.e., a yield of about 78%. The distillate obtained is monophasic, with the MeOH in it enabling homogenization of DCM and water. The global mass balance of the experimentation is presented in Figure 6. The produced distillate was conserved to purify the DCM once the operating conditions of the purification step were fixed. The global mass error was 3.12%, which is relatively correct considering the mass of effluent treated and the volatility of the solvents.

Robustness of Distillation. The impact of feed degradation on distillation was evaluated. Distillation of a mixture of 90% industrial effluent/10% withdrawal of continuous distillation performed previously (essentially MeOH and heavy compounds) was conducted. The azeotrope obtained had a composition of 93.3% DCM, 6.3% MeOH, and 0.4% water, which was quite similar to the azeotrope previously obtained. Thus, the azeotrope quality had not been modified by the feed composition variation, nor had the DCM yield obtained.

4. PURIFICATION OF THE DCM PRESENT IN THE AZEOTROPE

For reinjection in the chemical synthesis, the regenerated DCM has to reach the quality specifications presented above.

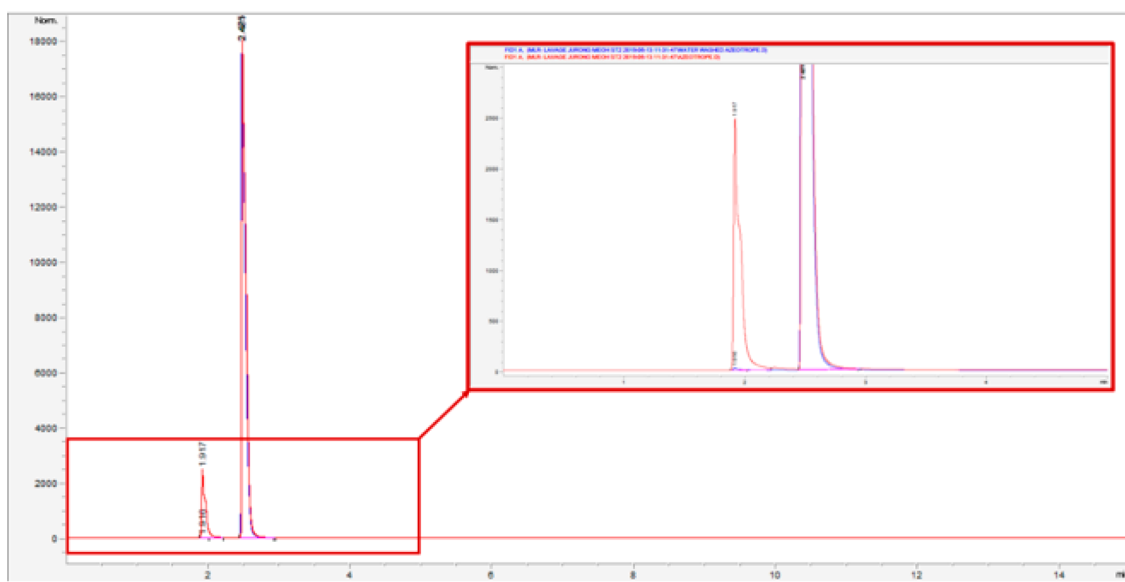


Figure 8. GC analysis of azeotrope before (red) and after (blue) washing.

To remove MeOH and water, two purifications were identified: water washing and membrane pervaporation. Both these processes were studied to determine feasibility and productivity, and their efficiency to remove methylal was evaluated to determine whether the distillation yield could be increased.

4.1. Water Washing. ProSim Simulations. A water wash of the azeotrope followed by decantation could be considered in order to purify the DCM. First, ProSim simulations were conducted to evaluate the influence of the operating temperature and the influence of the ratio of the azeotrope mass/water mass on the recovered DCM quality and yield (Figure 7). The model used for these simulations was the modified UNIFAC (Dortmund) 1993 model, which accurately transcribed the experimental data concerning batch distillation conducted at lab scale.

The impact of the temperature on the DCM purity and yield obtained was evaluated for a $m_{\text{azeo}}/m_{\text{water}}$ ratio equal to 1. Results showed that a decrease in temperature led to an improvement of the DCM quality and an increase in the efficiency of the operation. However, the wash/decantation temperature could not be set below 1 °C due to the water content of the mixture and the risk of freezing. Whatever the operating temperature tested, the specification for the water content could not be reached. Carrying out the wash and decantation at 1 °C led to obtaining a DCM with a purity close to the stated specifications without any risk of freezing the mixture.

The variation of $m_{\text{azeo}}/m_{\text{water}}$ ratio during the wash and decantation operation at 1 °C was studied. An increase in the $m_{\text{azeo}}/m_{\text{water}}$ ratio led to a degradation in the quality of the DCM recovered as the heavy phase of the decantation. The specification in MeOH (<0.1% w/w) could be reached for $m_{\text{azeo}}/m_{\text{water}}$ ratios lower than 1.8 when the operation was carried out at a temperature of 1 °C. The simulations showed that the specification in water (<0.05% w/w) was impossible to reach at this operating temperature because the $m_{\text{azeo}}/m_{\text{water}}$ ratio had no effect on the water content in the purified DCM. However, the results of the simulations also showed that the

increase of the $m_{\text{azeo}}/m_{\text{water}}$ ratio led to an increase in the recovery efficiency of the DCM.

Experimental Water Washing. In order to validate the ProSim simulations, a wash of the azeotrope recovered at the top of the distillation column was conducted with an $m_{\text{azeo}}/m_{\text{water}}$ ratio of 1. The wash and decantation was performed at 1 °C. As shown in the chromatograms obtained before (red) and after (blue) washing (Figure 8), the heavy part recovered after decantation—the washed azeotrope—is purified of methanol.

A quantification by GC with internal standard and KF analysis gave the results shown in Table 5. The purified DCM

Table 5. Wash and Decantation Step Efficiency and Yield

	% DCM w/w	% MeOH w/w	% water w/w	% residue on evaporation w/v
Azeotrope obtained by distillation	94.3%	5.55%	0.15%	0.002%
DCM purified by water wash and decantation	99.8%	0.08%	0.08%	0.002%

recovered after decantation was compliant with regard to the MeOH content, but the specification for the water content (KF < 0.05% w/w) was not reached. The residue on evaporation was evaluated, and the result attained the quality specification <0.1% w/v. The DCM recovery yield reached 89.8% (titrated) from the washing step.

Methylal Behavior during Water Washing. It was shown that the distillation yield was driven by the methylal presence in the distillate. However, if the purification step could eliminate methylal, the distillation yield could be increased. Water washing of a distillate fraction containing methylal was done with different pH's. The results are presented in this section.

