MINISTRY OF EDUCATION
University Politehnica of Bucharest
Faculty of Chemical Engineering and Biotechnologies

***Doctoral School* Chemical Engineering and Biotechnologies**

ABSTRACT

PhD Thesis

Decision No. 851 from 09.06.2022

Products of biological interest with biomedical implicațions separated by membrane processes

PhD student:

Eng. Ch. Ioana Alina Dimulescu (NICA)

Supervisor:

***Prof.dr.eng.* Gheorghe NECHIFOR**

June 2022, Bucharest

MINISTRY OF EDUCATION
University Politehnica of Bucharest
Faculty of Chemical Engineering and Biotechnologies

***Doctoral School* Chemical Engineering and Biotechnologies**

ABSTRACT

PhD Thesis

Decision No. 851 from 09.06.2022

Products of biological interest with biomedical implicațions separated by membrane processes

PhD student:

Ing. ch. Ioana Alina Dimulescu (NICA)

Doctoral Commission

President	**Prof. Hab. Dr. Eng. Ștefan Ioan VOICU**	from	**University Politehnica of Bucharest**
Supervisor	**Prof. Dr. Eng. Gheorghe NECHIFOR**	from	**University Politehnica of Bucharest**
Referent	**Prof. Dr. Eng. Ioan MĂMĂLIGĂ**	from	**Gheorghe Asachi Iasi Technical University**
Referent	**Prof. Hab. Dr. Simona Gabriela BUNGĂU**	from	**Oradea University**
Referent	**Prof. Dr. Eng. Gabriel Lucian RADU**	from	**University Politehnica of Bucharest**

Bucharest -2022

CONTENTS

INTRODUCTION

The elaboration of the doctoral thesis "Products of biological interest with biomedical implications separated by membrane processes" represents par excellence, an applicative activity, combined with fundamental activity. The application activity aims to isolate products of biological interest (amino acids, chemical species with potential toxicity) with biomedical implications separated by membrane processes.

The study is part of the research concerns in the country and abroad for obtaining products purified by membrane processes.

The thesis addresses a topic of practical importance and presents the results achieved in order to obtain new membranes for the separation of products of biological interest with biomedical applications.
The doctoral thesis is part of the broad topic "Obtaining biological products with applications in biotherapy using immunologically active fractions" which provided both the general research framework and the technical-scientific arguments for the development of publications and patent applications.

The degree of novelty

The paper presents an original and novel part, the results of which can be used in the pharmaceutical and medical industries.

The doctoral thesis consists of three parts: part A - synthesis of literature data, which includes chapter 1, part B - the experimental part structured in two chapters and part C consists of - elements of originality, general conclusions and research perspectives.

The first chapter "Membranes and membrane processes" is a study with reference to recent information on methods of obtaining, characterizing and applying membrane processes.

The second chapter "Characterization and obtaining of selective composite membranes applied in processes of separation of biological compounds" in the experimental part section presents two of the representative results of the research from the doctoral research stage.

Chapter 2. Characterization and Obtaining Selective Composite Membranes Applied in Biological Compound Separation Processes Approaches "Separation of Nitrophenols from Liquid Membranes with Magnetic Properties" magnetic nanoparticles with iron and doped with recovered silver, by electrolysis, for the transport of o- and m- nitrophenols, chemical species with recognized toxic potential.

Chapter 3 entitled "Separation of amino acids by cellulosic-polypropylene-derived composite membranes" addresses the transport of biological chemical species of interest (amino acids) for separation and / or concentration by composite membranes.

The paper concludes with General Conclusions, Elements of Originality and Research Development Perspectives.

In the last part of the doctoral thesis, the dissemination of experimental results was carried out by publishing scientific papers in specialized journals, by presenting scientific papers at domestic and international symposia and by conducting papers in patents.

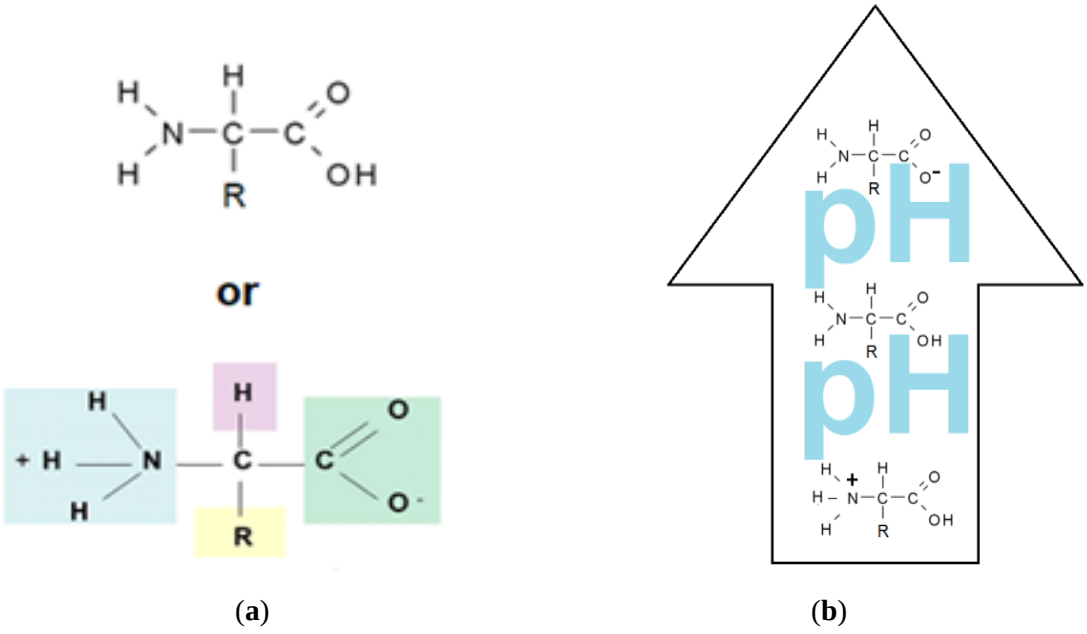
CHAPTER 3.

Separation of amino acids by cellulosic-polypropylene-derived composite membranes

3.1. Introduction

Amino acids are substances whose biological role, when incorporated into protein molecules, neurotransmitters or hormones and in precursors of other molecules, has led to a continuous development of fundamental and applied research [1, 2]. The simultaneous presence in the molecule of amino acids, of a basic, amino group (-NH_2) but also of an acid group, carboxyl (-COOH), close spatially (Figure 1a), gives these substances unique physical-chemical and biological properties [3, 4]. Of course, one of the important aspects of this structure is given by the presence of electrical charges in amino acids [5-7], regardless of the pH of the aqueous solution in which they are found (Figure 1 b). Simultaneously, the chemical properties of the amino and carboxyl groups make the amino acids the molecules of greatest interest in modifying, by grafting, the properties of various organic and inorganic materials [8-11].

All these characteristics, but also the multiple chemical, biological and biomedical applications make it necessary to recover amino acids from any source, even when their concentration is low [12-17].



(**a**) (**b**)

Figure 1. The chemical structure of amino acids (a) and the ionic forms depending on the pH of aqueous solution in which they are found (b).

The properties of an amino acid will also be influenced by the R group, which can give the molecule specific interactions: hydrophobic, hydrophilic or redox, depending on the atoms that make it up [18, 19]. All these characteristics of amino acids allowed researchers to address the most varied techniques and methods of separation, among which some of those involving membranes are presented in Table 1.

Table 1. Membrane amino acids separation techniques and methods

Methods or techniques	Gradient	Refs.
Dialysis (D), Hemodialysis (HD)	Δc	[20,21,22]
Ion-exchange membranes (IEM)	Δc, ΔE	[23,24,25]
Electro dialysis (ED)	ΔE	[26,27]
Electro-ultrafiltration (EUF)	ΔE, Δp	[28-33]
Ultrafiltration (UF)	Δp	[34-37]
Nanofiltration (NF)	Δp	[38-43]
Molecularly imprinted polymeric membranes (MIPM)	Δp	[44]
Liquid membranes (LM)	Δc	[45,46,47]
Other processes (Adsorption, Polyelectrolyte nanoparticles, Composite membranes, Combined processes, Molecular recognition)	Δc, ΔE, Δp	[48-59]

Sources of amino acid are among the most diverse, but mainly hydrolysates in the food industry have been addressed: milk, meat, fish, wine or animal skin processing, agriculture and biotechnology.

Each method or process of membrane separation, concentration or purification of amino acids has advantages and disadvantages and must be correlated with the processing system, so as to meet both selectivity and productivity requirements [60].

This paper addresses the recuperative separation of three amino acids (alanine, phenylalanine and methionine) from synthetic solutions, using membranes from cellulosic derivatives (cellulose acetate, 2-hydroxyethyl-cellulose, and methyl 2-hydroxyethyl-cellulose or sodium carboxymethyl-cellulose) in polypropylene hollow fiber matrix.

3.2. Materials and methods

3.2.1. Materials

3.2.1.1. Chemicals

The materials used in the present work were of analytical purity. They were purchased from Merck (Merck KGaA, Darmstadt, Germany): sodium hydroxide (NaOH) and hydrochloric acid solution (HCl, 35%).

The amino acids (alanine, phenylalanine and, methionine) and the cellulose derivatives (cellulose acetate (Product of USA), 2-hydroxyethyl-cellulose (product of USA), methyl 2-hydroxyethyl-cellulose (product of Belgium) and sodium carboxymethyl-cellulose (Product of USA)) were purchased from Aldrich Chemistry (Merck KGaA, Darmstadt, Germany).

The purified water, characterized by a conductivity of 18.2 μS/cm, was obtained with a RO Millipore system (MilliQR Direct 8 RO Water Purification System, Merck, Darmstadt, Germany).

3.2.1.2. Membrane support

The hollow fibers polypropylene support membranes (PPM) were provided by GOST Ltd., Perugia, Italy. Their characteristics are presented in Figure 2 [61, 62].

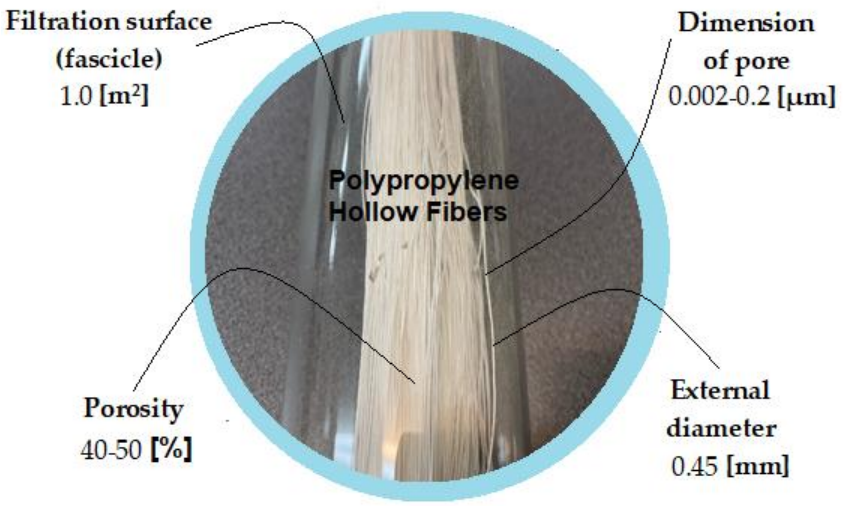


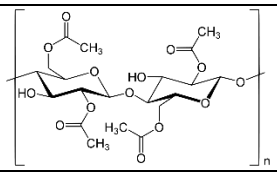
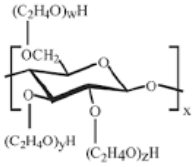
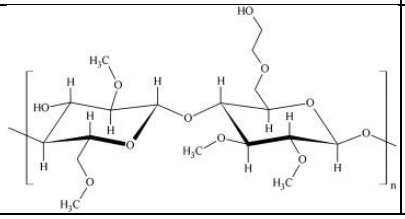
Figure 2. The characteristics of the hollow fibers polypropylene support membranes (PPM)

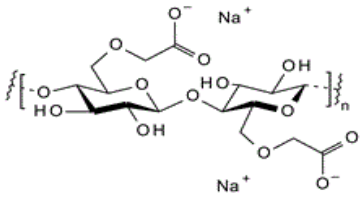
2.2. Impregnated cellulose derivatives polypropylene membrane preparation (Cell-D-PPM)

2.2.1. Obtaining the cellulose derivatives solution

The cellulosic derivatives (cellulose acetate, 2-hydroxyethyl-cellulose, methyl 2-hydroxyethyl-cellulose or sodium carboxymethyl-cellulose), having the characteristics indicated in Table 2, were solubilized in a mass concentration of 2%, in a mixture of methylene chloride : methyl alcohol = 2 : 1. For this, the glass vessel in which the mixture of solvents and the corresponding amount of polymer were introduced, was placed in an ultrasonic bath (Elmasonic S, Elma Schmidbauer GmbH, Singen, Germany) for four hours, observing the complete dispersion and obtaining the polymeric solution. The obtained solutions were filtered using a metal sieve with 40µm x 40µm meshes and then placed in closed containers for 24 hours in order to remove bubbles.

