TECH PAPERS

# SOLVENT BASED MEMBRANE NANOFILTRATION FOR PROCESS INTENSIFICATION

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Communication

# Solvent Based Membrane Nanofiltration for Process Intensification

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A large-scale mobile pilot installation for organic solvent nanofiltration has been designed to facilitate the transfer of this new promising technology for process intensification to industry. The installation, suitable for all requirements ranging from proof of principle testing to pilot scale production, is mobile and can be equipped both with ceramic and polymeric membranes. The pilot is full ATEX, meets the regulatory requirements of pharmaceutical and fine chemical manufacturing and is available to customers on a rental basis. In this paper, the technical specifications of the pilot unit, possible applications and some successful case studies are presented.

**Keywords:** Organic solvent nanofiltration, Pilot installation, Pilot testing, Process intensification

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## 1 Introduction

Organic solvent nanofiltration (OSN) is an emerging technology since it offers an economically interesting alternative separation process that has the added advantage of often leading to a more sustainable process [1]. Allowing non-thermal, energy-efficient and highly-selective separation, OSN has the potential to replace part of the huge number of traditional, mainly thermal separation processes currently used in the chemical and pharmaceutical industry [2].

Until about 10 years ago, it was hardly possible to treat organic solvent-based solutions with nanofiltration due to the lack of solvent-stable membranes and in-depth know-how of processing such streams. However, currently several high-performance OSN membranes exist, both polymeric and ceramic, at a sufficient level of development and commercially available.

In order to profit from the full potential of OSN, some remaining challenges and market demands need to be solved. One of these important market demands is more extensive demonstration of the technology by relevant pilot testing [1]. Testing the various applications at pilot scale is a must, since it is common practice that end-users only choose for new developments that have been already implemented at reference sites, or at least technically proven at larger scale.

## 2 Pilot Scale OSN Installation

Nowadays, some OSN pilot test facilities exist with current membrane suppliers. However, to facilitate independent pilot-testing for potential end-users, VITO has designed and recently acquired a large-scale nanofiltration installation suitable for use with virtually all organic solvents (full installation ATEX EEx IIB T4). Recognizing the enormous potential of the new technology for the pharmaceutical and fine-chemical industry (see Section 3), the installation was designed to meet the good manufacturing practice (GMP) requirements imposed upon pharmaceutical manufacturing: apparatus and components meet the required high quality levels with respect to cleanability (fully drainable and cleaning in place possible), materials (AISI 316L), surface roughness ($Ra = 0.8\,\mu m$), certification, etc. Furthermore, to avoid any restrictions of membrane choice, the equipment allows for the use of both ceramic membranes ($3 \times 19$ channel elements with a length of 1.2 m, total membrane surface $0.75\,m^2$) and polymeric membranes ($1 \times 4$-040 inch spiral-wound module with a diameter of 4 inch and a length of 40 inch, total membrane surface about $6\,m^2$), both under optimal conditions. Especially this compatibility with both ceramic and polymeric membranes is a unique feature of this installation.

A simplified flow sheet of the pilot is shown in Fig. 1. The installation is build following the usual two-pump design. The solvent is pumped out of a 400-L tank by a high pressure pump up to the working pressure and is circulated by a circulation pump at high flow rate (adjustable) over the membrane module (cross flow operation). The dedicated feed tank of 400 L allows for inert gas blanketing and is in-

