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Trabajo Fin de Grado

Fabricación y caracterización de membranas poliméricas biocompatibles de poliacrilonitrilo mediante inversión de fases para su aplicación en proliferación y diferenciación de células neuronales

(Synthesis and characterization of biocompatible polyacrylonitrile membranes by phase inversion technique for proliferation and differentiation of neural cells)

Para acceder al Titulo de

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TÍTULO	**Fabricación y caracterización de membranas poliméricas biocompatibles de poliacrilonitrilo mediante inversión de fases para su aplicación en proliferación y diferenciación de células neuronales**		
AUTOR	**Charlotte Juveneton**		
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TITULACIÓN	*Grado en Ingeniería Química*	**FECHA**	Febrero 2015

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PLANTEAMIENTO DEL PROBLEMA/SCOPE

El cerebro humano es uno de los órganos más complejos del cuerpo. En comparación con los animales, el cerebro humano es mucho más complicado y por tanto, los modelos de cerebro animal no reproducen realmente la complejidad del comportamiento del cerebro humano. Debido a que los mecanismos de las enfermedades, los medicamentos y otros estímulos no se pueden simular fielmente con modelos de cerebro no humanos, y su estudio en cerebros vivos es difícil y limitado, una idea que se propone es el desarrollo de modelos de cerebro humano *in vitro* de forma que puedan sustituir a los actuales modelos de cerebros de raton (Bae & Walsh, 2013)
Estos "mini cerebros" se construyen a partir de la proliferación *in vitro* de células madre y su diferenciación en células neuronales y en tejido cerebral. Los tejidos resultantes deben integrar todas las características de los cerebros humanos y desarrollar sus mismas respuestas funcionales.

En el presente trabajo, se propone como objetivo estudiar la fabricación de la membrana polimérica que servirá como soporte (scaffold) de crecimiento celular y que integrará el bioreactor para el desarrollo de un cerebro humano *in vitro*. La membrana polimérica a desarrollar debe poseer alta permeabilidad para permitir el transporte adecuado de los nutrientes hasta las células y tejidos.
El desarrollo de estas membranas poliméricas de alta permeabilidad se fabricarán utilizando la técnica de inversión de fases. El polímero a utilizar es el poliacrilonitrilo (PAN), que es un material biocompatible y de probada eficacia en la proliferación de células neuronales (Morelli et al., 2012). Se estudiará la influencia de usar diferentes baños de coagulación en el proceso de fabricación en las propiedades físicas (morfología de la membrana, porosidad, hidrofilicidad, etc.) y de transporte.

RESULTADOS /RESULTS

Se han preparado por inversión de fases membranas planas de PAN mediante un procedimiento similar al utilizado en anteriores trabajos del grupo (Gómez, 2014) usando una disolución polimérica al 10% en peso de PAN en N-metilpirrolidona (NMP) y como coagulantes agua (W), etanol (EtOH) e isopropanol (IPA)

El uso de W como coagulante dio lugar a la morfología de membrana más diferente. Sin embargo, usar EtOH o IPA produjo una estructura de membranas muy similar de acuerdo a las imágenes SEM. La menor velocidad de intercambio difusional entre el disolvente (NMP) y los coagulantes en el orden siguiente: W>EtOH>IPA, dio lugar a una menor porosidad y tamaño de poros. La porosidad y tamaño de poros más altos fueron por tanto en las membranas PAN/W. En cuanto a las membranas PAN/EtOH y PAN/IPA, la porosidad se encontraba en entre 10-34 % y el tamaño de poros entre 9-14 nm (rango de ultrafiltración) y su estructura era en general bastante compacta. Además, las membranas con espesor más delgado de PAN/EtOH y PAN/IPA presentaban transparencia que es una cualidad deseable para la evaluación en línea de cultivos celulares mediante técnicas ópticas como la microscopía confocal.
Las medidas de ángulo de contacto de agua mostraban valores entre 16-35º para todas las membranas, lo que indica un alto grado de hidrofilicidad. Esto hace esperar, que a pesar de los bajos valores de porosidad y tamaño de poro de las membranas PAN/EtOH y PAN/IPA se obtengan altos flujos de agua. Efectivamente, los valores de permeancia de estas membranas (225 y 160 L/h.m².bar para PAN/EtOH y PAN/IPA respectivamente) están en el rango de valores de otras membranas utilizadas en previos estudios de proliferación de células neuronales (Morelli et al., 2012)

CONCLUSIONES / CONCLUSIONS

Las membranas de PAN fabricadas en este trabajo presentan una morfología bastante compacta (poco porosa), que se atribuye principalmente a la baja concentración de polímero en la disolución polimérica utilizada durante el proceso de fabricación. Esta baja concentración de polímero produjo una viscosidad baja de la disolución y por tanto una mala distribución de la lámina durante el proceso de casting o extendido de la disolución. Esto produjo a su vez una alta variabilidad en el espesor de las membranas fabricadas y una compactación por gravedad de las membranas PAN/EtOH y PAN/IPA que precipitan más lentamente que la PAN/W.
Asi pues, aunque los resultados de permeabilidad y las cualidades del material hacen que estas membranas parezcan prometedoras para la proliferación de células neuronales, se necesita mejorar en futuros trabajos el método de fabricación para optimizar las propiedades de morfología y porosidad de las membranas así como la homogeneidad del método de fabricación.

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TÍTULO	**Synthesis and characterization of biocompatible polyacrilonitrile membranes by phase inversion technique for proliferation and differentiation of neural cells**		
AUTOR	**Charlotte Juveneton**		
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TITULACIÓN	*Degree in Chemical Engineering*	**FECHA**	February 2015

PLABRAS CLAVE/KEYWORDS

Biocompatible flat membranes, Neural cell proliferation and differentiation, phase inversion technique, polyacrylonitrile, tissue engineering

PLANTEAMIENTO DEL PROBLEMA/SCOPE

The human brain is one of the more complicated and mysterious organs in the human body. Compared to animals, the human brain is lot more complex and for this reason no animal model truly reports the complexity of the human brain behaviour. As the effect of diseases, drugs and others stimuli was not clearly simulated on non-human brains, and their study on alive human brain is complicated and technically limited, the idea of developing *in vitro* human cerebral models has been proposed as a promising alternative to current *in vivo* mice models (Bae & Walsh, 2013).
These "mini brains" should be developed *in vitro* from the proliferation of stem cells and their differentiation into different neural lineages and further neural tissues. These neural tissues have to integrate all the characteristics and functionality of human brain.
The present work aims at evaluating the fabrication of a polymeric membrane able to support the proliferation of cells *in vitro* which would be integrated in a bioreactor. The new bioreactor must hold highly permeable polymeric membranes (scaffolds).
The development of these highly permeable polymeric membranes will be made by phase inversion of a biocompatible polymer, polyacrylonitrile (PAN), already proved as a good biomaterial to promote neural cell proliferation (Morelli et al., 2012). The influence of different coagulation baths on the physical (morphology, porosity, hydrophobicity, etc.) and transport properties will be studied.

RESULTADOS /RESULTS

By using a 10% w/w solution of PAN in N-methylpyrrolidone (NMP), flat membranes were fabricated by phase inversion process following similar procedure as previously reported (Gomez, 2014) using water (W), ethanol (EtOH) and isopropanol (IPA) as coagulants.
The use of W as coagulant presented the most different membrane morphology. However, between using EtOH or IPA, both membranes presented similar structure in the SEM images. Slower diffusion exchange between the solvent (NMP) and non-solvent (diffusion rate in the following order: W>EtOH>IPA) resulted in obtaining smaller pore size and porosities. Higher porosity and pore size was observed for PAN/W membranes. Regarding PAN/EtOH and PAN/IPA membranes, the obtained values of porosity (10-34 %), as well as pore size were very low, in the range of 9-14

nm (ultrafiltration range) and their structure is relatively dense in general. Besides, PAN/EtOH and PAN/IPA membranes presented transparency (at low membrane thickness) which is a desirable property for the evaluation on-line of cell cultures using optical equipment, such as confocal imaging techniques.
Measurements of water contact angle were in the range of 16-35º, showing that PAN membranes are highly hydrophilic and therefore, despite the low porosities and pore size, high water flux of the membranes PAN/EtOH and PAN/IPA is expected.
The water permeance values for PAN/EtOH and PAN/IPA membranes (225 and 160 L/h.m².bar respectively) are in the range of previous works indicating that the studied membranes can be used for neural cells proliferation (Morelli et al., 2012).

CONCLUSIONES / CONCLUSIONS

The PAN membranes fabricated in the present work presented quite dense morphology and low porosity, attributed mainly to the low polymer concentration used during the fabrication method. This low polymeric concentration led to low polymer solution viscosities and bad solution distribution during the casting process. This caused a high variability in the membrane thickness and compaction by gravity of the membranes PAN/EtOH and PAN/IPA that precipitated more slowly during the coagulation. Therefore, although the results of permeability and other qualities of the PAN material are promising for neural cell proliferation, further improvement of the fabrication method is recommended for future work to optimize the membrane morphology and porosity as well as homogeneity of the membranes.

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A mi familia y amigos, que siempre creyó en mí y me dan animó para seguir adelante.

Charlotte Juveneton

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1. Approach

1.1 Introduction

The human brain is one of the more complicated and mysterious organs in the human body. The various functions of the brain and their implications are multiple. Compared to animals, the human brain is lot more complex and for this reason no animal model truly report the complexity of the human brain behaviour: for example, the animal brain mostly used to simulate the human brain is the mouse's one, but simulating human cerebral disease on a mouse brain, whose cerebral cortex is 100 time smaller, is very limited. The techniques available to analyse directly on human brain are very limited and the experimentation with living human brains is rather complicated. Therefore, it is compulsory to promote the quest for scientific alternatives to accurately evaluate the behaviour of human brain, its disease mechanisms and diagnosis techniques and the best treatments to be supplied to the patients [1].

As the effect of diseases, drugs and others stimuli was not clearly simulated on non-human brains, the idea of developing *in vitro* human cerebral models has been proposed as a promising alternative to current *in vivo* mice models. However, due to the difficulty on regenerating brain tissues *in vitro*, the development of this technology is a challenge. Lancaster *et al*. [2] have provided a major leap to this technology by developing a method to grow miniature human brain like structures (cerebral organoids) from embryonic stem (ES) cells *in vitro*. They also demonstrated that human cerebral organoids permit to model human diseases in a better way than do mice brain models. These "mini brains" have to integrate all the characteristic of human brain from the embryonic development to a complete adult cerebral cortex: these brains could be the next step to model human diseases. [3]

When human and mouse ES cells are cultured in special conditions, they can produce organoids with strong common points with precursors of various brain structures. Under these conditions, these organoids are able to self–organized and differentiate themselves into the target organs (e.g. meninges, hippocampus, retina or neurons). Based upon this idea, *Lancaster et al.* developed a culture system for human ES cell-derived, in a three-dimensional system. This technique of culture introduces ES cells embedded in droplets of Matrigel (a gelatinous protein mixture) within a spinning bioreactor, providing the structural support and

the nutrient/oxygen exchange that allows growth of larger and complex organoids (up to 4 mm in diameter). However, the organoids are still not sufficiently large to reproduce the human brain synapsis, and further research must be done.

In the present work, an alternative system, represented in Figure 1.1, to develop an *in vitro* human brain is proposed. The proposed system integrates a complete bioreactor that is composed of: membrane that will be the support of cell proliferation and differentiation, a special bioreactor configuration simulating a vascularized tissue and the control of some operating variables. The most important point for the improvement in the design of the bioreactor is based on the amelioration of the transport properties in order to reduce the mass transport resistances to the oxygen delivery to the cells and maximize the artificial vasculature of the regenerated tissues. This innovative bioreactor could permit obtaining *in vitro* human cerebral models able to produce reliable data of the human brain behaviour; this data could be applied to study diagnostic techniques and therapeutics in the biomedical and pharmaceutical sectors and to provide a better comprehension of the human brain reactions.