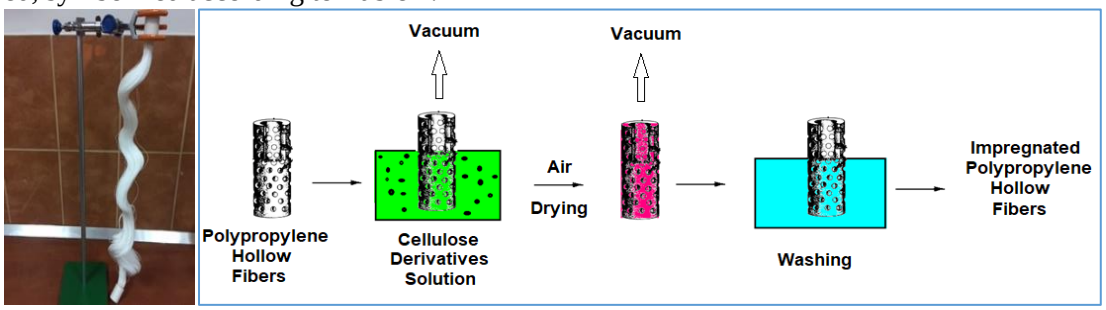
Table 2. The characteristics of cellulosic derivatives under test and the membranes obtained.

Cellulose Derivatives (Cell-D)	**Chemical formula**	**Molar weight**	**Membrane symbol**
cellulose acetate (CA)		50,000	CA-PPM
2-hydroxy-ethylcellulose (HEC)		380,000	HEC-PPM
methyl 2-hydroxyethyl-cellulose (MHEC)		N/A	CHEC-PPM

sodium carboxymethyl-cellulose (NaCMC)		90,000	NaCMC-PPM

3.2.2.2. Obtaining cellulose derivatives impregnated on polypropylene fibers membranes (Cell-D-PPM) [63, 64]

For impregnation of support hollow fiber membranes, the polymer solution the polymer solution was placed in a glass cylindrical vessel with measured capacity and then the fiber bundle was immersed (Figure 3) with the heads out of the solution and coupled to a preliminary vacuum pump. The fibers were coupled to the vacuum pump to remove the air and when the pressure difference increases, the pump switched-off automatically. The system was maintained in this state for 10 minutes, after which the impregnated fibers were removed above the polymer solution. After 30 minutes, the fibers were placed in the vacuum oven, at 60 °C, to remove the solvent mixture. After this stage the fibers were placed in a 1 L vessel with deionized water and after about an hour, they could be used in the permeation process. Four types of membranes were obtained, symbolized according to Table 2.



(**a**) (**b**)

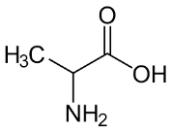
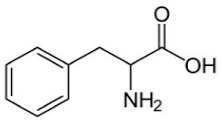
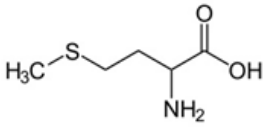
Figure 3. Schematic depiction of the impregnation procedure: (**a**) hollow polypropylene fiber bundles; and (**b**) scheme of the stages of the impregnation procedure.

3.2.3. Permeation procedures

In the source phase (SP) the synthetic solution of the considered chemical species (amino acids – Table 3), with a concentration of 0.150-0.250 mol/L, is introduced in the installation (Figure 4). The pH of the source phase is made with hydrochloric acid solution 0.01 mol/L, deionized water or sodium hydroxide 0.1 mol/L. The receiving phase (RP) is formed in all cases from deionized water. The volume of the source phase is 10 L, and of the receiving phase is 1 L. The operating flows are the same for all experiments, for operational reasons already studied [64, 65, 66]. Thus, for the source phase the flow in the pertraction module is 5 L/min, and the flow of the receiving phase is 0.1 L/min. In order to determine the amino acids separation performances, a 1 mL of solution is taken periodically and analyzed for spectrophotometric analysis (CamSpec Spectrophotometer) [67, 68, 69]. For the receiving phase, the operation is performed through capillaries while for the source phase the operation is performed outside the capillaries (Figure 4).

Table 3. The characteristics of the tested amino acids (at 25°C)

Amino acid	**Chemical formula**	**Molar weight (g/mol)**	**Solubility (g/L)**	**Isoelectric point (Ip)**	**Acidity constants (pKa)**

Alanine		89.09	167.2	6.11	2.35 (carboxyl), 9.87 (amino)
Phenylalanine		165.19	26.9	5.91	2.58 (carboxyl), 9.13 (amino)
Methionine or 2-amino-4-(methylthio) butanoic acid		149.21	56.6	5.74	2.28 (carboxyl), 9.21 (amino)

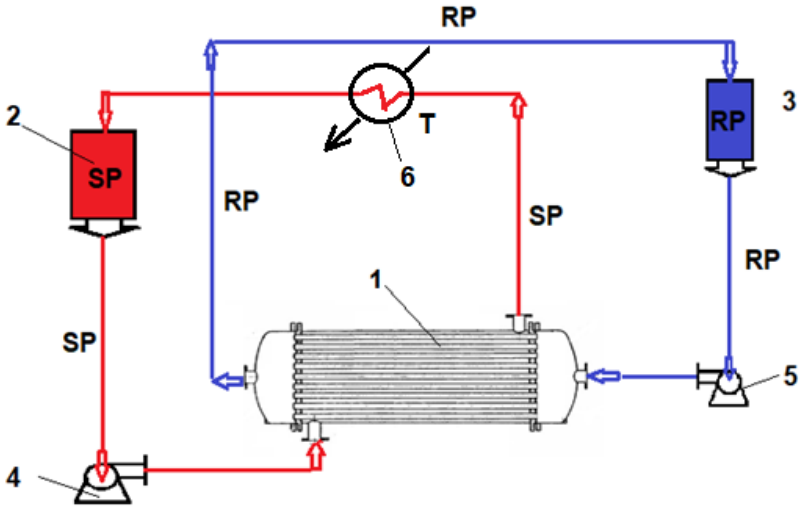


Figure 4. Depiction of the operational scheme with the pertraction module: SP – source phase, RS – receiving phase. **1**. hollow fiber pertraction module; **2**. SP reservoirs; **3**. RP reservoirs; **4**. SP pump; **5**. RP pump; **6**. T thermostat.

The fluxes from the source phase [70] were determined against the measured permeate mass within a determined time range, applying the following equation:

$$J = \frac{M}{S \cdot t} \quad (\text{mg}/(\text{m}^2\ \text{s})) \text{ or } ((\text{mol})/(\text{m}^2\ \text{s})) \tag{1}$$

where: M – permeate mass (g or mol), S – effective surface of the membrane (m^2), t – time (s) necessary to collect the permeate volume.

The extraction efficiency (EE%) for the species of interest using the concentration of the solutions [71] was calculated as follows:

$$EE(\%) = \frac{(c_0 - c_f)}{c_0} \cdot 100 \tag{2}$$

where: c_f – final concentration of the solute (considered chemical species), c_o – initial concentration of solute (considered chemical species).

The same extraction efficiency can also be computed based upon the absorbance of the solutions, as in:

$$EE(\%) = \frac{(A_0 - A_S)}{A_0} \cdot 100 \quad (3)$$

where: A_0 – initial absorbance of sample solution, A_s – current absorbance of the sample.

2.4. Equipment

The microscopy studies, scanning electron microscope (SEM) and high-resolution SEM (HR SEM), were performed using a Hitachi S4500 system (Hitachi High-Technologies Europe GmbH, Mannheim, Germany). Thermal characterizations were performed using a Netzsch Thermal Analyzer (Netzsch - Gerätebau GmbH, Selb, Germany).

The thermal analysis TG-DSC for the cellulose samples (~20 mg) was performed with a Netzsch STA 449C Jupiter apparatus. The samples were placed in an open crucible made of alumina and heated with 10 $K \cdot min^{-1}$ from room temperature up to 900 °C, under the flow of 50 mL min^{-1} dried air. An empty alumina crucible was used as reference.

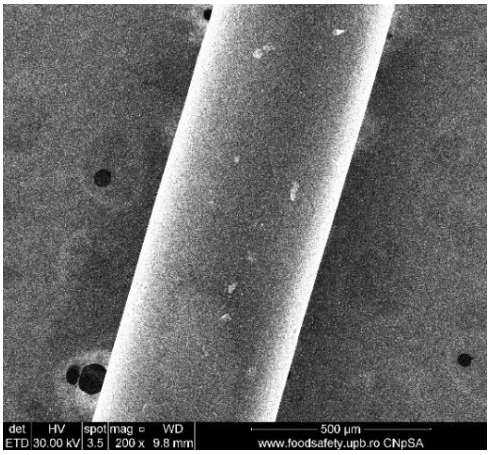
Spectroscopy Bruker Tensor 27 FTIR with a Diamond Attenuated Total Reflection - ATR (Bruker) was used to study the interactions between the chemicals used in the mem- branes developed. FTIR analysis was recorded in the range of 500 to 4000 cm^{-1}. UV-VIS analysis was performed on a Spectrometer CamSpec M550 (Spectronic CamSpec Ltd., Leeds, UK). Other devices used were as follows: ultrasonic bath (Elmasonic S, Elma Schmidbauer GmbH, Singen, Germany), vacuum oven (VIOLA—Shimadzu, Bucharest, Romania).

3. Results

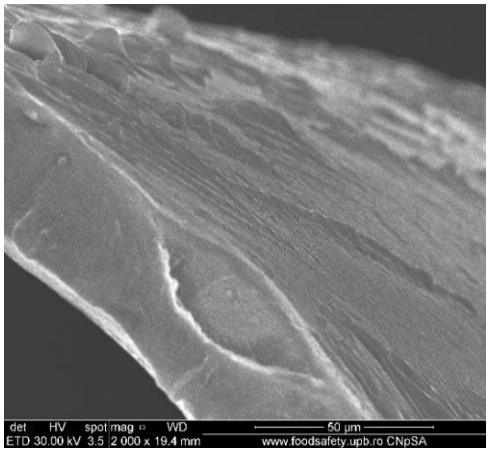
3.1. Scanning Electron Microscopy studies (SEM, and HFSEM and EDAX)

The surface morphology of the considered samples was analyzed using a scanning electron microscope (SEM), high-resolution scanning electron microscope (HR-SEM) and energy dispersive X-ray analysis (EDAX). All samples were properly dried prior to the microscopy analysis and were sufficiently coated with a sputtered gold layer of 400 Å.

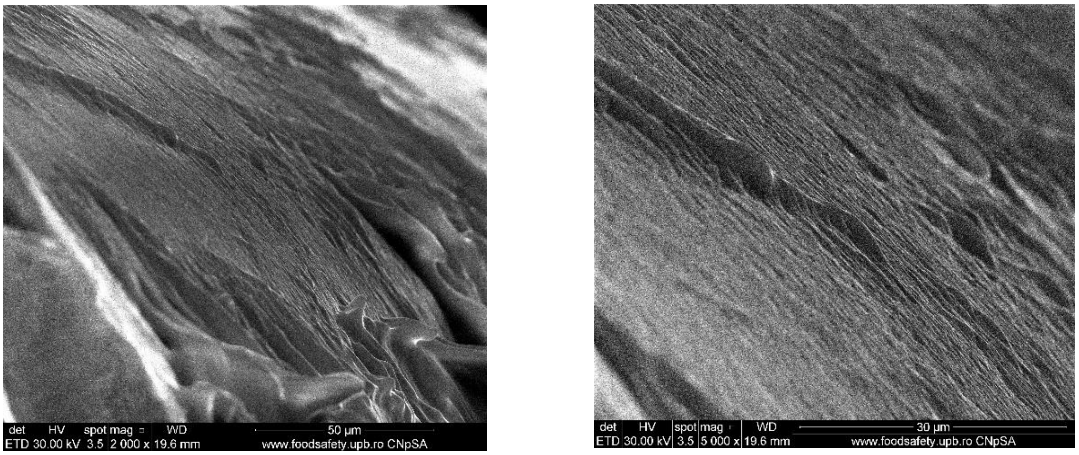
The results of the image analysis are presented in Figures 5, 6, 7 and 8. The compositional surface (EDAX) of the support membrane and two impregnated membranes were illustrated by figure 9.