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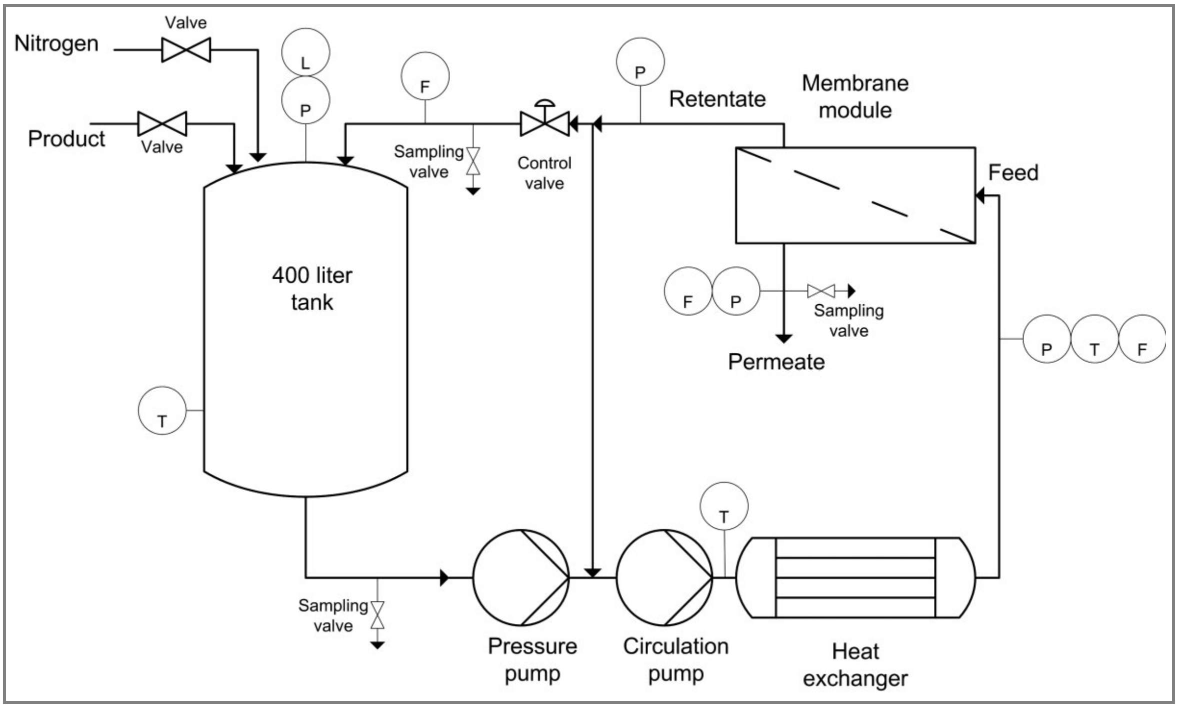

**Figure 1.** Simplified P&ID of the mobile OSN pilot. Sampling points as well as real-time monitoring points for pressure (P), temperature (T), flow rate (F) and tank level (L) are shown.

strumented to monitor temperature, pressure, and liquid level. Two spray heads allow for efficient cleaning. The main technical characteristics of the installation are summarized in Tab. 1. The installation is connected to a computer for real-time monitoring and data acquisition (pressures, temperatures, tank level, cross-flow velocity, and flux). Sampling points for tank outlet, permeate, and retentate are foreseen since no inline analysis is available. The pilot was designed to be mobile (two transportable frames) and can be rented for testing either at VITO or on-site at the end-user. A picture of the installation is shown in Fig. 2.

**Table 1.** Main technical specifications of the mobile OSN pilot.

| Parameter | Pilot specification |
|---|---|
| Operating pressure | 0 – 45 bar |
| Maximum temperature | 50 °C ATEX, 80 °C non-ATEX |
| Minimum feed volume | 80 L |
| Maximum circulation flow | 7000 L h$^{-1}$ |
| Maximum permeation flow | 500 L h$^{-1}$ |
| Skid dimensions | Skid 1: 2.6 m × 1.5 m × 1.9 m |
| (length × width × height) | Skid 2: 1.2 m × 1.2 m × 2.5 m |

## 3 Application Potential of OSN

OSN in general has a broad application potential in various production processes in many different industrial sectors such as the food, (petro)chemical, pharmaceutical sector and other chemistry-related industries [3]. Currently, there are only a limited number of implemented OSN processes running at industrial scale, but the number is growing steadily.

