

Kinetic Control Concept for the Diffusion Processes of Paracetamol Active Molecules Across Affinity Polymer Membranes

Sanae Tarhouchi (✉ sanae.tarhouchi@gmail.com)

University of Hassan II Casablanca

Rkia Louafy

University of Hassan II Casablanca

El Houssine EL Atmani

University of Hassan II Casablanca

Miloudi Hlaïbi

University of Hassan II Casablanca

Research Article

Keywords: Facilitated extraction, affinity membranes, permeability, apparent diffusion coefficient, association constant, kinetic, and energetic controls

Posted Date: April 26th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-418338/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Kinetic control concept for the diffusion processes of Paracetamol active molecules across affinity polymer membranes.

Sanae Tarhouchi^{1*}, Rkia Louafy¹, El Houssine. EL Atmani¹, Miloudi Hlaïbi¹

¹Laboratoire Génie des Matériaux pour Environnement et Valorisation (GeMEV), Faculté des Sciences Ain Chock PB 5366, Maârif, Hasssan II University of Casablanca (UH2C), Maroc.

PPR2 Project: Ministry of Higher Education, Scientific Research and Management Training - National Center for Scientific and Technical Research

*Corresponding author: Tel: 212 641421113, orcid.org/0000-0003-3658-9577, **Email:** sanae.tarhouchi@gmail.com

Abstract

Background: Paracetamol compound remains the most used pharmaceutical as an analgesic and antipyretic for pain and fever. It has been detected in aquatic environments. The recovery of this compound from wastewater is one of the important operations carried out by modern industries. Its recovery is especially important for environmental protection. Currently, research is focused on membrane technology that has gained considerable interest over the last decades due to the various advantages that it presents.

Result: Our work reports the selective extraction of paracetamol from liquid solution using two types of affinity polymer membranes: (i) polymer inclusion membrane (**PIM**) and (ii) grafted polymer membrane (**GPM**). The same extractive agent, gluconic acid (**GA**), is used for both. After total characterization, the developed membranes were adopted. Kinetic and thermodynamic models have been used to determine the values of various macroscopic parameters, permeability (**P**), and initial flux (**J₀**), to understand the membrane performance. The same techniques have been used to determine the values of different microscopic parameters, association constant (**K_{ass}**), and apparent diffusion coefficient (**D***) that determine the interaction between the paracetamol substrates and the extractive agent, necessary for the diffusion of paracetamol molecules through the membrane. Similarly, the effects of initial concentration (**C₀**), acidity (pH), and temperature were examined.

Conclusion: The experimental results allow the determination of values of activation and thermodynamic parameters (**E_a**, **ΔH[#]**, **ΔS[#]**, **ΔH[#]_{dis}**, and **ΔH[#]_{th}**). The results explain the membrane performances and confirm that the energetic or kinetic aspects control the mechanisms related to the oriented processes. The results also indicate that it is possible to recycle wastewater and eliminate contaminants such as paracetamol.

Keywords: Facilitated extraction, affinity membranes, permeability, apparent diffusion coefficient, association constant, kinetic, and energetic controls.

Introduction

In the last few decades, increasing attention has been paid to pharmaceutical industries that generate liquid wastes containing several pollutants and toxic substances [1–5]. These pollutants induce undesirable effects on the ecosystem and can potentially cause unexpected consequences and unintended effects on living organisms [5–9]. Consequently, the treatment of these wastes becomes a major environmental issue for modern pharmaceutical industries and scientific research institutions. New technologies for the extraction, separation, and elimination of organic or inorganic substances and the recovery of several value-added molecules for evaluating these releases must be developed [10–13] to minimize and reduce the rate of formation of toxic products [14].

Paracetamol, also known as acetaminophen or para-acetyl aminophenol, is one of the major active pharmaceutical ingredients used in many medicines as an analgesic and antipyretic. It is used (alone or in combination with other analgesics) to treat mild-to-moderate pain or fever [15–17], and it is one of the drugs used widely without prescription. This compound is currently a drug of choice (after acetylsalicylic) for numerous people worldwide [18]. It is one of the components of numerous pharmaceutical products. Due to these commercial and medical uses, modern industries use special methods to develop this active ingredient, which is not effectively removed by conventional methods during wastewater treatment. Thus they remain in municipal effluents. Different concentrations of paracetamol have been detected in various parts of the world [19, 20]. Long-term exposure to drugs containing this active pharmaceutical ingredient can cause serious damage to humans and other animals [21–24]. Paracetamol presents some strange and life-threatening effects like liver damage, which leads to fulminant liver failure (with a high rate of morbidity and mortality) [25]. Therefore, its recovery and extraction from industrial liquid waste is the need of the hour. Paracetamol is an acylated aromatic amide [26] that belongs to the family of anilides (derivatives of aniline) (Additional file 1: Figure S1).

Paracetamol, ($C_8H_9NO_2$) is a fat-soluble weak organic acid ($pK_a = 9.5$) that is found in its ionized form in the stomach and small intestine where it is absorbed. Its maximum absorption in the UV region is at 244 nm in an acidic solution. Today various industrial synthesis methods are used to produce paracetamol. However, most of the synthetic route involves acylation of para-aminophenol in the presence of acetic anhydride.

In recent years, various membrane processes have been reported for various applications [27–29] (such as removal, purification, recovery, and extraction of organic compounds present in liquid wastewater). Membrane-based technology has become immensely important and has attracted much

attention as a valuable technology for many industries. It is an environmentally friendly alternative that considerably reduces the volume of used chemical products, and minimal energy is consumed during the process. These methods are successfully applied in several fields, such as environment, energy, health, water treatment, cosmetic, food, chemical, and pharmaceutical industries. Depending on their structure, composition, and morphology, a wide range of membranes (including organic polymer membranes) can be developed for use in different fields. These favorable properties and functionalities exhibit clear and important advantages compared to other separation and extraction techniques such as resin separation, liquid-liquid extraction (ELL), solid-phase extraction (EPS), and chromatography [30–34]. These properties help in determining the selectivity parameters in particular.

In general, the extraction mechanism through a membrane is based on facilitated diffusion. These oriented membranes that promote facilitated extraction are now the subject of several studies. The studied membranes include the affinity membranes (for purification and recovery of organic molecules from aqueous solutions), supported liquid membranes (SLMs), polymer inclusion membranes (PIMs), and grafted polymer membranes (GPMs) [35–38]. This technology combines extraction and stripping operations in a single step. Due to the simple preparation steps, stability, better mechanical properties, good chemical resistance, better mechanical properties, and particularly, stable integration of the extractive agent into the polymer support, special attention is paid to PIMs and GPMs [39–42].

We aimed to improve the treatment process in the pharmaceutical industry. Accordingly, in our laboratory, experiments related to the facilitated extraction process of paracetamol, which is used here as a model drug to evaluate the extraction capabilities of the membrane process, were carried out to extract the active substances from the liquid solution. Our challenge was to determine the proper and selective extractive agent for the fabrication of a stable and efficient membrane for extracting paracetamol. We also aimed to evaluate the parameters to achieve high recovery, high throughput, and low consumption time. This extraction process was performed using **PIM** and **GPM** containing gluconic acid (**GA**) (Additional file 1: Figure S2) as the extractive agent. The prepared membranes were characterized by two spectroscopic techniques: (i) Fourier transform infrared spectroscopy (FTIR) and (ii) scanning electron microscopy (SEM) techniques to confirm the presence of the extractive agent in the polymeric support. The developed membranes were used to perform oriented processes for facilitated extraction and to recover paracetamol substrates under the influence of initial substrate concentration, acidity, and temperature of the medium. The dynamics of mass transfer and the effect of the different factors on the process of extracting the paracetamol substrate were

discussed. The kinetically determining step, which controls the rate of paracetamol extraction when PIMs and GPMs are used, has been elucidated by analyzing the kinetic data.

Experimental section

Reagent

Paracetamol was purchased from ICN Biomedicals. All polymers, polyvinyl alcohol (PVA) ($M_w = 72\,000\text{ g/mol}$), polysulfone (PSU) ($M_w = 35\,000\text{ g/mol}$), polyvinyl-pyrrolidone (PVP) ($M_w = 45\,000\text{ g/mol}$), GA ($M_w = 218, 2\text{ g/mol}$), and the solvent *N,N*-dimethylformamide (DMF, 99.8%) and dimethylsulfoxide (DMSO, > 99.8%), are commercial products (Aldrich, Fluka).

The paracetamol concentration (C_R) in the receiving phase was measured ($\lambda_{\max} = 244\text{ nm}$) using a UV–visible spectrophotometer. A single-beam type monochromator, Helios γ Rayleigh U.V.-2601) was used to analyze the solutions. An Infrared spectrophotometer (AVATAR 360 FTIR ESP) was used to plot the FTIR spectra to identify the presence of extractive agents in the polymer matrix. Similarly, the SEM technique (ZEISS EVO40 EP) was used to produce different micrographs and study the morphology and porosity of the developed membranes.

Membrane preparation

To conduct the oriented processes of the facilitated extraction of paracetamol, we have prepared two types of polymer membranes **PIM** and **GPM**, based on polyvinyl alcohol and polysulfone as polymer supports with the same extractive agent (**GA**).

The adopted **GPM** was developed according to the following experimental protocol [43]: A precise amount (3 g) of polysulfone polymer dissolved in 13 mL of dimethylformamide (DMF) was introduced into a closed bottle to isolate the mixture from the air. The system was stirred for 12 h until polysulfone was completely solubilized. Next, a 0.625 g of polyvinylpyrrolidone (PVP) was added to this homogeneous solution, followed by slow addition of the weighed mass of the extractive agent. The mixture was stirred for 3 to four days to completely solubilize the extractive agent to produce a homogeneous phase. The resulting phase was cast on a glass plate and then spread with a ruler. This glass plate was rapidly immersed in a bath containing distilled water. The solvent DMF leaves the membrane matrix and a rigid membrane in the form of a paper (phase inversion method) was obtained [44, 45]. After this operation, the GPM membrane was dried, its mass (0.030 g) and thickness ($l = 162\ \mu\text{m}$) were determined. Its total surface area (10 cm^2) was measured and the concentration of the extractive agent $[\mathbf{T}]_0 = 0.20\text{ mol L}^{-1}$ was calculated.

PIM [46] was prepared by dissolving 10 g of polyvinyl alcohol (PVA) in a mixture of 20 mL of DMSO and 80 mL of distilled water. The mixture was stirred for 24 h at a temperature of 120 °C to dissolve the PVA in the solution. In this homogeneous solution, a precise amount of the extractive agent (**GA**) was added slowly under a condition of constant stirring to avoid polymer aggregation. The resulting solution was poured carefully into a Petri dish, placed on a stove at a temperature in the range of 70 to 80 °C to completely evaporate the solvent. The PIM obtained by this experimental protocol (heat vulcanization method) was homogenous, transparent, flexible, and mechanically strong. Its thickness was measured ($l = 228 \mu\text{m}$) and the extractive agent concentration was calculated ($[\text{T}]_0 = 0.30 \text{ mole.L}^{-1}$).

Experimental methods and adopted materials

(Additional file 1: Figure S3) shows the experimental cell used for carrying out the facilitated extraction processes for extracting paracetamol. It consists of two compartments of identical volume separated by the developed membrane. The feed phase (**F**) contained the paracetamol solution in the concentration range of 0.01 M to 0.08 M, and the receiving phase (**R**) contained distilled water. The aqueous phase volume was 70 mL in each compartment. The system was immersed in a thermostatic bath (**TB**) containing water to maintain a constant temperature throughout the experimental procedure. Homogeneity was ensured by using a multi-station magnetic stirrer.

Samples were collected from the receiving phase every 30 min and were measured at a wavelength of 244 nm using an ultraviolet-visible (UV-visible) spectrophotometer to determine C_R in the receiving phase. The acidities of the aqueous solutions (feed phase and receiving phase) were measured using a pH meter (HANNA Instruments HI 8519N). The pH was adjusted with an analytical grade solution of hydrochloric acid. The thicknesses of the developed membranes, which were specified in the preceding paragraph, were measured using an electronic micrometer (Mitutoyo). A knowledge of these values is necessary to calculate the membrane volume to determine the fixed concentration $[\text{T}]_0$ of GA in the membrane phase.