(**a**)

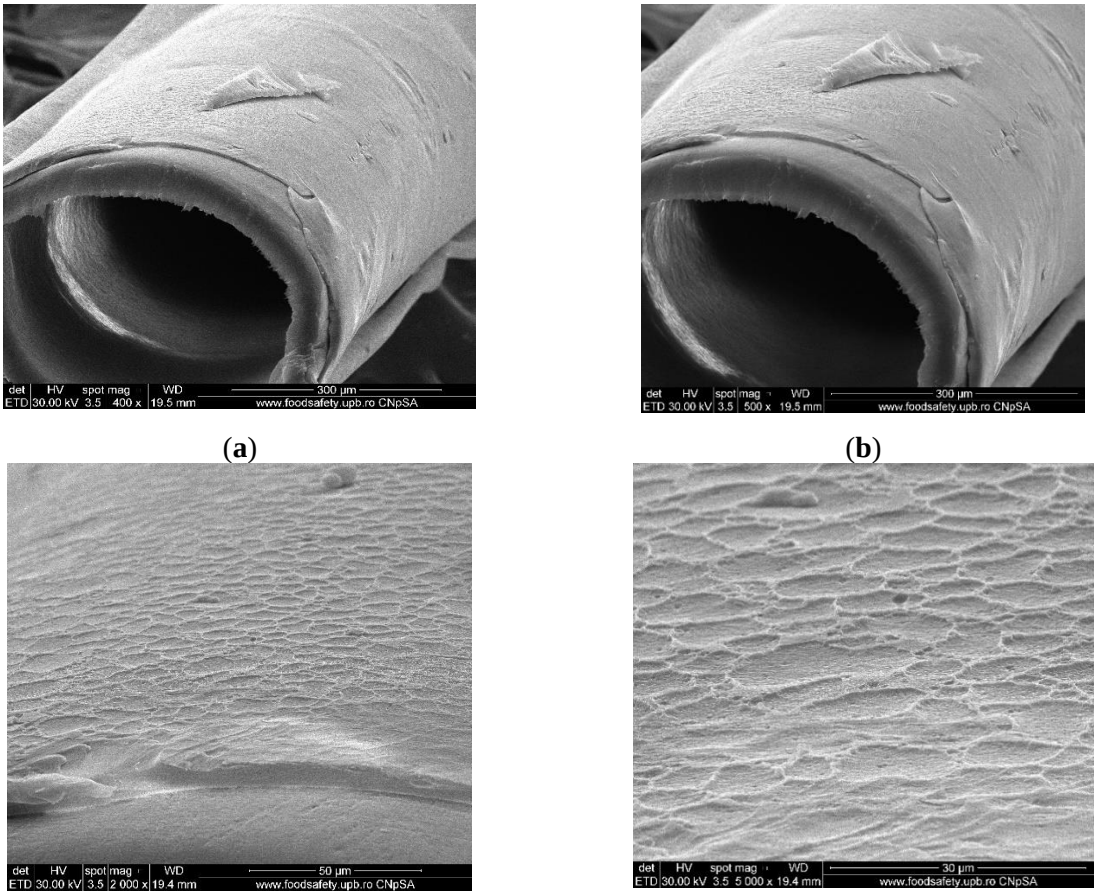


(**b**)



(**c**) (**d**)

Figure 5. Morphology CA-PPM membranes: (**a**) view; (**b**) cross-section; (**c**) and (**d**) surface detail.



(**a**) (**b**)

(**c**) (**d**)

Figure 6. Morphology HEC-PPM membranes: (a) view; (b) cross-section; (c) and (d) surface detail.

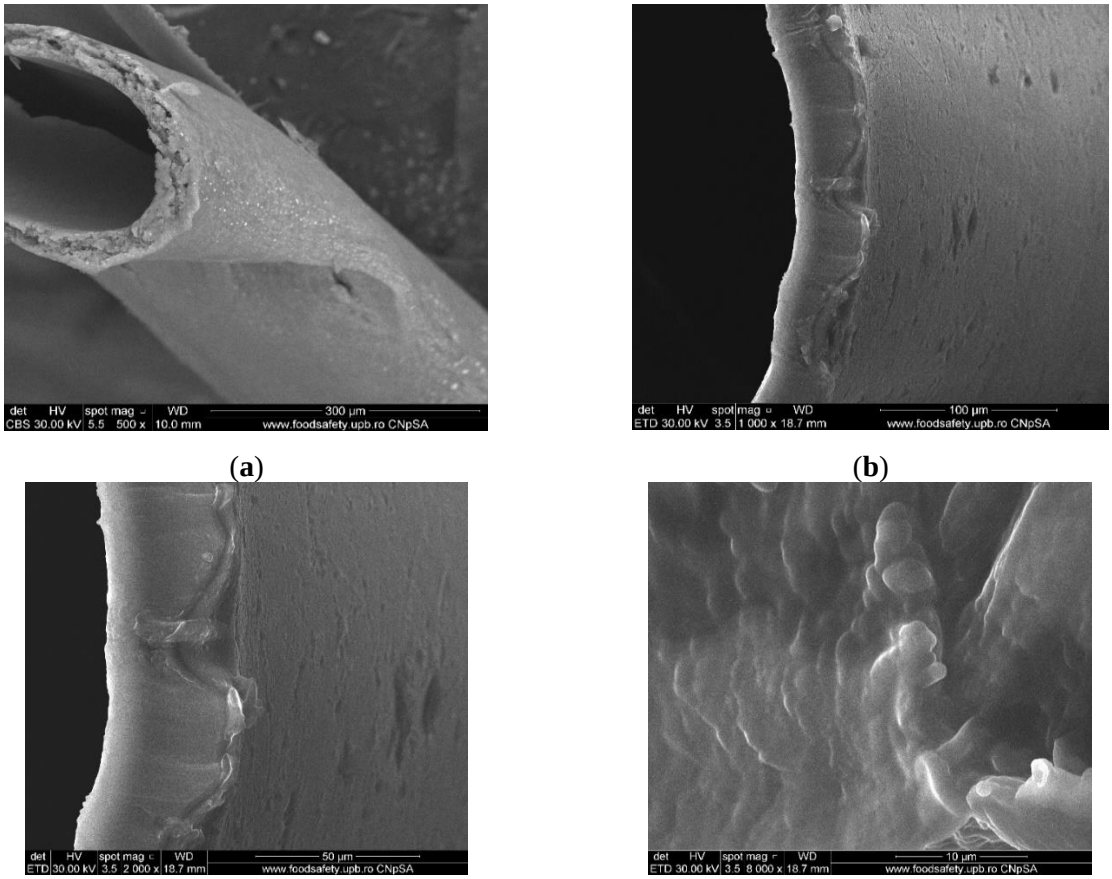
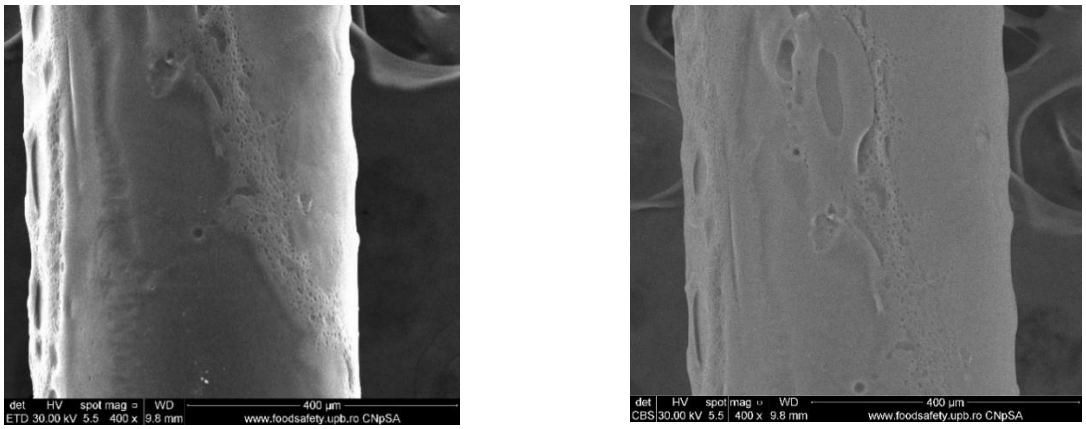
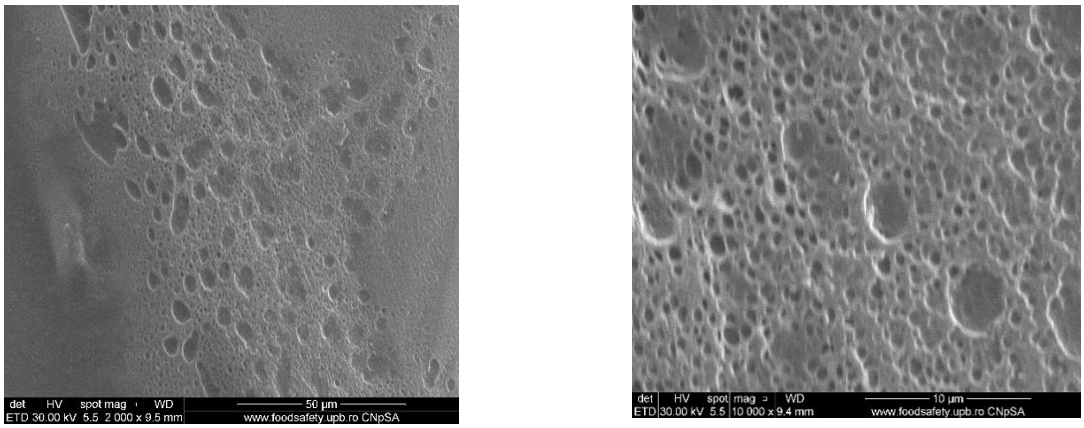


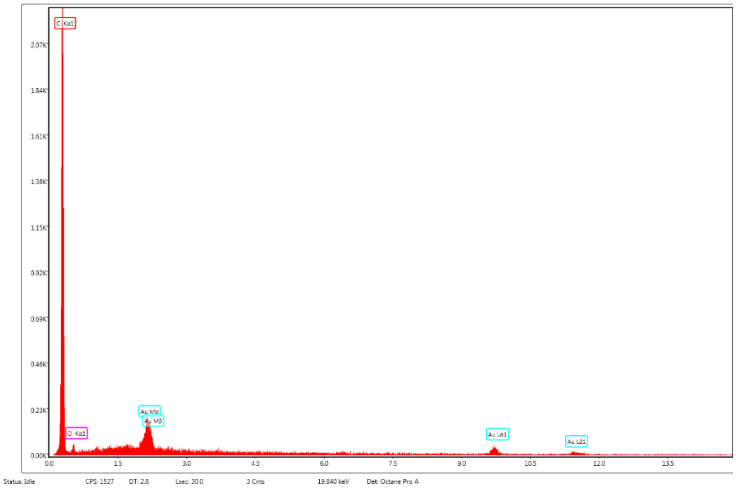
Figure 7. Morphology MHEC-PPM membrane: (**a**) membrane cross-section; (**b**) detail from a); (**c**) membrane surface; (**d**) detail from (**c**).



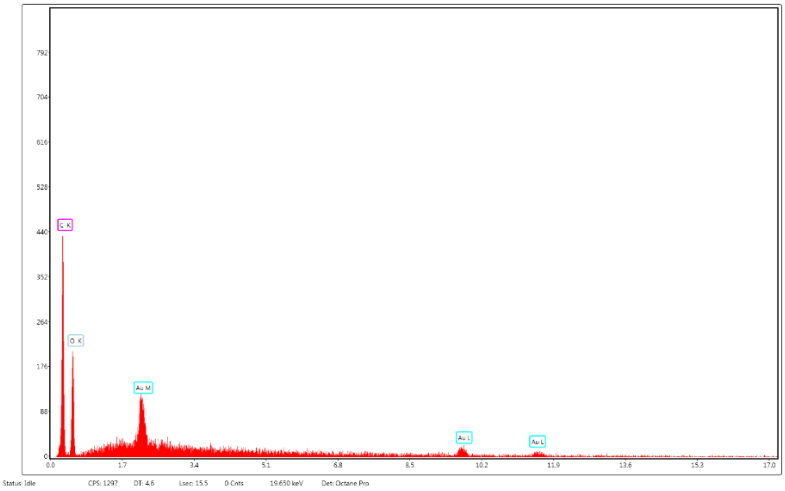


(**c**) (**d**)

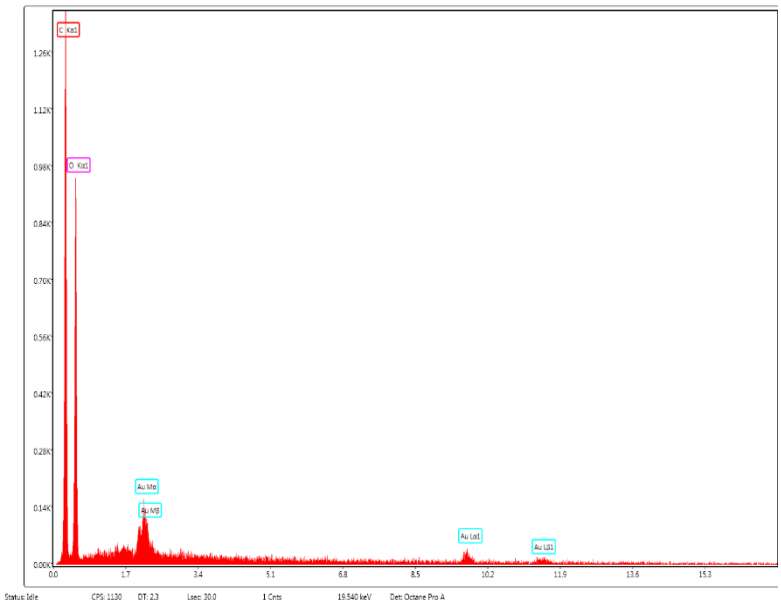
Figure 8. Morphology NaCMC-PPM membranes: (**a**) view; (**b**) detail from (a); (**c**) surface; (**d**) detail from (c).