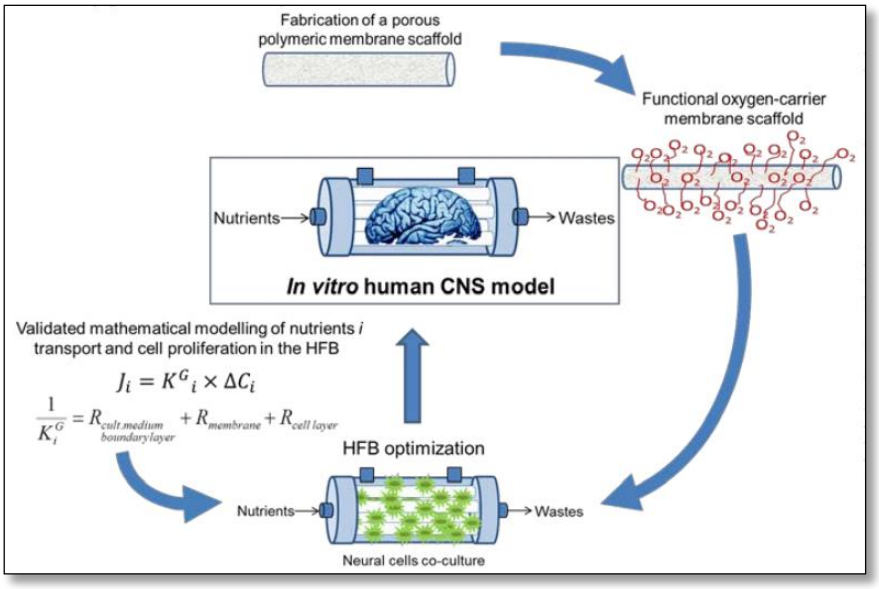


Figure 1.1: Conceptual design of the integral process of in-vivo human brain model

The new bioreactor must hold highly permeable polymeric membranes (scaffolds). The development of these scaffolds will be the aim of the present project.

1.2 Scaffolds

One of the main areas of research in tissue engineering and cell proliferation is the design of the scaffolds or three-dimensional structures on which cell growth occurs. The majority of the cultivated cells in tissue engineering need to adhere to a solid surface to grow. Therefore, the surface of the support structure or scaffold on which the cell adhesion and proliferation takes place as well as the transport properties through these scaffolds have an influence on cell growth and tissue formation.

For the application in proliferation and differentiation of cells, the scaffolds should have some special properties:

- *Biocompatibility*:

The materials used in the manufacture of the scaffold must not have any adverse biological reaction.

- *Promote cell adhesion, diffusion and proliferation*:

The scaffold must induce cell adhesion and proliferation on its surface and cell diffusion across its three-dimensional structure for the regulation of cell growth and differentiation. This property is directly related to the surface morphology and porous structure.

- *Good transport properties*:

The scaffolds need to provide a proper transport of nutrients to the cells while removing waste products. High porosity, good connection between pores and good mechanical strength are, therefore, necessary characteristics of the scaffolds.

In order to make scaffolds, various materials can be used and they can be classified depending on the required mechanical properties for the various applications in biomedical engineering. Two groups can be established: one for “soft” application such as cardiovascular or musculoskeletal tissue and the other one for “hard” applications such as bone tissue [4].

In general, a large range of polymers can be used for “soft” applications whereas for “hard” applications, rigid polymers, ceramic or metal are used [4]. There are a lot of advantages to use polymers in this area, they are biocompatible, easy to process and shape, and have a good mechanical strength. Besides, the properties of the polymers can be easily tailored.

Among the different polymers that can be applied for tissue engineering applications, polyacrylonitrile (PAN) is a biocompatible polymer, have a hydrophilic behaviour and in addition this polymer has a nitrile group that can be chemically functionalized. Furthermore, the application of a PAN copolymer has been already proven to give good results [5] for the proliferation of neural cell lineages and it is non-biodegradable which preserves its stability for long term use in *in vitro* human brain models.

1.3 Fabrication Process: phase inversion

The behaviour of cells under *in vitro* culture conditions is influenced by the structure of the scaffolds, which depends on the manufacturing method employed. Particularly for polymeric scaffolds, the phase inversion process is a very versatile method to fabricate a scaffold with tailoring properties to adapt to the necessary characteristics that an adequate scaffold should gather which have been mentioned before. The phase inversion process is a fast and cheap method that can be easily used and allows the fabrication of reproducible membranes of different polymeric materials.

To fabricate flat polymeric films (or membranes) by phase-inversion technique, the polymeric solution is extended on a glass support, introduced into a coagulation bath of a solvent immiscible with the polymer, but miscible with the solvent of the polymeric solution. The polymer coagulation occurs due to the exchange between the solvent of the polymer solution and the coagulation bath solvent (non-solvent of the polymer), driven by concentration difference. The exchange rate depends on the affinity between the non- solvent and the solvent: it is faster when the affinity between the two solvents is high [6]. During the process of phase separation by immersion, in which an instantaneous precipitation occurs, a dense top layer is usually formed and below this layer, there is a zone with macropores. If the precipitation is not instantaneous, and depending on the exchange rate between both solvents, the obtained membrane might have a microporous/nanoporous structure with different pore size [7].

This fabrication method has been used in various different works on the subject. Membrane fabrication by phase inversion is commonly used to make flat membranes with others polymers like PCL [8] or for example some hollow fibers made of PAN [5] or others polymers like poly(vinylchloride)/polystyrene/poly(ethylene glycol) [9]. In all these works, phase inversion techniques were applied to perform these membranes.

1.4 Objective

The aim of this project is the fabrication of flat membranes of a biocompatible polymer, polyacrylonitrile (PAN), by casting and phase inversion, to be applied at *in vitro* neural cell proliferation and differentiation.

The influence of different coagulation baths (water, ethanol and isopropanol) on the physical (morphology, porosity, hydrophobicity, etc.) and transport properties will be studied in order to determine the most promising PAN membrane herein fabricated to be applied for neural cell proliferation.

2. Development

2.1. Polymer solvent and non-solvent selection

In this study, to prepare the polymer solution of PAN, three different solvents were first considered: N-methylpyrrolidone (NMP) [10], tetrahydrofurane (THF) and dimethylformamide (DMF) [5].

The DMF was discarded because to solve PAN, the solution had to be heated at 70°C [5] and working at room temperature was preferable.

Regarding THF, this is a very common solvent for the measurement of molecular weight in Gel Permeation Chromatography (GPC) while NMP is also a common polymer solvent and it was used in some previous works on the subject (i.e. PAN membranes [9][10] and Poly-caprolactone (PCL) flat membranes [8])

To be sure of the selection of NMP as solvent and to determine the coagulants, the solubility space study was introduced for NMP and THF solvents first and then for water (W), ethanol (EtOH) and isopropanol (IPA) as possible coagulants.

The distance between the solvent, NMP or THF respectively, and the PAN ($\Delta\delta_{s\text{-}p}$) in the solubility space was calculated according to the following equation: [11]

$$\Delta\delta_{s-p} = (4.\left(\delta_{d,s} - \delta_{d,p}\right)^2 + \left(\delta_{p,s} - \delta_{p,p}\right)^2 + \left(\delta_{h,s} - \delta_{h,p}\right)^2)^{1/2} \qquad \textit{Equation 1}$$

Where δ_d, δ_p, δ_s represents the dipole, polar and hydrogen bonding components, respectively, of the solubility parameter (δ_t); the subscript *s* represents the solvent (NMP, THF) or non-solvent (water, EtOH or IPA) and the subscript *p* represents the polymer (PAN).

Furthermore, the total solubility parameter δ_t is defined as follows (Equation 2):

$$\delta_t = (\delta_d^2 + \delta_p^2 + \delta_h^2)^{1/2} \qquad \textit{Equation 2}$$

2.2 Preliminary determination of the concentration of the polymer solution

Before starting the fabrication of the PAN polymeric membranes, it was necessary to determine the adequate concentration of PAN in the solution. An important parameter to establish the optimal polymer concentration in a polymer solution is the viscosity. The viscosity of the polymer concentration was measured using a rotational viscometer (Fungilab, Alpha Series). In order to measure the viscosity, a small volume (8-10 mL) of the polymer solution was placed into a container inside the viscometer and a spindle was placed in the equipment. The spindle type and rotation velocity were selected depending on the viscosity range expected. Therefore, two different spindles, TL5 at 0.5 rpm to measure viscosities up to 5000 cP and TL6 at 5 rpm and 6 rpm to measure viscosities up to 6000 and 5000 cP, respectively, were used during experiments.

According to previous works [10][12][13], the most common range of PAN concentration in the polymer solution, using different type of solvents for phase inversion casting in membrane fabrication, was found to be between 10 and 20% by weight (%w/w). Therefore, the viscosity the polymer solutions was measured by progressively increasing the PAN concentration from 10 to 20 %w/w in the different solvents under selection.

2.2 Experimental methodology

2.2.1 Fabrication of PAN membranes using phase inversion casting

For the preparation of the PAN flat membranes, a polymer solution was prepared using a 10% w/w of PAN (MW 150000 Da, Sigma - Aldrich) using NMP (99 %, Extra Pure, Acros Organic) as solvent.

To facilitate the solution of the PAN in the solvent, this solution was stirred using a mechanical stirrer for 24 h up to complete solution and homogenization of the PAN. Afterwards, the polymer solution was filtered through a metal mesh filter with pore diameter of 25 µm (Figure 2.1) to remove any traces of not solved polymer or particles, in order to avoid any imperfection in the manufacturing of the membranes.

Figure 2.1: Filter wire mesh, filter flask and vacuum pump.

After filtering, the solution was left in a glass flask (Figure 2.2) tightly capped (in order to avoid the evaporation of the solvent) for degassing for 24 h.

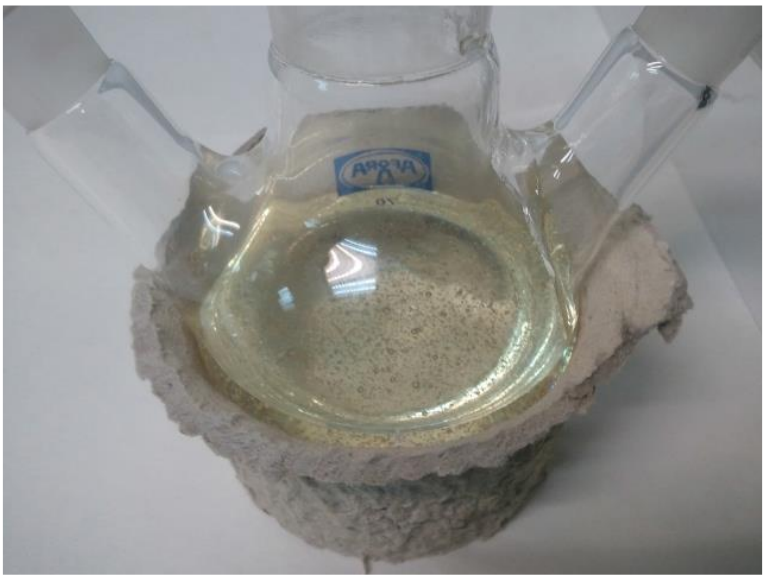


Figure 2.2: 10% w/w PAN solution in NMP filtered and ready for degassing

After verification that the solution is free of bubbles, the solution was ready to be used. During the casting, a small amount of the solution was poured on a glass plate with no surface defects, and with a casting knife the solution was extended along the glass plate. The casting knife was previously adjusted to a height of 200 µm.