Theoretical models for quantification of processes

The facilitated extraction processes for substrate **S** was conducted using an affinity polymer membrane. The process depends on the formation and the dissociation of the substrate-extractive agent entity (**ST**) at the membrane-solution interfaces and in the membrane phase during the diffusion of the substrate. To quantify the processes carried out and to study the performances of the adopted membranes, kinetic and thermodynamic models based on the first and second Fick's laws

and a saturation law of the extractive agent (**T**) by the substrate (**S**) have been developed in the laboratory [43, 46–49]. The following relationships were established.

$$P \times (t - t_I) = (l \times V / S) [1/2 \times \ln(C_0/C_0 - 2C_R)], \quad (1)$$

$$J_0 = (D^*/l) \times [[T]_0 \times K_{ass} \times C_0 / (1 + K_{ass} \times C_0)]. \quad (2)$$

l: Membrane thickness (cm), *S*: Membrane active area (cm²) and *V*: Receiving phase volume (cm³).
*C*₀, *C*_R, and *[T]*₀: initial substrate concentration in the feed phase (mol. L⁻¹), substrate concentration in the receiving phase at time *t* (mole.L⁻¹) and extractive agent concentration in the organic phase (mole.L⁻¹), respectively.

P: Membrane permeability (cm². s⁻¹), *J*₀: Substance initial flux across the membrane (mmole.s⁻¹.cm⁻²), *K*_{ass}: Association constant of entity **ST** (L.mole⁻¹), and *D*^{*}: Apparent diffusion coefficient of the substrate **S** through the membrane phase (cm².s⁻¹).

Determination of macroscopic parameters *P* and *J*₀

If the kinetic model is verified, after an induction time (*t*_I), the function (–Ln (*C*₀–2*C*_R) versus time) evolves linearly. The slope (*a*) of the obtained straight line allows the determination of the permeability parameter *P* according to the following equation [50, 51].

$$P = (a * V * l) / 2S \quad (3)$$

The initial flux *J*₀ can be calculated from the permeability coefficient *P* by the following equation:

$$J_0 = (P \times C_0) / l. \quad (4)$$

Determination of microscopic parameters *D*^{*} and *K*_{ass}

To determine the nature of the movement of the substrate **S** during its diffusion through the membrane phase and to elucidate the mechanism that governs the studied processes, it is necessary to determine the values of the microscopic parameters *D*^{*} and *K*_{ass}. We used the Lineweaver–Burk method (L–B) to linearize the expression in equation 2, according to the following equation [52, 53]:

$$1/J_0 = (l/D^*) \times [(1/([T]_0 \times K_{ass})) \times (1/C_0) + (1/[T]_0)] \quad (5)$$

The linear evolution of the term 1/*J*₀ = *f* (1/*C*₀) (from equation 5) allows us to confirm that the thermodynamic model is based on the interaction of the substrate (**S**) with the extractive agent (**T**). The interaction in the membrane phase was checked. Similarly, the values of slopes (*p*) and

intercepts (**OO**) of the obtained straight line segments are used to calculate the values of D^* and K_{ass} according to the following equation:

$$K_{ass} = \text{intercept}(\mathbf{OO})/\text{slope} \quad \text{And} \quad D^* = (l/\mathbf{OO}) \times (1/[T]_0) \quad (6)$$

Determination of activation and thermodynamic parameters

The initial flux is related to the temperature factor by the Arrhenius law [54, 55], according to the following equation:

$$J_0(T) = A_j \exp(-E_a/RT) \quad (7)$$

R : gas constant ($8.314 \text{ J.mol}^{-1}.\text{K}^{-1}$). A_j : proportional term to the favorable interactions ($\text{mole}^{-1}.\text{s}^{-1}.\text{m}^2$), E_a : transition state activation energy of the formation-dissociation reaction of the entity (**TS**) (J.mole^{-1}).

The expression was linearized according to the following equation:

$$\ln J_0 = \left(((-E_a)/R) \times (1/T) + \ln A_j \right) \quad (8)$$

The values of activation parameters E_a and A_j were determined from the slope and the intercept of the linear function $\ln(J_0) = f(1/T)$. According to the transition state theory (Eyring theory), these values allow the calculation of the activation enthalpy ΔH^\ddagger (J.mole^{-1}) and entropy ΔS^\ddagger ($\text{J.K}^{-1}.\text{mole}^{-1}$) parameters from the following equation:

$$\Delta H^\ddagger = E_a - 2500 \text{ (J.mol}^{-1}) \quad \text{And} \quad \Delta S^\ddagger = R(\ln A_j - 30,46) \text{ (J.K}^{-1}.\text{mol}^{-1}) \quad \text{at } 298 \text{ }^\circ\text{K} \quad (9)$$

The thermodynamic enthalpy parameter ΔH_{th}^\ddagger (Kj.mol^{-1}) represents the amount of energy exchanged during the equilibrium reaction related to the formation of the **ST** entity. The value of this parameter is determined directly from the slope of the linear representation of Van't Hoff's law (equation 10).

$$\ln(K_{ass}) = (-(\Delta H_{th})/RT) + cste \quad (10)$$

On the other hand, according to the transition state theory, for an elementary reaction, this important thermodynamic parameter is related to the activation enthalpies, association ΔH_{ass}^\ddagger , and dissociation ΔH_{dis}^\ddagger (Kj.mol^{-1}) by the following relation:

$$\Delta H_{th} = \Delta H_{ass}^\ddagger - \Delta H_{diss}^\ddagger \quad (11)$$

Results and discussion

Fourier Transform-Infrared (FTIR) Analysis

After drying the sample for 48 h to remove traces of residual water and solvent, the obtained membranes (PSU-PVP) and (PSU-PVP-AG) were characterized by the IRTF-spectroscopy technique to record the vibration bands corresponding to the membrane components. FTIR spectra (Figure 1) were plotted and recorded using an Avatar 360 FT-IR ESP spectrometer. The analysis of the ATR-FTIR spectrum of the prepared membrane reveals the presence (at around 3350 cm^{-1}) of a characteristic broad absorption band corresponding to the alcohol (OH) group. A peak at 1720 cm^{-1} was also observed, which was attributed to the vibration of the C=O group of GA. This result proved that the extractive agent was successfully grafted onto the surface of the PSU membrane.

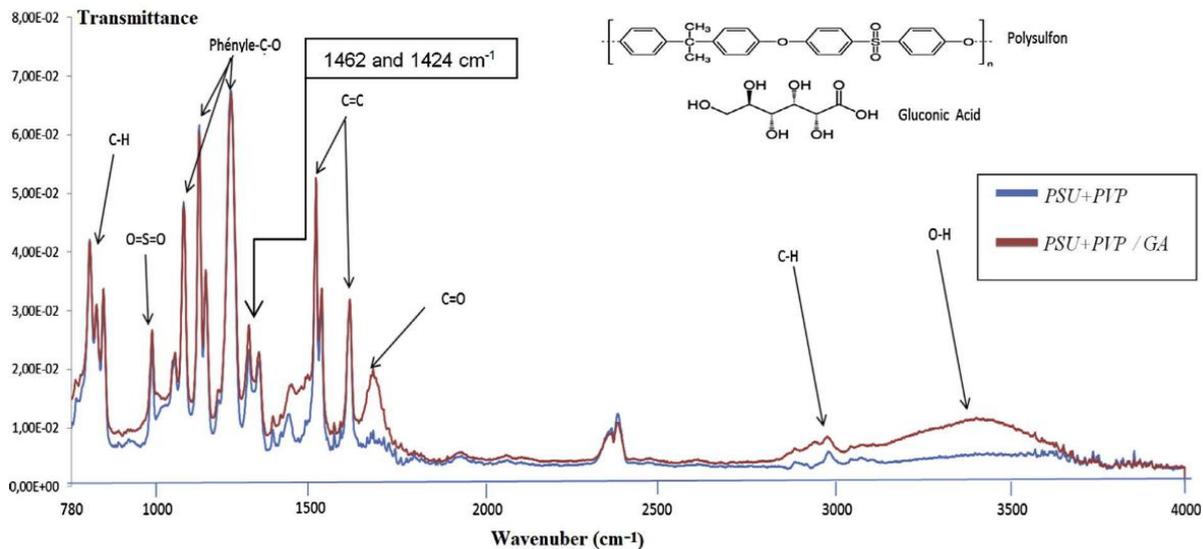


Figure 1. ATR-FTIR spectrum of the developed membrane PSU/PVP-GA

Scanning Electron Microscopy (SEM) Analysis

Various samples of the elaborated membranes were visualized using the SEM (JEOL NeoScope JCM-500) technique. The samples were irradiated with an electron beam (15 kV). This study was carried out under suitable magnification. Electrons were precisely focused for better visualization of the membrane surface and to properly record SEM micrographs of the upper surface of the polymer support (PSU + PVP) and the GPM membrane (PSU + PVP + GA). SEM images (1000 magnification) of the membranes with different compositions are grouped in the scheme of Figure 2. The SEM micrograph, presented in Figure 2.a, represents the morphology of the polymer support (PSU-PVP). A considerably smooth and dense surface without apparent porosity was observed. Figures 2.b and 2.c reveal that the extractive agent was efficiently grafted onto the

membrane phase. It also influenced the structure, morphology, and porosity of the polymeric support. The synthesized membrane contained pores along the membrane width (surface layers; Figures 2.b and 2.c).

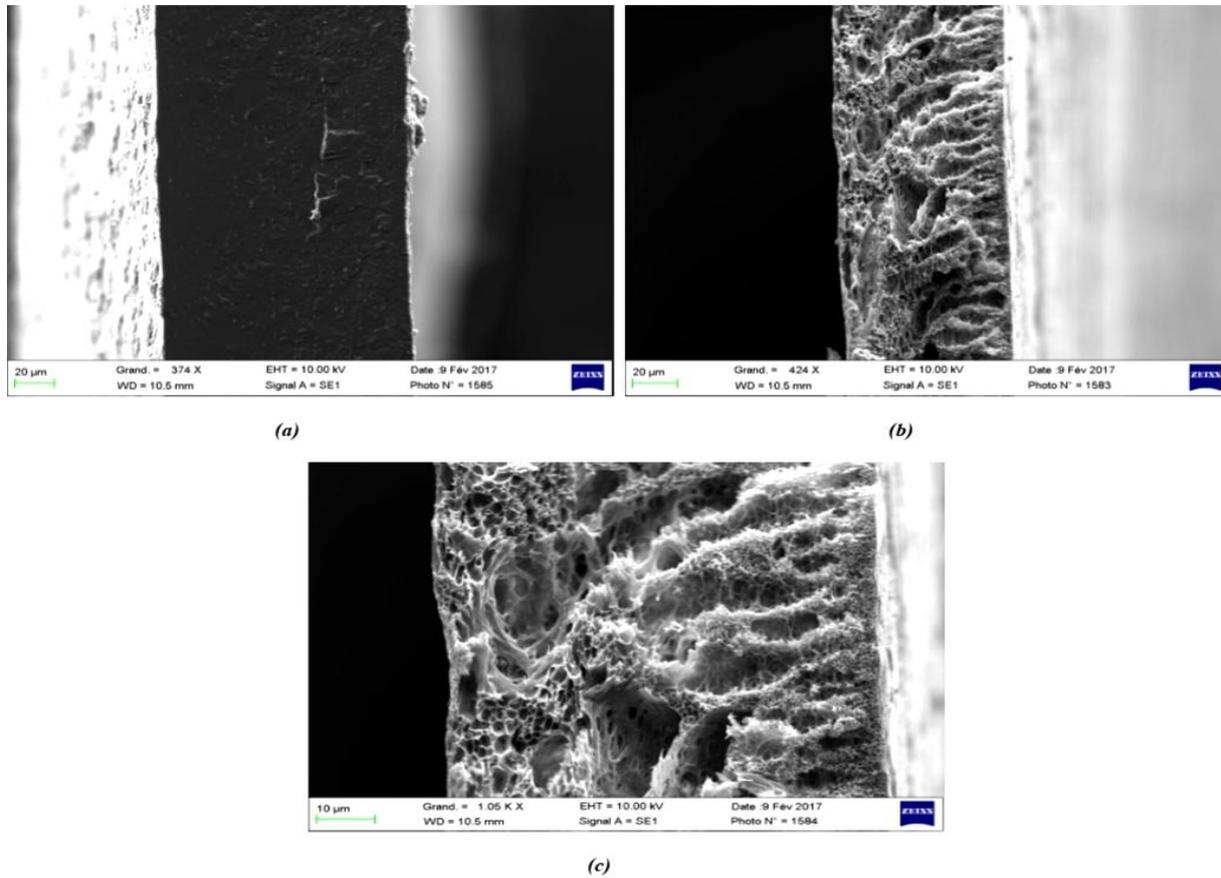


Figure 2. SEM micrographs: a) support polymer surface and cross-section (PSU/PVP), b), and c) membrane cross-section (PSU/PVP-GA)

The PIM was analyzed and characterized using the spectroscopic techniques used for characterizing the membrane described in the previous section. The results indicated and proved that the extractive agent was trapped in the polymer matrix of the membrane whose porosity increased with the concentration of the extractive agent.