(**a**)



(**b**)



(**c**)

Figure 9. Energy dispersive X-ray analysis (EADX) on: (**a**) polypropylene hollow fiber membrane (PPM); (**b**) impregnated membranes (CA-PPM) and (**c**) impregnated membranes (MHEC-PPM).

3.2. Thermal analysis

The thermal analysis generated the results materialized in the diagrams presented in Figure 10 and Figure 11, representing analysis results (TG and DSC) for cellulose derivatives, polypropylene hollow fibers, and impregnated polypropylene hollow fibers. The diagrams were recorded up to 900 °C, with a heating speed of 10 °C·min^{-1}.

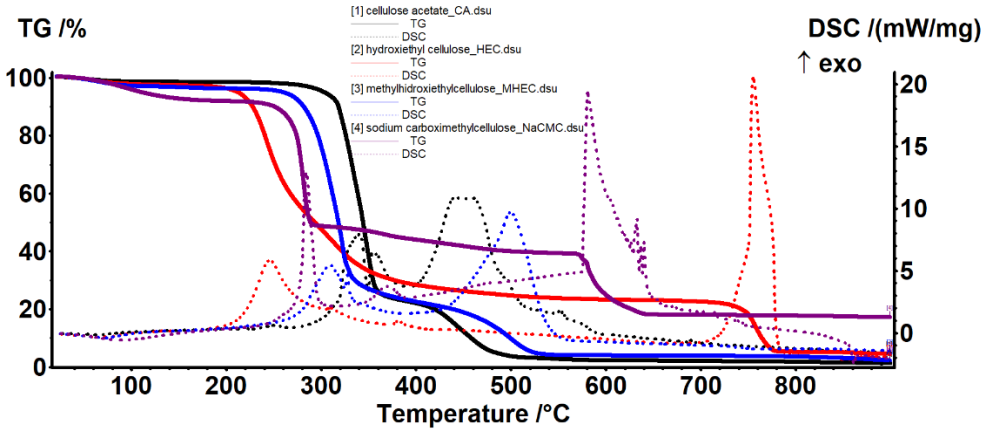


Figure 10. The superposed thermal diagrams for: (**1**) cellulose acetate (CA); (**2**) 2-hydroxyethyl cellulose (HEC); (**3**) methyl 2-hydroxyethyl-cellulose (MHEC); and (**4**) sodium carboxymethyl-cellulose (NaCMC).

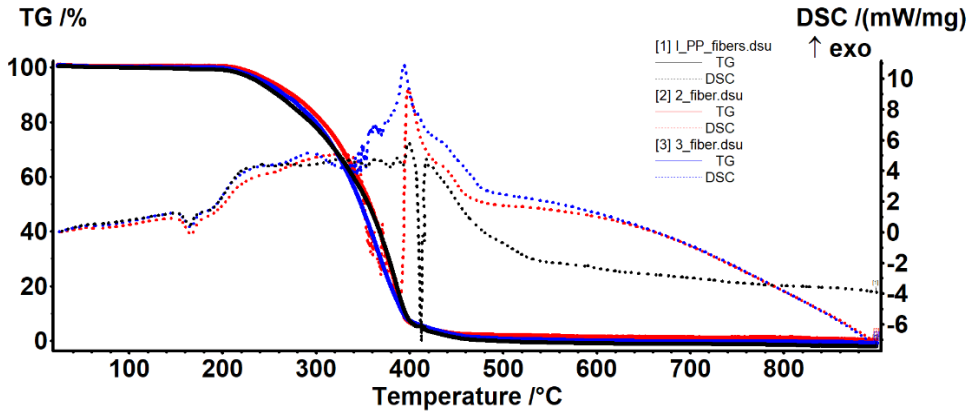
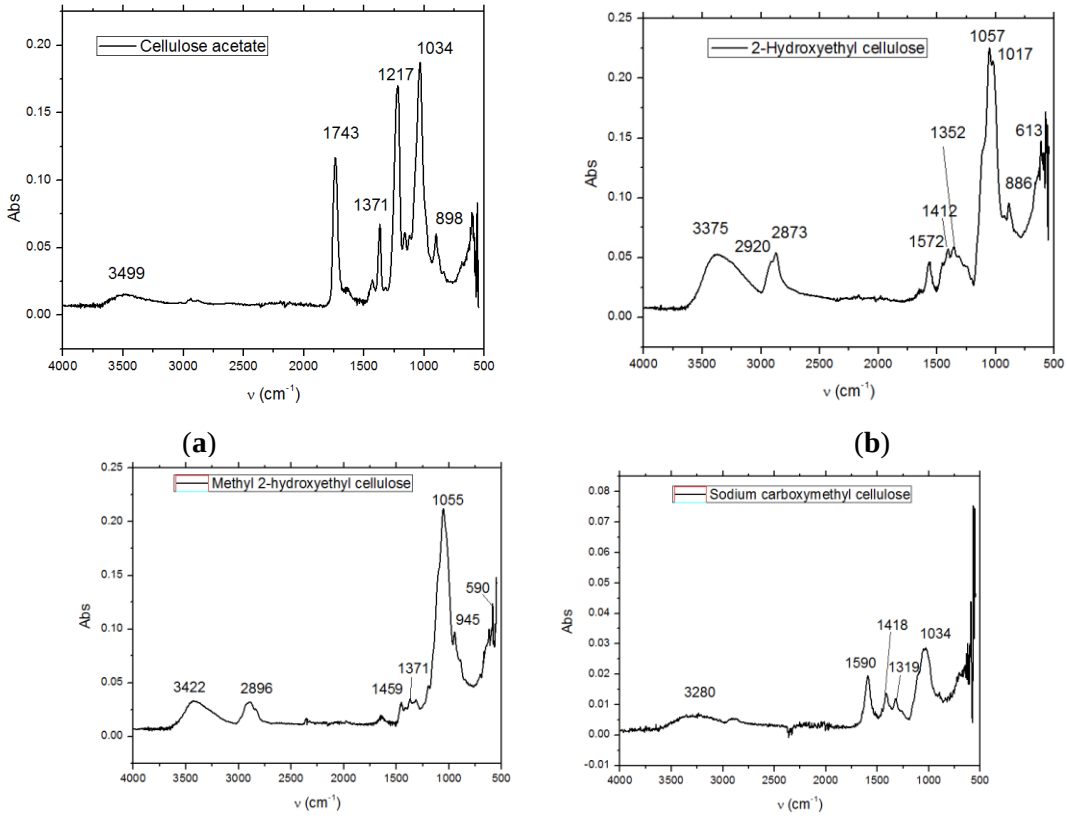


Figure 11. The superposed thermal diagrams for: (**1**) polypropylene hollow fibers (PPM); (**2**) CA-PPM impregnated polypropylene fibers; and (**3**) MHEC-PPM impregnated polypropylene fibers.

3.3. FTIR analysis

Figure 12 presents the FTIR spectra of the obtained membranes. Their characterization were obtained directly onto the solid samples, using the Bruker Tensor 27 with ATR diamond for the materials in this study.



(**a**) (**b**)

(**c**) (**d**)

Figure 12. The Fourier transform infrared spectroscopy (FT-IR) spectrum of the impregnated membranes: (**a**) CA-PPM; (**b**) HEC-PPM; (**c**) MHEC-PPM; (**d**) NaCMC-PPM.

3.4. Performance of the amino acids removal process

The results of amino acids permeation through the prepared membranes are given in Figures 13-15. The main operating parameters and their influence on the evolution of the target chemistry species separation are presented.

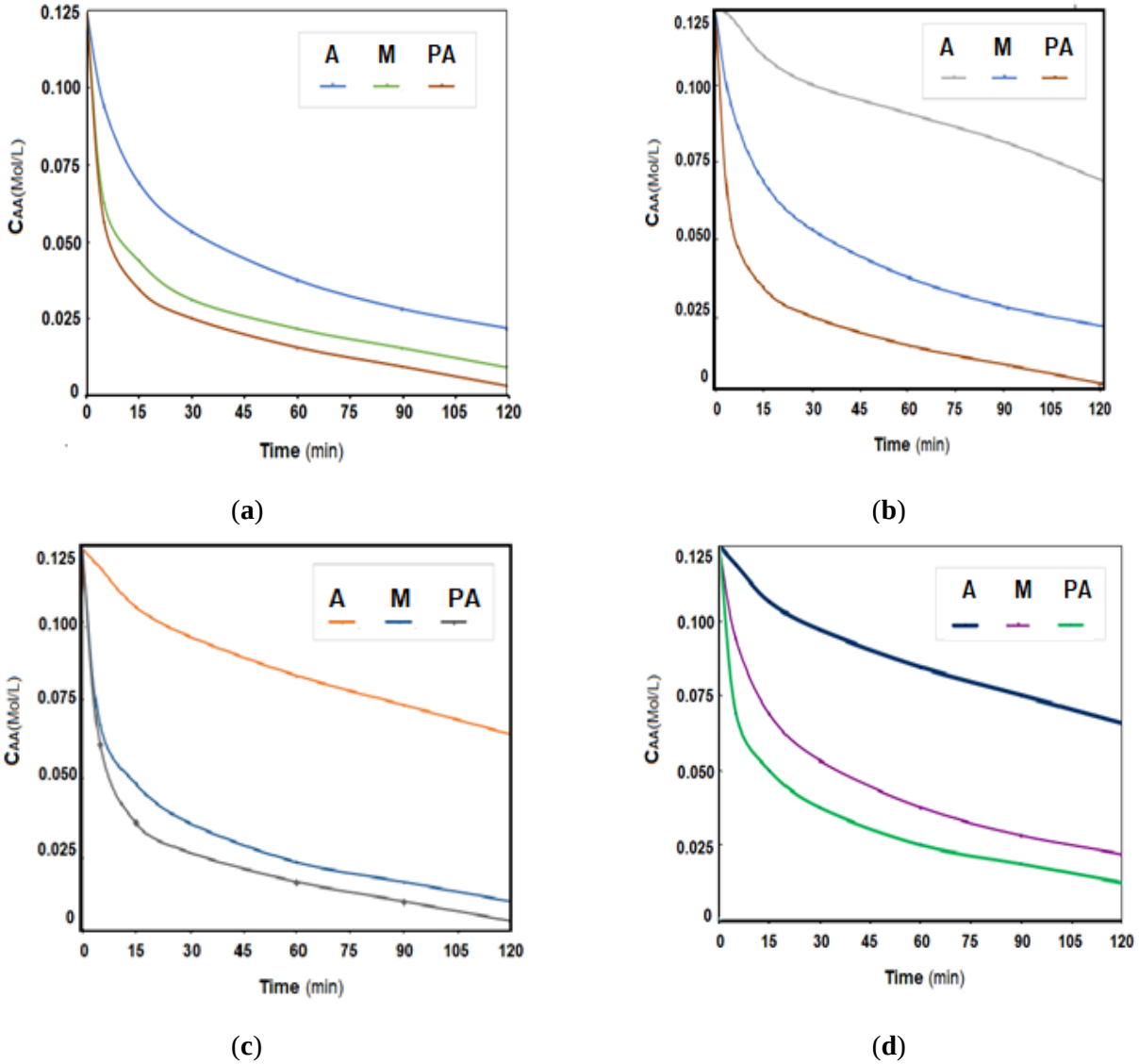


Figure 13. Variation of source phase amino acid concentration depending on the operating time at pH_{SP}=12 and pH_{RP}=7: (**a**) CA-PPM; (**b**) HEC-PPM; (**c**) MHEC-PPM; and (**d**) NaCMC-PPM. **A**=alanine; **M**=methionine, and **PA**=phenylalanine.