To evaluate the behavior of the methylal regarding a water wash, a fraction of distillate containing 3.5% (area) of methylal was washed with water. The $m_{\text{azeo}}/m_{\text{water}}$ ratio of the experimentation performed was 1, and the wash and decantation was conducted at 4 °C (not optimized). The

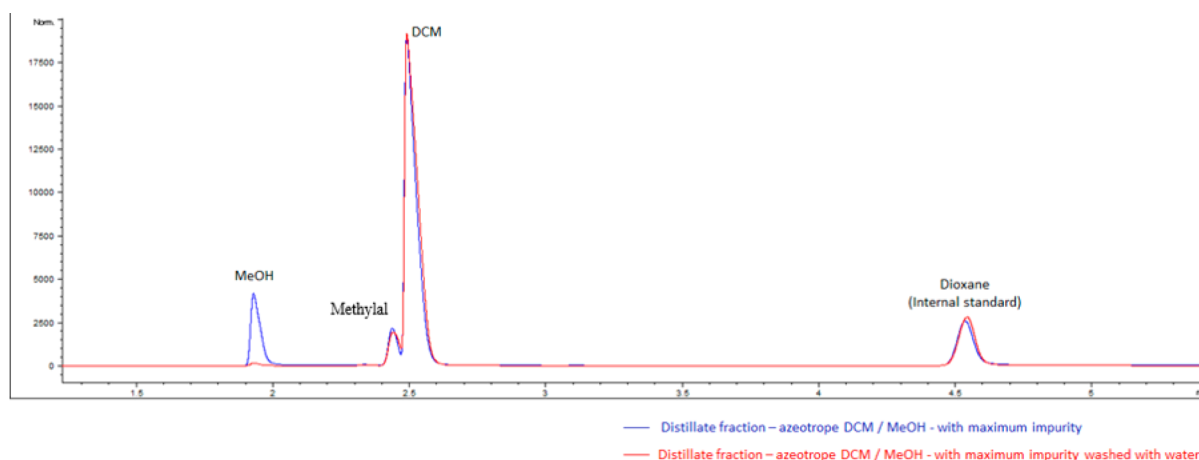


Figure 9. GC analysis of azeotrope with methylal before (blue) and after (red) water wash

results of the GC analysis of azeotrope with methylal (blue) vs washed azeotrope (red) are compared in Figure 9.

These chromatograms show that the methylal remained in the DCM fraction while MeOH was transferred in the aqueous phase. Thus, if the second purification step envisaged was a water wash, the methylal RT = 2.44 could not be tolerated in the distillate, which implied that the distillation yield was still driven by the methylal presence in the distillate.

The efficiency of acid water washing on methylal removal was evaluated. In order to do this, a fraction of distillate containing 3.5% (area) of methylal was washed with HCl 1 N with a mass ratio of 1 in the mix at 20 °C. Acid washing did not remove the methylal. A washing of the azeotrope containing 3.5% (area) methylal was performed with NaOH 1 N in a mass ratio of 1 at 20 °C (not optimized). This washing eliminated about 48.3% (titrated) of methylal (Figure 10). The heavy phase (the regenerated DCM) was washed a second time with NaOH 1 N in a mass ratio of 1 at 20 °C (not optimized). As is shown in Figure 10, this second washing totally removed the methylal.

Two basic washings were necessary to remove the methylal, generating DCM losses in the aqueous phases (about 4.5% titrated) and a large quantity of aqueous phase containing DCM residues. In these conditions, this treatment option seems to be of no interest.

4.2. Pervaporation. One of the options investigated for the purification of the DCM in the azeotrope DCM/MeOH/water was pervaporation involving a separation based on the compounds' polarity difference and their affinity toward the membrane. The installations used for the experiments are described in the Materials and Methods section. In order to totally immerse the NIR probe in the feed reactor, a volume of about 2 L (2.526 kg) of azeotrope was introduced into the reactor. The initial composition of this synthetic azeotrope given by the NIR was 94.3% w/w in DCM, 5.55% w/w in MeOH, and 0.15% w/w in water. The feed flow was not controlled during this experiment. The pervaporation was conducted until a DCM quality in the feed reactor was obtained with these specifications: DCM purity >99% w/w, MeOH content <0.1% w/w, and water content <0.05% w/w. This quality was obtained after a filtration time of about 3 h. Figure 11a, Figure 11b, and Figure 11c show the evolution of the content for each species considered in the pervaporation feed tank, measured by NIR over the course of the operation.

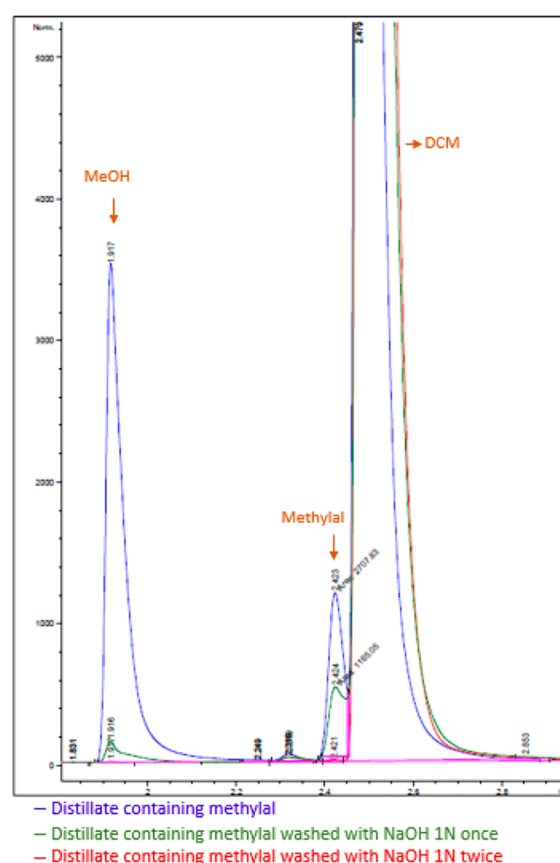


Figure 10. GC analysis of azeotrope with methylal (blue) washed once (green) and washed twice (red) with NaOH 1 N.

A linear elimination of water and MeOH during the first 40 min of filtration was observed before the slope slightly reduced. This observation could be explained by the reduction of permeate flow with the decrease of water and MeOH concentrations in the feed. The good impermeability of the membrane for DCM was confirmed by this result. Once the NIR announced a quality of DCM conforming with the specifications, the pervaporation operation was stopped. At the end of the purification, the permeate recovered in nitrogen traps was collected and analyzed by GC to determine its composition. The loss of DCM which had passed through the membrane and recovered in the nitrogen traps represented 5%