Influence of the initial substrate concentration (C_0) on the performance of the fabricated membranes

In this section, we have examined the effect of C_0 on the evolution of macroscopic parameters P and J_0 for the facilitated extraction processes of paracetamol (through all the fabricated membranes). Indeed, we have studied the processes at different C_0 (**0.08M**, **0.04M**, **0.02M**, and **0.01M**) at pH = 1 and T = 298 K. At all concentrations, the kinetic model has been verified, and the function $-\ln(C_0 - 2C_R) = f(t)$ generated straight lines (Figure 3). The values of P and J_0 , determined

from the slopes of these straight lines (according to the expressions in equations 3 and 4), have been presented in **Table 1**.

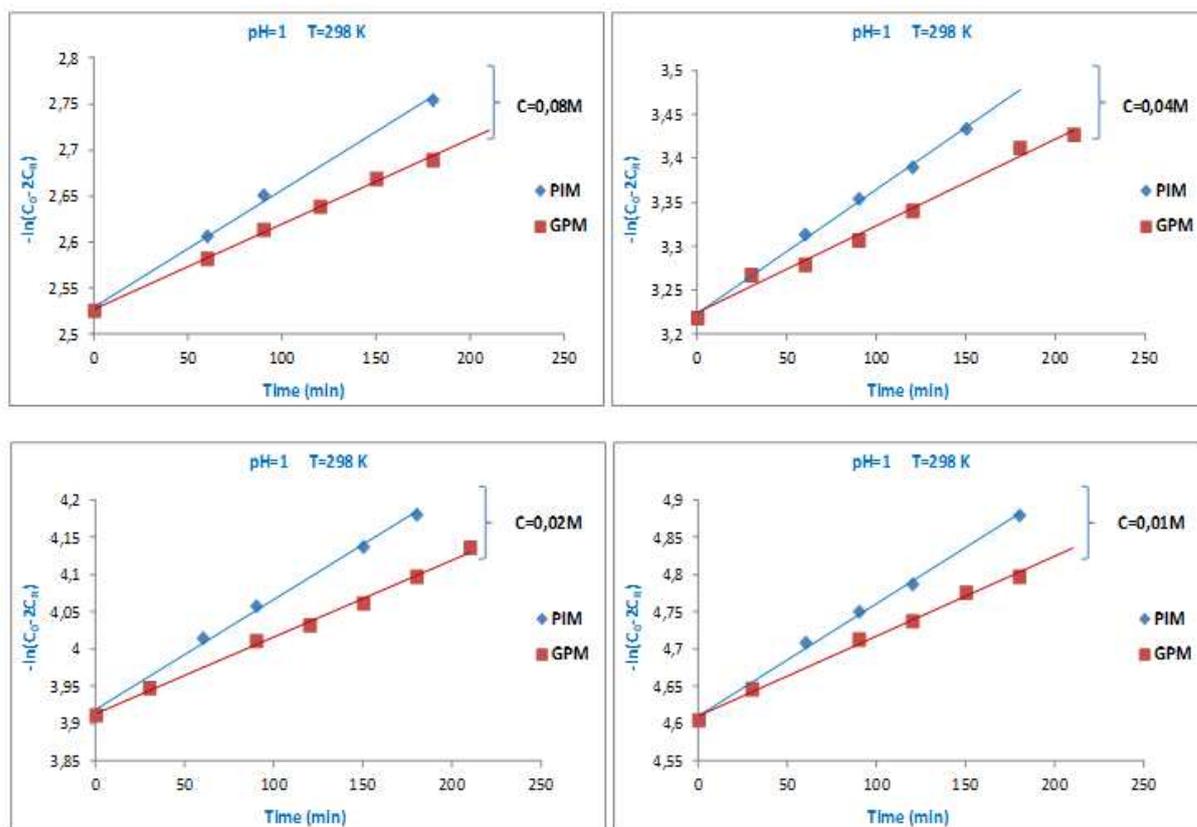


Figure 3. Evolution of the kinetic function $-\ln(C_0 - 2C_R) = f(t)$ describing the extraction processes of paracetamol through the developed membranes at different concentrations C_0 , $\text{pH}=1$ and $T=298\text{ K}$

Table 1. Evolution of P and J_0 parameters for extraction oriented processes of the paracetamol substrate at $T = 298\text{ K}$

Membrane type	PIM		GPM	
C_0 initial concentration	$P \cdot 10^7$ ($\text{cm}^2 \text{s}^{-1}$)	$J_0 \cdot 10^5$ ($\text{mmol.s}^{-1}.\text{cm}^{-2}$)	$P \cdot 10^7$ ($\text{cm}^2.\text{s}^{-1}$)	$J_0 \cdot 10^5$ ($\text{mmol.s}^{-1}.\text{cm}^{-2}$)
0.08 M	18.112	0.636	9.374	0.462
0.04 M	20.235	0.355	10.053	0.248
0.02 M	20.962	0.184	10.458	0.129
0.01 M	21.446	0.094	10.851	0.067

Analysis of the results grouped in **Table 1** demonstrates that the used membranes are effective extractors of paracetamol. The PIM membrane was more efficient than the GPM membrane. However, it was noticed that permeability P increases, and initial flux J_0 and C_0 decrease.

Acidity factor influence the evolution of paracetamol extraction processes

To investigate the effect of acidity (feed and receiving aqueous solutions) on the efficiency of extraction through the adopted membranes, a series of experiments were performed at different pH (1, 2, and 3). Different substrate concentrations (0.01 M–0.08 M) were used for the experiments. The values of the macroscopic parameters P and J_0 were determined at each pH value (Table 2). The Lineweaver–Burk (L–B) representation $1/J_0 = f(1/C_0)$ was plotted using the values of initial fluxes. The slopes and intercepts of the straight lines are shown in Figure 4. The D^* and K_{ass} values (microscopic parameters) were estimated. The results are presented as histograms in Figure 5.

Table 2. Evolution of P and J_0 with pH during the extraction of paracetamol at $C_0 = 0, 01$ M and $T = 298$ K

Membrane type	PIM		GPM		
	pH	$P \cdot 10^7$ ($\text{cm}^2 \cdot \text{s}^{-1}$)	$J_0 \cdot 10^5$ ($\text{mmol} \cdot \text{s}^{-1} \cdot \text{cm}^{-2}$)	$P \cdot 10^7$ ($\text{cm}^2 \cdot \text{s}^{-1}$)	$J_0 \cdot 10^5$ ($\text{mmol} \cdot \text{s}^{-1} \cdot \text{cm}^{-2}$)
1		20.189	0.317	10.184	0.226
2		19.579	0.301	9.911	0.219
3		19.241	0.296	9.775	0.215

According to the results grouped in Table 2, it is clear that the pH of the aqueous solutions does not significantly influence the extraction oriented processes followed for the extraction of paracetamol. On the other hand, it has been confirmed that the performance of the PIM membrane is better than that of the GPM membrane.

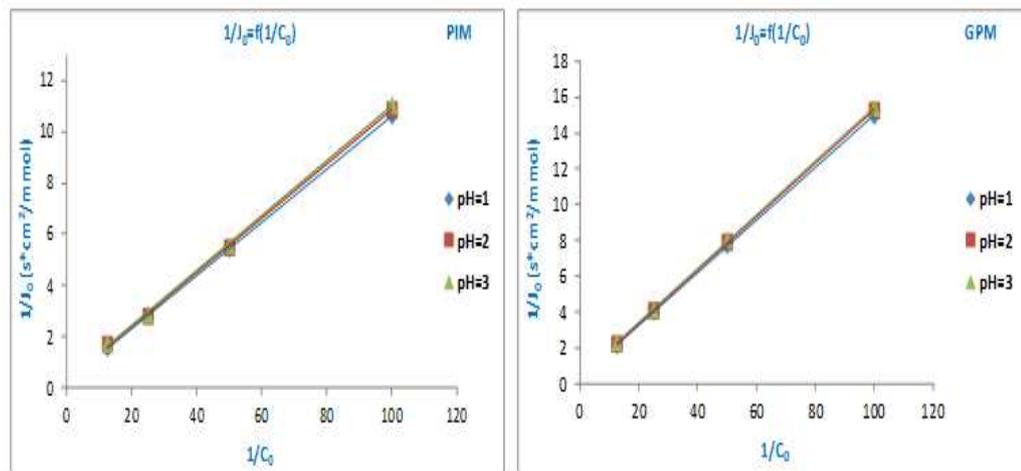


Figure 4. Lineweaver–Burk representations ($1/J_0 = f(1/C_0)$) for facilitated extraction processes across PIM and GPM membranes

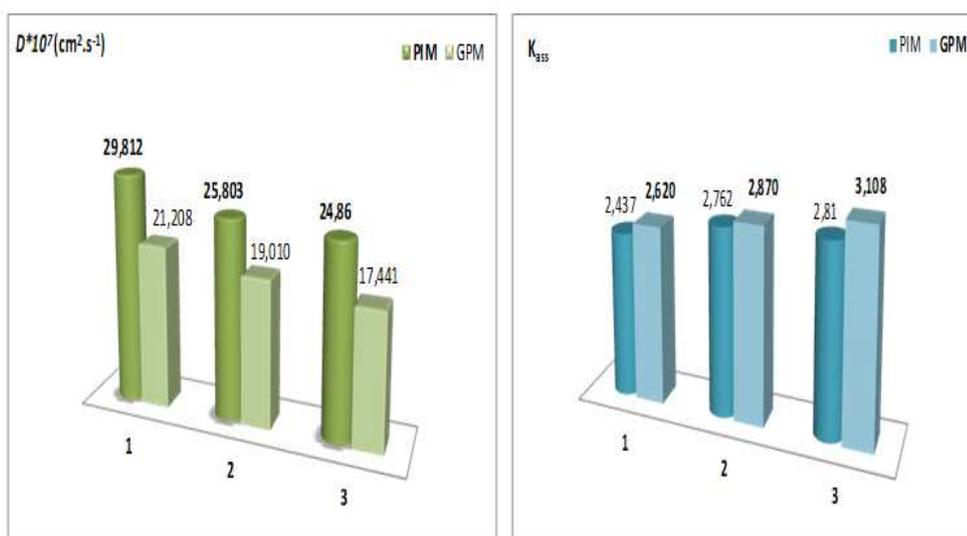


Figure 5. Influence of acidity on the parameters D^* and K_{ass} associated with the diffusion of paracetamol molecules through the developed PIM and GPM membranes

As can be seen from Figure 5, the apparent diffusion coefficient D^* and association constant K_{ass} vary inversely. The highest values of D^* and the lowest K_{ass} value, are obtained for the most efficient membrane (PIM). These results explain the performances of the developed polymer membranes. The interactions between the paracetamol molecules and the extractive agent were studied using the thermodynamic model.

Temperature influence on the evolution of oriented extraction processes of paracetamol

The values of the macroscopic parameters (P) and (J_0) were determined at different temperatures (298, 303, and 308 K) to assess the influence of temperature on the facilitated extraction processes. The experiments were conducted at $\text{pH}=1$. C_0 was varied in the range of 0.08 M to 0.01 M. This study is very important to explain the performances of developed membranes and to elucidate the mechanisms related to these oriented processes.

Table 3. Evolution of P and J_0 parameters depending on the temperatures at which the extraction oriented processes of paracetamol substrate are conducted at $C_0 = 0,01$ M.