Immediately after the extension of the solution, the glass plate with the casted polymer solution was immersed in the coagulation bath aiming at the polymer precipitation (Figure 2.3). Three different coagulation baths were used: ultra-pure water (W, MilliQ, Millipore), ethanol (EtOH, technical, Acros Organics) and iso-propanol (IPA, 99.9%, Oppac). The membranes obtained were coded according to the solvent employed during coagulation, as: PAN/W, PAN/EtOH and PAN/IPA using W, EtOH and IPA as coagulants, respectively.

Once the polymer film has coagulated, the membrane is spontaneously separated from the glass plate. Afterwards, the membrane was transferred to a second coagulation bath with the same composition as the first one. To ensure complete coagulation of the polymer, the membrane was left into this bath during 24 hours.

Figure 2.3: Glass plate and PAN polymer solution immersed in the coagulation bath for the exchange of the solvent and non-solvent to promote the PAN precipitation

Then, traces of the solvent and non-solvent were completely cleaned by immersing the membranes into ultrapure water for 48 hours. The water was changed 3 times a day to ensure a complete solvent removal in the membrane. This step is really important to be sure that there is no solvent (NMP) remaining in the membrane structure because during the utilisation of the membranes, this product could cause several damages to the *in vitro* system.

The PAN flat membranes were stored in water until their use in further characterization studies.

In order to evaluate the better procedure to store dried PAN membranes, different preservative solutions to retain the mechanical stability and microstructure morphology of the membrane were tested. The composition of the preservative solutions was: 100% glycerol (99%, Panreac, Spain), 50%v/v glycerol/water, 25%v/v glycerol/water and 100% IPA. The membranes were immersed during 24 h in the preservative solution and then, were left air drying for 24 h. The flexibility of the dried membranes was tested and compared to the membranes not immersed on preservative and left air drying.

2.2.2 Physical characterization of membranes

❖ Thickness of the membrane:

The thickness of the membranes (δ) was measured by using an electronic micrometer (Model Standard, Serie 293, Mitutoyo).

❖ Porosity:

Membrane porosity (ε) can be defined as the void fraction, that is, the pore volume divided by the total volume of the membrane (Equation 3).

$$\varepsilon(\%) = \frac{V_T - V_M}{V_T} . 100 \qquad \textit{Equation 3}$$

Where V_T is the total volume (cm^3) of the sample (membrane and pores) and V_M is the volume of the membrane without pores (cm^3).

The porosity was determined by using the gravimetric method described by *Alsalhy et al.* [9]. In summary, the porosity was evaluated using two different types of solvents: water and kerosene. The initially humid samples (containing water) were weighted (W_1 (g)) with a balance (AT21 Comparator, Mettler Toledo) in order to determine the water porosity. Then the membranes were introduced into a vacuum oven (Vaciotem-T, P- Selecta) for 24 hours, at 30°C and 200 mbar. Once dried, the samples were weighed again (W_2 (g)) and immersed in kerosene for another 24 hours. After this immersion, the samples were weighted for the third time (W_3 (g)). Before weighting the humid samples (W_1 and W_3) the excess of liquid on the membrane surface was carefully removed. The porosity is finally calculated according to Equations 4 and 5: [9]

$$\varepsilon_w(\%) = \frac{(W_1 - W_2)/\rho_w}{[\,(W_1 - W_2)/\rho_w + W_2/\rho_p} . 100 \qquad \textit{Equation 4}$$

$$\varepsilon_k(\%) = \frac{(W_3 - W_2)/\rho_k}{[\,(W_3 - W_2)/\rho_k + W_2/\rho_p} . 100 \qquad \textit{Equation 5}$$

With: $\boldsymbol{\varepsilon}_w$ and $\boldsymbol{\varepsilon}_k$ are the average porosity obtained for water or kerosene, respectively; ρ_k represents the density of the kerosene: 0.82 g/cm^3 (at room temperature), ρ_w represents the water density: 1 g/cm^3 (at room temperature); ρ_p represents the density of the PAN: 1,184 g/cm^3 (Sigma Aldrich).

❖ Scanning Electron Microscopy (SEM)

The structure and morphology of the surface and cross section of the membranes were analysed by the technique of scanning electron microscopy (SEM, EVO MA 15, Carl Zeiss) applying a voltage of 12.6 kV. To study the cross section, the samples were prepared and fractured by immersion in liquid nitrogen. Before realizing the SEM analysis, the samples of both cross section and surface were maintained at 30 °C and 200 mbar overnight.

For the measurement, the samples were coated with a thin gold film: method known as "gold sputtering". These experiments were conducted at the laboratory of the Division of Science and Engineering Materials (LADICIM) of the University of Cantabria.

❖ Water contact angle

When a drop of a fluid is set on a flat surface, it takes a special form that depends on the nature of the surface and the forces between the fluid and the surface of the membrane. The angle formed between the contact point of the drop and the surface of the membrane, is called contact angle (θ), as it can be seen in the Figure 2.4. The water contact angle, θ_w, is useful to study the degree of hydrophobicity of the surface. Hydrophilic surfaces show values of $\theta_w<90^o$ whereas for hydrophobic surfaces, this value is higher than 90^o [14].

Figure 2.4: Measurement of the contact angle

The static water contact angle was measured as follows: a water drop is set on the membrane surface with the help of a syringe and pictures of the angle formed between the water drop and the membrane surface (θ_w) were taken. The measurement of θ_w was performed using the software Meazure 2.0 (C Thing Software, USA).

❖ Transparency

Transparency might be a very valuable property to facilitate on-line optical measurements (microscopy techniques) of the evolution of cell behaviour (adhesion and proliferation, as well as tissue differentiation) on the membranes in a bioreactor. The transparency of the PAN membranes was evaluated qualitatively. Pictures of the membranes were taken to show the influence of the coagulation bath on the degree of transparency of the membrane.

❖ Characterization of transport properties: clean water flux

For the determination of transport properties of membranes, we measured the clean water flux by using a dead-end flow filtration system (Figure 2.5).

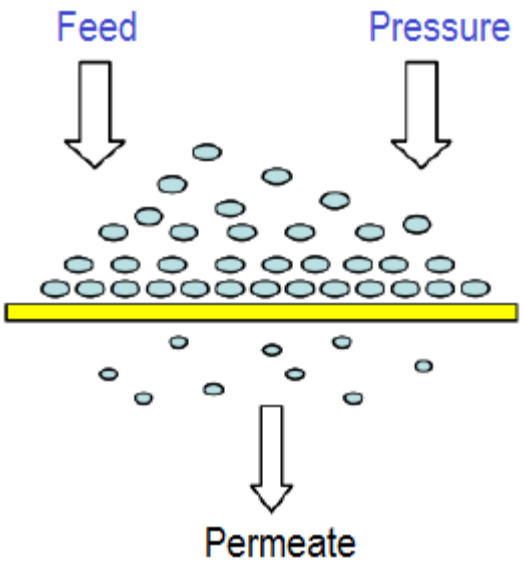


Figure 2.5: Mechanism of transport of the molecules through a Dead-End Flow Filtration System

The dead-end flow experimental system can be seen in Figure 2.6.

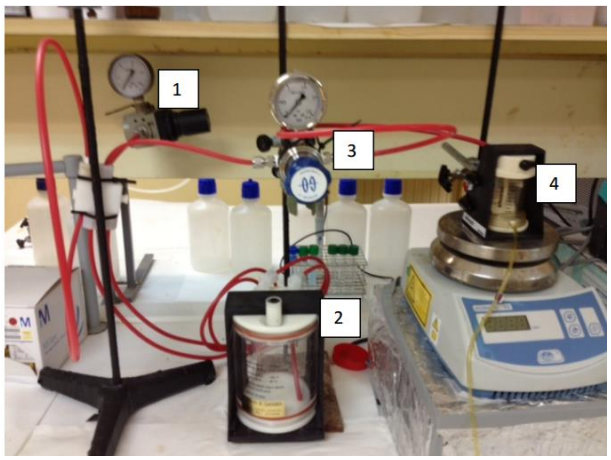


Figure 2.6: Dead-end flow experimental system

This experimental system is composed of a manual air pressure reducer valve(0-10 bar) set to 2 bars (1), a pressurized feed tank of 1L (Millipore) (2), a liquid pressure reducer (0-2.5 bar) (3), and a cell membrane (Amicon Cell), with a filtration effective area of 13.4 cm^2 (4).

The water flux of the membrane was measured during 8 hours, under a constant transmembrane pressure of 0.2 bar, typical in a perfusion bioreactor (between 0.1-0.3 bar) [15]. For the determination of the water flux, the volume (L) of water permeated across the membrane during the 8 hours of experiment was collected at different time intervals, thus obtaining the permeate flow rate ($L.h^{-1}$). By dividing this flow rate by the effective membrane area, we obtained the permeate flux ($L.m^{-2}.h^{-1}$).

One of the most important parameters that characterize the transport properties of the membranes is the hydraulic permeance or permeance coefficient of water, K_w. To determine K_W, Equation 6 was used [14]:

$$J_w = K_w \,.\, \Delta P \qquad \textit{Equation 6}$$

Where J_w is the permeate flux ($L.m^{-2}.h^{-1}$), K_w is the water permeance of the membrane ($L.m^{-2}.h^{-1}.bar^{-1}$) and ΔP is the pressure applied to the membrane (bar).

2.3 Results and discussion

❖ Polymer solvent and non-solvent selection

As previously reported, the selection of the combination of solvent and non-solvents of PAN in the present study was done by analysing the solubility space of the polymer by using the Equations 1 and 2. According to this procedure the following table was established:

Table 2.1: Solubility parameters and solubility space of potential solvents and non-solvents of PAN

PAN and Coagulation bath	δ_d $(MPa)^{1/2}$	δ_p $(MPa)^{1/2}$	δ_h $(MPa)^{1/2}$	δ_t $(MPa)^{1/2}$	$\Delta\delta_{s\text{-}p}$ $(MPa)^{1/2}$	Litterature
PAN	18.2	16.2	6.8	25.3	-	[16]
NMP	18	12.3	7.2	22.9	3.9	[17]
THF	16.8	5.7	8	19.5	10.9	[18]
Water	15.6	16	42.3	47.8	35.9	[17]
EtOH	15.8	8.8	19.4	26.5	15.4	[19]
IPA	15.8	6.1	16.4	23.6	14.7	[19]

Low value of $\Delta\delta_{s\text{-}p}$ means a high solubility of PAN in the solvent, indicating that it is a good solvent for the polymer under study: in this case, these calculations show that the NMP is the best solvent for PAN because it presents the lower value of $\Delta\delta_{s\text{-}p}$. The value of $\Delta\delta_{s\text{-}p}$ for the set THF-PAN is much higher than for NMP-PAN and very proximate to the value of $\Delta\delta_{s\text{-}p}$ for IPA-PAN, which could indicate a very low or null solubility of PAN in THF at room temperature. This observation was confirmed experimentally. After 24 hours of stirring of the mixture of PAN (10%w/w) in THF the polymer was not soluble. For this reason, the NMP was chosen as the only solvent to be tested in the present study.

Furthermore, the higher the difference of the total solubility parameter δ_t between the solvent and non-solvent is, the more intense the exchange between them is and the faster the polymer coagulates [20].

Table 2.1 indicates that W, EtOH and IPA are good coagulants for PAN and that the affinity between the non-solvents and the polymer is in the following order: W>EtOH>IPA.

❖ Polymer concentration

Considering that, between the two solvents under consideration, THF and NMP, only NMP could solve PAN, the viscosity of the PAN in NMP was considered for further analysis, increasing progressively the PAN concentration up to reach viscosity values of the polymeric solution that could fit in the range of those values experimentally used for phase inversion [10, 12-13]. The viscosity required for casting is in the following range: 2000-6000 cP [21].