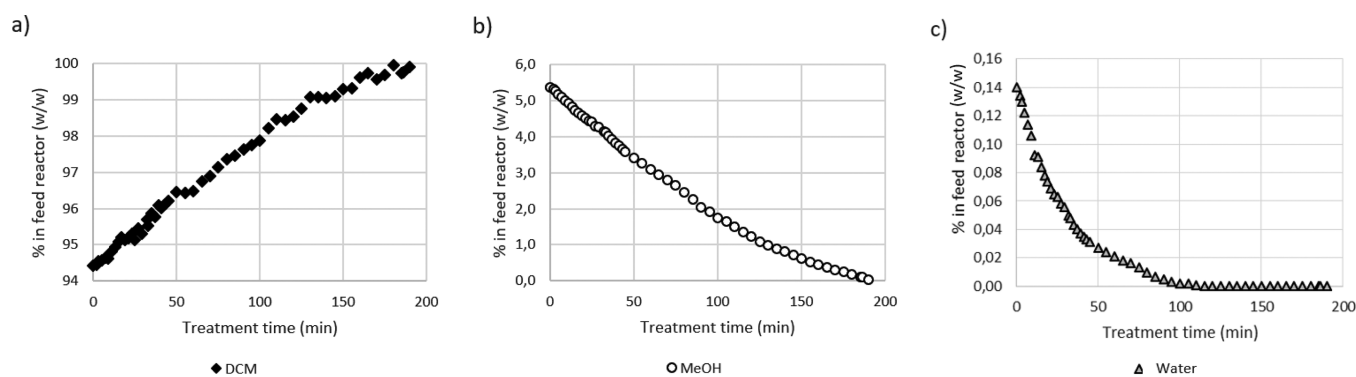


Figure 11. Evolution of (a) DCM purity, (b) MeOH content, and (c) water content in the feed reactor over the pervaporation time.

of the DCM mass loaded in the feed reactor. Thus, the DCM yield from the pervaporation step is 95% (titrated). As is shown in Table 6, the DCM obtained reached the quality

Table 6. Pervaporation Step Efficiency and Yield

	% DCM w/w	% MeOH w/w	% water w/w	% residue on evaporation w/v
Azeotrope obtained by distillation	94.3%	5.55%	0.15%	0.002%
DCM purified by pervaporation	99.96%	0.0037%	0.003%	0.002%

specifications for MeOH and water content, unlike the DCM recovered after wash/decantation for which the water content remained higher than 0.05% w/w.

Once the feasibility of DCM purification had been proved, a scale-up was made on a semipilot installation containing 7 membranes (total membrane area = 1.05 m²). On this pilot, the impacts of the feed pressure, flow, and temperature were studied. Optimizations were performed on a synthetic mixture before validating the improved operating conditions on the azeotrope recovered during continuous distillation of the industrial effluent. Pervaporation was conducted at 3 bar (absolute pressure) and 20 °C. The monitoring of DCM purification was identical to the experiment conducted at atmospheric pressure in terms of DCM yield, productivity, and purification (Figure 12). There was no impact from pressure on purification. Therefore, pressure could be used as a tool for

reaching higher operating temperatures. In fact, at 3 bar, the boiling point of DCM is increased to about 70 °C. This pressure allows operation at a higher temperature while ensuring the feed will remain liquid.

Two circulation flows were tested (645 L·h⁻¹ and 1170 L·h⁻¹) in order to evaluate the impact on DCM purification. Both flows represented turbulent circulation in the membrane channels, with a Reynolds number of 17,000 and 30,000, respectively. A higher feed flow did not increase productivity but did aggravate the DCM loss in the permeate as is shown in Figure 13, leading to a lower DCM yield. This phenomenon is even more important when a high feed flow is combined with a high feed temperature. A pervaporation test under atmospheric pressure at 33 °C and with a circulation flow of 1,180 L·h⁻¹ gave a DCM yield of 47% for a productivity of only 2.5 kg_{DCM}·h⁻¹·m⁻². Therefore, a low feed flow was considered the best option for the optimized operating conditions

Pervaporation of synthetic mixtures was conducted at 10–15–20–28 °C (at atmospheric pressure) and at 41 °C (at 3 bar in order to keep the pervaporation feed in the liquid state). The purification of DCM over the period was followed by NIR, and the results are presented in Figure 14. An increase in temperature led to an increase in process productivity. This is quite positive because it implied a smaller unit for the industrial scale. However, DCM passed more easily through the membrane at higher temperature, making the DCM yield decrease somewhat. The DCM yield is also lower than that obtained at lab scale: 95% (titrated) at lab scale and 83% at

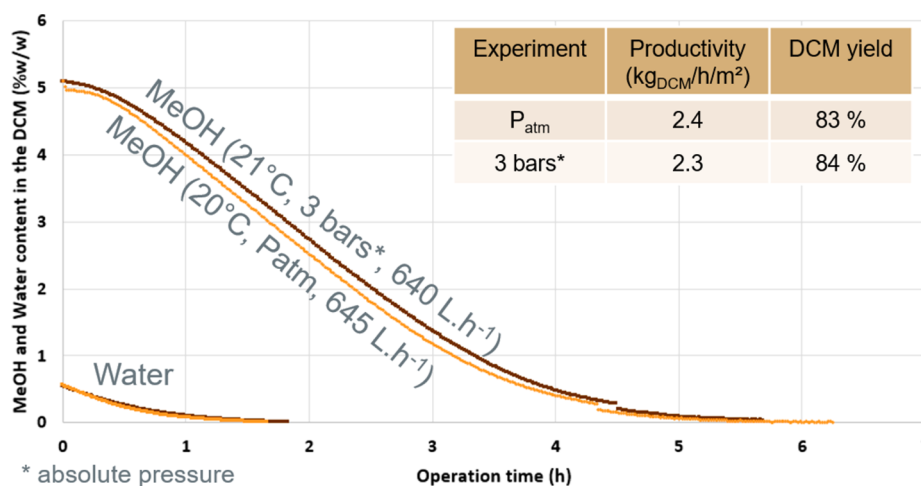


Figure 12. Impact of feed pressure on DCM purification by pervaporation.

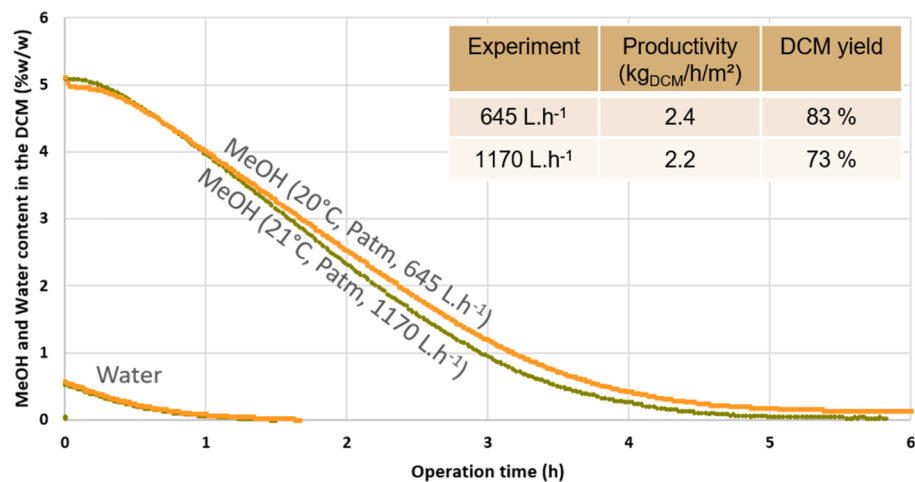


Figure 13. Impact of feed flow on DCM purification by pervaporation.