Membrane type	PIM		GPM	
	$P \cdot 10^7$ (cm ² s ⁻¹)	$J_0 \cdot 10^5$ (mmol.s ⁻¹ .cm ⁻²)	$P \cdot 10^7$ (cm ² . s ⁻¹)	$J_0 \cdot 10^5$ (mmol.s ⁻¹ .cm ⁻²)
298 °K	20.189	0.317	10.184	0.226
303 °K	22.052	0.347	11.811	0.26
308 °K	23.505	0.366	12.267	0.273

The values of macroscopic parameters P and J_0 have been summarized in **Table 3**. The data reveals the impact of temperature on the facilitated extraction processes employed for isolating paracetamol. In addition, an increase in temperature leads to an increase in membrane performance. It was noted that the permeability through the **PIM** membrane was higher than the permeability of the **GPM** membrane at all temperatures. To complete our study, we plotted the L–B curve ($1/J_0 = f(1/C_0)$). The data obtained at every temperature point was plotted. The linear evolution verified the result obtained from the thermodynamic model. Slopes and intercepts of the straight lines were obtained following equation 6 (Figure 6). The values of the apparent diffusion coefficient D^* and the association constant K_{ass} associated with the movement of the paracetamol molecules when they diffuse through each membrane were also determined. The values for these specific parameters and their evolution are presented by the histograms in Figure 7. The opposite trends exhibited by these parameters confirmed the results obtained from the oriented processes conducted at different temperatures. The enhanced membrane performance can be potentially explained by the high D^* values obtained at high temperatures.

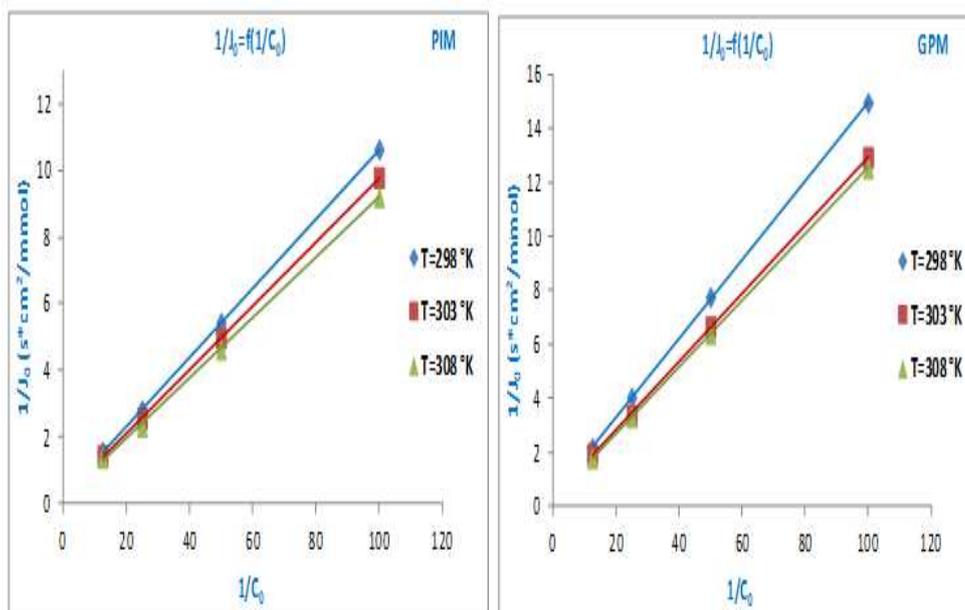


Figure 6. The L–B curved ($1/J_0 = f(1/C_0)$) for the oriented extraction processes employed for extracting paracetamol through PIM and GPM membranes at different temperatures

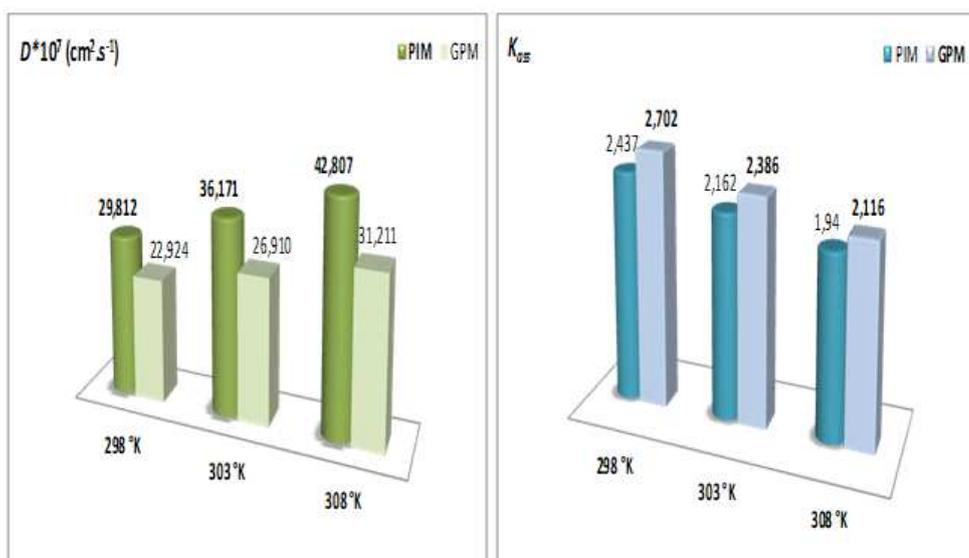


Figure 7. The opposite trends exhibited by D^* and K_{ass} , characteristics of paracetamol movement during the extraction oriented processes through elaborated membranes

The opposite evolution trends observed for K_{ass} and D^* indicate an important characteristic of the extraction oriented processes that occur through the affinity polymer membranes. Indeed, at high temperatures, the degree of diffusion of the paracetamol molecules was high. The low stability of the entity (ST) responsible for the diffusion of these substrate molecules (S) indicates that these molecules migrate from one site to another of the extractive agent. Successive association/dissociation reactions led to the formation of the (ST) entity. During the oriented processes, the diffusion of substrate molecules occurs following a mechanism where the molecules successively jump from one fixed site to another of the extractive agent immobilized in the membrane phase (Additional file 1: Figure S4).

The scheme in (Additional file 1: Figure S4) describes the mechanism of *successive jumps* and explains the good performances of these polymer membranes during the extraction of paracetamol.

Several models have been used to elucidate the mechanisms of extraction of organic and metal ions. Theories derived from these models are important for interpreting the results obtained for the current systems. These can help in designing more efficient and selective systems. Indeed, the literature reports several studies on the application of extraction procedures of various compounds that have been used as anti-inflammatories and analgesics and are found in wastewater. T. Razo-Lazcano et al. [56–58] examined the structure and the effect of pharmaceuticals on different types of extraction processes.

The reviews and papers published by Hlaibi et al. [59, 60] have indicated that the interaction between the substrate and the extractive agent assists the migration of organic compounds through a membrane. The formation of a “substrate-extractive agent,” the stabilities of which depend on the structure of the compounds and the nature of interaction sites, was observed. On the other hand, a jumping mechanism [61, 62], in which the substrate moves while binding successively to several fixed carriers (considered as a complexation site), similar to the case of an ion-exchange membrane, was studied. Reversible association-dissociation reactions leading to the formation and decomposition of an unstable “host-guest” complex were carried out. The jumping mechanism, frequently seen for cases when **PIM** is used [63, 64], is characterized by a percolation threshold, which corresponds to the minimal concentration of the carrier required to produce a measurable flux. The existence of a percolation threshold is highlighted when the influence of the concentration of the carrier on the permeability of the membrane is studied.

Activation and thermodynamic parameters for the extraction studied processes

To confirm the results, to elucidate the *energetic* or *kinetic aspect* that controls the mechanism of the studied processes, and to explain the performances of the fabricated membranes, it is necessary to determine the values of the activation and thermodynamic parameters (E_a , ΔH_{ass}^\ddagger , ΔS^\ddagger , ΔH_{diss}^\ddagger , and ΔH_{th}) corresponding to the transition state of the substrate diffusion step across each organic membrane phase. For this, we have studied Arrhenius and Van't Hoff relationships (Eqs. 8 and 10) for the extraction-oriented processes. The J_0 and K_{ass} values were determined, and the straight line segments were plotted (Figure 8). The slopes and intercepts calculated from these straight line segments were used to determine the values of the activation parameters E_a and A_j . The thermodynamic parameter ΔH_{th} was also studied. The activation enthalpies ΔH_{ass}^\ddagger and ΔH_{dis}^\ddagger and the activation entropy ΔS^\ddagger were calculated following equations 9 and 11.

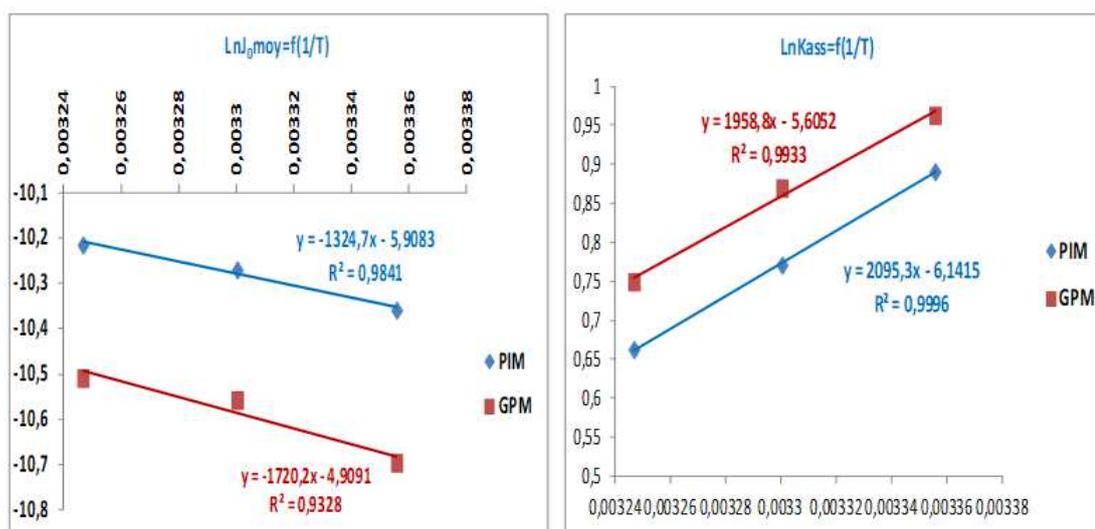


Figure 8. Evolution of Arrhenius and Van't Hoff relationships for the extraction-oriented processes followed for extracting paracetamol through the PIM and GPM membranes

Table 4 presents the values of all the activation and thermodynamic parameters. Analysis of the activation parameters indicates that the transition state corresponding to the diffusion step requires little energy (E_a and ΔH^\ddagger). On the other hand, the negative activation entropy (ΔS^\ddagger) indicates a late transition state, and the transition state depends on the structures of the substrate and extractive agent. It also depends on the orientation of their interaction sites.

Table 4. Activation and thermodynamic parameters corresponding to the transition state of the extraction process occurring through developed membranes

Activation Parameters	E_a (kJ.mol ⁻¹)	ΔH^\ddagger_{ass} (kJ.mol ⁻¹)	ΔS^\ddagger (J.mol ⁻¹ .K ⁻¹)	ΔH_{th} (kJ.mol ⁻¹)	ΔH^\ddagger_{diss} (kJ.mol ⁻¹)
PIM	11.008	8.531	-302.221	-17.420	25.952
GPM	14.295	11.818	-293.918	-16.286	28.10

The evolution of these parameters is described by the table 4. The results indicate that a favorable orientation of the interaction sites is required to achieve a good association between the paracetamol molecules and GA in the transition state with the bidentate sites ($\Delta S^\ddagger = -300 \text{ J.mol}^{-1}.\text{K}^{-1}$) (Additional file 1: Figure S5 and Figure S6). On the other hand, the low values of the important parameters (ΔH^\ddagger_{ass} and ΔH^\ddagger_{dis}) reveal the *kinetic control aspect* of the mechanisms of the oriented processes leading to good membrane performances even at low temperatures. This *kinetic control aspect* for the diffusion of paracetamol molecules through affinity polymer membranes can be ascribed to *the structure of the molecules and the pharmacological and biological activities of these molecules that diffuse through cell membranes at a constant temperature.*

Conclusion

The results described in this work are very interesting and can help elucidate and understand the different parameters and steps necessary for the realization of membrane oriented processes performed for extracting paracetamol (through two types of affinity polymer membranes). Indeed, two types of polymer membranes (**PIM** and **GPM**) were developed following the heat vulcanization and phase inversion methods using the same extractive agent (**GA**). Different techniques have been used to characterize the composition, morphology, and porosity of the developed membranes and the concentration of the extractive agent included and immobilized in the membrane phases. Detailed studies have been carried out with these two membranes to determine the optimal experimental and technical conditions required for the oriented processes employed for extracting high-value paracetamol. Several kinetic, thermodynamic, and activation parameters were determined under different experimental conditions. The evolution of all these parameters with C_0 of paracetamol, acidity (**pH**), and temperature (**T**) of the aqueous phases was studied, and the membrane performance was quantified. The mechanisms of the oriented processes were also determined.