The viscosity of the polymer solution must be high enough to preserve the consistency of the casted solution but not too high because the higher the polymer concentration the lower the porosity of the membrane will be. Based on these considerations, a 10% w/w solution of PAN in NMP was tested. The results can be seen in the following Table 2.2:

Table 2.2: Viscosity experimental results

Spindle	Velocity (RPM)	Average viscosity (cP)
TL 5	0.6	3594 ± 30
TL 6	6	3630 ± 40
TL 6	5	3623 ± 15

As the prepared solution was in the range indicated by literature it was considered sufficient to perform casting process for the fabrication of membranes by phase inversion technique [21]. Therefore, it was not necessary to test higher polymer concentrations. Besides, the higher the polymer concentration is, the lower the porosity of the membrane is usually achieved by phase inversion [4].

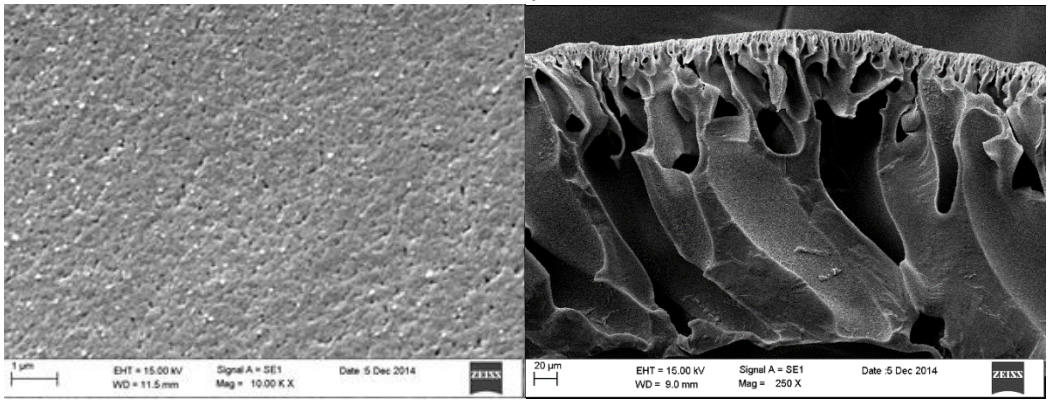
2.3.1 Physical Characterization

To realize all the characterization experiments, between 3 and 5 samples were tested for each type of membrane, PAN/W, PAN/EtOH or PAN/IPA. This multiplicity of samples was necessary to prove the reproducibility of the properties of the membranes.

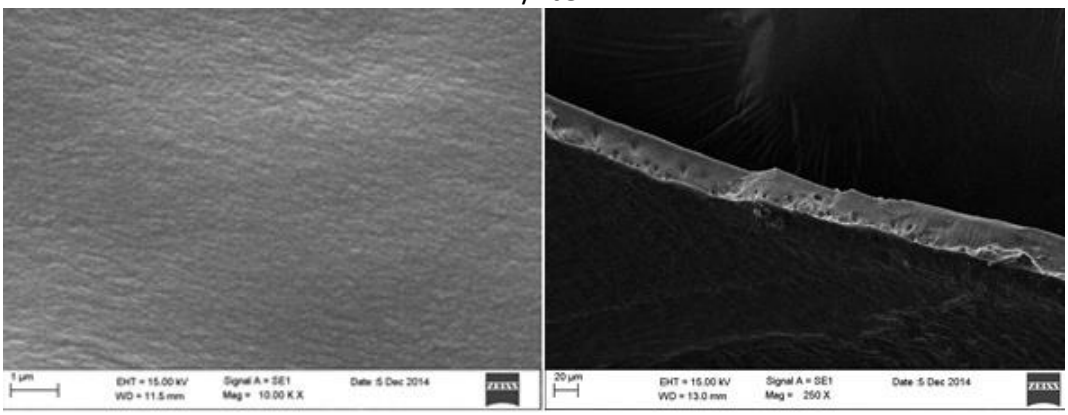
- Scanning Electron Microscopy (SEM)

The structure and morphology of the surface and cross section of the PAN membranes are shown in Figure 2.7.

PAN/W



PAN/EtOH



PAN/IPA

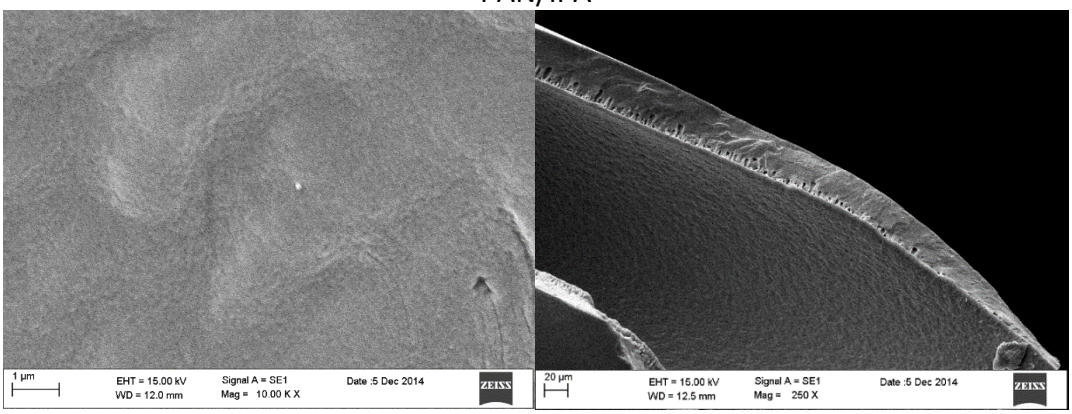


Figure 2.7: SEM Pictures of the PAN membrane surface (left picture, magnification: x10 000) and cross section (right picture, magnification: x250) using different coagulation baths

PAN/EtOH and PAN/IPA membranes presented a quite dense surface while PAN/W had small pores, already visible at the SEM x 10000 magnifications, uniformly scattered through its surface. Regarding the cross section pictures, the three membranes presented asymmetric structures, however, PAN/EtOH and PAN/IPA had mainly dense cross sections, similarly to the surface images, and small macrovoids located only at the upper part of the membrane.

On the other hand, PAN/W membranes had high macrovoids structure distributed in the whole cross section of the membrane. This structure points to a high porosity of PAN/W membranes, while PAN/EtOH and PAN/IPA membranes presented qualitatively very low porosity.

The polymer concentration used in the present study (10%w/w) can be considered very low in comparison with other works. In general, the lower the polymer concentration, the higher the porosity of the membranes is [13, 22]. According to SEM images, this statement was true only in the case of PAN/W, while it was not the case for PAN/EtOH and PAN/IPA membranes. This could be attributed to the low viscosity of the polymer solution and the slower coagulation rate of PAN/EtOH and PAN/IPA membranes in comparison to PAN/W membranes. As the exchange between NMP and W is fast, PAN/W membranes were coagulated fast and the internal porous structure was preserved. However, the slow exchange between EtOH and NMP, and IPA and NMP (see affinities in Table 2.1) slowed down the polymer coagulation favouring that the gravity affected the porous structure by compacting the polymer. In this case, the viscosity of the polymer solution, which usually helps holding the thickness of the polymer up to the coagulation takes place, was too low so the solution rapidly compacted by gravity reducing importantly the membrane thickness as it can be seen in Figure 2.7.

❖ Porosity and thickness of the membrane

Table 2.3 shows the results of the measurements of the thickness of the different membranes (δ), and the porosity in water (ε_w) and kerosene (ε_k) according to Equations 4 and 5, expressed as average values ± error.

Table 2.3: Thickness and porosity of PAN/W, PAN/IPA and PAN/EtOH membranes

Membranes	δ (µm)	ε_w (%)	ε_k(%)
PAN/W	229 ± 12	94 ± 2	80 ± 3
PAN/EtOH	276 ± 130	87 ± 4	10 ± 5
PAN/IPA	93 ± 7	89 ± 6	34 ± 11

As the casting knife height was set at 200 µm, δ should be ≤ 200 µm. For PAN/IPA, the thickness value seems to match the expected results. The thickness of PAN /W is slightly higher than expected but this value is verified by SEM pictures whereas for PAN/EtOH the thickness measured with the micrometer and by using the SEM pictures are different. An important deviation is observed for the thickness of this membrane; the membrane used for clean water flux were all very thick meanwhile the one used for the SEM experiment was in the low range of thickness indicated in the table. That is why PAN/EtOH thickness measured by using SEM pictures is not really representative of the measurements presents above. The high values of δ for PAN/W and PAN/EtOH could result from the measurement of the membrane thickness from a side of the membrane where the polymer solution has been flowed to while the glass plate was tilted during the casting and phase inversion procedure. This effect was observed experimentally during the casting process and it was attributed to the low viscosity of the polymer solution.

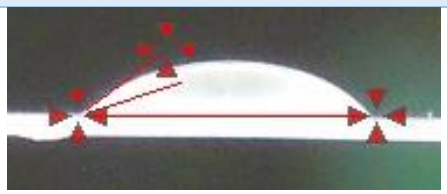
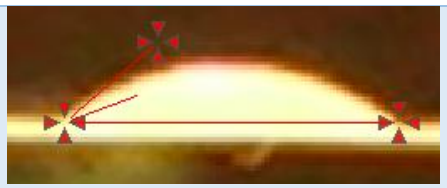
Regarding the porosity, water and kerosene porosity values are in agreement with SEM images for PAN/W membranes. However, for PAN/EtOH and PAN/IPA membranes the values of water porosity are really high in comparison to kerosene porosity. Besides, these values are not realistic compared with the SEM pictures of membranes: these photos show really dense membranes with few pores. These results could be due to the high hydrophilic characteristics of the PAN membranes: they might retain water into their pores and even swell the membrane by water adsorption.

The measurements performed with kerosene were more in agreement with the SEM images in Figure 2.7: porosity values obtained with kerosene indicate that PAN/IPA membranes had higher porosity than PAN/EtOH membranes. Compared to the results of kerosene porosity obtained for poly-ε-caprolactone (PCL) membranes fabricated by phase inversion in previous works of the group [8] (around 80%), the porosity of the studied PAN membranes is much lower.

❖ Static Water Contact Angle

Table 2.4 shows representative pictures of contact angle for samples of PAN/W, PAN/EtOH, PAN/IPA expressed as average values ± error.

Table 2.4: Average static water contact angle of PAN membranes

Membranes	Pictures	Water Contact angle Θ_w(°)
PAN/W		16° ± 2
PAN/EtOH		39° ± 10
PAN/IPA		35° ± 3

These results showed that the three types of PAN membranes, independently of the coagulation bath employed, presented hydrophilic character (contact angle lower than 90°).

In addition the difference between contact angles of the PAN/EtOH and PAN/IPA membranes is not significant.

The obtained values are lower than those reported in the literature for PAN membranes (60° ± 3°) but these PAN membranes were still hydrophilic [5]. However, the polymer was actually a PAN copolymer (with very high contribution of PAN in its molecule), the molecular weight (MW 40000 Da), composition of the polymer solution (the weight ratio was 15/15/70 for PAN, PVP and DMF, respectively) and the membrane macrostructure (the obtained membranes were hollow fibers) of the PAN membrane was not the same.

❖ Transparency

Table 2.5 shows the pictures illustrating qualitatively the transparency of the 3 type of PAN membrane. In general, transparency is a desirable property for the evaluation on-line of cell cultures using optical equipment, such as confocal imaging techniques.

Table 2.5: Pictures and transparency of PAN membranes

Membranes	Transparency Pictures
PAN/W	
PAN/EtOH	 
PAN/IPA	

The transparency of the membrane depends of its thickness: the higher the thickness of the membrane is, the higher the opacity is. As the studied membranes have different thickness, their degree of transparency was different. PAN/W membranes were white and not much transparent. On the other hand, regarding PAN/EtOH and PAN/IPA membranes, the thinnest they were, the most transparent they looked.