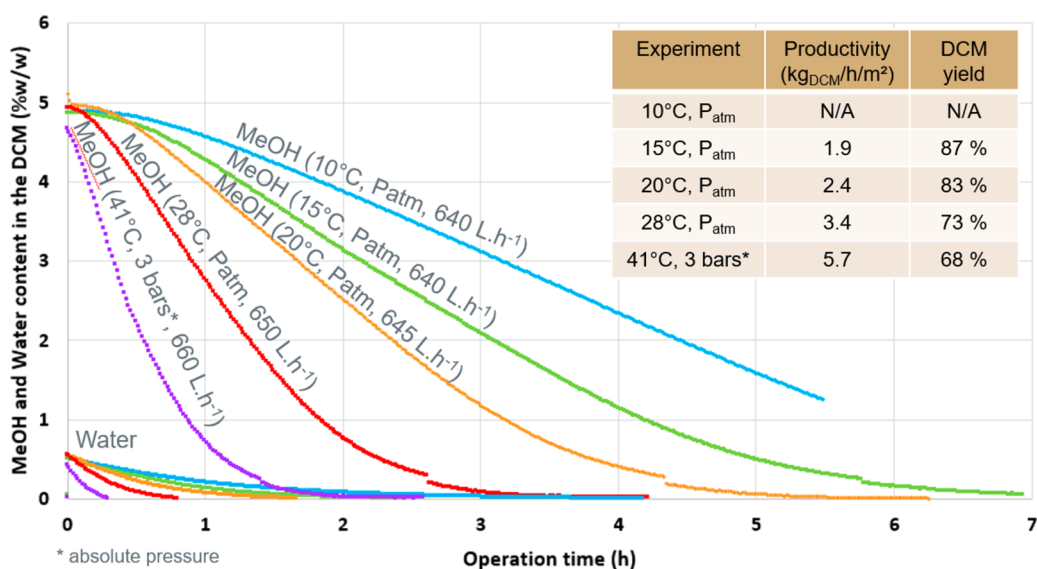


Figure 14. Impact of temperature on DCM purification by pervaporation

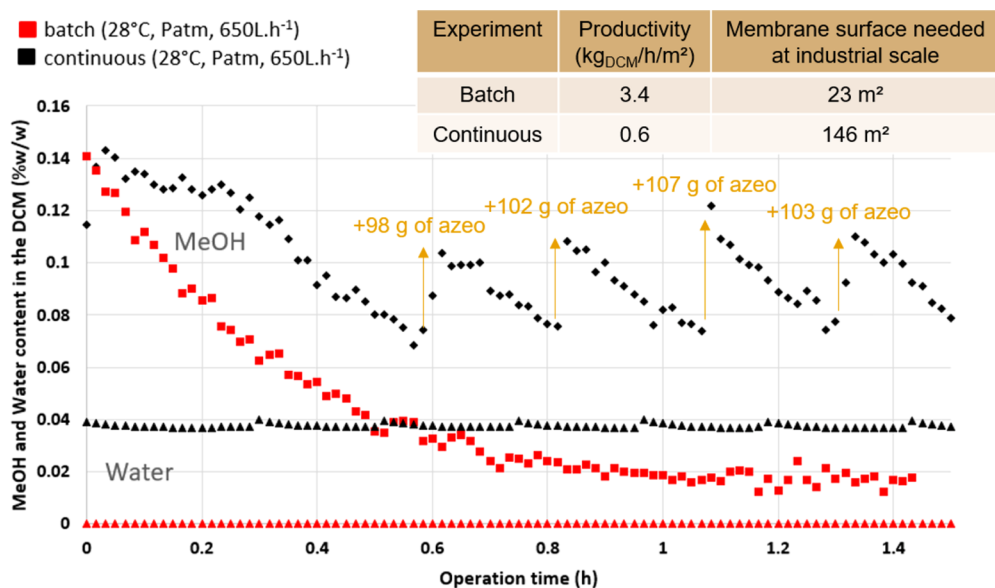


Figure 15. Comparison between batch and continuous processes under the same operating conditions.

Table 7. Separation Factors at the End of the Pervaporation Step

	$\alpha_{\text{MeOH,DCM}}$	$\alpha_{\text{Water,DCM}}$	$\alpha_{\text{Water,MeOH}}$	DCM yield (%)	Productivity ($\text{kg}_{\text{DCM}}\cdot\text{h}^{-1}\cdot\text{m}^{-2}$)
20 °C, P_{atm} , 645 $\text{L}\cdot\text{h}^{-1}$	5.99	5.99	1.00	84	2.3
21 °C, $P = 3$ bar, 640 $\text{L}\cdot\text{h}^{-1}$	6.20	6.22	1.00	83	2.4
21 °C, P_{atm} , 1170 $\text{L}\cdot\text{h}^{-1}$	3.69	3.74	1.01	73	2.2
10 °C, P_{atm} , 640 $\text{L}\cdot\text{h}^{-1}$	N/A	N/A	N/A	N/A	N/A
15 °C, P_{atm} , 640 $\text{L}\cdot\text{h}^{-1}$	7.96	7.90	0.99	87	1.9
28 °C, P_{atm} , 650 $\text{L}\cdot\text{h}^{-1}$	3.70	3.70	1.00	73	3.4
41 °C, $P = 3$ bars, 660 $\text{L}\cdot\text{h}^{-1}$	3.14	3.14	1.00	68	5.7
Continuous. 28 °C, P_{atm} , 650 $\text{L}\cdot\text{h}^{-1}$	3.63	3.66	1.01	73	0.6

semipilot scale for the same operating conditions (20 °C, atmospheric pressure). This is because the increase in membrane surface facilitates the passage of DCM through the membrane. Nevertheless, a recycling of the permeate in the distillation feed could overcome this loss of DCM in the permeate, making the DCM yield for the pervaporation step equal to 100%. The operating conditions will be chosen depending on the equipment selected for condensation. Optimized operating conditions were considered for the higher temperature values: 41 °C at 3 bar if the industrial condenser enables condensation of all the permeate eliminated during the process. If this is not the case, the temperature will have to be slightly reduced in order to limit the permeate flow to be condensed.

The installation was initially designed for batch purposes; therefore, real continuous experiments could not be carried out. Accordingly, semicontinuous pervaporation was tested at semipilot scale. The feed tank was regularly opened in order to inject a small quantity of azeotrope while a purge valve removed some regenerated DCM from the tank. As before, the whole process was monitored by NIR in order to have an inline and live analysis of the environment and to know when a new addition of azeotrope/removal of regenerated DCM was needed. As is shown in Figure 15, the operation conducted in semicontinuous mode implies that water content is roughly constant at 0.04%, while in batch mode the water content of the retentate remains at 0.0% since the water passes entirely through the membrane. The water content in the pervaporation feed influences the permeate flux. In the presence of water, the passage of MeOH through the membrane is reduced and the productivity of the pervaporation is degraded. Indeed, the continuous process is only focused on the end of pervaporation, while the batch process also includes the beginning of pervaporation, which is quicker to treat. Therefore, in order to process the same flow in continuous mode, one would require a membrane surface ten times larger than for a batch process.