Finally, original ideas regarding the kinetic and energetic control aspects that help elucidate the mechanism of the oriented processes (through affinity polymer membranes) have been presented in this work. The *kinetic control* affected the mechanism of extraction of this biologically active compound (paracetamol) through the two developed membranes. Good membrane performance was observed even at low temperatures. In fact, the paracetamol molecules can potentially diffuse through the cell walls having well-adapted structures at a constant temperature. Consequently, the kinetic control of the extraction processes of paracetamol is an original idea, and the studies produced logical results. It can be correlated to the molecular structures of paracetamol and the extractive agent. The effect of temperature on the diffusion of paracetamol molecules through the membrane phases was not significant.

Additional file

Figure S1. Structure of gluconic acid. **Figure S2.** 1-hydroxy-4-acetaminobenzene (paracetamol). **Figure S3.** Representation of the facilitated extraction cell. **Figure S4.** Mechanism of successive jumps on fixed sites during the facilitated extraction process followed for extracting paracetamol through the PIM-GA membrane **Figure S5.** Possible interaction sites between paracetamol and gluconic acid. **Figure S6.** Interaction sites between paracetamol and gluconic acid (Chemdraw).

Abbreviations

$[T]_0$: Concentration of carrier in the membrane phase (mol.l^{-1}); C_0 : initial concentration of paracetamol in the feed phase (mol.l^{-1}); C_R : concentration of paracetamol in the receiving phase (mol.l^{-1}); P : permeability of the membrane ($\text{cm}^2.\text{s}^{-1}$); J_0 : initial flux ($\text{mmol.s}^{-1}.\text{cm}^{-2}$); D^* : apparent diffusion coefficient ($\text{cm}^2.\text{s}^{-1}$); K_{ass} : association constant; l : membrane thickness (μm); t : time (s); V : volume of the receiving phase (cm^3); S : active area of the membrane (cm^2); T : temperature ($^{\circ}\text{K}$); R : ideal gas constant ($\text{J.mol}^{-1}.\text{K}^{-1}$); E_a : activation energy (KJ.mol^{-1}); $\Delta H_{ass}^{\ddagger}$: activation association enthalpy (KJ.mol^{-1}); $\Delta H_{diss}^{\ddagger}$: activation dissociation enthalpy (KJ.mol^{-1}); ΔS^{\ddagger} : activation entropy ($\text{KJ.mol}^{-1}.\text{K}^{-1}$); ΔH_{th} : thermodynamic enthalpy (KJ.mol^{-1}).

Authors' contributions

ST did most of the experiment and wrote the manuscript. RL and El-H did the preparation and characterization of the membrane. MH helped in editing the English language beside adding some paragraphs to the text. All authors read and approved the final manuscript.

Author Information

¹Laboratoire Génie des Matériaux pour Environnement et Valorisation (GeMEV), Faculté des Sciences Ain Chock PB 5366, Maârif, Hasssan II University of Casablanca (UH2C), Maroc.

Acknowledgments

The authors wish to thank the Ministry of Higher Education and Scientific Research (MESRSFC) and the National Center of Scientific and Technical Research (CNRST) for their financial support PPR2 Project.

Competing Interest

All authors declare that they have no competing interest, financial or personal, which may influence the work reported in this paper.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Not applicable.

Funding

Not applicable

References

1. Ang, W. L; Mohammad, A. W; Hilal, N; Leo, C.P. A review on the applicability of integrated / hybrid membrane processes in water treatment and desalination plants. *Desalination* **2015**, 363, 2–18.
2. Boleda, M. R; Galceran, M. T; Ventura, F. Validation and uncertainty estimation of a multiresidue method for pharmaceuticals in surface and treated waters by liquid chromatography-tandem mass spectrometry. *J. Chromatogr. A* **2013**, 1286, 146–158.
3. Kümmerer, K. The presence of pharmaceuticals in the environment due to human use - present knowledge and future challenges. *J. Environ. Manage* **2009**, 90, 2354–2366.
4. Shi, X; Leong, K. Y; Ng, H. Y. Anaerobic treatment of pharmaceutical wastewater: A critical review. *Bioresour. Technol* **2017** 245, 1238–1244.
5. COLLETTE-BREGAND, M; JAMES, A; MUNSHY, C; BOCQUENÉ, G. Contamination des milieux aquatiques par les substances pharmaceutiques et cosmétiques Etat des lieux et perspectives. *Etat des lieux Perspec* **2009**.
6. Wang, Y; Huang, H; Wei, X. Influence of wastewater pre-coagulation on adsorptive filtration of pharmaceutical and personal care products by carbon nanotube membranes. *Chem. Eng. J* **2018** 333, 66–75.
7. Comtois-Marotte, S; Chappuis, T; Gilbert, N; Lajeunesse, A; Taktek, S; Desrosiers, M; Veilleux, E; Sauvé, S. Analysis of emerging contaminants in water and solid samples using high resolution mass spectrometry with a Q Exactive orbital ion trap and estrogenic activity with YES-assay. *Chemosphere* **2017**, 166, 400–411.
8. Garcia-Rodríguez, A; Fontas, C; Matamoros, V; Almeida, M.I.G.S; Carttal R.W; Kolev, D.S. Development of a polymer inclusion membrane-based passive sampler for monitoring of sulfamethoxazole in natural waters. Minimizing the effect of the flow pattern of the aquatic system. *Microchem. J* **2016** 124, 175–180.
9. Defarges, T. M; Guerbet, M; Massol, J. Impact des médicaments sur l'environnement : état des lieux , évaluation des risques , communication. *Thérapie* **2011**, 66, 335–340.
10. Galambos, I; Molina, J. M; Jaray, P; Vatai, G; Bekassy-Molnar, E. High organic content industrial wastewater treatment by membrane filtration. *Desalination* **2004**, 162, 117–120.
11. Tang, Y; Liu, W; Wan, J; Wang, Y; Yang, X. Two-stage recovery of S-adenosylmethionine using supported liquid membranes with strip dispersion. *Process Biochem* **2013**, 48, 1980–1991.
12. Zouhri, A; Ernst, B; Burgard, M. Bulk Liquid Membrane for the Recovery of Chromium(VI)

- from a Hydrochloric Acid Medium Using Dicyclohexano-18-crown-6 as Extractant- Carrier. *Sep. Sci. Technol* **1999**, 34, 1891–1905.
13. Kumar, S; Babu, B. V. Separation of carboxylic acids from waste water via reactive extraction. *Int. Conv. Water Resour. Dev. Manag* **2008**.
 14. LaPara, T. M; Nakatsu, C. H; Pantea, L. M; Alleman, J. E. Aerobic biological treatment of a pharmaceutical wastewater: Effect of temperature on COD removal and bacterial community development. *Water Res* **2001**,35, 4417–4425.
 15. Allegaert, K. & van den Anker, J. N. Perinatal and neonatal use of paracetamol for pain relief. *Semin. Fetal Neonatal Med* **2017**, 22, 308–313.
 16. Anderson, B. J. Paracetamol (Acetaminophen): Mechanisms of action. *Paediatr. Anaesth* **2008**,18, 915–921.
 17. Erlewyn-Lajeunesse, M. D. S; Koppens, K; Hunt, L.P; Chinnick, P.J; Davies, P; Higginson, I.M, Benger, J.R . Randomised controlled trial of combined paracetamol and ibuprofen for fever. *Arch. Dis. Child* **2006**, 91, 414–416.
 18. Bosch, M. E; Sánchez, A. J. R; Rojas, F. S; Ojeda, C. B. Determination of paracetamol: Historical evolution. *Journal of Pharmaceutical and Biomedical Analysis* **2006**, 42, 291–321.
 19. Ziylan, A; Ince, N. H. The occurrence and fate of anti-inflammatory and analgesic pharmaceuticals in sewage and fresh water: Treatability by conventional and non-conventional processes. *J. Hazard. Mater* **2011**,187, 24–36.
 20. Parolini, M. Toxicity of the Non-Steroidal Anti-inflammatory Drugs (NSAIDs) acetylsalicylic acid, paracetamol, diclofenac, ibuprofen and naproxen towards freshwater invertebrates: a review. *Sci. Total Environ* **2020**,740, 140043.
 21. Kosjek, T; Heath, E; Krbavcic, A. Determination of non-steroidal anti-inflammatory drug (NSAIDs) residues in water samples. *Environ. Int* **2005**, 31, 679–685.
 22. Andrezzi, R; Raffael, M; Nicklas, P. Pharmaceuticals in STP effluents and their solar photodegradation in aquatic environment. *Chemosphere* **2003**, 50, 1319–1330.
 23. Stumpf, M; Ternes, T. A; Wilken, R; Rodrigues, S. V; Baumann, W. Polar drug residues in sewage and natural waters in the state of Rio de Janeiro , Brazil. *Sci. Total Environ* **1999**, 225, 135–141.
 24. Comeau, F; Surette, C; Brun, G. L; Losier, R. The occurrence of acidic drugs and caffeine in sewage effluents and receiving waters from three coastal watersheds in Atlantic Canada. *Sci. Total Environ* **2008**, 396, 132–146.
 25. Ghaffar, U. B; Tadvi, N. A. Paracetamol Toxicity: A Review Paracetamol Toxicity: A Review Epidemiology of Toxicity. *J. Contemp. Med. Dent* **2015**. doi:10.18049/jcmad/232

26. Toussaint, K; Yang, X.C; Zielinski, M.A; Reigle, K.L; Sacavage, S.D; Nagar, S; Raffa, R.B. What do we (not) know about how paracetamol (acetaminophen) works? *J. Clin. Pharm. Ther* **2010**, 35, 617–638.
27. Zidi, C; Tayeb, R; Dhahbi, M. Comparaison entre le transport facilité à travers une Membrane à Liquide Supporté (MLS) du phénol et de la vanilline extraits de milieux aqueux (Comparison between facilitated transport through a Supported Liquid Membrane (SLM) of phenol and vanillin extr. *J. Mater. Environ. Sci* **2014**, 5, 779–782.
28. O. Kebiche Senhajdji; S. Sahi; N. Kahloul; S. Tingry; M. Benamor; P. Seta. EXTRACTION DU Cr(VI) PAR MEMBRANE POLYMERE A INCLUSION. *Sci. Technol. A* **2008**, 43–50.
29. Dzygiel, P; Wiczorek, P. P. Supported liquid membranes and their modifications: Definition, classification, theory, stability, application and perspectives. in *Liquid Membranes* **2010**, 73–140. doi:10.1016/B978-0-444-53218-3.00003-9
30. Strathmann, H. Membranes and Membrane Separation Processes ,1. Principles. *Ullmann's Encyclopedia of Industrial Chemistry* **2011**. doi:10.1002/14356007.a16
31. Charcosset, C. Procédés membranaires à application pharmaceutique et biotechnologique. *Itbm-Rbm* **2006**, 27, 1–7.
32. Baudot, A; Flourey, J; Smorenburg, H. E. Liquid-liquid extraction of aroma compounds with hollow fiber contactor. *AIChE J* **2001**, 47, 1780–1793.
33. Liu, X; Ma, Y; Cao, T; Tan, D; Wei, X; Yang, J; Yu, L. Enantioselective liquid-liquid extraction of amino acid enantiomers using (S)-MeO-BIPHEP-metal complexes as chiral extractants. *Sep. Purif. Technol* **2019**, 211, 189–197.
34. Shintani, H. Liquid-Liquid Extraction vs Solid Phase Extraction in Biological Fluids and Drugs. *Int. J. Clin. Pharmacol. Toxicol* **2013**.
35. Jean, E., Villemin, D., Hlaibi, M. & Lebrun, L. Heavy metal ions extraction using new supported liquid membranes containing ionic liquid as carrier. *Sep. Purif. Technol* **2018**, 201, 1–9.
36. Xie, R; Chu, L.-Y; Deng, J.-G. Membranes and membrane processes for chiral resolution. *Chem. Soc. Rev* **2008**, 37, 1243–1263.
37. Ershad, M; Almeida, M. I. G. S; Spassov, T. G; Cattrall, R. W. & Kolev, S. D. Polymer inclusion membranes (PIMs) containing purified dinonylnaphthalene sulfonic acid (DNNS): Performance and selectivity. *Sep. Purif. Technol* **2018**, 195, 446–452.
38. Galiano, F; Briceñob, K; Marinao, T; Molinoc, A; Christensenb K.V; Figoli, A . Advances in biopolymer-based membrane preparation and applications. *J. Memb. Sci* **2018**, 564, 562–586.
39. O'Rourke, M; Cattrall, R. W; Kolev, S. D; Potter, I. D. The extraction and transport of organic