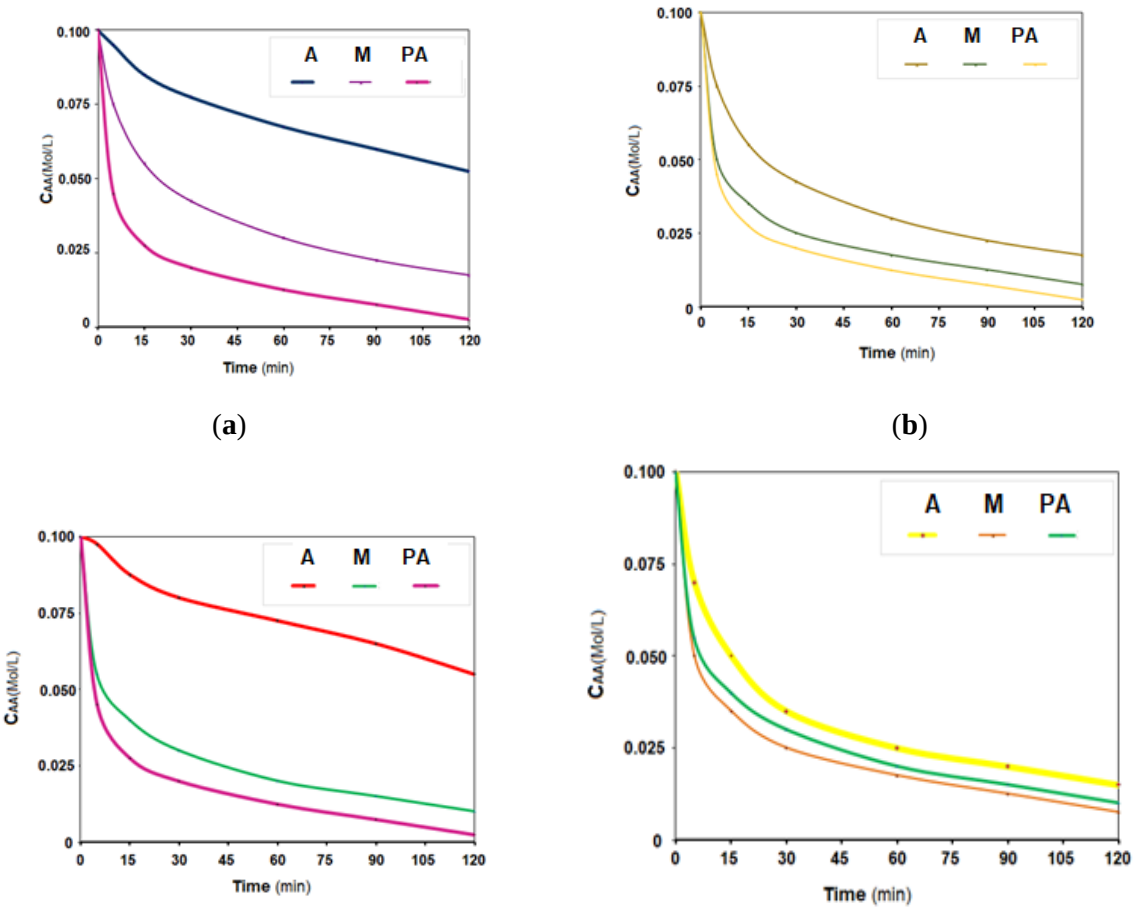
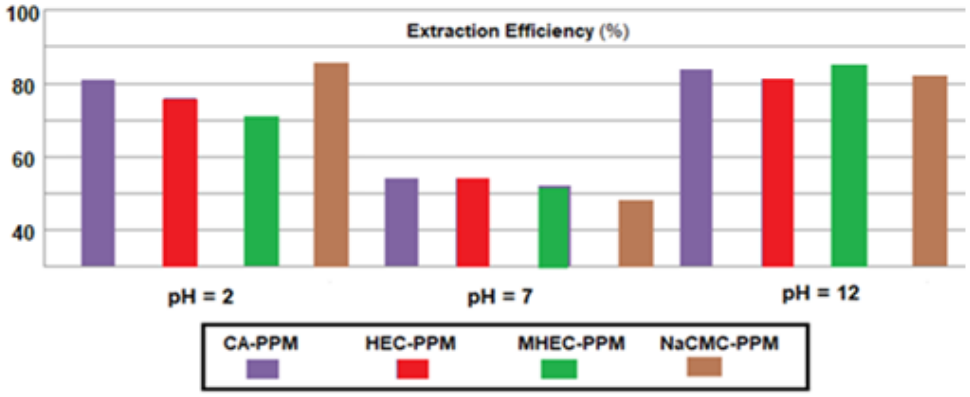
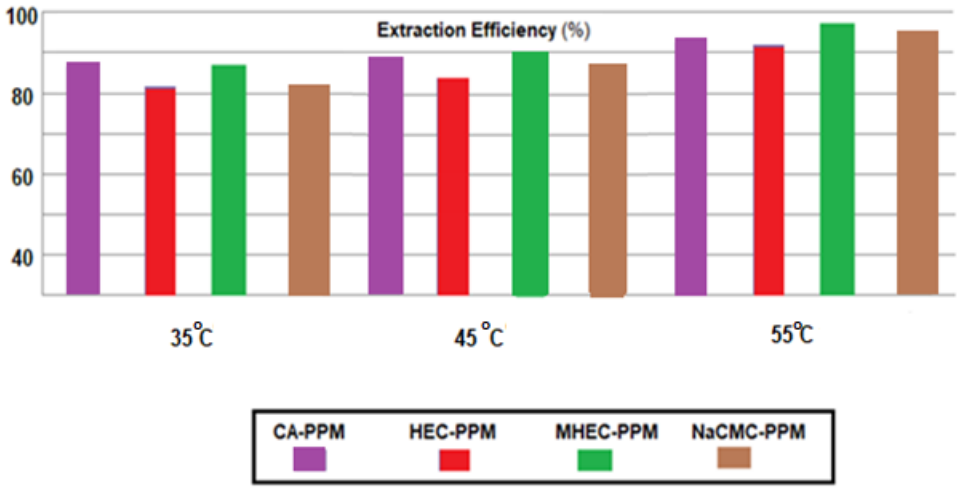


Figure 14. Variation of source phase amino acid concentration depending on the operating time at pH_{SP}=2 and pH_{RP}=7: (**a**) CA-PPM; (**b**) HEC-PPM; (**c**) MHEC-PPM; and (**d**) NaCMC-PPM. **A**=alanine; **M**=methionine, and **PA**=phenylalanine.





(**b**)

Figure 15. The phenylalanine extraction efficiency EE (%) variation versus: (**a**) the pH of the source phase (SP) for the prepared membranes; and (**b**) the temperature of source phase (SP) for the prepared membranes.

4. Discussion

The separation, concentration and purification of amino acids concerns researchers from various fields of activity: chemistry, biochemistry, engineering, medicine or the environment. Remarkable results were obtained in this field through membrane processes, but further research considers both the recovery of amino acids from poor sources and the creation of physical-chemically resistant biocompatible membranes – especially for sterilization or cleaning in order to reuse or maintain process performance.

Obviously, the concern of cellulose derivatives usage for amino acid recovery through membrane processes it is understandable. These derivatives are compatible with the biological environment and biological chemical species, in our case amino acids and their bio-resources. Likewise, the cellulose derivatives have a natural, specific interaction with amino acids, and the chemical modifications of this interaction are very important.

4.1. Membranes and material membranes characterization

4.1.1. Thermal characteristics

Among the physical characteristics of the membranes and membrane materials proposed for study the mechanical ones are provided by the support matrix of polypropylene hollow fiber. But in the practice of membrane processes, the working temperature as well as the temperature of regeneration-washing or of sterilization is very important. Hence, the need to determine the thermal behavior of both membrane materials and impregnated membranes obtained. (Figures 10, 11, 16 and 17, Table 4 and 5).

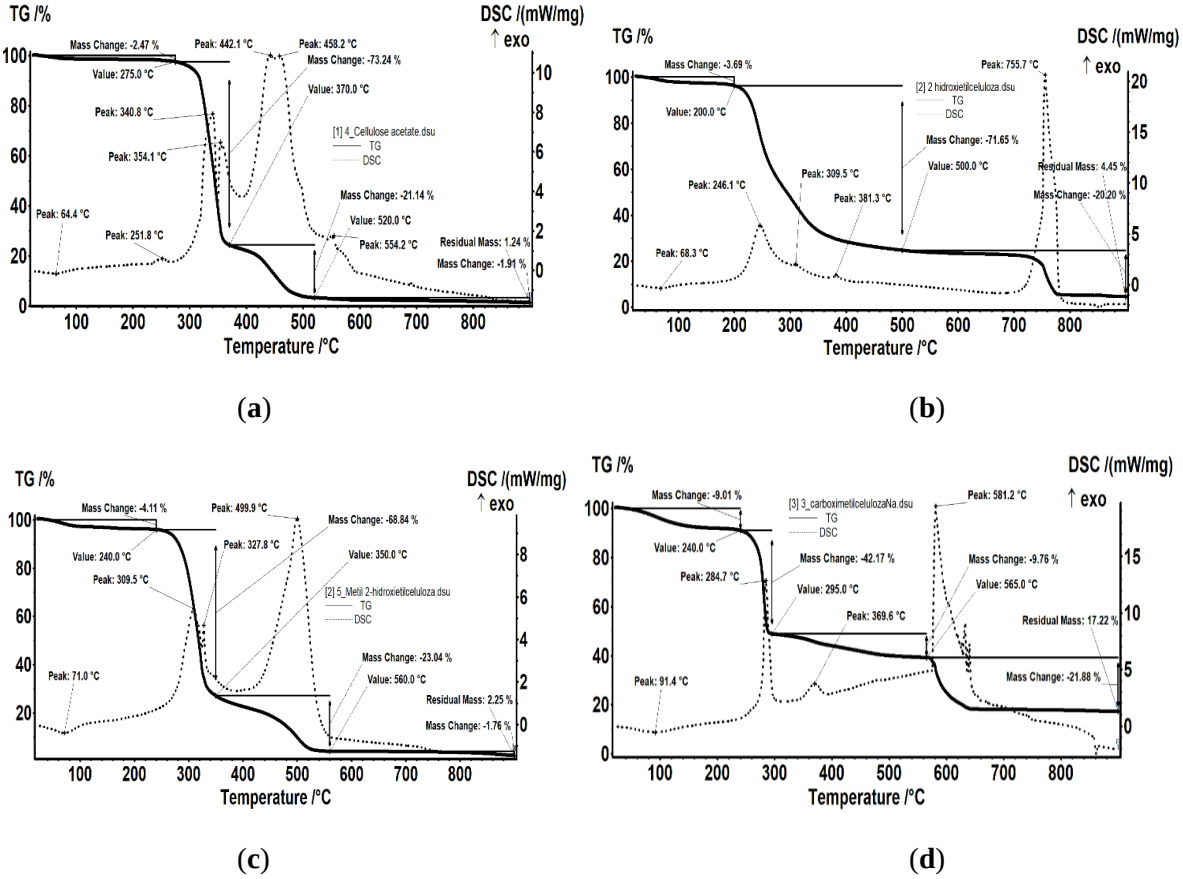


Figure 16. Thermal diagrams for: (**a**) cellulose acetate (CA); (**b**) 2-hydroxyethyl cellulose (HEC); (**c**) methyl 2-hydroxyethyl-cellulose (MHEC); (**d**) sodium carboxymethyl-cellulose (NaCMC).

The cellulose acetate test (Figure 16 a) is thermally stable up to 275 °C. The test loses 2.47% of its initial mass, most likely due to the water (moisture) absorbed, the process being accompanied by a weak endothermic effect at 64.4 °C. A weak exothermic effect is also observed at 251.8 °C, corresponding to a process of partial oxidation of the organic molecule. Degradative oxidation starts at 275 °C, the test loosing 73.24% up to 370 °C. The process is accompanied by two separate exothermic peaks, at 340.8 and 354.1 °C, corresponding to the degradation of the acetate and cellulose group. The carbon mass remaining after initial degradation is eliminate in the range 370-520 °C, through oxidation, the process being accompanied by an exothermic intense, wide effect, with two maxima at 442.1 and 458.2 °C.

The 2-hydroxyethyl cellulose test (Figure 16b) loses 3.69% of its initial mass in the range RT-200 °C, probably water absorbed by the hydroxyethyl cellulose powder. The process is accompanied by a weak endothermic effect, at 68.3 °C. After 200 °C the main process of oxidative degradation takes place, the mass loose continuing slowly until 500 °C. During this interval, 71.65 % of the initial mass is lost. The process is accompanied by several exothermic effects with maxima at 246.1, 309.5 and 381.3 °C.

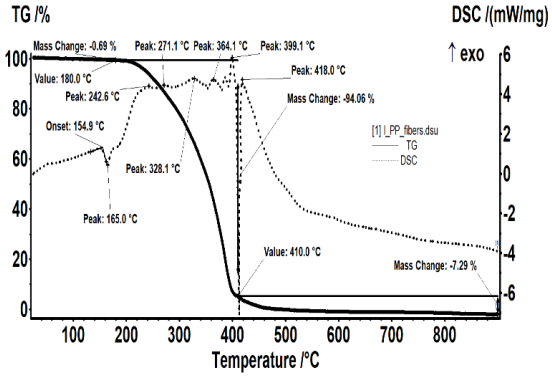
The methyl 2-hydroxyethyl cellulose test (Figure 16 c) looses 4.11% of its initial mass, most likely the absorbed water, the process being accompanied by a weak endothermic effect, with a minimum at 71 °C. The degradative oxidation process took place in the interval 240-350 °C, the test loosing 68.84%. The process is accompanied by two separate, asymmetric, exothermic peaks at 309.5 and 327.8 °C, corresponding to the degradation of cellulose and to the lateral groups, respectively. The remaining carbon mass following the initial degradation is eliminated in the interval 350-560 °C, by oxidation, the process being accompanied by an exothermic, intense, wide, asymmetric effect with the maximum at 499.9 °C.