2.3.2 Clean water flux experiments

❖ Clean water flux characterisation

In the following Figures 2.8 and 2.9, representative results of the clean water flux of PAN/EtOH and PAN/IPA membranes for a pressure of 0.2 bar are shown.

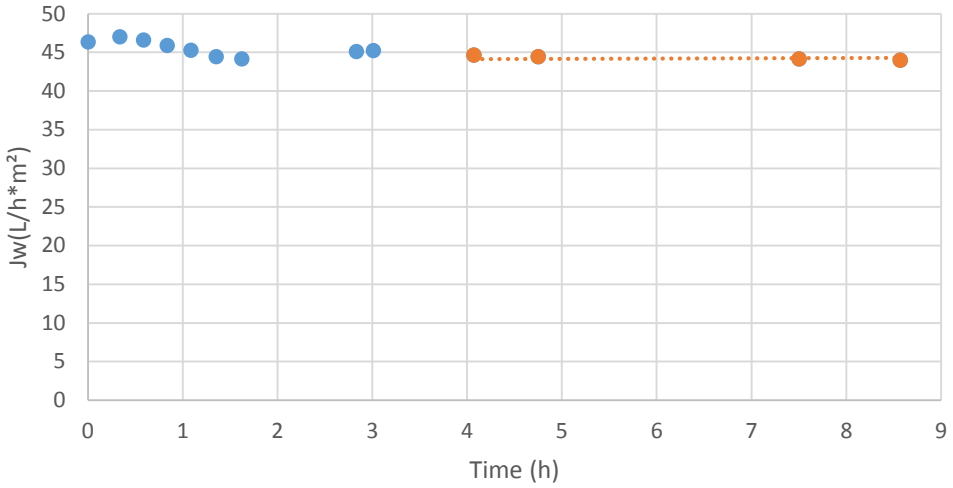


Figure 2.8: Change with the time of clean water flux of PAN/EtOH membrane in dead-end configuration system

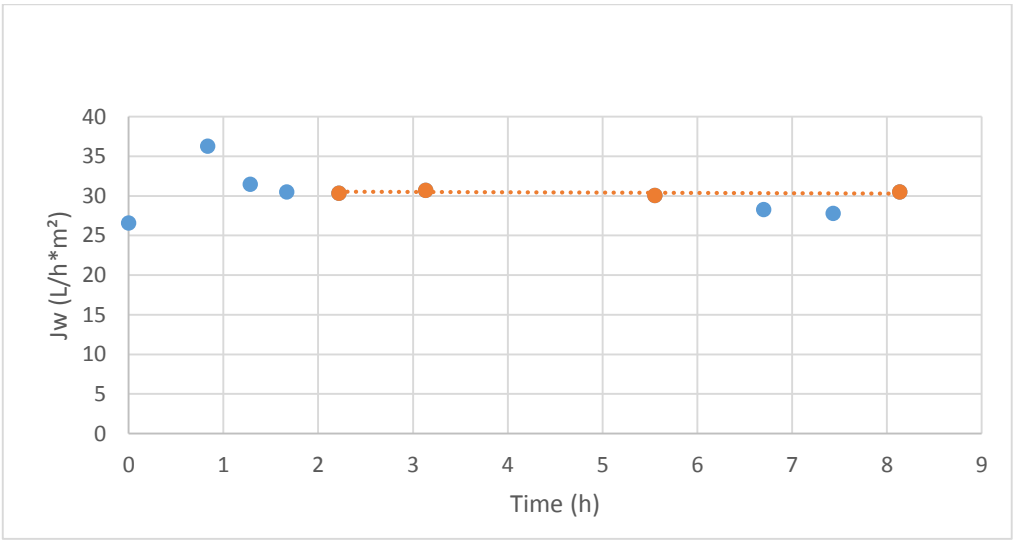


Figure 2.9: Change with the time of clean water flux of PAN/IPA membrane in dead-end configuration system

As it can be seen in the figures above, the values of the clean water flux are about 44.3 ± 3.5 L/h.m² for the PAN/EtOH membrane and 33.4 ± 1.5 L/h.m² for the PAN/IPA membrane. In the previous work [8], the initial clean water flux of PCL membranes for a pressure of 0.4 bar was 1124 ± 135 and 2069 ± 169 L/h.m², respectively for PCL/EtOH and PCL/IPA, but an important compaction of the membrane was observed during the development of the water flux experiments and at steady state, the clean water flux was reduced up to 156 ± 58 and 186 ± 61 L/h.m² respectively for PCL/EtOH and PCL/IPA. On the contrary, the herein fabricated PAN membranes presented a stable water flux during the experiments, indicating no compaction of the membrane when subjected to the transmembrane pressure of 0.2 bar, typical in a perfusion bioreactor [15].

The hydraulic permeance was calculated by Equation 6 considering the applied transmembrane pressure ΔP of 0.2 bar (Table 2.6):

Table 2.6: Experimental results of clean water flux at 0.2 bar and hydraulic permeance of PAN membranes

Membranes	Clean water flux (L/h.m²)	Permeance (L/h.m².bar)
PAN/EtOH	45 ± 4	225 ± 20
PAN/IPA	32 ± 3	160 ± 15

Based on various works and publications, comparisons of transport properties between the PAN flat membranes of this study and others polymer membranes for biomedical application have been made in Table 2.7.

Table 2.7: Comparison between different polymers for biomedical applications

Polymer	Solvent	Polymer/ solvent (% w/w)	Coagulation bath	Permeance K_w	Literature
PAN	NMP	10/90	EtOH	225	Present study
			IPA	160	Present study
PAN/PVP	DMF	15/15/70	Water	239	[5]
PCL	NMP	15/85	EtOH	150	[8],[23]
			IPA	100	[8],[23]
PEEK	DMF	10/90	Water	4000	[24]
	DMA	18/82	Water	89	[5]

As the Table 2.7 shows, various polymers can be used for biomedical application. For instance, *Morelli and al* [5] fabricated also PAN-based hollow fibers by phase inversion. For these PAN membranes, the polymer solution contained Poly Vinyl Pyrrolidone (PVP); this agent permits to open pores after being leached out of the membrane structure. The obtained clean-water flux is 48 ± 5 L/h.m² (at 0.2 bar) and permeance is 239 L/h.m².bar: these values are in the same range than those attained in the present study, indicating that PAN membranes herein fabricated are acceptable for the envisaged application. Comparing to PCL membranes made by phase inversion in almost same experimental conditions (polymer concentration: 15% w/w; solvent: NMP; coagulation baths: water, EtOH, IPA; fabrication by phase inversion) during previous work [8], the values of hydraulic permeance were in the same range than the one of PAN membranes: for PCL/EtOH and PCL/IPA membranes hydraulic permeance were 390 ± 145 and 394 ± 16 L/h.m².bar, respectively.

The hydraulic permeance values in the present study are in the range of previous works indicating that the herein studied PAN membranes could be used for tissue engineering applications.

Furthermore, by using Hagen-Poiseuille equation (which is valid for parallel and capillary pores) the average pore size of the membrane could be estimated (Equation 7)

$$J_W = \frac{\varepsilon . r^2}{8 . \eta . \tau} . \frac{\Delta P}{\Delta x} \qquad \textit{Equation 7}$$

Where: J_w is the dead-end clean water flux, ΔP the pressure applied to the membrane, ε the porosity, r the average radius of the pore's membrane, η the water viscosity and τ the tortuosity (a value of 2 was considered). By using this expression, an estimation of the pore radius of PAN/EtOH and PAN/IPA membranes was estimated. The results are presented in the Table 2.8.

Table 2.8: Experimental values of pore radius for PAN/EtOH and PAN/IPA membranes

Membranes	Pore radius (nm)
PAN/EtOH	7.1 ± 0.3
PAN/IPA	4.5 ± 0.3

The obtained values are in accordance with the morphology seen in the SEM images. With this range of pore radius, the obtained membranes are in the category of ultrafiltration membrane [25].

2.3.3 Preservative solution

Table 2.9 shows the results about the mechanical stability of the dried PAN membranes after being immersed on different preservative solutions.

Table 2.9: Results of the influence of the type of preservative solutions on the mechanical stability of the dried PAN membranes

Membranes	Preservative	Membrane's state
PAN/W	25% v/v glycerol/W	Flexible
	50% v/v glycerol/W	**Flexible, better elasticity**
	100% glycerol	Flexible
	100% IPA	Brittle
PAN/EtOH	25% v/v glycerol/W	Like plastic behaviour
	50% v/v glycerol/W	**Really flexible**
	100% glycerol	Very flexible
	100% IPA	Brittle, multiple breakings
PAN/IPA	25% v/v glycerol/W	Flexible
	50% v/v glycerol/W	**Flexible**
	100% glycerol	Flexible
	100% IPA	Brittle, multiple breakings

It is worth noting, that when the membranes were air dried without using any preservative solution, the PAN membranes were brittle and fractured easily when handle.

Based on the observations reported in Table2.9, IPA was excluded because it makes the samples very brittle as well. Furthermore, the preservative made with 25 v/v glycerol/W was not suitable: some PAN membrane samples were flexible after immersion in this preservative but it was not sufficient for the PAN/EtOH membrane that was not entirely flexible. As 50% v/v glycerol/W was sufficient to provide a good environment for the PAN membranes, it was considered that 100% glycerol was too high. Therefore, the 50% v/v glycerol/W solution was elected as preservative solution when the dried storage of PAN membranes must be done.

3. Conclusions

3. Conclusions and Perspectives for furthers enquiries

This project has developed the study and analysis of physical and transport properties of flat membranes, manufactured by phase inversion from polyacrylonitrile (PAN) and the influence of the use of different coagulation baths (water (W), ethanol (EtOH) and isopropanol (IPA)) on the physical and transport properties of the membranes was evaluated.

The flat PAN membranes presented in the present work were fabricated with a low polymer concentration (10%w/w). The low polymer concentration was expected to promote high porosities on the casted membranes. However, this low polymer concentration led to low solution viscosities and so to a bad distribution of the polymeric solution during the casting process (the repartition of the polymer solution was not regular on the entire surface of the glass support). During the immersion in the coagulation bath, glass support was tilted and the polymer solution flowed on its surface and so, the polymer solution was not present in an equal thickness on the casted film. This caused a high variability in the membrane thickness. Besides, the low viscosity of the polymer solution could favour the compaction by gravity of the PAN/EtOH and PAN/IPA membranes during the coagulation caused by a slow precipitation of the polymer and a bad preservation of the rigid structure that could kept the porosity and membrane thickness. Hence an interesting further improvement must focus on the fabrication method and particularly on the polymer concentration in order to enhance the homogeneity and reproducibility of the membranes by phase inversion as well as of structural and morphological factors.

Regarding the morphology of the structure, due to the compaction phenomenon previously described, PAN/EtOH and PAN/IPA membranes presented low porosity (10 and 34 %, respectively). The pore size was 9 and 14 nm for PAN/EtOH and PAN/IPA respectively which corresponded to a range in the ultrafiltration type of membranes. The low water contact angle (39 and 35^{o}) for both membranes indicates high hydrophilic character, which is in agreement with the high hydraulic permeances (225 and 160 L/m^2.h.bar) achieved for PAN/EtOH and PAN/IPA membranes despite the low porosities of these membranes. Therefore, the results are promising for neural cell proliferation.

Additionally, the transparency observed for the thinnest PAN/EtOH and PAN/IPA membranes is much desired for their application during on-line evaluation of cell culture behaviour using microscopic techniques.

For furthers enquiries, and once the fabrication method has been optimized, it is proposed to carry out the study of transport properties of nutrients such as BSA (Bovine Serum Albumin), one of the proteins present in higher concentration in the cell culture medium commonly formulated with DMEM protein (Dulbecco's Modified Eagle Medium) supplemented with serum, typically FBS (Foetal Bovine Serum). The BSA, due to his high molecular size, gives a higher risk to cause an effect of fouling or clogging of the membranes and this has to be verified.