**Figure 2.** Picture of the mobile OSN pilot.

With respect to the food sector, OSN offers potential in solvent-intensive extraction processes, such as in the edible oil industry. Currently one specific application of OSN is commercialized, i.e., deacidification of sunflower oil. Energy savings are substantial, and very efficient removal of fatty acids can be achieved. The very favorable economics lead to payback times of no more than 6 to 24 months [1]. The required initial investment for these typically large-volume applications is however quite high and hampers further implementation.

The petrochemical sector has actually triggered the development of solvent resistant polymeric nanofiltration membranes, and has also seen the first industrial OSN implementation at large scale, i.e., the Max/deWax plant at Exxon Mobile's refinery in Beaumont, Texas. The installation dedicated to recovering solvent (a mixture of toluene and methyl ethyl ketone) used for dewaxing waxy lube oil feed streams, was recently awarded the Kirkpatrick Honor Award of the chemical engineering industry. This hybrid OSN-distillation process, implemented already in 1998 and treating approximately 11 000 $m^3$ of waxy feed per day allowed for significant cost (4×) and space (5×) reductions in comparison to the conventional, entirely distillation based solvent recovery process. The net benefit was calculated to be about $ 6 million per year, leading to a payback time of just one year [4]. Various other thermal separations of organic solvent-based product mixtures could be replaced with more cost-efficient OSN.

The pharmaceutical and fine-chemical sectors, where solvent-intensive processes are omnipresent and a clear need for more efficient, preferably non-thermal separations exists, are perceived as the most attractive industries where OSN can pre-eminently deploy its capabilities. OSN allows for the facile, safe and low-cost recovery, concentration or purification of the target molecules. Pharmaceutical and fine-chemical products are often sensitive to high processing temperatures and, therefore, OSN offers an attractive low-temperature separation solution. Other drivers are the ease of use, ability to flexibly integrate OSN with upstream and downstream (separation) processes, selectivity and yield improvement. Possible applications encompass the concentration of pharmaceutical products or intermediates, their purification (e.g. removal of unwanted high/medium molecular weight species such as oligomers and polymers), their transfer from one synthesis solvent to another one (non-thermal solvent exchange), and the recovery of expensive homogeneous catalysts from post-reaction mixtures. Moreover, coupling of OSN membranes directly to the chemical reactor offers novel, unique capabilities such as in situ product recovery, or shifting of the reaction equilibrium leading to increased product yields and/or decreased impurity levels. The pharmaceutical sector is envisioned to be a key application area where small and medium sized OSN units could assist process engineers in product development as well as batch productions. The implementation of OSN in larger scale production processes is not likely to take place until the technology is demonstrated at pilot scale and has proven long-term performance stability.

One lucrative application of OSN in the pharmaceutical industry is the recovery of active pharmaceutical ingredients (APIs) from solvent waste streams. These waste streams, typically about 250 $m^3$ per year, contain about 1 wt % of APIs and are currently mainly disposed by incineration. OSN offers the opportunity of a low-temperature concentration up to approximately 10 wt % of API. The resulting concentrate stream can easily be re-directed to the existing downstream processing train, leading to an efficient API recovery and a direct profit of about 1 million euro per year. OSN installations for such processes are typically small – using an estimated flux of 5 $L\,h^{-1}m^{-2}$ membrane surfaces of about 15 $m^2$ are typically required – and therefore not capital-intensive. Payback times of less than one year are easily feasible. An OSN-based, fully GMP, API recovery process was recently implemented at Glaxo Smith Kline, UK [5].

It can be stated that the chemical and related sectors (including the pharmaceutical sector) may be specifically interested in ceramic rather than polymeric membranes due to their higher temperature stability, greater stability in basic or acidic media and easier storage of the membranes in between test or batch production campaigns. Indeed, typical streams in the chemical industry often contain either acids or bases. Moreover, in case of temperature stable products, filtration at higher temperatures can avoid solute precipitation or lower the viscosity of the stream to be filtrated.