- molecules using polymer inclusion membranes. *Solvent Extr. Res. Dev* **2009**, 16, 1–12.
40. Nghiem, L. D; Mornanea, P; Potter, I.D; Perera, J. M; Cattrall, R. W; Kolev, D.D. Extraction and transport of metal ions and small organic compounds using polymer inclusion membranes (PIMs). *J. Memb. Sci* **2006**, 281, 7–41.
 41. Fontas, C; Tayeb, R; Dhahbib, M; Gaudichet, E; ThomINETTE, F; Royd, P; Steenkeste, K; Fontaine-Aupart M.P; Tingry, S; Tronel-Peyroz, E; Seta, P. Polymer inclusion membranes: The concept of fixed sites membrane revised. *J. Memb. Sci* **2007**, 290, 62–72.
 42. Zaidi, S. M. J; Mauritz, K. A; Hassan, M. K. Membrane Surface Modification and Functionalization. *Fonct. Polym* **2018**, 1–26. doi:10.1007/978-3-319-95987-0_11
 43. Razo-lazcano, T. A; López-munive, Y; González-muñoz, M. P. Ibuprofen Recovery from Aqueous Solutions by Supported Liquid Membranes. *Int. J. Membr. Sci. Technol* **2015**, 2, 21–29.
 44. Vilt, M. E; Ho, W. S. W. Supported liquid membranes with strip dispersion for the recovery of Cephalexin. *J. Memb. Sci* **2009**, 342, 80–87.
 45. Román-hidalgo, C; Martín-valero, M. J; Fernández-torres, R; Callejón-mochón, M; Bello-lópez, M. Á. New nanostructured support for carrier-mediated electromembrane extraction of high polar compounds. *Talanta* **2017**, 162, 32–37.
 46. Tbeur, N; Rhlalou, T; Hlaïbi, M; Langevin, D ; Metayer, M; Verchere, J.F. Molecular recognition of carbohydrates by a resorcinarene. Selective transport of alditols through a supported liquid membrane. *Carbohydr. Res* **2000**, 329, 409–422.
 47. Hlaïbi, M; Tbeur, N; Benjjar, A; Kamal, O; Lebrun, L. Carbohydrate – resorcinarene complexes involved in the facilitated transport of alditols across a supported liquid membrane. *J. Memb. Sci* **2011**, 377, 231–240.
 48. Munro, T. A; Smith, B. D. Facilitated transport of amino acids by fixed-site jumping Amino acids are transported with high fluxes through plasticized cellulose triacetate membranes containing large amounts of quaternary tetraalkylammonium salts ; similar. *Chem. Commun* **1997**, 22, 2167–2168.
 49. Ren, X; Jia, Y; Lu, X; Shi, T; Ma, S. Preparation and characterization of PDMS-D2EHPA extraction gel membrane for metal ions extraction and stability enhancement. *J. Memb. Sci* **2018**, 559, 159–169.
 50. Smith, J. A. R; B. D. Facilitated Transport of Small Carbohydrates through Plasticized Cellulose Triacetate Membranes . Evidence for Fixed-Site Jumping Transport Mechanism Facilitated transport through liquid membranes has been investigated for more than 30 years as a potentia. *J. Am. Chem. Soc* **1997**, 119, 2765–2766.

51. White, K. M; Smith, B. D; Duggan, P. J; Sheahan, S. L; Tyndall, E. M. Mechanism of facilitated saccharide transport through plasticized cellulose triacetate membranes. *J. Memb. Sci* **2001**, 194, 165–175.
52. Mouadili, H; Majid, S; Kamal, O; ElAtmani, EL.H; Touaj, K; Lebrun, L; Hlaïbi, M. New grafted polymer membrane for extraction , separation and recovery processes of sucrose , glucose and fructose from the sugar industry discharges. *Sep. Purif. Technol* **2018**, 200, 230–241 (2018).
53. Haponska, M; Trojanowska, A; Nogalska, A; Jastrzab, R; Gumi, T; Tylkowski, B. PVDF Membrane Morphology — Influence of Polymer Molecular Weight and Preparation Temperature. *Polymers (Basel)* **2017** ,9, 718.
54. Kang, G. dong; Cao, Y. ming. Application and modification of poly(vinylidene fluoride) (PVDF) membranes - A review. *J. Memb. Sci* **2014**, 463, 145–165.
55. El Atmani, E.H; Benelyamani, A; Mouadili, H; Tarhouchi, S; Majid , S; Touaj, K; Lebrun, L; Hlaibi, M. The oriented processes for extraction and recovery of paracetamol compound across different affinity polymer membranes . Parameters and mechanisms. *Eur. J. Pharm. Biopharm* **2018**, 126, 201–210.
56. Hassoune, H; Rhlalou, T; Verchère, J. F. Mechanism of transport of sugars across a supported liquid membrane using methyl cholate as mobile carrier. *Desalination* **2009**, 242, 84–95.
57. Kamal, O ; Eljaddi,T; El Atmani, EL.H; Touarssi, I; Mourtah, I; Lebrun, L; Hlaibi, M. Process of facilitated extraction of vanadium ions through supported liquid membranes . Parameters and mechanism. *Adv. Mater. Sci. Eng* **2017**, 1–12.
58. Eljaddi, T; Hor, M; Benjjar, A; Riri, M; Mouadili, H; Mountassir, Y; Hlaibi, M. New Supported Liquid Membrane for Studying Facilitated Transport of U (VI) Ions Using Tributyl Phosphate (TBP) and Tri-n-Octylamine (TOA) as Carriers from Acid Medium. *BAOJ Chem* **2015** ,1, 1–9.
59. Touaj, K; Tbeur, N; Hor, M ;Verchère, J.F; Hlaïbi, M. A supported liquid membrane (SLM) with resorcinarene for facilitated transport of methyl glycopyranosides : Parameters and mechanism relating to the transport. *J. of Membrane Sci* **2009**, 337, 28–38.
60. Chaouqi,Y; Rachid Ouchn, R; Eljaddi, T; Amane, J; Elbouchti, M; Cherkaoui,O; Hlaibi,M. Oriented Processes for Extraction and Recovery of Blue P3R Dye across Hybrid Polymer Membranes : Parameters and Mechanism. *J. Membr. Sci. Res* **2019**, 5, 303–309.
61. Touarssi, I; Mourtah,I; Chaouqi,Y; Kamal, O; Sefiani,N; Lebrun, L Hlaïbi, M. Conceptualization and quantification of oriented membrane processes for recovering vanadium ions from acidic industrial discharges. *J. Environ. Chem. Eng* **2019**, 7.

62. Louafy, R; Benelyamani, A; Tarhouchi, S; Kamal,O; Touaj,T; Hlaibi,M. Parameters and mechanism of membrane-oriented processes for the facilitated extraction and recovery of norfloxacin active compound. *Environ. Sci. Pollut. Res* **2020**.
63. Chaouqi, Y; Ouchn, R; Touarssi, I ; Mourtah, I ; El Bouchti, M; Lebrun, L; Cherkaoui, O; Hlaibi, M. Polymer Inclusion Membranes for Selective Extraction and Recovery of Hexavalent Chromium Ions from Mixtures Containing Industrial Blue P3R Dye. *Ind. Eng. Chem. Res* **2019**, 58, 18798–18809.
64. Eyring, H. The Activated Complex in Chemical Reactions. *J. Chem. Phys* **1935**, 3, 107–115.

Figures

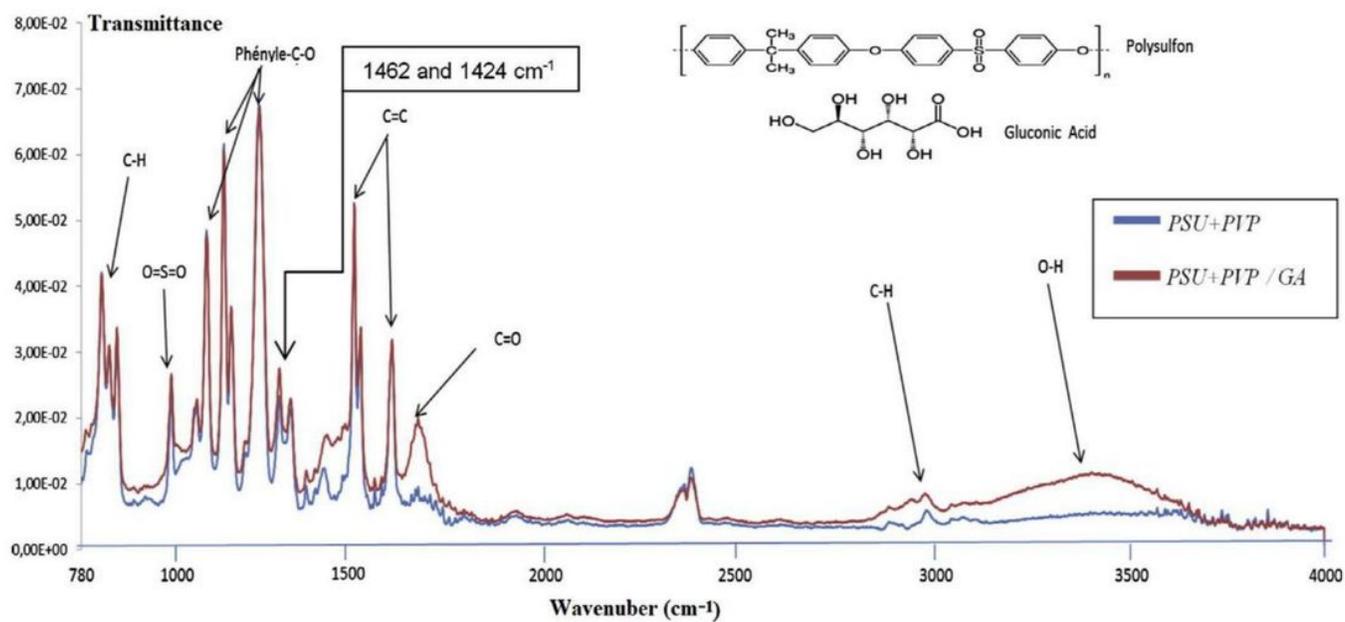
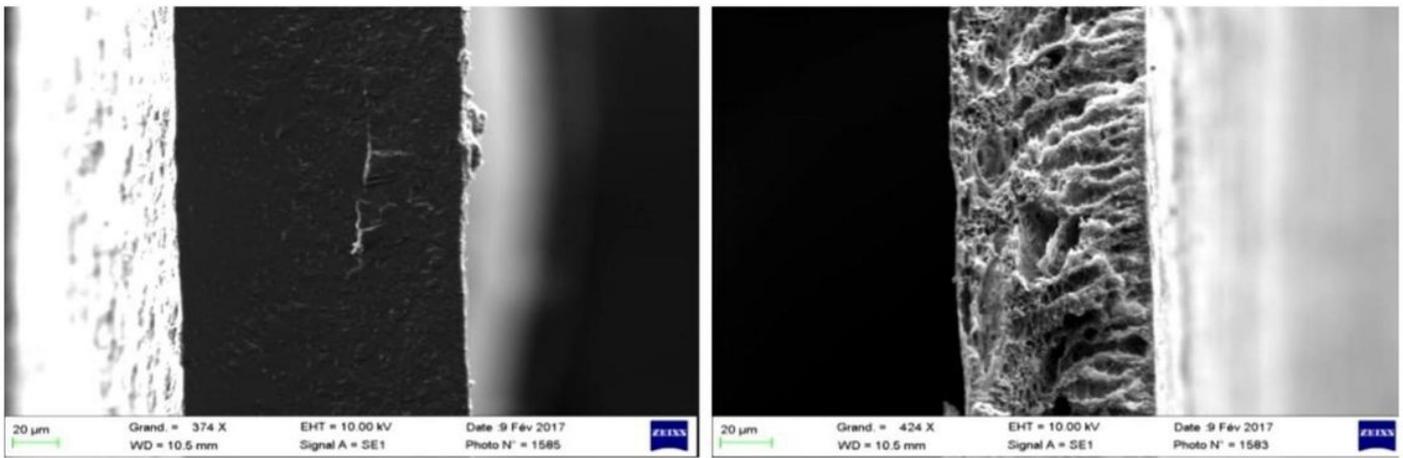