The sodium carboxymethyl-cellulose test (Figure 16d) looses 9.01% of its initial mass in the interval RT-240 °C, probably having a higher water content absorbed by the carboxymethyl-cellulose powder. The process is accompanied by a weak endothermic effect, at 91.4°C. The main oxidative degradation takes place in the range 240-295 °C (42.17% of its initial mass is eliminated), the mass loss continuing slowly until 565 °C (another 9.76% is still eliminated). The processes are accompanied by exothermic effects with maxima at 284.7 °C and 369.6 °C. After 565 °C, there is a mass loss of 17.22% accompanied by a strong exothermic effect, with a maximum at 581.2 °C, most likely due to the decomposition of sodium carbonate and the reaction with the mass of the crucible mass (Al_2O_3).

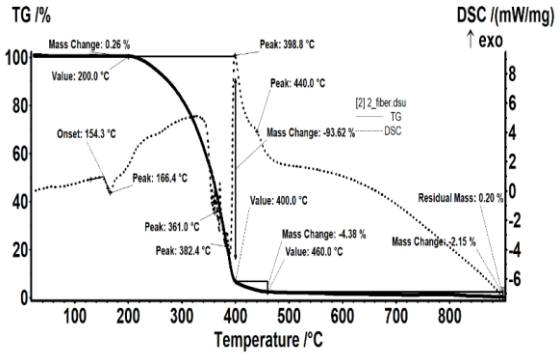
Table 4. Main thermal characteristics of the used cellulose derivatives

Sample	Water content	Mass loss 200-400 °C	Mass loss 400-800 °C	Residual mass
CA	2.47%	76.35%	20.31%	1.24%
HEC	3.71%	67.92%	23.17%	4.45%
MHEC	4.11%	73.63%	19.06%	2.25%
NaCMC	9.02%	47.84%	26.28%	17.22%

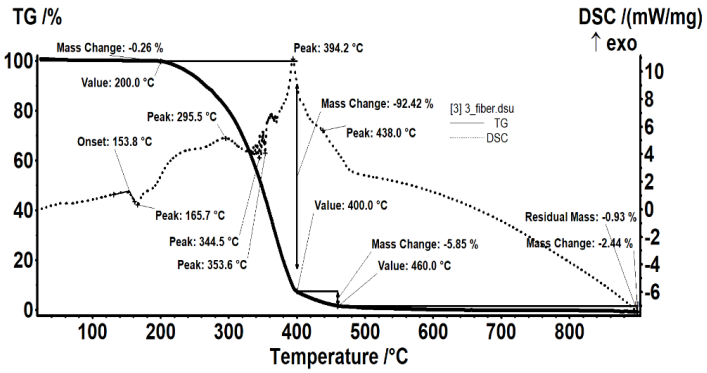
For impregnated membranes that have provided the best separation results (CA-PPM and MHEC-PPM), the thermal diagrams indicate behaviors close to the support fiber, but with specificities that must be taken into account, especially for operation, regeneration or thermal sterilization (Figure 17 and Table 5).



(**a**)



(**b**)



(**c**)

Figure 17. Thermal diagrams for hollow fiber membranes: (**a**) PPM; (**b**) CA-PPM; (**c**) MHEC-PPM.

The sample PPM (Figure 17 a) is relatively stable up to 180°C, with 0.69% recorded mass loss. In the same time, a small endothermic effect is present on the DSC curve, with onset at 154.9 °C and a peak at 165.0 °C. This effect corresponds to the melting of the polypropylene. Between 180 and 410 °C the PPM fibers suffered an oxidative degradation, the recorded mass loss being 94.06%. The effects on DSC curve are a mix of endothermic (decomposing reactions) and exothermic (partial oxidation) effects, with the latest being more intense than former. In the 410-500 °C interval, the oxidation of the carbonaceous mass is achieved with a mass loss of 7.29%. The process is accompanied by a strong exothermic effect, asymmetric, with a maximum at 418.0 °C.

The sample PPM-CA (Figure 17 b) is stable up to 200 °C, the recorded mass loss being 0.26%. In the same time, a small endothermic effect is present on the DSC curve, with onset at 154.3 °C and a peak at 166.4 °C. This effect corresponds to the melting of the polypropylene. Between 200 and 400 °C the sample presents a mass loss of 93.62%. The effects on DSC curve starts with an exothermic, broad one, with peaks at 240 and 327.5 °C, followed by a series of endothermic peaks. This indicates that first process is an oxidation of the polymeric fiber, followed by a series of decompositions. The carbonaceous mass obtained towards end decomposition starts to burn and a strong, sharp exothermic peak can be observed at 398.8 °C. The final oxidation process takes place quick up to 460 °C, with a recorded mass loss of 4.38%, and proceeds slowly after, with another 2.15% mass loss up to 900 °C.

The sample PPM-MHEC (Figure 17c) is stable up to 200 °C, the recorded mass loss being 0.26%. In the same time, a small endothermic effect is present on the DSC curve, with onset at 153.8 °C and a peak at 165.7 °C. This effect corresponds to the melting of the polypropylene. Between 200 and 400 °C the sample presents a mass loss of 92.42%. The first effect on DSC curve is exothermic, broad, asymmetric, with peaks at 235 and 295.5 °C, and indicates that some oxidation processes are responsible for the mass lost in the first part. There are multiple endothermic effects around 350 °C, which indicate the predominance of decomposition processes. The carbonaceous mass obtained by the end of the decomposition starts to burn and a strong, sharp exothermic peak can be observed at 394.2 °C. The final oxidation process takes place quickly up to 460 °C, with a recorded mass loss of 5.85%, and proceeds slowly after, with another 2.44% mass loss up to 900 °C.

Table 5. Main thermal characteristics of the hollow fiber membranes

Sample	PP melting onset (°C)	PP melting peak (°C)	Decomposition start (°C)	$T_{10\%}$ (temperature for 10% mass loss) (°C)
1_PP_fiber (support)	154.9	165.0	180	258
2_fiber (CA-impregnated)	154.3	166.4	200	274
3_fiber (MHEC-impregnated)	153.8	165.7	200	266

4.1.2. Chemical structure and composition

The chemical structure of the chosen cellulosic derivatives was highlighted through Fourier transform infrared spectroscopy (FT-IR), in which the functional groups that can interact specifically with the amino acids considered are observed (Figure 12 and Table 5).

Table 5. The main structural characteristics identified through Fourier transform infrared spectroscopy (FT-IR)

Cellulose derivatives	Wave numbers of the interesting groups for the considered interactions (cm^{-1})

	ν O-C- δ O-C-O	δ-CH_2 δ O-H	δ-CH_2	ν C=O	ν C-H	ν O-H
CA	1034	1371	1410	1743	2960s	3499
HEC	1057	1352	1412	-	2987	3374
MHEC	1055	1371	1420	-	2896	3422
NaCMC	1034	1319	1418	-	2940	3280

ν = vibration; δ = deformation

The chemical structure of the four cellulosic derivatives which impregnate the membranes indicates possibilities of interaction with the amino acids or their ionic forms, both by hydrogen or dipole-dipole bonds (given by the carboxyl or amino groups) and by hydrophobic interactions of hydrocarbon chains. This statement is strengthened by the character of the radical R (Figure 1a) of the considered amino acids: aromatic hydrophobic (phenylalanine) or aliphatic hydrophobic (alanine and methionine).

Of course, depending on the pH of operation in the separation with the considered membranes, the complexity of the amino acid – cellulose derivative interaction must be taken into account. The superficial composition determined through energy dispersive spectroscopy analysis (EDAX) of impregnated membranes Cell-D-PPM (Figure 9 b and c), compared with the PPM support membrane (Figure 9a) shows the appearance in different concentrations of oxygen atoms on the surface. This concentration of the oxygen atoms on the surface of the membrane will be responsible for the attraction of the amino acid, but the migration inside the impregnated membrane depends on the overall composition of the cellulose derivative used for impregnation.

4.1.3. Membrane morphology

From the images obtained through scanning electron microscopy (SEM) and high resolution scanning electron microscopy (HR-SEM) some common features of the obtained impregnated membranes can be highlighted, but also several specificities, as follows:

- Impregnation of the membranes takes place superficially and adherently, without the cellulosic derivative reaching the inside of propylene hollow fiber membrane (Figure 5a, Figure 6a, Figure 7a and Figure 8a);
- The layer of cellulosic derivative from the surface of the membranes has about 5 μm (Figure 6 a, b, and c) being highlighted in the detail depicted in Figure 18;

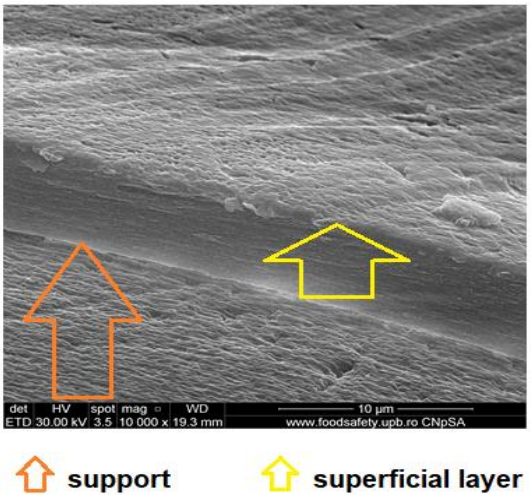
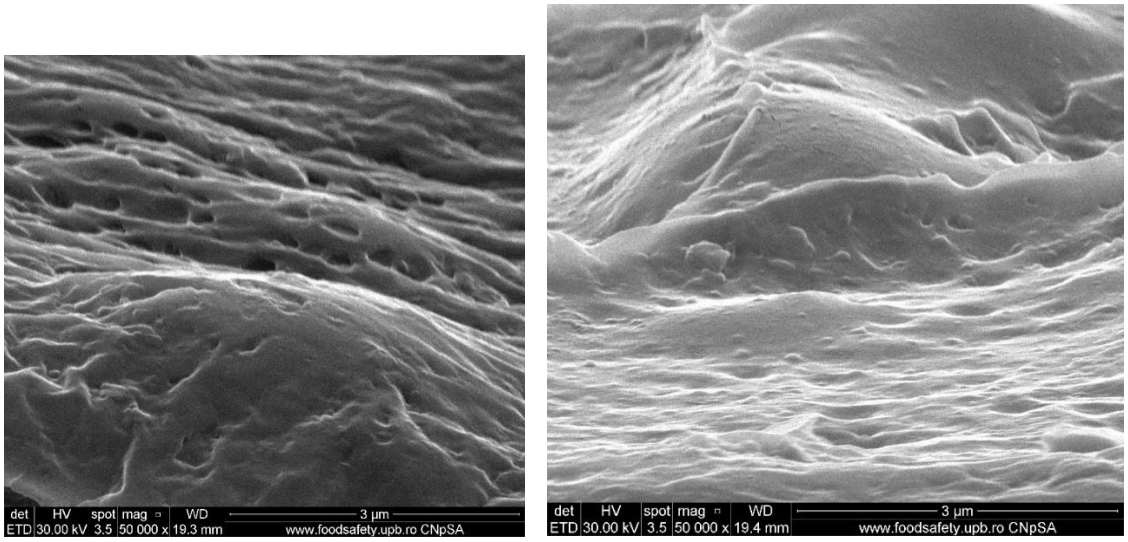


Figure 18. Detail of the superficial layer from the cellulose derivatives on the polypropylene hollow fiber

- The surface layer of cellulosic derivative has a microstructure specific to nanofiltration membranes (Figure 5d, Figure 6d, Figure 7d and Figure 8d), highlighted in two significant details in Figure 19.



(**a**) (**b**)

Figure 19. Detail of the superficial layer from the cellulose derivatives: (**a**) cellulose acetate and (**b**) 2-hydroxyethyl cellulose.

4.2. The effect of the composition of the impregnated membrane on the recovery of amino acids

The first pertraction tests of the chosen amino acids, alanine, phenylalanine and methionine, considered the study of the evolution of amino acids in source phase, in a determined interval of 120 minutes (Figure 13 and 14). The pH of the feeding solution was equal to 12 (Figure 13) and 2, respectively (Figure 14), to have the certainty of the formation of the carboxyl anion, in the first case and of the ammonium cation, in the second case (Figure 1b and Table 3). The receiving phase consists of pure water (pH=7) so that when re-extracted from the membrane the amino acid reaches the shape specific to the isoelectric point (Figure 20). The working temperature was 25 °C in the whole membrane system.

The concentration of the three amino acids decreases rapidly in the first 60 minutes of operation, after which the decrease is slower, or a level is created (Figures 13 and Figure 14). The lowest decrease rate is in all cases for alanine, followed by methionine, and phenylalanine.

However, some peculiarities stood out:

- The difference in transfer rate is large between alanine and the other two amino acids, especially for HEC-PPM, MHEC-PPM and NaCMC-PPM membranes, at pH=12, as well as for CA-PPM and MHEC-PPM membranes, at pH=2;
- The transfer rates differ less in the case of CA-PPM at pH=12, as well as for HEC-PPM and NaCMC at pH=2.