## 4 Succesfull OSN Cases

VITO has been involved in research and development on OSN since the end of the 90's. Besides its own membrane developments, several feasibility tests for industrial customers were performed. Successful separation processes over the course of the years include, amongst others, diafiltration processes to remove unwanted solvent from chemical or pharmaceutical product streams (impurity levels down to 100 ppm are easily feasible), recovery and re-use of homogeneous catalysts and removal of unwanted oligomer and polymer by-products [6, 7]. One of the diafiltration applications has been implemented in Belgium using ceramic membranes at a scale of 72 $m^2$ membrane surface area, after long-term pilot testing at a scale of 5 $m^2$.

Recently a membrane-assisted process was developed to perform reactions that require high dilution for sufficient product yield [8]. Typical examples of such reactions are macrocyclization reactions where high dilution avoids the formation of polymers due to intermolecular reactions. The high dilution leads to low productivity – down to 50 kg in a batch reactor of 6000 L [9] – high solvent use (typically 100 to 1000 $L\,mol^{-1}$) and, thus, high production costs. In the new membrane-assisted process called VID (volume-intense dilution) the substrate is added at a low concentration from a feed tank at a high concentration, while the solvent needed for substrate dilution is recovered in situ. Fig. 3 shows the process scheme of the VID process.

The proof of principle of the process was demonstrated for a representative macrocylization reaction, i.e., a Mitsunobu reaction to form a 13-membered ring, shown in Fig. 4. Tests were performed in two typical reaction solvents, dichloromethane (DCM) and tetrahydrofuran (THF), using both ceramic and polymeric OSN membranes. The tests