Nevertheless, from an economic perspective, continuous pervaporation remains the better option for the industrial process. A quick technical–economical evaluation shows that one square meter of pervaporation membrane costs about \$1k (USD). Assuming a 3-year lifetime, a continuous process represents a complementary maintenance cost of around $\$40\text{k}\cdot\text{y}^{-1}$ compared to the batch process. However, for coupling a batch pervaporation process with a continuous distillation column, at least two additional storage tanks are necessary. One storage tank represents an investment of about \$1,000k, which makes batch pervaporation more expensive than the continuous process. Therefore, for the industrial unit, a continuous process is recommended.

Separation factors were determined for each experiment once the DCM purity reached the quality specification in the feed (Table 7). At this time, all the water and almost all the MeOH is recovered in the permeate; thus, the separation factor $\alpha_{\text{Water,MeOH}}$ is equal to 1. As expected, the separation factors involving the DCM ($\alpha_{\text{MeOH,DCM}}$ and $\alpha_{\text{Water,DCM}}$) are dependent on the DCM yield of the pervaporation. The average flux of each component was calculated (Table 8). The

Table 8. Average Flux of Water, MeOH, and DCM during the Pervaporation Step

	J_{Water} ($\text{g}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$)	J_{MeOH} ($\text{g}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$)	J_{DCM} ($\text{g}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$)
20 °C, P_{atm} , 645 $\text{L}\cdot\text{h}^{-1}$	1.1	2.8	5.9
21 °C, $P = 3$ bar, 640 $\text{L}\cdot\text{h}^{-1}$	1.0	2.7	6.3
21 °C, P_{atm} , 1170 $\text{L}\cdot\text{h}^{-1}$	1.3	3.0	10.4
10 °C, P_{atm} , 640 $\text{L}\cdot\text{h}^{-1}$	N/A	N/A	N/A
15 °C, P_{atm} , 640 $\text{L}\cdot\text{h}^{-1}$	0.7	1.9	4.0
28 °C, P_{atm} , 650 $\text{L}\cdot\text{h}^{-1}$	2.3	4.3	14.3
41 °C, $P = 3$ bars, 660 $\text{L}\cdot\text{h}^{-1}$	6.3	7.3	27.4
Continuous. 28 °C, P_{atm} , 650 $\text{L}\cdot\text{h}^{-1}$	0.02	0.5	N/A

fluxes of water and MeOH were not strongly impacted by the increase in feed flow; at $T = 20$ °C, J_{Water} is equal to about $1.0\text{ g}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ and J_{MeOH} is equal to about $2.9\text{ g}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$. However, the feed flows impacted the DCM flux and this varied from 6 to $10.4\text{ g}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$, with the feed flow increased from 640 $\text{L}\cdot\text{h}^{-1}$ to $1170\text{ L}\cdot\text{h}^{-1}$. This flux variation is directly linked to the DCM yield obtained during the pervaporation step. Increasing the temperature leads to increased permeability for each component. J_{Water} , J_{MeOH} , and J_{DCM} are multiplied respectively by 9, 4, and 7 when the pervaporation temperature is increased from 15 to 41 °C.

Pervaporation tests were performed on an azeotrope spiked with methylal in order to evaluate if the methylal was passing through the membranes during purification, which would enable the distillation yield to be increased. A synthetic mixture initially containing 91.0% DCM, 5.6% MeOH, 3.0% methylal, and 0.4% water was treated by pervaporation. As is shown in Figure 16, the methylal was retained by the pervaporation membranes. At the end of the process, the retentate was composed of 96.2% DCM, 0.05% MeOH, 3.74% methylal, and 0.01% water. Thus, the DCM regeneration yield was limited by the distillation of methylal during the first regeneration step.

As was mentioned previously, to limit DCM losses in the pervaporation step, the permeate could be recycled in the distillation feed. It was important to evaluate the impact of this recirculation on the distillation operation especially for distillate quality and distillation yield (=methylal behavior).

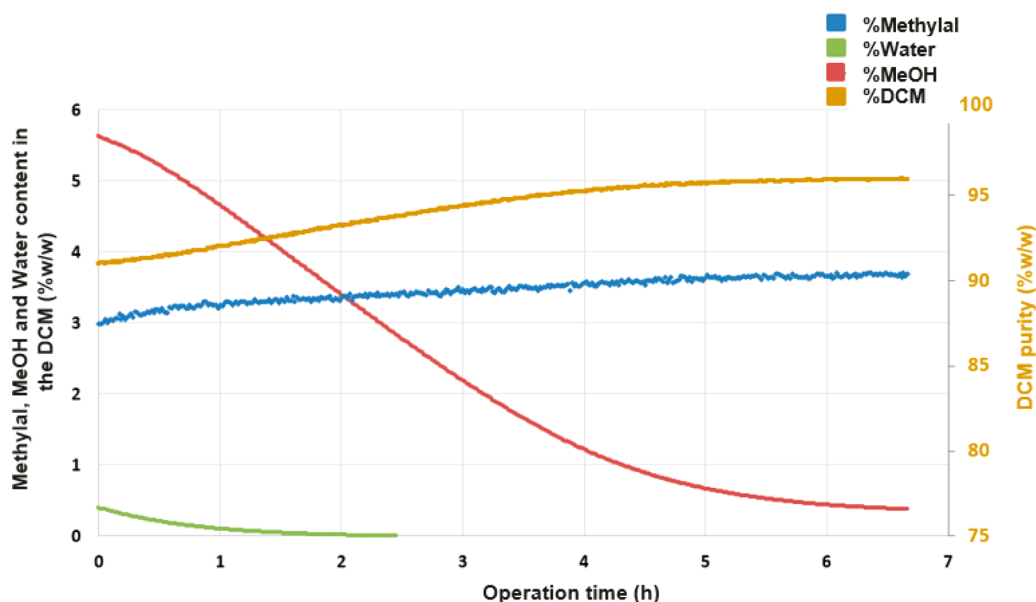


Figure 16. Methylal behavior during DCM purification by pervaporation.