Following these permeation tests the authors considered that membranes CA-PPM and MHEC-PPM were selected for thermal characterization (TA) and surface analysis (EDAX) (Figures 13b and c-AT and, Figures 9b and c-EDAX).

Considering the amino acid flows (Table 6), depending on the nature of cellulose derivative that forms the impregnated membrane, it can be seen that there are significant differences in the flow of the three amino acids.

Table 6. The fluxes of the cellulose derivatives membranes at pH=2 and pH=12 of the source phase (**A**=alanine; **M**=methionine, and **PA**=phenylalanine)

pH source phase	Membrane flux (μMol/m^2·s)											
	CA-PPM			HEC-PPM			MHEC-PPM			NaCMC-PPM		
	A	M	PA	A	M	PA	A	M	PA	A	M	PA
2	83.3	186.1	241.6	180.5	222.5	244.5	69.4	208.5	227.8	194.4	229.0	230.8
12	236.1	277.0	300.4	83.2	235.6	305.4	111.4	280.5	305.5	97.2	236.1	278.0

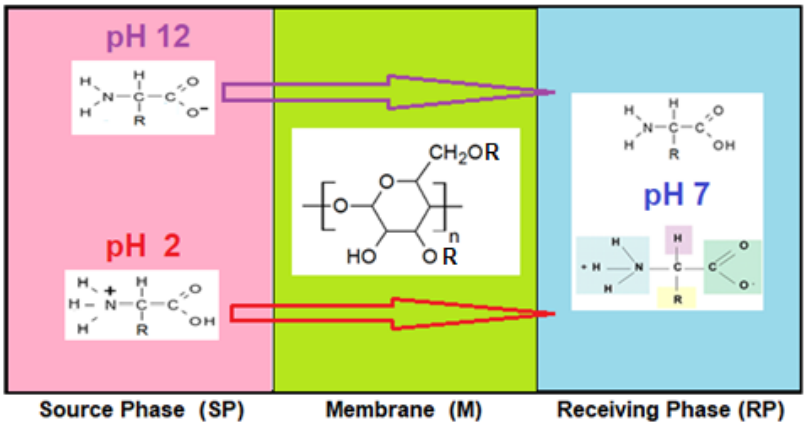
The results obtained show that phenylalanine has the highest fluxes through all four types of membranes, followed by methionine and alanine. pH does not change this order, but suggests the possibility of selective separation of the three amino acids, more obvious being the separation of alanine from phenylalanine.

Of the four kinds of membrane, the most suitable for recuperative separation of the considered amino acids are those based on cellulose acetate and methyl 2-hydroxyethyl-cellulose.

4.3. The effect of pH and solubitility of amino acids on the flow through impregnated membranes

The flow performances were also found in the efficiency of phenylalanine extraction, chosen for the highest transfer rates found in all previous experiments for all four types of membrane (Figure 15 a). Depending on the pH of the source phase, the following succession was obtained:

$$EE_{pH\ 12} = EE_{pH\ 2} > EE_{pH\ 7} \quad (4)$$



(**a**) (**b**)

Figure 20. The transport mechanism of the amino acids at (**a**) pH=2 and pH=12 for the source phase (SP); and (**b**) pH=7 (pure water) in the receiving phase (RP).

Determination of the efficiency of extraction of the amino acids from source solutions of pH=12, at temperatures of 35, 45 and 55 °C, shows that the separation efficiency grows with increasing temperature for all four types of membranes (Figure 15b). A more pronounced effect can be seen in the case of HEC-

PPM and NaCMC-PPM membranes, which could correlate with higher hydrophilicity of membranes based on the two cellulosic derivatives. However, the usage of these impregnation derivatives is limited by the solubility of the polymeric layer in the source solution, which would lead over time to significant losses and drastic decreases in membrane thickness, known in the literature of the membranes as 'membrane washing' [72].

Which was somewhat surprising in the preliminary experiments was the behavior of alanine, whose rate of transfer through membranes is the lowest, sometime even suggesting the possibility of its separation methionine or phenylalanine. One explanation that would answer to the results presented in figures 13, 14 and 15a would be that the solubility of alanine is much higher than that of the other two amino acids (Table 3), which would lead to an important retention of it in the source phase.

The argument presented is even more valid as the transfer of phenylalanine is in all cases higher than that of methionine. Thus, it could be generalized that that the transfer flow (***J***) of amino acids through the studied membranes grows in this order:

$$\boldsymbol{J}_{phenylalanine} > \boldsymbol{J}_{methionine} > \boldsymbol{J}_{alanine} \tag{5}$$

which would thus be correlated with the solubility in pure water ($\boldsymbol{S_o}$) of the amino acids:

$$\boldsymbol{So}_{phenylalanine} < \boldsymbol{So}_{methionine} < \boldsymbol{So}_{alanine} \tag{6}$$

The results can be explained by the fact that in aqueous solution the amino acids participates in proton exchange equilibria which are controlled by pH:

$$HOOC\text{- }CHR\text{ -}NH_2 + H_3O^+ \leftrightarrow HOOC\text{- }CHR\text{ -}NH_3^+ + HOH \tag{7}$$

$$HOOC\text{- }CHR\text{ -}NH_2 + HOH \leftrightarrow {}^-OOC\text{- }CHR\text{ -}NH_2 + H_3O^+ \tag{8}$$

Based on these balances, the acidity constants are defined:

$$K_{a_1} = \frac{[HOOC-CHR-NH_2][H_3O^+]}{[HOOC-CHR-NH_3^+]} \tag{9}$$

$$K_{a_2} = \frac{[OOC-CHR-NH_2][H_3O^+]}{[HOOC-CHR-NH_2]} \tag{10}$$

The degree of formation of these chemical species can be assessed with the following relationships:

$$\alpha_0 = \frac{1}{1+10^{pK_{a_2}-pH}+10^{pK_{a_1}+pK_{a_2}-2pH}} \tag{11}$$

$$\alpha_1 = \frac{1}{1+10^{pK_{a_1}-pH}+10^{pH-pK_{a_2}}} \tag{12}$$

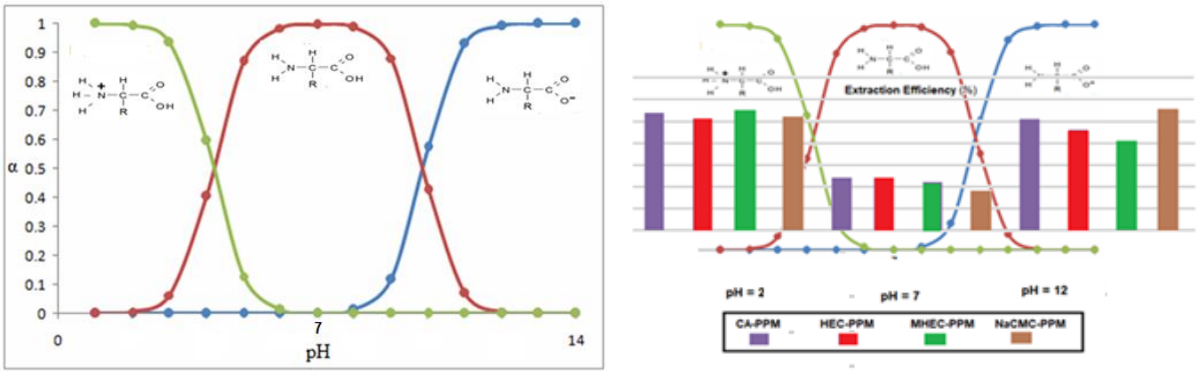
$$\alpha_2 = \frac{1}{1+10^{pH-pK_{a_1}}+10^{2pH-pK_{a_1}-pK_{a_2}}} \tag{13}$$

in which α_0, α_1, α_2 represent, respectively, the degrees of formation of the species ${}^-OOC\text{-}CHR\text{-}NH_2$, $HOOC\text{- }CHR\text{ -}NH_2$, and $HOOC\text{- }CHR\text{ -}NH_3^+$, in the aminophenol solution.

The actual solubility (S) of the considered amino acid is a function of pH and the solubility in pure water (S_o), which explains the behavior of the amino acid in the pertraction process:

$$S = S_0 \cdot f(\alpha) \tag{14}$$

With these relations one can illustrate the speciation diagram for a generic amino acid with: pK_{a1}= 2.30 and pK_{a2}= 9.20 (Figure 21):



(**a**) (**b**)

Figure 21. The speciation diagram of an amino acid, as a function on pH: (**a**) diagram; and (**b**) the diagrams superposed on the efficiency extraction from Figure 15a.

Based on the analysis of the speciation diagram, the pH conditions for the formation of the different chemical species of the studied amino acids can be anticipated, so as to obtain the optimal results in separation.

5. Conclusions

Amino acids are substances whose chemical and biochemical impact are quite remarkable. A special place in the study of the amino acids is occupied by their recovery from various sources, through a multitude of separation methods and techniques in which the membranes occupy a special place.

The present paper addressed the recuperative separation of three amino acids (alanine, phenylalanine and methionine) from synthetic solutions, using membranes from cellulose derivatives (cellulose acetate, 2-hydroxyethyl-cellulose and methyl 2-hydroxylethyl-cellulose or sodium carboxymethyl-cellulose) in polypropylene hollow fiber matrix.

In order to determine the basic characteristics, the separation performances of the considered amino acids (retention, flow and selectivity) and the morphological and structural ones, the membranes and membrane materials were analyzed by specific techniques: scanning electron microscopy (SEM), high resolution SEM (HR-SEM), Fourier transform infrared spectroscopy (FT-IR), energy dispersive spectroscopy (EDS) and thermal-gravimetric analyzer (TGA).

The support offered by polypropylene hollow fibers confers physical-chemical resistance, and cellulosic derivatives used for impregnation contribute to the separation performances of prepared impregnated membranes.

The results of the separation are influenced by the pH of the source phase and the solubility of the amino acids considered, the best results as flow and extraction efficiency being obtained when the source phase has a pronounced acidic or basic pH, and the receiving phase has a neutral pH (pure water).

Among the amino acids, the highest transmembrane fluxes and extraction efficiency are offered by phenylalanine, then methionine and finally alanine. This succession is closely correlated with the solubility of the amino acids studied in water, a high solubility in water leading to a low transfer rate and separation efficiency.

The considered cellulosic derivatives (cellulose acetate, 2-hydroxyethyl-cellulose, methyl 2-hydroxyethyl-cellulose or sodium carboxymethyl-cellulose) have a similar behavior in the separation process, but following the experiments, cellulose acetate and methyl 2-hydroxyethyl-cellulose are recommended for the realization of impregnated membranes. Although when increasing the operating temperature from 25 to 55 °C the performance of membranes impregnated with 2-hydroxyethyl-cellulose and sodium carboxymethyl-cellulose increases, still the use of these membranes at high temperature raises the problem of degradation by the solubilization-washing phenomenon.

C. General conclusions and research perspectives

C.1.General conclusions

The elaboration of the doctoral thesis "Products of biological interest with biomedical implications separated by membrane processes" represents par excellence, an applied research activity, combined with fundamental research activity. Applied research refers to the separation of products of biological interest (amino acids, chemical species with toxic potential) with biomedical implications separated by membrane processes.

The synthesis of the literature (Chapter 1) highlighted some significant research directions of membranes and membrane processes:

- Currently known membranes are classified both by the nature, structure and type of material of which they are made and by the scope
- Depending on the nature of the material, the membranes are natural and synthetic
- Depending on the structure, the membranes are porous and non-porous (dense)
- By type of material: polymeric and inorganic
- In terms of pore distribution, porous or non-porous membranes can be isotropic (symmetrical), anisotropic (asymmetrical) or composite
- Methods of obtaining membranes refer to homogeneous neutral membranes, ion exchange membranes, liquid membranes
- The membrane processes described are microfiltration, ultrafiltration, electrodialysis and reverse osmosis.
- Liquid membranes are classified into three categories: bulk, emulsion and sustained (on support)
- In recent years, a number of new membrane processes have developed: piezodialysis, diafiltration, membrane distillation and pervaporation.
- The interest in thermally directed processes has been updated by the development of a new process called membrane distillation.
- The separation of compounds of biological interest (amino acids, proteins, chemical species with toxicological impact) with the help of membranes has been widely studied due to numerous applications in environmental protection, purification of proteins from various biological environments, reduction of organic water load, recovery of valuable products grocery shop.

The Experimental Part section (Chapters 2 and 3) presents two of the representative results of the research in the doctoral research internship:

In Chapter 2. liquid membranes are used on the support of microporase polypropylene fibers based on n-octanol and n-decanol containing magnetic nanoparticles with iron and doped with recovered silver, by electrolysis, for the transport of o- and m-nitrophenols, species chemicals with recognized toxic potential.

Nanoparticles that have a silver or iron oxide component are by far the most widely used both as individual nanoparticles and as composite, hybrid, or smart nanoparticles containing both silver and iron oxides.