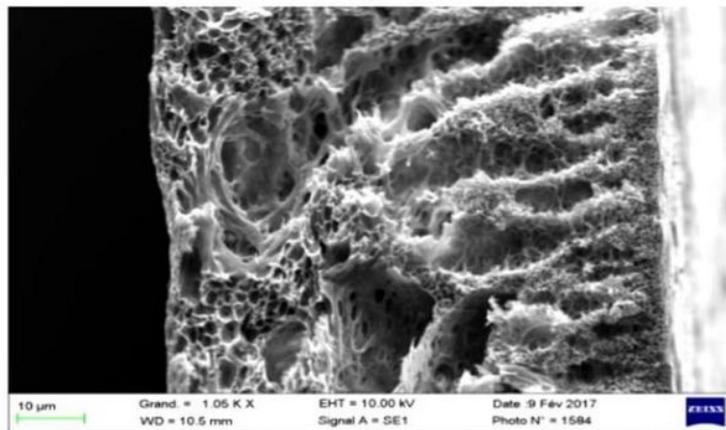
Figure 1

ATR-FTIR spectrum of the developed membrane PSU/PVP-GA



(a)

(b)



(c)

Figure 2

SEM micrographs: a) support polymer surface and cross-section (PSU/PVP), b), and c) membrane cross-section (PSU/PVP-GA)

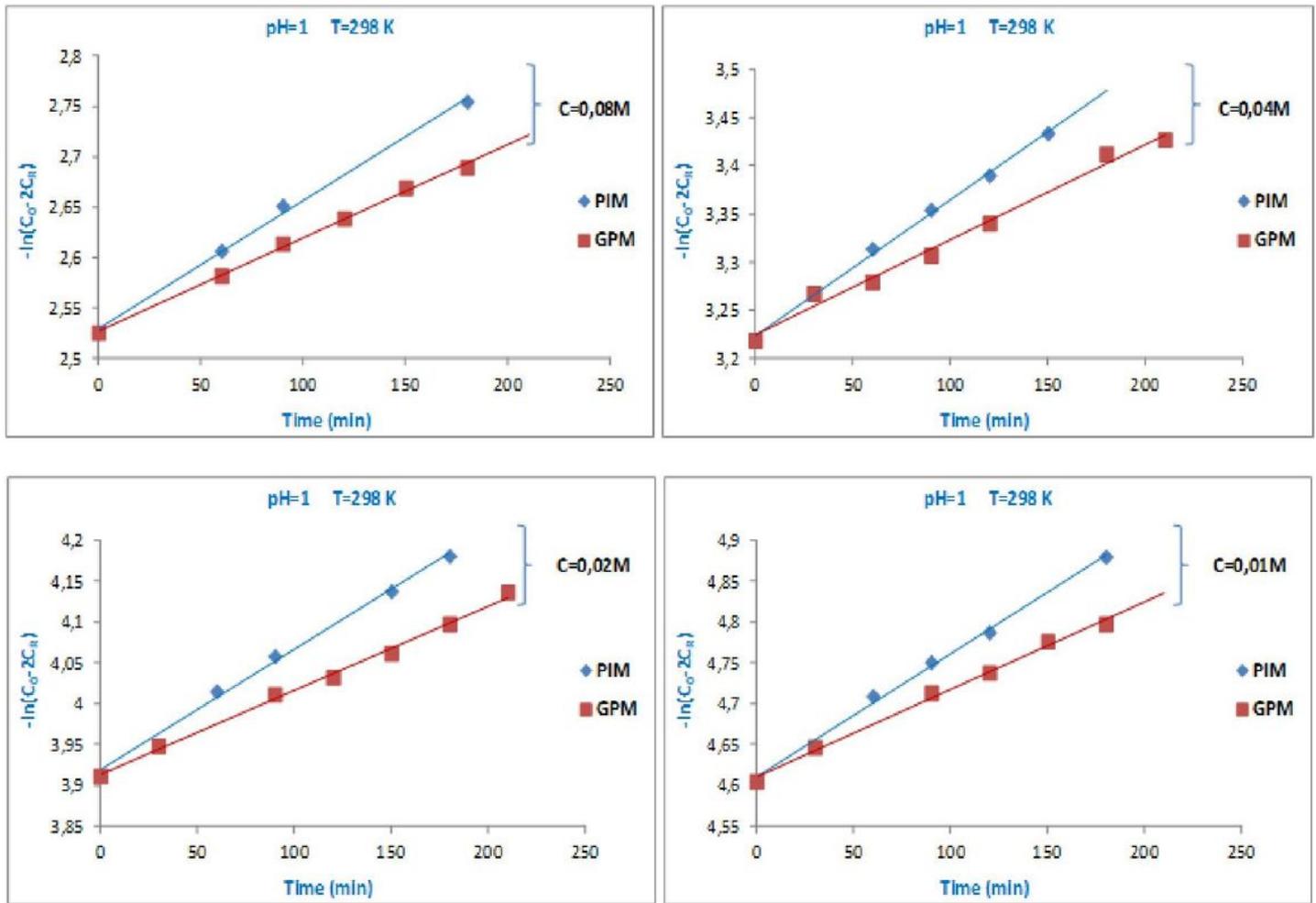


Figure 3

Evolution of the kinetic function $-\ln(C_0 - 2C_R) = f(t)$ describing the extraction processes of paracetamol through the developed membranes at different concentrations C_0 , $\text{pH}=1$ and $T=298\text{ K}$

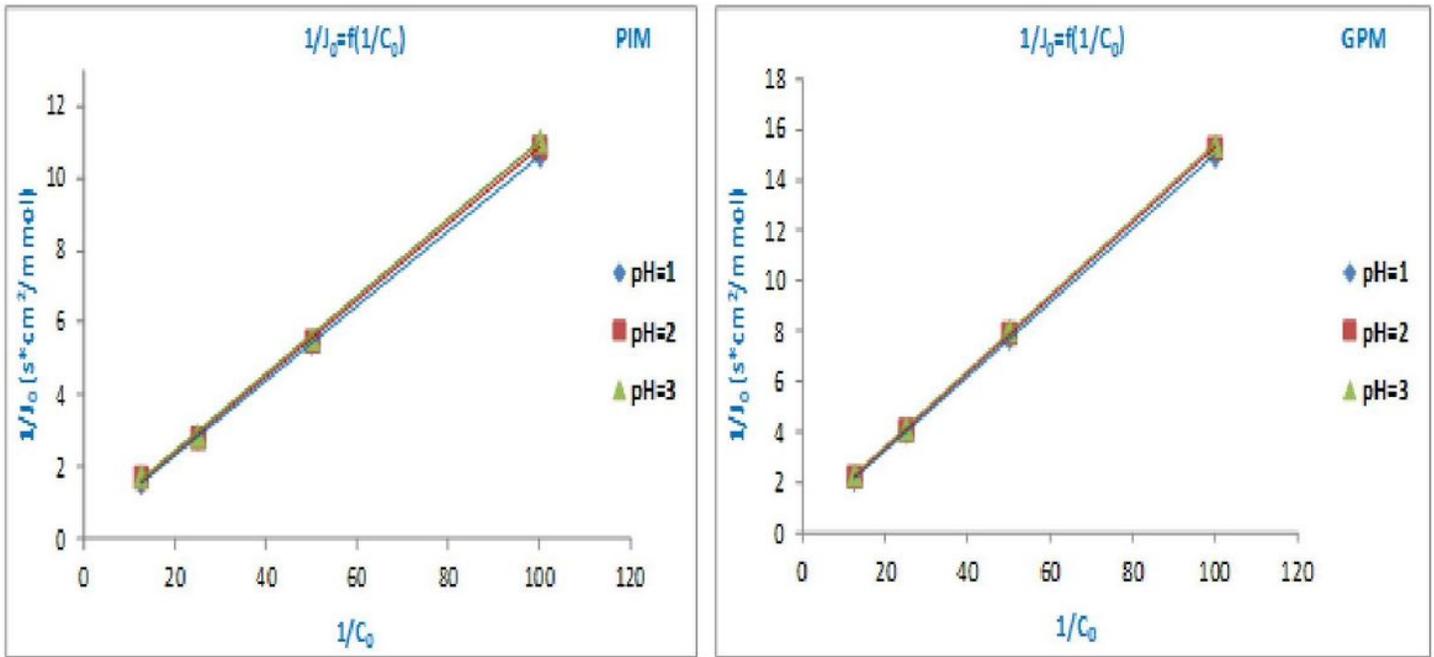


Figure 4

Lineweaver–Burk representations ($1/J_0 = f(1/C_0)$) for facilitated extraction processes across PIM and GPM membranes

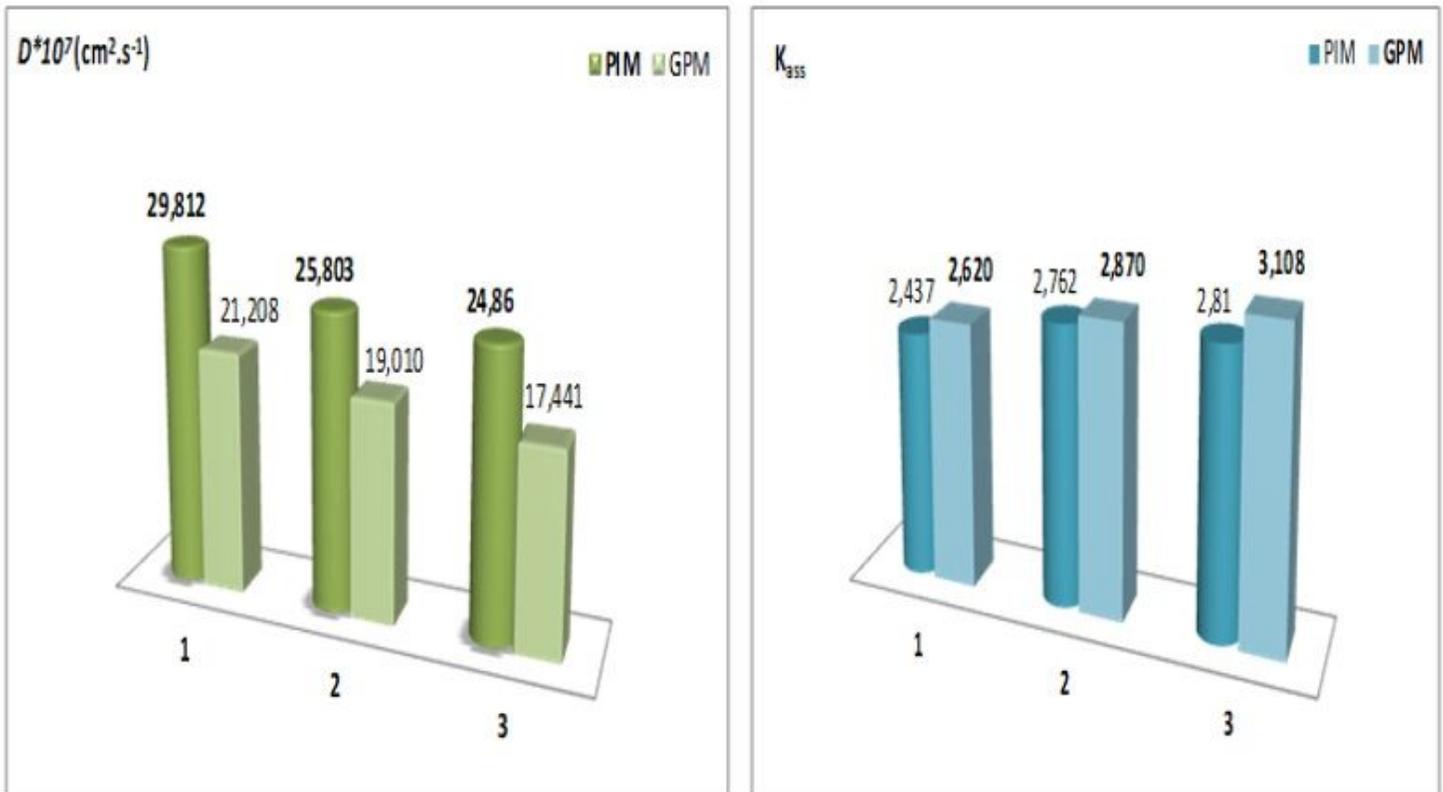


Figure 5

Influence of acidity on the parameters D^* and K_{ass} associated with the diffusion of paracetamol molecules through the developed PIM and GPM membranes