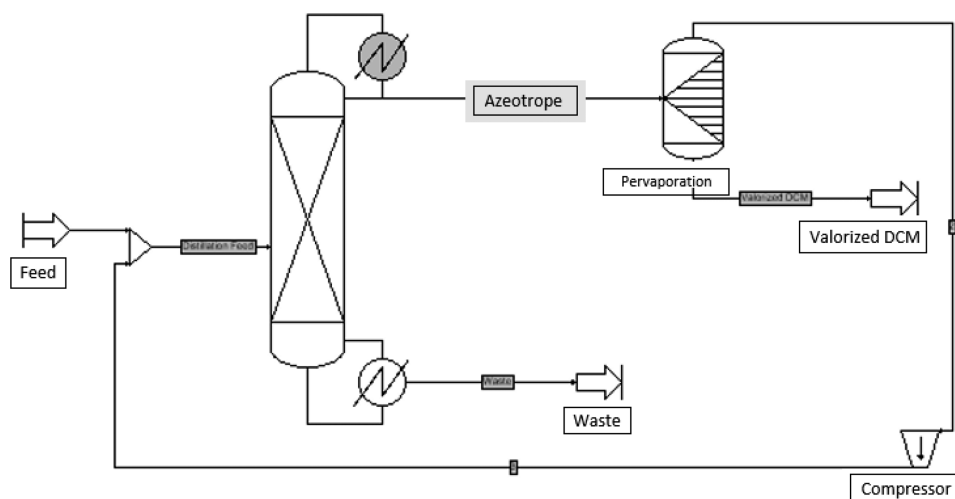


Figure 17. Simulation of continuous DCM regeneration with permeate recirculation.

Simulations were conducted on ProSimPlus in order to collect some answers (Figure 17). The industrial effluent was injected in the distillation column and the distillate was treated by pervaporation. For illustrating pervaporation, a separator was used and the partition coefficient obtained experimentally was set, as were the temperature and pressure. The permeate was condensed using a compressor before being recycled toward the distillation feed.

The simulation results showed that the distillation is not modified by the recirculation of permeate. In fact, permeate flux is not significant compared to distillation feed flow. Depending on the pervaporation conditions, the amount of DCM recovered in the permeate will vary and could lead to a more significant modification of the distillation feed. The quantity of azeotrope distilled increases with the DCM content in the distillation feed. The distillation operating parameters will have to be determined according to the operating conditions chosen for the pervaporation step.

4.3. Industrial Effluent Purification after Azeotrope Distillation. The azeotrope collected after distillation of

industrial effluent was purified by pervaporation. The results were compared to those obtained with synthetic fluxes under similar operating conditions (Figure 18). The behavior of both treated solvent mixtures was quite similar. The productivity of the real effluent azeotrope purification was slightly higher because the initial mixture contained more water, which is the compound with the most affinity with the membrane, so the transfer was accelerated. In addition, pervaporation of industrial effluent azeotrope was conducted at 2 °C higher than for the synthetic mixture. This temperature difference could also explain the faster purification.

The regenerated DCM obtained was analyzed by the Control Laboratory, and the purity of DCM was equal to 99.87%. All the impurities were found to be within the specifications required (less than 0.1% w/w for MeOH, methylal, and heavy compounds, less than 0.05% w/w for water).

The presence of amylene, the DCM stabilizer, was detected in GC and is currently undergoing quantification. If the stabilizer content is lower than expected, the DCM

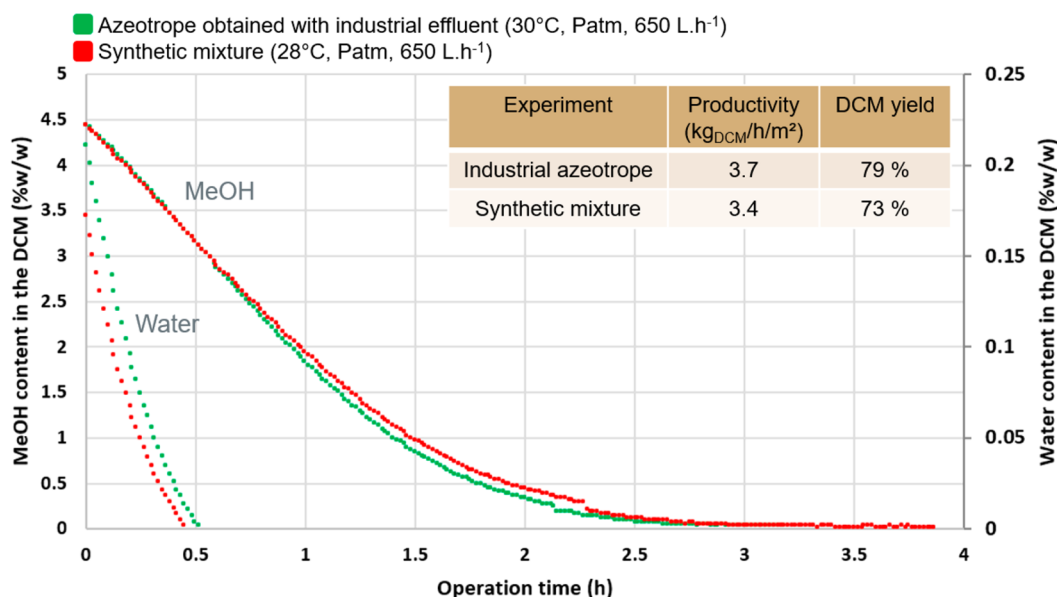


Figure 18. Comparison of industrial azeotrope vs synthetic mixture pervaporation.

regeneration process will include the addition of a small quantity of amylene. Finally, a sample of this regenerated DCM was sent to teams of chemists in order to perform a use-test. The result will enable evaluation of whether or not the regeneration process has affected the chemistry of the active substance produced.

5. PROJECTIONS

5.1. Industrial Installation. The quantity of industrial effluent produced by the plant is about 2,100 t·year⁻¹ or around 44 t·week⁻¹ (running for 48 weeks a year). Therefore, the feed flow of the distillation under consideration is about 260 kg·h⁻¹. The DCM feed content varies from 28% to 40% w/w. This means that between 68 and 100 kg·h⁻¹ of DCM could be recovered in the distillate and be purified by pervaporation. The study described above concludes that the industrial effluents behaved the same way as the synthetic mixtures. Therefore, the optimized operating conditions obtained with synthetic mixtures can be applied for the industrial scaling of the process. For the pervaporation step, the recommended operating conditions are a continuous unit working at 30 °C, at P_{atm} , and with a low circulation flow. This implies a membrane surface of about 150 m² in order to treat the 260 kg·h⁻¹ of industrial effluent. This value is calculated from a distillation DCM yield of 80%, which was the highest value experimentally obtained. Further tests will enable us to conclude if it is possible to reach a 90% distillation DCM yield—and therefore a 90% DCM yield for the whole process with permeate recycling—as announced by the ProSim simulations. Finally, the 90% DCM regeneration reduces the global purchase and destruction costs of solvents by about 15%, in terms of the entire production process. First estimations of Return On Investment (ROI) for a regeneration installation composed of a distillation column and a pervaporation unit show that the installation costs may be recouped in 3 years.