Once characterized the transport of nutrients, the next step of study for these membranes could be performing *in vitro* cell culture assays in order to determine the reliability of these PAN membranes for an application in neural cell proliferation.

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5. Appendix

5.1 Safety data sheet for Polyacrylonitrile (PAN)

SIGMA-ALDRICH sigma-aldrich.com

FICHA DE DATOS DE SEGURIDAD

de acuerdo el Reglamento (CE) No. 1907/2006
Versión 5.2 Fecha de revisión 06.11.2014
Fecha de impresión 29.01.2015

SECCIÓN 1: Identificación de la sustancia o la mezcla y de la sociedad o la empresa

1.1 Identificadores del producto

Nombre del producto : Polyacrylonitrile

Referencia : 181315
Marca : Aldrich
REACH No. : Un número de registro no está disponible para esta sustancia, ya que la sustancia o sus usos están exentos del registro, el tonelaje anual no requiere registro o dicho registro está previsto para una fecha posterior
No. CAS : 25014-41-9

1.2 Usos pertinentes identificados de la sustancia o de la mezcla y usos desaconsejados

Usos identificados : Reactivos para laboratorio, Fabricación de sustancias

1.3 Datos del proveedor de la ficha de datos de seguridad

Compañía : Sigma-Aldrich Química, S.L.
Ronda de Poniente, 3
Apdo.Correos 276
E-28760 TRES CANTOS -MADRID

Teléfono : +34 91 6619977
Fax : +34 91 6619642
E-mail de contacto : eurtechserv@sial.com

1.4 Teléfono de emergencia

Teléfono de Urgencia : 704100087

SECCIÓN 2: Identificación de los peligros

2.1 Clasificación de la sustancia o de la mezcla

No es una sustancia o mezcla peligrosa de acuerdo con el Reglamento (CE) No. 1272/2008.

2.2 Elementos de la etiqueta

2.3 Otros Peligros
Esta sustancia/mezcla no contiene componentes que se consideren que sean bioacumulativos y tóxicos persistentes (PBT) o muy bioacumulativos y muy persistentes (vPvB) a niveles del 0,1% o superiores.

SECCIÓN 3: Composición/información sobre los componentes

3.1 Sustancias

Formula : C3H3N
No. CAS : 25014-41-9

Según la normativa aplicable no es necesario divulgar ninguno de los componentes.

SECCIÓN 4: Primeros auxilios

4.1 Descripción de los primeros auxilios

Si es inhalado
Si aspiró, mueva la persona al aire fresco. Si ha parado de respirar, hacer la respiración artificial.

En caso de contacto con la piel
Eliminar lavando con jabón y mucha agua.

En caso de contacto con los ojos
Lavarse abundantemente los ojos con agua como medida de precaución.

Si es tragado
Nunca debe administrarse nada por la boca a una persona inconsciente. Enjuague la boca con agua.

4.2 Principales síntomas y efectos, agudos y retardados
Los síntomas y efectos más importantes conocidos se describen en la etiqueta (ver sección 2.2) y / o en la sección 11

4.3 Indicación de toda atención médica y de los tratamientos especiales que deban dispensarse inmediatamente
Sin datos disponibles

SECCIÓN 5: Medidas de lucha contra incendios

5.1 Medios de extinción

Medios de extinción apropiados
Usar agua pulverizada, espuma resistente al alcohol, polvo seco o dióxido de carbono.

5.2 Peligros específicos derivados de la sustancia o la mezcla
Óxidos de carbono, Óxidos de nitrógeno (NOx)

5.3 Recomendaciones para el personal de lucha contra incendios
Si es necesario, usar equipo de respiración autónomo para la lucha contra el fuego.

5.4 Otros datos
Sin datos disponibles

SECCIÓN 6: Medidas en caso de vertido accidental

6.1 Precauciones personales, equipo de protección y procedimientos de emergencia
Evite la formación de polvo. Evitar respirar los vapores, la neblina o el gas.
Equipo de protección individual, ver sección 8.

6.2 Precauciones relativas al medio ambiente
No se requieren precauciones especiales medioambientales.

6.3 Métodos y material de contención y de limpieza
Limpiar y traspalar. Guardar en contenedores apropiados y cerrados para su eliminación.

6.4 Referencia a otras secciones
Para eliminación de desechos ver sección 13.

SECCIÓN 7: Manipulación y almacenamiento

7.1 Precauciones para una manipulación segura
Debe disponer de extracción adecuada en aquellos lugares en los que se forma polvo.
Ver precauciones en la sección 2.2

7.2 Condiciones de almacenamiento seguro, incluidas posibles incompatibilidades
Almacenar en un lugar fresco. Conservar el envase herméticamente cerrado en un lugar seco y bien ventilado.
Clase alemán de almacenamiento (TRGS 510): Sólidos No Combustibles

7.3 Usos específicos finales
Aparte de los usos mencionados en la sección 1.2 no se estipulan otros usos específicos

SECCIÓN 8: Controles de exposición/protección individual

8.1 Parámetros de control

Componentes con valores límite ambientales de exposición profesional.
No contiene sustancias con valores límites de exposición profesional.

8.2 Controles de la exposición

Controles técnicos apropiados
Procedimiento general de higiene industrial.

Protección personal

Protección de los ojos/ la cara
Use equipo de protección para los ojos probado y aprobado según las normas gubernamentales correspondientes, tales como NIOSH (EE.UU.) o EN 166 (UE).

Protección de la piel
Manipular con guantes. Los guantes deben ser inspeccionados antes de su uso. Utilice la técnica correcta de quitarse los guantes (sin tocar la superficie exterior del guante) para evitar el contacto de la piel con este producto. Deseche los guantes contaminados después de su uso, de conformidad con las leyes aplicables y buenas prácticas de laboratorio. Lavar y secar las manos.

Los guantes de protección seleccionados deben de cumplir con las especificaciones de la Directiva de la UE 89/686/CEE y de la norma EN 374 derivado de ello.

Protección Corporal
Elegir la protección para el cuerpo según sus caraterísticas, la concentración y la cantidad de sustancias peligrosas, y el lugar específico de trabajo., El tipo de equipamiento de protección debe ser elegido según la concentración y la cantidad de sustancia peligrosa al lugar específico de trabajo.

Protección respiratoria
Proteccion respiratoria no requerida. Donde la protección sea deseada Usar respiradores y componenetes testados y aprobados bajo los estandards gubernamentales apropiados como NIOSH (EEUU) o CEN (UE)

Control de exposición ambiental
No se requieren precauciones especiales medioambientales.

SECCIÓN 9: Propiedades físicas y químicas

9.1 Información sobre propiedades físicas y químicas básicas

a)	Aspecto	Forma: sólido
b)	Olor	Sin datos disponibles
c)	Umbral olfativo	Sin datos disponibles
d)	pH	Sin datos disponibles
e)	Punto de fusión/ punto de congelación	Sin datos disponibles
f)	Punto inicial de ebullición e intervalo de ebullición	Sin datos disponibles
g)	Punto de inflamación	Sin datos disponibles
h)	Tasa de evaporación	Sin datos disponibles
i)	Inflamabilidad (sólido, gas)	Puede formar concentraciones de polvo combustible en el aire.
j)	Inflamabilidad superior/inferior o límites explosivos	Sin datos disponibles
k)	Presión de vapor	Sin datos disponibles
l)	Densidad de vapor	Sin datos disponibles
m)	Densidad relativa	Sin datos disponibles
n)	Solubilidad en agua	Sin datos disponibles

o)	Coeficiente de reparto n-octanol/agua	Sin datos disponibles
p)	Temperatura de auto-inflamación	Sin datos disponibles
q)	Temperatura de descomposición	Sin datos disponibles
r)	Viscosidad	Sin datos disponibles
s)	Propiedades explosivas	Sin datos disponibles
t)	Propiedades comburentes	Sin datos disponibles

9.2 Otra información de seguridad
Sin datos disponibles

SECCIÓN 10: Estabilidad y reactividad

10.1 Reactividad
Sin datos disponibles

10.2 Estabilidad química
Estable bajo las condiciones de almacenamiento recomendadas.

10.3 Posibilidad de reacciones peligrosas
Sin datos disponibles

10.4 Condiciones que deben evitarse
Sin datos disponibles

10.5 Materiales incompatibles
Agentes oxidantes fuertes

10.6 Productos de descomposición peligrosos
Otros productos de descomposición peligrosos - Sin datos disponibles
En caso de incendio: véase sección 5

SECCIÓN 11: Información toxicológica

11.1 Información sobre los efectos toxicológicos

Toxicidad aguda
Sin datos disponibles

Corrosión o irritación cutáneas
Sin datos disponibles

Lesiones o irritación ocular graves
Sin datos disponibles

Sensibilización respiratoria o cutánea
Sin datos disponibles

Mutagenicidad en células germinales
Sin datos disponibles

Carcinogenicidad

IARC: No se identifica ningún componente de este producto, que presente niveles mayores que o igual a 0,1% como agente carcinógeno humano probable, posible o confirmado por la (IARC) Agencia Internacional de Investigaciones sobre Carcinógenos.

Toxicidad para la reproducción
Sin datos disponibles

Toxicidad específica en determinados órganos - exposición única
Sin datos disponibles

Toxicidad específica en determinados órganos - exposiciones repetidas
Sin datos disponibles

Peligro de aspiración
Sin datos disponibles

Información Adicional
RTECS: sin datos disponibles

SECCIÓN 12: Información ecológica

12.1 Toxicidad
Sin datos disponibles

12.2 Persistencia y degradabilidad
Sin datos disponibles

12.3 Potencial de bioacumulación
Sin datos disponibles

12.4 Movilidad en el suelo
Sin datos disponibles

12.5 Resultados de la valoración PBT y mPmB
Esta sustancia/mezcla no contiene componentes que se consideren que sean bioacumulativos y tóxicos persistentes (PBT) o muy bioacumulativos y muy persistentes (vPvB) a niveles del 0,1% o superiores.

12.6 Otros efectos adversos

Sin datos disponibles

SECCIÓN 13: Consideraciones relativas a la eliminación

13.1 Métodos para el tratamiento de residuos

Producto
Ofertar el sobrante y las soluciones no-aprovechables a una compañía de vertidos acreditada.

Envases contaminados
Eliminar como producto no usado.

SECCIÓN 14: Información relativa al transporte

14.1 Número ONU
ADR/RID: - IMDG: - IATA: -

14.2 Designación oficial de transporte de las Naciones Unidas
ADR/RID: Mercancía no peligrosa
IMDG: Not dangerous goods
IATA: Not dangerous goods

14.3 Clase(s) de peligro para el transporte
ADR/RID: - IMDG: - IATA: -

14.4 Grupo de embalaje
ADR/RID: - IMDG: - IATA: -

14.5 Peligros para el medio ambiente
ADR/RID: no IMDG Marine pollutant: no IATA: no

14.6 Precauciones particulares para los usuarios
Sin datos disponibles

SECCIÓN 15: Información reglamentaria

La hoja técnica de seguridad cumple con los requisitos de la Reglamento (CE) No. 1907/2006.

15.1 Reglamentación y legislación en materia de seguridad, salud y medio ambiente específicas para la sustancia o la mezcla

Sin datos disponibles

15.2 Evaluación de la seguridad química

Para este producto no se ha llevado a cabo una evaluación de la seguridad química

SECCIÓN 16: Otra información

Otros datos

La información indicada arriba se considera correcta pero no pretende ser exhaustiva y deberá utilizarse únicamente como orientación. La información contenida en este documento esta basada en el presente estado de nuestro conocimiento y es aplicable a las precauciones de seguridad apropiadas para el producto. No representa ninguna garantía de las propiedades del producto. La Corporación Sigma-Aldrich y sus Compañías Afiliadas, no responderán por ningún daño resultante de la manipulación o contacto con el producto indicado arriba. Diríjase a www.sigma-aldrich.com y/o a los términos y condiciones de venta en el reverso de la factura o de la nota de entrega.