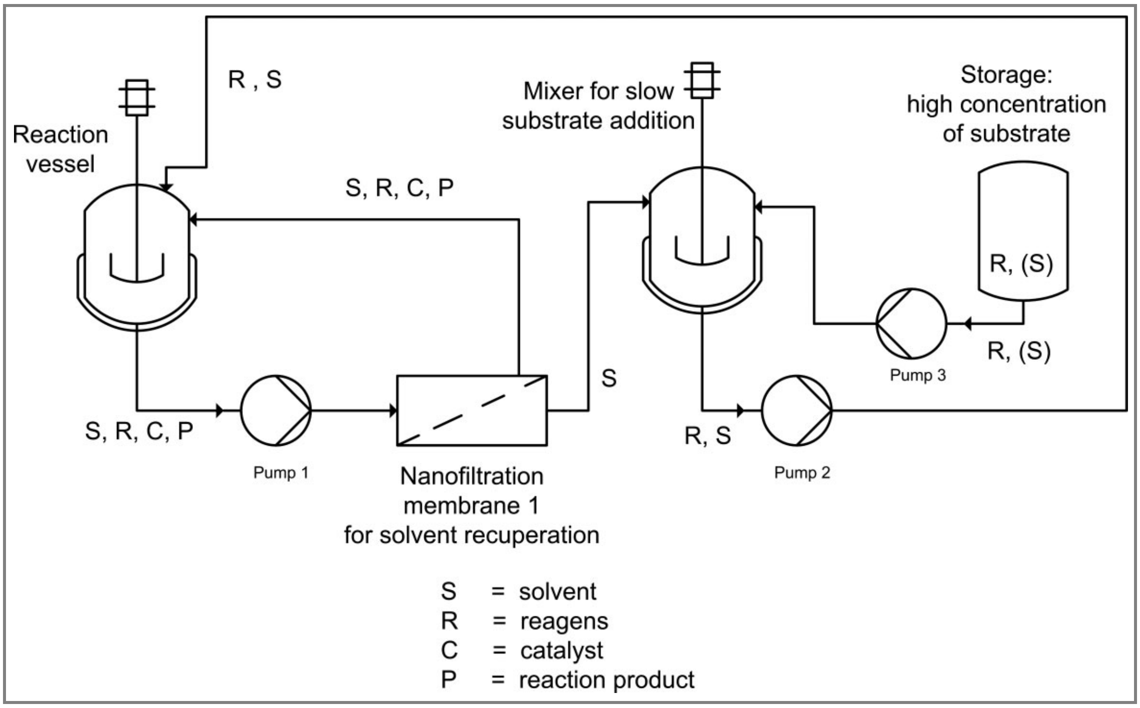

**Figure 3.** Process scheme of the new membrane-assisted dilution process developed.

have shown that the yields obtained with the new process is at least similar to the yields acquired in batch reactions performed at the same concentration, and is independent of the reaction concentration, as shown in Fig. 5. In addition, in contrast to batch reactions, substantial decrease of solvent use can be achieved with process mass intensity [10] reductions of more than 40 % realized in a non-fully optimized system. The VID process is applicable not only for macrocylization reactions but for all other reactions profiting from high dilution, e.g., reactions suffering from substrate inhibition or precipitation. The process is not limited to OSN, but can also be applied using other types of membrane processes as reverse osmosis or aqueous ultrafiltration, depending on the properties of the reaction mixture and the reactive species.

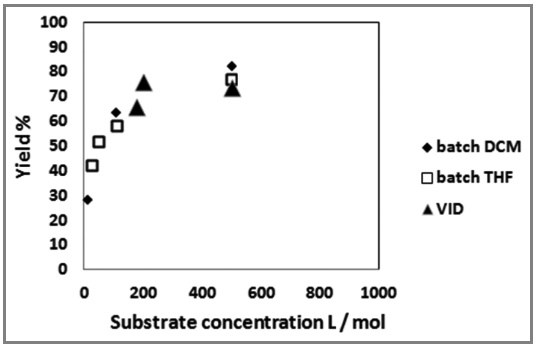

**Figure 5.** Yields for the Mitsunobu test reaction when performed in batch (using DCM or THF as reaction solvent) and when performed using the new VID process.

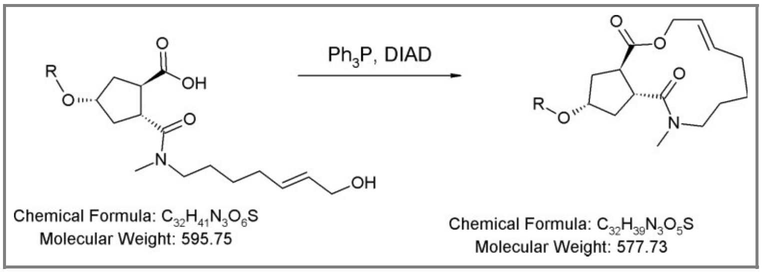

**Figure 4.** Mitsunobu reaction chosen as test reaction for the new OSN-assited VID process.

## 5 Conclusion

To support the implementation of the emerging high-potential membrane process OSN in industry, VITO offers the use of a mobile pilot installation, specifically designed to meet GMP requirements and to allow testing with both polymeric and ceramic membranes. An overview was given on the potential of OSN, and the implementations already performed in different industrial sectors. Moreover, a new successful membrane-assisted process, VID, was described allowing for efficient, volume-intense performance of reactions that normally require economically unfavorable high dilutions.

## Abbreviations

| | |
|---|---|
| API | active pharmaceutical ingredient |
| DCM | dichloromethane |
| GMP | good manufacturing practice |
| OSN | organic solvent nanofiltration |
| THF | tetrahydrofuran |
| VID | volume intense-dilution |

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Organic solvent nanofiltration is an emerging technology that offers an economically interesting alternative for common separation processes. The broad potential of this new sustainable separation technique in the chemical industry is discussed. A pilot installation meeting all the requirements needed for proof of principle testing and pilot scale batch production is described.