5.2. Reflections on MeOH Regeneration. Regeneration of the MeOH contained in the distillation bottom is under study. Indeed, global MeOH regeneration represents an additional 15% reduction in the purchase and destruction

costs for the whole process. Therefore, the potential economic gains justify the exploration of how to regenerate the MeOH. Here again, the complexity of the mixture makes regeneration by single distillation impossible. After the distillation of the azeotrope from the industrial effluent, the bottom of the column was collected and analyzed. The mixture was composed of 65.54% MeOH, 8.65% DCM, 5.14% methylal, 4.00% water, and 16.67% nonvolatile compounds. A different unit process may be envisaged to recover the MeOH. First of all, simulations of distillation were performed in order to determine the behavior of the mixture with regard to the number of theoretical trays, reflux ratio, feed position and presence of side draw. The theoretical results need to be compared with the experimental data to evaluate the veracity of the thermodynamic model used. Experimentation will also serve to observe the behavior of the fluxes, especially the viscosity of withdrawal which can be mainly composed of heavy compounds. If one single distillation step is not enough to recover MeOH with the expected quality specifications, it is possible to envisage a third distillation step or a pervaporation step with an adapted membrane. Indeed, the membranes used in this study do not allow separation of the MeOH and methylal. Laboratory tests to perform membrane screening will allow a separation coefficient to be obtained and the feasibility of MeOH purification by pervaporation to be evaluated.

6. CONCLUSION

This study presents a means of solvent regeneration applied to a targeted pharmaceutical effluent. The complexity of the industrial azeotropic mixture means that regeneration by a single step is impossible. The use of water washing followed by decantation and pervaporation has been studied because these separation processes are not limited by the boiling point of solvents. Only the pervaporation process made it possible to attain the quality specifications for reintroducing the regenerated DCM in the chemistry synthesis. The simulation run on continuous distillation showed that about 90% of the DCM engaged in the distillation can be recovered in the distillate with an azeotropic composition of 93.6% DCM, 6.0% MeOH, and 0.4% water. It is important to check that there is

no methylal in the distillate because the pervaporation used as a purification step retains this compound. Pervaporation testing conducted at lab scale and semipilot scale showed that increasing the temperature, pressure (if a temperature increase is needed to keep the feed liquid), and circulation flow leads to a faster DCM purification but an increase in the passage of DCM through the membrane and, thus, a decrease in the DCM yield. The permeate recycling toward the distillation feed aims at limiting DCM losses and enables the pervaporation operating conditions to be adapted according to the distillate flow without being blocked by the pervaporation yield. Finally, the regenerated DCM obtained by distillation followed by pervaporation presents the quality specifications required (DCM purity >99.8% w/v, MeOH content <0.1% w/v, and water content <0.05% w/v), and a chemical use-test should confirm that it can be recycled in the chemical synthesis. A projection considering the flow of industrial effluent treated in continuous mode was made for the design of the processing unit on an industrial scale. The regeneration process presented here overcomes technological barriers, when considering that the treated azeotrope mixture represents a real economic issue, with significant reduction in new solvent use and management costs, and it offers environmental benefits thanks to solvent regeneration.

AUTHOR INFORMATION

Corresponding Author

Morgane Le Hir – Sanofi Chimie, Laboratoire Génie des Procédés 1, Process Engineering, Global Chemistry Manufacturing & Control (CMC), 04200 Sisteron, France; orcid.org/0000-0002-5775-022X; Phone: +33 (0)4 92 33 30 62; Email: morgane.lehir@sanofi.com

Authors

Adrien Magne – Aix Marseille Univ., CNRS, Centrale Marseille, M2P2 UMR 7340, Equipe Procédés membranaires (EPM), Europole de l'Arbois, BP80, 13545 Aix en Provence Cedex, France

Thomas Clair – Sanofi Chimie, Laboratoire Génie des Procédés 1, Process Engineering, Global Chemistry Manufacturing & Control (CMC), 04200 Sisteron, France

Emilie Carretier – Aix Marseille Univ., CNRS, Centrale Marseille, M2P2 UMR 7340, Equipe Procédés membranaires (EPM), Europole de l'Arbois, BP80, 13545 Aix en Provence Cedex, France

Philippe Moulin – Aix Marseille Univ., CNRS, Centrale Marseille, M2P2 UMR 7340, Equipe Procédés membranaires (EPM), Europole de l'Arbois, BP80, 13545 Aix en Provence Cedex, France

Notes

The authors declare no competing financial interest.

NOMENCLATURE

API active pharmaceutical ingredient
DCM dichloromethane
GC gas chromatography
KF Karl Fischer
MEK methyl ethyl ketone
MeOH methanol
 m_{azeo} mass of azeotrope

m_{water} mass of water
NIR near infra-red
PVA polyvinyl alcohol
REACH registration, evaluation, authorization, and restriction of chemicals
RMSECV root mean square errors of cross validation
ROI return on investment
RR reflux ratio
RT retention rate
THF tetrahydrofuran
TTN theoretical trays number
VOCs volatile organic compounds
% w/v % weight/volume
% w/w % weight/weight

REFERENCES

- (1) Triolet, J.; INRS, Institut National de Recherche et de Sécurité. Panorama de l'utilisation Des Solvants En France Fin 2004 - Article de Revue - INRS. *INRS - Hygiène et sécurité du travail - Cahiers de notes documentaires - 2e trimestre*; 2005.
- (2) Boust, C.; INRS, Institut National de Recherche et de Sécurité. *Fiche Solvants, Les Hydrocarbures Halogénés*. ED 4223; 2011.
- (3) Schucht, S.; Denize, C.; Brignon, J.-M. Données technico-économiques sur les substances chimiques en France: Dichloromethane. *DRC-15-136881-12175A* **2015**, 95.
- (4) Kumar, P.; Gogia, A.; Kakar, A.; Miglani, P. An Interesting Case of Characteristic Methanol Toxicity through Inhalational Exposure. *J. Fam. Med. Prim. Care* **2015**, 4 (3), 470–473.
- (5) Menges, N. The Role of Green Solvents and Catalysts at the Future of Drug Design and of Synthesis; 2018. DOI: [10.5772/intechopen.71018](https://doi.org/10.5772/intechopen.71018).
- (6) Aranda, R. M. M.; López-Sanz, J. Green Solvents for Pharmaceutical Industry. In *Green Solvents I: Properties and Applications in Chemistry*; Mohammad, A., Ed.; Springer Netherlands: Dordrecht, 2012; pp 147–173. DOI: [10.1007/978-94-007-1712-1_4](https://doi.org/10.1007/978-94-007-1712-1_4).
- (7) Cue, B. W.; Zhang, J. Green Process Chemistry in the Pharmaceutical Industry. *Green Chem. Lett. Rev.* **2009**, 2 (4), 193–211.
- (8) Slater, C. S.; Savelski, M. Towards a Greener Manufacturing Environment. *Innov. Pharm. Technol.* **2009**, 29, 78–83.
- (9) Seyler, C.; Capello, C.; Hellweg, S.; Bruder, C.; Bayne, D.; Huwiler, A.; Hungerbühler, K. Waste-Solvent Management as an Element of Green Chemistry: A Comprehensive Study on the Swiss Chemical Industry. *Ind. Eng. Chem. Res.* **2006**, 45 (22), 7700–7709.
- (10) Tóth, A. J.; Gergely, F.; Mizsey, P. Physicochemical Treatment of Pharmaceutical Process Wastewater: Distillation and Membrane Processes. *Period. Polytech., Chem. Eng.* **2011**, 55 (2), 59–67.
- (11) Deegan, A. M.; Shaik, B.; Nolan, K.; Urell, K.; Oelgemöller, M.; Tobin, J.; Morrissey, A. Treatment Options for Wastewater Effluents from Pharmaceutical Companies. *Int. J. Environ. Sci. Technol.* **2011**, 8 (3), 649–666.
- (12) Byrne, F. P.; Jin, S.; Paggiola, G.; Petchey, T. H. M.; Clark, J. H.; Farmer, T. J.; Hunt, A. J.; Robert McElroy, C.; Sherwood, J. Tools and Techniques for Solvent Selection: Green Solvent Selection Guides. *Sustainable Chem. Processes* **2016**, 4 (1), 7.
- (13) Tiwari, A. Study of Various Solvent Recycling and Treatment Methods in a Pharmaceutical Manufacturing Plant. *Int. J. Pharm. Pract. Pharm. Sci.* **2019**, 1 (2), 55–61.
- (14) Pandey, N. K.; Rajeev, R.; Joyakin, C. V.; Anand, P. V.; Velavendan, P.; Mudali, U. K.; Natarajan, R. Development of Solvent Regeneration Process. *Desalin. Water Treat.* **2014**, 52 (40–42), 7637–7644.
- (15) Nemeth, B.; Lang, P.; Hegely, L. Optimisation of Solvent Recovery in Two Batch Distillation Columns of Different Size. *J. Cleaner Prod.* **2020**, 275, 122746.