Silver is recovered from residues of silver chloride from university teaching and research activities (UPB).

Silver is recovered by solubilizing silver chloride in hydrochloric acid, sodium thiosulfate and ammonia, and electrolytes containing [AgCl2] -, [Ag (S2O3) 2] 3- or [Ag (NH3) 2] + are subjected to cyclic voltammetry (from -0.5 to +1.23 V), in a cell with pure iron anode and cathode and platinum reference electrode.

Three types of nanoparticles are obtained:

- [AgCl2] - denoted NP1
- [Ag (S2O3) 2] 3- denoted NP2
- [Ag (NH3) 2] + denoted NP3

whose dispersion in n-octanol or n-decanol provides the membrane material for liquid membranes on a support of microporous polypropylene fibers:

The separation of the target substances (o-nitrophenol and m-nitrophenol) in oscillating magnetic field shows that overall, the extraction performances (extraction efficiency-EE and flux -J) increase in the order:

EENP3> EENP1> EENP2

JNP3> JNP1> JNP2

The efficiency of separation with Ag-doped magnetic nanoparticles is correlated with their saturation magnetization and their silver content.

It is thus possible to suggest a dependence of the total flow of nitrophenol through the diffusion-solubilization membrane, convection and silver-assisted transport:

Jtotal = Jdifuzie + Jconvectiv + Jasiatat

In other words, the total flux cumulates the effect of the solvent, magnetization and silver content:

Jnitrophenol = Solvent + JNP + JAg

Chapter 3 addresses the transport of some biological chemical species of interest (amino acids) for separation and / or concentration through composite membranes.

Amino acids are substances whose chemical and biochemical impact is quite remarkable. A special place in the study of amino acids is occupied by their recovery from various sources, through a multitude of methods and techniques of separation in which the membranes occupy a special place.

The present work addressed the recovery of three amino acids (alanine, phenylalanine and methionine) from synthetic solutions, using membranes from cellulose derivatives (cellulose acetate, 2-hydroxyethyl cellulose and methyl 2-hydroxyethyl cellulose or sodium carboxymethyl cellulose).) in hollow polypropylene fiber matrix.

To determine the basic characteristics, the separation performances of the considered amino acids (retention, flow and selectivity) and of the morphological and structural ones, membranes and membrane materials were analyzed by specific techniques: scanning electron microscopy (SEM), high resolution. SEM (HR-SEM), Fourier transform infrared spectroscopy (FT-IR), energy dispersive spectroscopy (EDS) and thermal-gravimetric analyzer (TGA).

The support provided by the hollow polypropylene fibers provides physico-chemical resistance, and the cellulose derivatives used for impregnation contribute to the separation performance of the prepared impregnated membranes.

The separation results are influenced by the pH of the source phase and the solubility of the amino acids considered, the best results in flow and extraction efficiency being obtained when the source phase has a pronounced acidic or basic pH and the receiving phase has a neutral pH (water pure).

Among the amino acids, the highest transmembrane fluxes and extraction efficiency are provided by phenylalanine, then methionine and finally alanine. This sequence is closely correlated with the solubility of the studied amino acids in water, a high solubility in water leading to a low transfer rate and separation efficiency.

The considered cellulose derivatives (cellulose acetate, 2-hydroxyethyl-cellulose, methyl 2-hydroxyethyl-cellulose or sodium carboxymethyl-cellulose) behave similarly in the separation process, but following the experiments, cellulose acetate and methyl 2-hydroxyethyl Cellulose are recommended for making impregnated membranes. Although increasing the operating temperature from 25 to 55 ° C increases the performance of membranes impregnated with 2-hydroxyethyl-cellulose and sodium carboxymethyl-cellulose, the use of these membranes at high temperature raises the problem of degradation by the phenomenon of solubilization-washing.

*C2. **Elements of originality in the doctoral thesis***

Three types of new materials were obtained in the thesis:

- Silver-iron oxide magnetic nanoparticles by electrochemical process.
- Magnetic dispersion composite membranes on microporous polypropylene support.
- Cellulosic composite membranes on microporous polypropylene support.

Two new separation processes involving composite membranes have been developed in the thesis:

- Separation in magnetic field through membranes magnetic dispersion on porous support.
- Separation by composite membranes cellulosic derivative-microporous support driven by the pH gradient.

Separations of chemical species of biological and biomedical interest were performed:

- Separation of nitrophenols by membranes magnetic dispersion on porous support.
- Separation of amino acids by composite membranes cellulosic derivative-microporous support.

*C3. **Research development perspectives***

The research carried out within the doctoral research program "Products of biological interest with biomedical implications separated by membrane processes" led to the development of new applications of separation processes through composite membranes in magnetic field and pH gradient.

Selective references

[132] *H. Bechhold,* Kolloidstudien mit der Filtrationsmethode, *Z. Physik Chem.* **60**, 257 (1907).

[133] *W.J. Elford,* Principles Governing the Preparation of Membranes Having Graded Porosities. The Properties of 'Gradocol' Membranes as Ultrafilters, *Trans. Faraday Soc.* **33**, 1094 (1937).

[134] *S. Loeb and S. Sourirajan,* Sea Water Demineralization by Means of an Osmotic Membrane, in *Saline Water Conversion–II, Advances in Chemistry Series Number 28,* American Chemical Society, Washington, DC, pp. 117–132 (1963).

[135] *Mulder, M.* Basic principles of membrane technology; Kluwer Academic Publishers: Netherlands, 1996; ISBN 0792309782.

[136] *Baker, R.W.* Membrane Transport Theory. In Membrane Technology and Applications; John Wiley&Sons Ltd, 2012 ISBN 0-470-85445-6.

[137] *Nechifor, G.; Popescu, G.* Asymmetric membranes prepared by immersion-precipitation technique. Rev. Roum. Chim. **1990**, *35*, 899.

[138] *Pusch, W., Walch, A. (1982)* Synthetic membranes – preparation, structure, and application. Angewandte Chemie International Edition in English, **21**, 660–685.

[139] Cath, *T.Y., Childress, A.E., Elimelech, M. (2006)* Forward osmosis: principles, applications, and recent developments. Journal of Membrane Science, **281**, 70–87.

[140] Sirkar, *K.K. (2008)* Membrane contactors. In Advanced Membrane Technology and Applications, N.N. Li, A.G. Fane, W.S.W. Ho, T. Matsuura (eds). John Wiley Sons, Inc., Hoboken, NJ, pp. 687–702.

[141] *Stanojević, M., Lazarević, B., Radić., D. (2003)* Review of membrane contactors designs and applications of different modules in industry. FME Transactions, **31**, 91–98.

[142] *Wang, Y., Ou, R., Wang, H., Xu, T. (2015)* Graphene oxide modified graphitic carbon nitride as a modifier for thin film composite forward osmosis membrane. Journal of Membrane Science, **475**, 281–289.

[143] *R.G. Blanck and W. Eykamp*, Fruit Juice Ultrafiltration, in Recent Advances in Separation Techniques-III, N.N. Li (ed.), AIChE Symposium Series Number 250, AIChE, New York, NY, p. 82 (1986).

[144] Hegab, *H.M., ElMekawy A., Barclay T.G., et al. (2015)* Fine-tuning the surface of forward osmosis membranes via grafting graphene oxide: performance patterns and biofouling propensity. ACS Applied Material Interfaces, **7**, 18004–18016.

[145] *F.V. Kosikowski*, Membrane Separations in Food Processing, in Membrane Separations in Biotechnology, W.C. McGregor (ed.), Marcel Dekker, New York, pp. 201–254 (1986).

[146] Soroush, *A., Ma, W., Silvino, Y., Rahaman, M.S. (2015)* Surface modification of thin film composite forward osmosis membrane by silver-decorated graphene-oxide nanosheets. Environmental Science: Nano, **2**, 395–405.

[147] Park, *M.J., Phuntsho, S., He, T., et al. (2015)* Graphene oxide incorporated polysulfone substrate for the fabrication of flat-sheet thin-film composite forward osmosis membranes. Journal of Membrane Science, **493**, 496–507.

[148] Priya, *D., Sivakumar, P., Sutha, M. (2014)* A review on desalination using membrane distillation:

[162] *M.C. Porter*, Ultrafiltration, in Handbook of Industrial Membrane Technology, M.C. Porter (ed.), Noyes Publication, Park Ridge, NJ, pp. 136–259 (1990).

[163] *L. Mir, W.* Eykamp and R.L. Goldsmith, Current and Developing Applications for Ultrafiltration, *Indust. Water Eng.* May/June 1 (1977).

[164] *B.R. Breslau and R.G. Buckley*, The Ultrafiltration of 'Whitewater', An Application Whose Time Has Come! *The 1992 Tenth Annual Membrane Technology/Separations Planning Conference*, Newton, MA (October 1992).

[165] *S. Loeb and S. Sourirajan*, Sea Water Demineralization by Means of an Osmotic Membrane, in Saline Water Conversion-II, Advances in Chemistry Series Number 38, Washington, DC (1963).

[166] *H. Strathmann*, Electrodialysis in Membrane Separation Systems, in Membrane Separation Systems, *R.W. Baker, E.L. Cussler, W. Eykamp, W.J. Koros, R.L. Riley* and *H. Strathmann* (eds), Noyes Data Corp., Park Ridge, NJ, pp. 396–420 (1991).

[167] *G.A. Pittner*, High Purity Water Production Using Reverse Osmosis Technology, in *Reverse Osmosis*, Z. Amjad (ed.), Van Nostrand Reinhold, New York (1993). REVERSE OSMOSIS 235

[169] *L. Mir, W.* Eykamp and R.L. Goldsmith, Current and Developing Applications for Ultrafiltration,

Indust. Water Eng. May/June 1 (1977).

[170] *F.V. Kosikowski*, Membrane Separations in Food Processing, in Membrane Separations in Biotechnology W.C.Mc Gregor (ed.), Marcel Dekker, New York, pp. 201–254 (1986).

[171] *C.F. Frith, Jr*, Electronic-grade Water Production Using Reverse Osmosis Technology, in Reverse Osmosis Technology, B.S. Parekh (ed.), Marcel Dekker, New York, pp. 279–310 (1988).

Published papers
Ioana Alina DIMULESCU (NICA)

1. Nechifor, A.C., Pîrțac, A., Albu, P.C., Grosu, A.R., Dumitru, F., **Dimulescu, I.A.,** Oprea, O., Pașcu, D., Nechifor, G., Bungău, S.G. Recuperative amino acids separation through cellulose derivative membranes with microporous polypropylene fiber matrix. (2021) ***Membranes***, 11 (6), art. no. 429,

2. Cotorcea, S., **Dimulescu, I.A.,** Pașcu, D., Bărdacă, C., Nechifor, G., Pîrțac, A. Membranes based on cellulose acetate recovered from cinematographic films for protein retention. (2021**)** ***UPB Scientific Bulletin, Series B: Chemistry and Materials Science,*** 83 (4), pp. 43-54.

3. **Dimulescu, I.A.,** Nechifor, A.C., Bărdacă, C., Oprea, O., Pașcu, D., Totu, E.E., Albu, P.C., Nechifor, G., Bungău, S.G. Accessible silver-iron oxide nanoparticles as a nanomaterial for supported liquid membranes. (2021) ***Nanomaterials,*** 11 (5), art. no. 1204,

4. Urducea, C.B., Nechifor, A.C., **Dimulescu, I.A.,** Oprea, O., Nechifor, G., Totu, E.E., Isildak, I., Albu, P.C., Bungău, S.G. Control of nanostructured polysulfone membrane preparation by phase inversion method. (2020) **Nanomaterials,** 10 (12), art. no. 2349, pp. 1-21.

5. Vesa, C.M., Popa, A.R., Bungau, S., Daina, L.G., Buhas, C., Judea-Pusta, C.T., Pasca, B., **Dimulescu, I.A.,** Zaha, D.C. Exploration of Insulin Sensitivity, Insulin Resistance, Early Insulin Secretion and β-cell Function, and Their Relationship with Glycated Hemoglobin Level in Normal Weight Patients with Newly Diagnosed Type 2 Diabetes Mellitus. (2019***) Revista de Chimie***, 70 (12), pp. 4217-4223. C

6. Popa, A.R., Pusta, C.T.J., Vesa, C.M., Bungau, S., Buhas, C.L., Sava, C., **Dimulescu, I.A.,** Zaha, D.C., Bustea, C. Prediction models of albumin renal excretion in type 2 diabetes mellitus patients. (2019) ***Revista de Chimie***, 70 (11), pp. 3802-3807.

7. Popa, A.R., Bungau, S., Vesa, C.M., Bondar, A.C., Pantis, C., Maghiar, O., **Dimulescu, I.A.,** Cseppento, D.C.N., Rus, M. Evaluating the efficacy of the treatment with benfotiamine and alpha-lipoic acid in distal symmetric painful diabetic polyneuropathy. (2019) ***Revista de Chimie***, 70 (9), pp. 3108-3114.