5.2 Data safety sheet for N-methylpyrrolidone (NMP)

ACROS ORGANICS

FICHA DE DATOS DE SEGURIDAD

Fecha de preparación 12-nov-2009 **Fecha de revisión** 19-abr-2012 **Número de revisión** 7

SECCIÓN 1. IDENTIFICACIÓN DE LA SUSTANCIA O LA MEZCLA Y DE LA SOCIEDAD O LA EMPRESA

Identificador del producto

Nombre del producto 1-Methyl-2-pyrrolidinone
Número de registro REACH 01-2119472430-46
Cat No. 127630000; 127630010; 127630025; 127630051; 127630250
Sinónimos 1-Methyl-2-pyrrolidone; N-Methylpyrrolidone; NMP

Usos pertinentes conocidos de la sustancia o de la mezcla y usos desaconsejados

Uso recomendado Reactivos para laboratorio
Usos desaconsejados No hay información disponible

Datos del proveedor de la ficha de datos de seguridad

Compañía
Acros Organics BVBA
Janssen Pharmaceuticalaan 3a
2440 Geel, Belgium
E-mail de contacto begel.sdsdesk@thermofisher.com

Teléfono de emergencia
Para obtener información en EE.UU., llame al: 800-ACROS-01
Para obtener información en Europa, llame al: +32 14 57 52 11

Número de emergencia, Europa: +32 14 57 52 99
Número de emergencia, EE.UU.: 201-796-7100

Número de teléfono de CHEMTREC, EE.UU.: 800-424-9300
Número de teléfono de CHEMTREC, Europa: 703-527-3887

SECCIÓN 2. IDENTIFICACIÓN DE LOS PELIGROS

Clasificación de la sustancia o de la mezcla
REGLAMENTO (CE) No 1272/2008

Corrosión o irritación cutáneas	Categoría 2
Lesiones o irritación ocular graves	Categoría 2
Toxicidad para la reproducción	Categoría 1B
Toxicidad sistémica específica del órgano blanco (única exposición)	Categoría 3

Clasificación de acuerdo con las Directivas de la UE 67/548/CEE ó 1999/45/CE
Para obtener el texto completo de las frases R y H mencionadas en este apartado, consultar el apartado 16

Símbolo(s) T - Tóxico
Frase(s) - R R61 - Riesgo durante el embarazo de efectos adversos para el feto
Combinación de frases de riesgo R36/37/38 - Irrita los ojos, la piel y las vías respiratorias

SECCIÓN 2. IDENTIFICACIÓN DE LOS PELIGROS

Elementos de la etiqueta

Palabra de advertencia **Peligro**

Indicaciones de peligro

H319 - Provoca irritación ocular grave
H315 - Provoca irritación cutánea
H335 - Puede irritar las vías respiratorias
H360D - Puede dañar al feto

Consejos de prudencia - EU (§28, 1272/2008)

P201 - Pedir instrucciones especiales antes del uso
P308 + P313 - EN CASO DE exposición manifiesta o presunta: Consultar a un médico
P261 - Evitar respirar el polvo/ el humo/ el gas/ la niebla/ los vapores/ el aerosol
P302 + P352 - EN CASO DE CONTACTO CON LA PIEL: Lavar con agua y jabón abundantes
P280 - Llevar guantes/ prendas/ gafas/ máscara de protección
P305 + P351 + P338 - EN CASO DE CONTACTO CON LOS OJOS: Aclarar cuidadosamente con agua durante varios minutos. Quitar las lentes de contacto, si lleva y resulta fácil. Seguir aclarando

Otros peligros

No hay información disponible.

SECCIÓN 3. COMPOSICIÓN/INFORMACIÓN SOBRE LOS COMPONENTES

Componente	No. CE.	Por ciento en peso	No. CAS	67/548/CEE Clasificación	CLP clasificación - Reglamento (CE) n ° 1272/2008	REACH No.

SECCIÓN 3. COMPOSICIÓN/INFORMACIÓN SOBRE LOS COMPONENTES

1-Methyl-2-pyrrolidone 872-50-4	EEC No. 212-828-1	99	872-50-4	Xi; R36/37/38 Repr.Cat.2; R61	Skin Irrit. 2 (H315) Eye Irrit. 2 (H319) Repr. 1B (H360D) STOT SE 3 (H335)	01-2119472430-46

Para obtener el texto completo de las frases R y H mencionadas en este apartado, consultar el apartado 16

SECCIÓN 4. PRIMEROS AUXILIOS

Descripción de los primeros auxilios

Contacto con los ojos Enjuagar inmediatamente con abundante agua, también debajo de los párpados, al menos durante 15 minutos. Consulte al médico.

Contacto con la piel Lavar inmediatamente con abundante agua durante al menos 15 minutos. Consulte al médico.

Ingestión No provocar el vómito. Consulte al médico.

Inhalación Sacar al aire libre. Si la respiración es difícil, darle oxígeno. Consulte al médico.

Notas para el médico Tratar sintomáticamente

SECCIÓN 5. MEDIDAS DE LUCHA CONTRA INCENDIOS

Medios de extinción

Medios de extinción apropiados
Usar agua pulverizada, espuma resistente al alcohol, polvo seco o dióxido de carbono. Enfriar los contenedores cerrados expuestos al fuego con agua pulverizada.

Medios de extinción que no deben utilizarse por razones de seguridad
No hay información disponible.

Peligros específicos derivados de la sustancia o la mezcla

Material combustible. Los contenedores pueden explotar si se calientan. Manténganse el producto y los recipientes vacíos lejos del calor y de las fuentes de ignición.

Recomendaciones para el personal de lucha contra incendios

Como en cualquier incendio, llevar un aparato respiratorio autónomo con demanda de presión, MSHA/NIOSH (aprobado o equivalente) y una ropa de protección total. La descomposición térmica puede llegar a desprender gases y vapores irritativos.

SECCIÓN 6. MEDIDAS EN CASO DE VERTIDO ACCIDENTAL

Precauciones personales, equipo de protección y procedimientos de emergencia

Utilícese equipo de protección individual. Asegúrese una ventilación apropiada. Retirar todas las fuentes de ignición.. Adóptense precauciones contra las descargas electroestaticas. Evitar el contacto con la piel, ojos y ropa.

Precauciones relativas al medio ambiente

No debe liberarse en el medio ambiente.

Métodos y material de contención y de limpieza

Retirar todas las fuentes de ignición. Empapar con material absorbente inerte. Adóptense precauciones contra las descargas electroestaticas. Guardar en contenedores apropiados y cerrados para su eliminación..

SECCIÓN 7. MANIPULACIÓN Y ALMACENAMIENTO

Precauciones para una manipulación segura

Usar sólo bajo un protector contra humos químicos.. Mantener apartado de las llamas abiertas, de las superficies calientes y de los focos de ignición. Adóptense precauciones contra las descargas electroestaticas. No hay que meterlo en los ojos, sobre la piel, o sobre la ropa. No respirar vapores o niebla de pulverización.

Condiciones de almacenamiento seguro, incluidas posibles incompatibilidades

Cerrar los recipientes herméticamente y mantenerlos en lugar seco, fresco y bien ventilado. Manténgase separado del calor y de las fuentes de ignición. Protéjase de la luz.

Usos específicos finales

SECCIÓN 8. CONTROLES DE EXPOSICIÓN/PROTECCIÓN INDIVIDUAL

Parámetros de control

Límites de exposición

Componente	Unión Europea	Reino Unido	Francia	Bélgica	España
1-Methyl-2-pyrrolidone	Possibility of significant uptake through the skin	STEL: 75 ppm 15 min STEL: 309 mg/m³ 15 min TWA: 25 ppm 8 hr TWA: 103 mg/m³ 8 hr Skin			Skin VLA-EC: 75 ppm 15 minutos VLA-EC: 309 mg/m³ 15 minutos VLA-ED: 25 ppm 8 horas VLA-ED: 103 mg/m³ 8 horas

Componente	Italia	Alemania	Portugal	Países Bajos	Finlandia
1-Methyl-2-pyrrolidone		MAK: 20 ppm 8 Stunden. vapour MAK: 82 mg/m³ 8 Stunden. vapour skin notation Skin Peak: 40 ppm Peak: 164 mg/m³ TWA: 20 ppm 8 Stunden. vapor exposure factor 2 TWA: 82 mg/m³ 8 Stunden. vapor exposure factor 2	Skin notation		TWA: 10 ppm 8 tunteina TWA: 40 mg/m³ 8 tunteina STEL: 20 ppm 15 minuutteina STEL: 80 mg/m³ 15 minuutteina Skin

Componente	Austria	Dinamarca	Suiza	Polonia	Noruega
1-Methyl-2-pyrrolidone	Skin STEL: 80 ppm 15 Minuten STEL: 320 mg/m³ 15 Minuten TWA: 20 ppm 8 Stunden TWA: 80 mg/m³ 8 Stunden	TWA: 5 ppm 8 timer TWA: 20 mg/m³ 8 timer	Skin STEL: 40 ppm 15 Minuten STEL: 160 mg/m³ 15 Minuten MAK: 20 ppm 8 Stunden MAK: 80 mg/m³ 8 Stunden	NDSCh: 240 mg/m³ 15 minutach NDS: 120 mg/m³ 8 godzinach	TWA: 5 ppm 8 timer TWA: 20 mg/m³ 8 timer STEL: 10 ppm 15 minutter. STEL: 30 mg/m³ 15 minutter. Skin

Componente	Bulgaria	Croacia	Irlanda	Chipre	Republica Checa
1-Methyl-2-pyrrolidone		Skin Notation TWA: 25 ppm 8 satima. TWA: 103 mg/m³ 8 satima. STEL: 75 ppm 15 minutama. STEL: 309 mg/m³ 15 minutama.	TWA: 25 ppm 8 hr. TWA: 101 mg/m³ 8 hr. Skin		

Componente	Estonia	Gibraltar	Grecia	Hungría	Islandia
1-Methyl-2-pyrrolidone	TWA: 50 ppm 8 tundides. TWA: 200 mg/m³ 8 tundides. STEL: 75 ppm 15 minutites. STEL: 300 mg/m³ 15 minutites.		TWA: 100 ppm TWA: 400 mg/m³		TWA: 50 ppm 8 klukkustundum. TWA: 200 mg/m³ 8 klukkustundum. Ceiling: 100 ppm Ceiling: 400 mg/m³

Componente	Letonia	Lituania	Luxemburgo	Malta	Romania
1-Methyl-2-pyrrolidone	TWA: 100 mg/m³	TWA: 50 ppm TWA: 200 mg/m³ STEL: 75 ppm STEL: 300 mg/m³			

Componente	Russia - TWA	Slovak Republic	Eslovenia	Suecia	Turquía
1-Methyl-2-pyrrolidone	MAC: 100 mg/m³		TWA: 19 ppm 8 urah vapor TWA: 80 mg/m³ 8 urah vapor Potential for cutaneous absorption STEL: 76 ppm 15 minutah vapor STEL: 320 mg/m³ 15 minutah vapor	STV: 75 ppm 15 minuter STV: 300 mg/m³ 15 minuter LLV: 50 ppm 8 timmar. LLV: 200 mg/m³ 8 timmar.	

Valores límite biológicos Este producto, tal como se suministra, no contiene ningún material peligroso con límites biológicos establecidos por los organismos reguladores regionales específicos.

Nivel obtenido sin efecto (DNEL) No hay información disponible.