- (16) Chapman, P. D.; Oliveira, T.; Livingston, A. G.; Li, K. Membranes for the Dehydration of Solvents by Pervaporation. *J. Membr. Sci.* **2008**, *318* (1), 5–37.
- (17) Ping, Z. *Déshydratation des alcools par pervaporation sur membranes hydrophiles: relation entre la nature et la structure des matériaux membranaires et le pouvoir séparateur des films*. PhD thesis, Institut National Polytechnique de Lorraine, 1994.
- (18) Sekkak, N.; Mas, A.; Berrada, M.; El Harfi, A.; Schue, F. Membranes Polysulfone et Polysulfone Modifié Pour La Deshydratation de l'éthanol Par Pervaporation. *Eur. Polym. J.* **2001**, *37* (8), 1543–1551.
- (19) Yu, C.; Liu, Y.; Chen, G.; Gu, X.; Xing, W. Pretreatment of Isopropanol Solution from Pharmaceutical Industry and Pervaporation Dehydration by NaA Zeolite Membranes. *Chin. J. Chem. Eng.* **2011**, *19* (6), 904–910.
- (20) Rollet, V. Transfert de Matière En Pervaporation Application à La Deshydratation de Mélanges Complexes. *These de doctorat*, Compiègne, 2000.
- (21) Vauclair, C. Déshydratation d'alcools à l'aide de Membranes Hydrophiles: Modélisation Du Transfert de Matière. *These de doctorat*, Caen, 1998.
- (22) Slater, C. S.; Savelski, M. J.; Moroz, T. M.; Raymond, M. J. Pervaporation as a Green Drying Process for Tetrahydrofuran Recovery in Pharmaceutical Synthesis. *Green Chem. Lett. Rev.* **2012**, *5* (1), 55–64.
- (23) La Rocca, T.; Carretier, E.; Dhaler, D.; Louradour, E.; Truong, T.; Moulin, P. Purification of Pharmaceutical Solvents by Pervaporation through Hybrid Silica Membranes. *Membranes* **2019**, *9* (7), 76.
- (24) Haaz, E.; Szilagyi, B.; Fozer, D.; Toth, A. J. Combining Extractive Heterogeneous-Azeotropic Distillation and Hydrophilic Pervaporation for Enhanced Separation of Non-Ideal Ternary Mixtures. *Front. Chem. Sci. Eng.* **2020**, *14* (5), 913–927.
- (25) Eliceche, A. M.; Carolina Daviou, M.; Hoch, P. M.; Ortiz Uribe, I. Optimisation of Azeotropic Distillation Columns Combined with Pervaporation Membranes. *Comput. Chem. Eng.* **2002**, *26* (4), 563–573.
- (26) Hoch, P.; Daviou, M.; Eliceche, A. Optimization of the Operating Conditions of Azeotropic Distillation Columns with Pervaporation Membranes. *Lat. Am. Appl. Res.* **2003**, 33.
- (27) Van Hoof, V.; Van den Abeele, L.; Buekenhoudt, A.; Dotremont, C.; Leysen, R. Economic Comparison between Azeotropic Distillation and Different Hybrid Systems Combining Distillation with Pervaporation for the Dehydration of Isopropanol. *Sep. Purif. Technol.* **2004**, *37* (1), 33–49.
- (28) Albert, M.; Hahnenstein, I.; Hasse, H.; Maurer, G. Vapor-Liquid and Liquid-Liquid Equilibria in Binary and Ternary Mixtures of Water, Methanol, and Methylal. *J. Chem. Eng. Data* **2001**, *46* (4), 897–903.
- (29) Huemer, H.; Wörtl, K.; Moser, F. A New Apparatus for Measurement of Liquid-Liquid Equilibrium Data, and Results for the Water-Methanol-Dichloromethane System at 20 and 60°C. *Fluid Phase Equilib.* **1983**, *11* (3), 311–323.
- (30) Zhu, Z.; Yu, X.; Ma, Y.; Yang, J.; Wang, Y.; Cui, P.; Li, X. Efficient Extractive Distillation Design for Separating Binary Azeotrope via Thermodynamic and Dynamic Analyses. *Sep. Purif. Technol.* **2020**, *238*, 116425.
- (31) Berg, L. Separation of Methylene Chloride from Methylal by Extractive Distillation. US 5051153 A, September 24, 1991.
- (32) ProSim ILogiciels & Services en Simulation de Procédés, <https://www.prosim.net/>.
- (33) Van Veen, H. M.; Rietkerk, M. D. A.; Shanahan, D. P.; van Tuel, M. M. A.; Kreiter, R.; Castricum, H. L.; ten Elshof, J. E.; Vente, J. F. Pushing Membrane Stability Boundaries with HybSi® Pervaporation Membranes. *J. Membr. Sci.* **2011**, *380* (1), 124–131.
- (34) Mafi, A.; Raisi, A.; Hatam, M.; Aroujalian, A. A Mathematical Model for Mass Transfer in Hydrophobic Pervaporation for Organic Compounds Separation from Aqueous Solutions. *J. Membr. Sci.* **2012**, *423–424*, 175–188.
- (35) Servel, C. Potentialités de la pervaporation dans les procédés hybrides de séparation. *Alimentation et Nutrition*; Université de Lorraine, 2014.