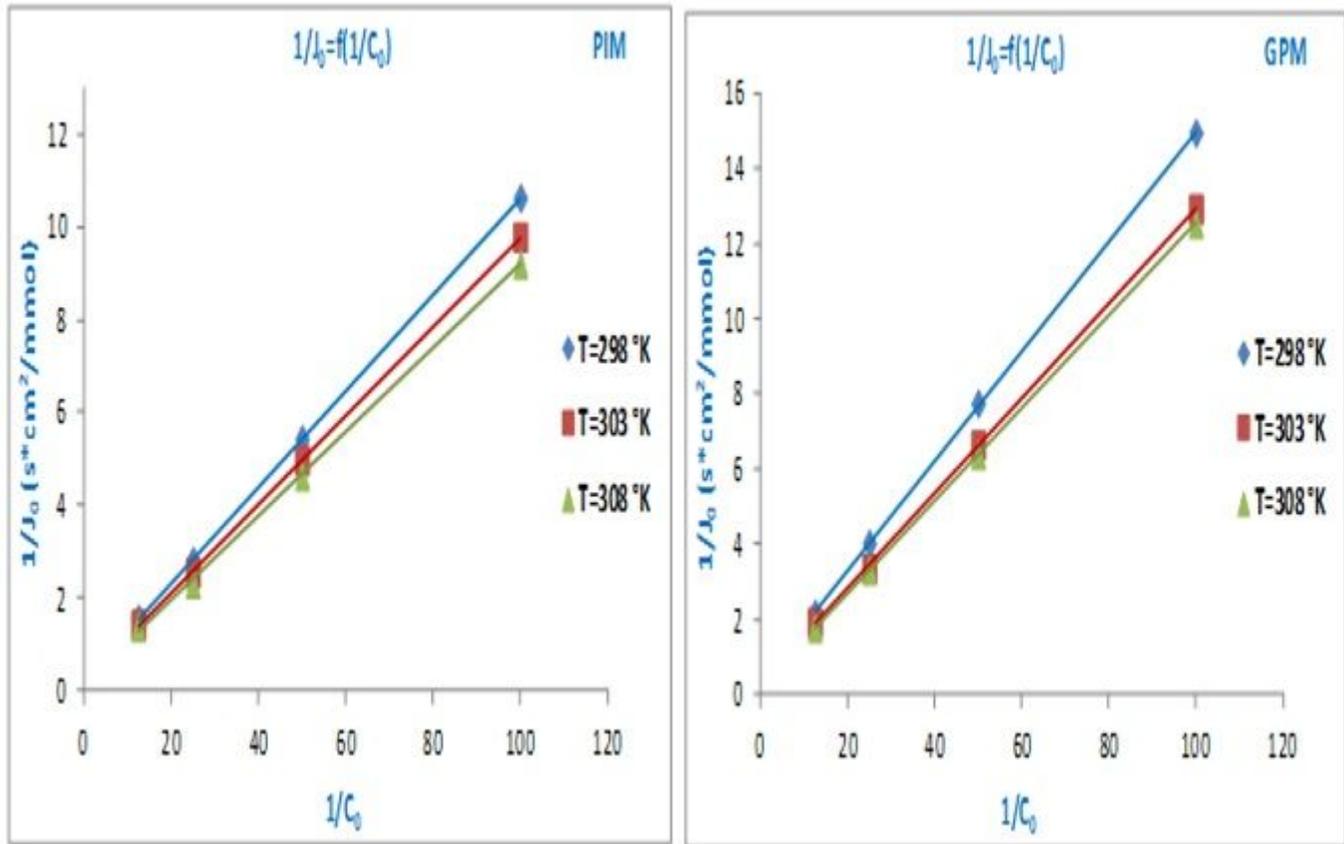


Figure 6

The L-B curved ($1/J_0 = f(1/C_0)$) for the oriented extraction processes employed for extracting paracetamol through PIM and GPM membranes at different temperatures

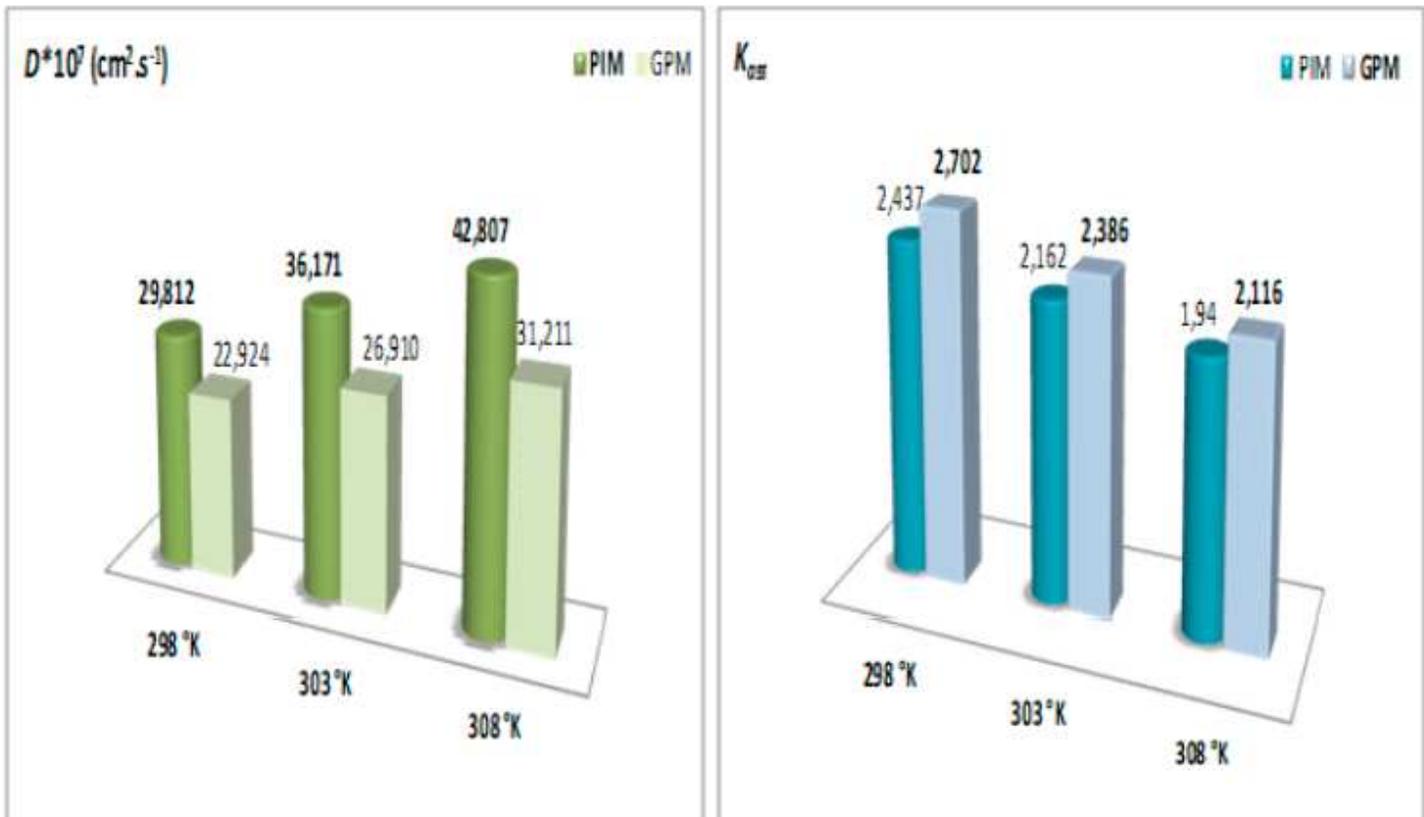


Figure 7

The opposite trends exhibited by D^* and K_{05} , characteristics of paracetamol movement during the extraction oriented processes through elaborated membranes

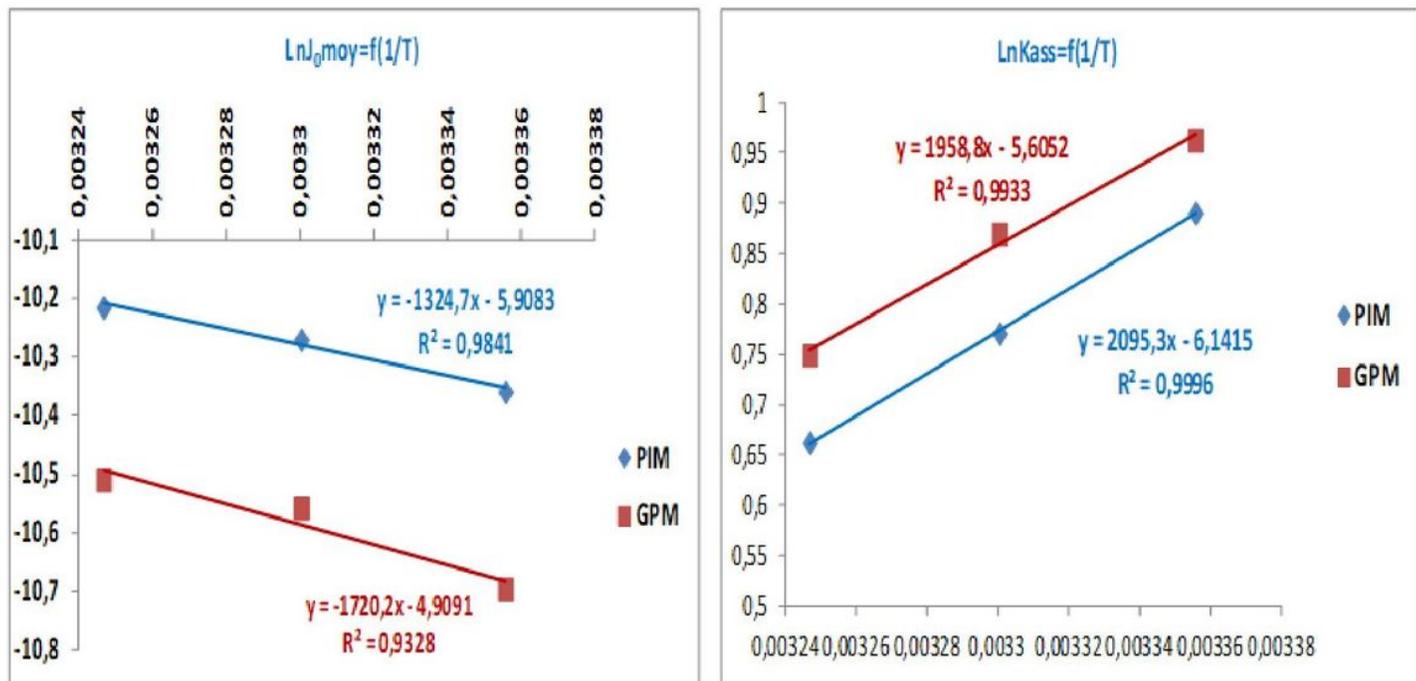


Figure 8

Evolution of Arrhenius and Van't Hoff relationships for the extraction-oriented processes followed for extracting paracetamol through the PIM and GPM membranes

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile1.docx](#)