Concentración prevista sin efecto (PNEC) No hay información disponible.

Controles de la exposición

Disposiciones de ingeniería Usar sólo bajo un protector contra humos químicos Asegurarse de una ventilación adecuada, especialmente en locales cerrados Asegúrese de que las estaciones de lavado de ojos y las duchas de seguridad estén localizadas cerca del sitio de trabajo

Protección personal

Protección de los ojos Gafas protectoras con cubiertas laterales

Protección de las manos Guantes protectores

Protección de la piel y del cuerpo Ropa de manga larga

Protección respiratoria Cuando los trabajadores estén expuestos a concentraciones por encima de los límites de exposición, deberán usar mascarillas apropiadas certificadas

Medidas de higiene Manipular con las precauciones de higiene industrial adecuadas, y respetar las prácticas de seguridad

Controles de exposición medioambiental No hay información disponible.

SECCIÓN 9. PROPIEDADES FÍSICAS Y QUÍMICAS

Estado físico	líquido
Aspecto	incoloro
Olor	similar a huevo podrido
pH	7.7-8.0 100 g/L aq.sol.
Presión de vapor	0.7 mbar @ 25 °C
Densidad de vapor	3.4 (Aire = 1.0)
Viscosidad	1.67 mPa s at 20 °C
Punto /intervalo de ebullición	202°C / 395.6°F@ 760 mmHg
Punto/intervalo de fusión	-24°C / -11.2°F
Punto de inflamación	91°C / 195.8°F
Temperatura de auto-inflamación	346°C / 654.8°F

Límites de explosión	
Inferior	1.3 vol %
superior	9.5 vol %
Solubilidad en agua	miscible
Gravedad Específicas	1.030
Fórmula molecular	C5 H9 N O
Peso molecular	99.13

SECCIÓN 10. ESTABILIDAD Y REACTIVIDAD

Reactividad

Estabilidad química

higroscópico. Sensible al aire. Sensible a la luz.

Posibilidad de reacciones peligrosas

Polimerización peligrosa	No hay información disponible
Reacciones peligrosas .	No hay información disponible.

Condiciones que deben evitarse

Productos incompatibles, Calor, llamas y chispas, Exposición al aire, Exposición al aire húmedo o al agua, Exposición a la luz.

Materiales incompatibles

Agentes oxidantes fuertes, Ácidos fuertes, Bases fuertes.

Productos de descomposición peligrosos

Monóxido de carbono. Dióxido de carbono (CO_2). óxidos de nitrógeno (NOx). Peróxidos.

SECCIÓN 11. INFORMACIÓN TOXICOLÓGICA

Información sobre los efectos toxicológicostoxicidad aguda

Toxicidad aguda

Información del Componente

Componente	DL50 Oral	DL50 cutánea	LC50 Inhalación
1-Methyl-2-pyrrolidone	3598 mg/kg (Rat)	2000 mg/kg (Rabbit) 2500 mg/kg (Rat)	3.1 mg/L (Rat) 4 h

Toxicidad crónica

Carcinogenicidad	Este producto no contiene compuestos químicos carcinógenos conocidos

Sensibilización	No hay información disponible.
efectos mutágenos	Se han producido efectos mutagénicos en microorganismos.
Efectos reproductivos	Los experimentos han demostrado la reproductividad de los efectos tóxicos en animales de laboratorio
Efectos del desarrollo	Sustancias conocidas que causan toxicidad desarrollada en humanos Riesgo durante el embarazo de efectos adversos para el feto
Teratogenicidad	Han ocurrido efectos teratogénicos en animales experimentales.
Órganos diana	Sistema respiratorio Ojos Piel Hígado Riñón bazo Sangre
Otros efectos adversos	Se han comunicado efectos tumorigénicos en animales de experimentación. Consulte la información completa en la entrada concreta de RTECS.
Información sobre disruptores endocrinos	Ninguna conocida

SECCIÓN 12. INFORMACIÓN ECOLÓGICA

Toxicidad

Efectos ecotoxicológicos

Componente	Algas de agua dulce	Peces de agua dulce	Microtox	Pulga de agua
1-Methyl-2-pyrrolidone	500 mg/L EC50 > 72 h	1072 mg/L LC50 96 h 4000 mg/L LC50 96 h 832 mg/L LC50 96 h 1400 mg/L LC50 96 h		4897 mg/L EC50 = 48 h

Persistencia y degradabilidad

No hay información disponible

Potencial de bioacumulación

No hay información disponible.

Componente	log Pow
1-Methyl-2-pyrrolidone	-0.46

Movilidad en el suelo

Resultados de la valoración PBT y MPMB

Otros efectos adversos

No hay información disponible

SECCIÓN 13. CONSIDERACIONES RELATIVAS A LA ELIMINACIÓN

Métodos para el tratamiento de residuos

Desechos de residuos / producto no utilizado Eliminar, observando las normas locales en vigor

Envases contaminados Los recipientes vacíos deben entregarse a gestores de residuos autorizados, para su eliminación

SECCIÓN 14. INFORMACIÓN RELATIVA AL TRANSPORTE

IMDG/IMO no regulado

ADR no regulado

IATA no regulado

SECCIÓN 15. INFORMACIÓN REGLAMENTARIA

Reglamentación y legislación en materia de seguridad, salud y medio ambiente específicas para la sustancia o la mezcla

Inventarios Internacionales

Componente	EINECS	ELINCS	NLP	TSCA	DSL	NDSL	PICCS	ENCS	China	AICS	KECL
1-Methyl-2-pyrrolidone	212-828-1	-		X	X	-	X	X	X	X	X

Leyenda

TSCA : Ley de Control de Sustancias Tóxicas estadounidense, apartado 8(b), Inventario
b EINECS/ELINCS : Inventario europeo de sustancias químicas comercializadas existentes/Lista europea de sustancias químicas notificadas
DSL/NDSL : Lista de Sustancias Domésticas Canadiense/Lista de Sustancias No Domésticas Canadiense
PICCS - Inventario filipino de sustancias y preparados químicos
ENCS - Inventario japonés de sustancias químicas existentes y nuevas
IECSC - Inventario chino de sustancias químicas existentes
AICS - Inventario australiano de sustancias químicas
KECL - Inventario coreano de sustancias químicas existentes y evaluadas

Evaluación de la seguridad química

ACROS ORGANICS

FICHA DE DATOS DE SEGURIDAD

1-Methyl-2-pyrrolidinone **Fecha de revisión** 19-abr-2012

SECCIÓN 16. OTRA INFORMACIÓN

El texto completo de las frases-R referidas en los puntos 2 y 3
R61 - Riesgo durante el embarazo de efectos adversos para el feto
R36/37/38 - Irrita los ojos, la piel y las vías respiratorias

Fecha de revisión 19-abr-2012
Resumen de la revisión

Razón de la revisión Secciones actualizadas (M)SDS (Hoja de datos de seguridad), 3.

La hoja técnica de seguridad cumple con los requisitos de la Reglamento (CE) No. 1907/2006
De responsabilidad
La información facilitada en esta Ficha de Datos de Seguridad es correcta, a nuestro leal saber y entender, en la fecha de su publicación. Dicha información está concebida únicamente como guía para la seguridad en la manipulación, el uso, el procesamiento, el almacenamiento, el transporte, la eliminación y la liberación, no debiendo tomarse como garantía o especificación de calidades. La información se refiere únicamente al material específico mencionado y puede no ser válida para tal material usado en combinación con cualquier otro material o en cualquier proceso salvo que se especifique expresamente en el texto.

Fin de la Ficha de Datos de Seguridad

5.3 Safety data sheet for Ethanol (EtOH)

oppac sa	**BOLETIN ANALISIS** **ALCOHOL ETÍLICO ABSOLUTO CON INDICADOR**	**ET-05-00-01** **Rev. 0**

LOTE Nº:
FECHA ANALISIS
GRADO: 99,9

Parámetro	Resultado	Unidades	Especificaciones	Método
Aspecto	Limpio incoloro	-	Limpio incoloro	CEE L 130 (1992) método 2
Contenido en agua	153	Ppm	<1000	Karl Fischer
Extracto seco	0,10	g/HI-AP	<1,5	CEE L 130 (1992) método 10
Acidez	0,10	g ácido acético g/HI PA	<1,5	CEE L 130 (1992) método 6
Esteres a 20ºC	0,00	g acetato de etilo /HI. PA	<1,3	CEE L 130 (1992) método 7 CPG
Aldehídos a 20ºC	0,21	g acetaldehído g/HI.PA	<0,8	CEE L 130 (1992) método 4 CPG
Alcoholes superiores	0,00	G 2-metilpropan-1-ol/HI de PA	<2	CPG método UNDG
Metanol	0	g/HI. AP	<10	Cee I130 (1992) método 9
Bases Nitrogenas	NA	g Nitrógeno/HI. AP	<0,2	Espectrometría visible
Test de Permanganato	26	mín. a 20ºC	>20	CEE L130 (1992) método 3
Olor	13,87	>9,5	Neutro	Método FA
Otras determinaciones				

Resultado sin desnaturalizante

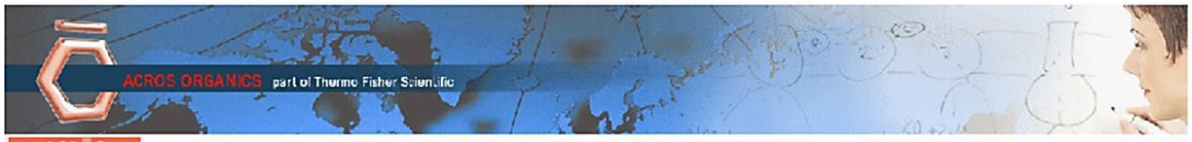
Desnaturalizante	Resultado	Unidad	Especificaciones
Bitrex	10,5	Mg/l alcohol como tal	>10

***NOTA**: Copia del certificado de análisis del original facilitado por el fabricante.*

***NOTA**: El presente Boletín de Análisis es una reproducción informatizada del original disponible en Productos OPPAC, S.A., motivo por el cual no va firmado.*

PRODUCTOS OPPAC, S.A.
Fdo. J. Peñalver

5.4 Safety data sheet for Isopropanol (IPA)



ACROS ORGANICS

Isopropanol, technical

MSDS Specifications Molfile Other grades

General	
Product Name	Isopropanol Isopropyl alcohol IPA 2-Propanol
CAS RN	67-63-0
ACD Code	MFCD00011674
Structure	
Molecular Formula	C3 H8 O
Molecular weight	60.10
Pack size	Catalog Qty / UM Price (EUR) 444250050 5 LT 29.40 Order Check stock
Physical	
Density (g/cm³)	0.785
Refractive index	1.376 - 1.378
Boiling Point (°C)	81 - 83
Melting Point (°C)	-89.5
Flash Point (°C)	12
Safety	
GHS Pictogram	
GHS Signal Word	Danger
GHS H statement	H336: May cause drowsiness or dizziness H319: Causes serious eye irritation H225: Highly flammable liquid and vapor
GHS P statement	P261: Avoid breathing dust/fume/gas/mist/vapors/spray P280: Wear protective gloves/protective clothing/eye protection/face protection P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing P210: Keep away from heat/sparks/open flames/hot surfaces. - No smoking P240: Ground/Bond container and receiving equipment
Hazard	 F: Highly flammable XI: Irritant
Risk	11: Highly flammable. 36: Irritating to eyes. 67: Vapours may cause drowsiness and dizziness.
Safety	7: Keep container tightly closed. 16: Keep away from sources of ignition - No smoking. 24/25: Avoid contact with skin and eyes. 26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
Other	
Parameter	EINECS 200-661-7 Solubility Solubility in water: Miscible Solubility in other solvents: Soluble in methanol, ethanol, methylene chloride, DMF and acetone Miscible with alcohol, ether and chloroform