source compartment and the same water volume is placed in the receiving phase compartment. We made several samples in the receiving phase at known time intervals. C_r is the substrate concentration in the receiving phase at time t, the concentration of substrate in the source phase at this time is $C_s = C_0 - C_r$. The equation that relates the flux J to C_r concentration of substrate S, is given by the relationship:

$$dCr/dt = J \times S/V \quad (1)$$

with S the membrane surface in contact with the source phase solution, V the receiving phase volume.

For a quasi-static state, the flux is related to the difference in concentrations of the two compartments.

$$J = P \times \Delta C / l \quad (2)$$

With, P membrane permeability and l the membrane thickness.

The slope (***a***) of the line $- \ln (C_0 - 2C_r) = f(t)$, gives the permeability P according to equation (3) (H. Hassoune)..

$$P = \boldsymbol{a} \times V \times l / 2S \quad (3)$$

b) Apparent diffusion coefficient *D and association constant K_{ass}.**

The facilitated transport of substrate S depends on the formation and dissociation of the substrate-carrier complex (TS) at the membrane-solution interfaces. The carrier T is insoluble in the aqueous phase while the substrate S is not soluble in the membrane organic phase.

We find that the macroscopic parameters ***P*** and $\boldsymbol{J_0}$ are proportional to the substrate initial concentration C_0, and have a Michaelis-Menten evolution, since for high substrate concentrations both parameters tend to limit values. In order to determine the microscopic parameters ***D**** and $\boldsymbol{K_{ass}}$, we use the Lineweaver-Burk method to linearize the expression of equation according to equation and draw the linear representation $1/J_0 = f(1 / C_0)$.

$$1/ J_0 = (l /D^*) \times [(1 / [T]_0 \times Kass) \times (1 / C_0) + (1 / [T]_0)] \quad (4)$$

$$\text{with: } K_{ass} = \text{intercept (OO)} / \text{slope (p)} \text{ and } D^* = (l / OO) * (1 / [T]_0) \quad (5)$$

3-3 Determination of activation parameters:

The flux ***J*** of the substrate S through the SLM, is related to the change in the source phase C_r concentration equation (1), this parameter varies with the temperature according to the Arrhenius relationship (D.J. Speed) given by equation (6) .

$$J_{(T)} = A_j \exp(-E_a/RT) \quad (6)$$

R is the gas constant (8.314 $J.mol^{-1}.K^{-1}$), A_J a constant (pre-exponential factor) whose value is proportional to the number of favourable interaction faces between the substrate and extractive agent (carrier), and $\boldsymbol{E_a}$ is the transition state activation energy

on the formation-dissociation reaction of complex (TS) at the membrane interfaces and in the SLM organic phase. After linearization we obtain:

$$\ln J_0 = -E_a / R * (1/T) + \ln A_j \qquad (7)$$

From the slope of the line ($\ln J_0 = f(1/T)$), we determine the E_a value. On the other hand, it is known from the activated complex theory, that $\boldsymbol{E_a}$ is related to the activation enthalpy ($\boldsymbol{\Delta H^{\#}}$) by the relation:

$$\boldsymbol{\Delta H^{\#}} = E_a - 2500 \quad (J.mol^{-1}) \text{ at } 298\ K \qquad (8)$$

While the activation entropy ($\boldsymbol{\Delta S^{\#}}$), is related to A_J constant by the equation:

$$\boldsymbol{\Delta S^{\#}} = R\,(\ln A_J - 30.46) \quad (J.K^{-1}.mol^{-1}) \text{ at } 298\ K \qquad (9)$$

4. Results and Discussions

4-1. Influence of the source phase acidity

a) Determination of the parameters: permeability *P* and the initial flux J_0:

Under the same experimental conditions, using the same SLM with the same carrier (methyl cholate), paracetamol transport was performed at different C_0 concentrations (C_0= 0.08M, 0.04M, 0.02M et 0.01M) of paracetamol in source phase, and for different acidities, pH = 1, 2, 2.5 or 3 (HCl). The experimental results verify the kinetic proposed model for this facilitated extraction process, and line segments represented by the graph of figure 3, shows the linear evolution of - ln ($C_0 - 2C_r$) terms versus time, provided by this model (H. Hassoune)

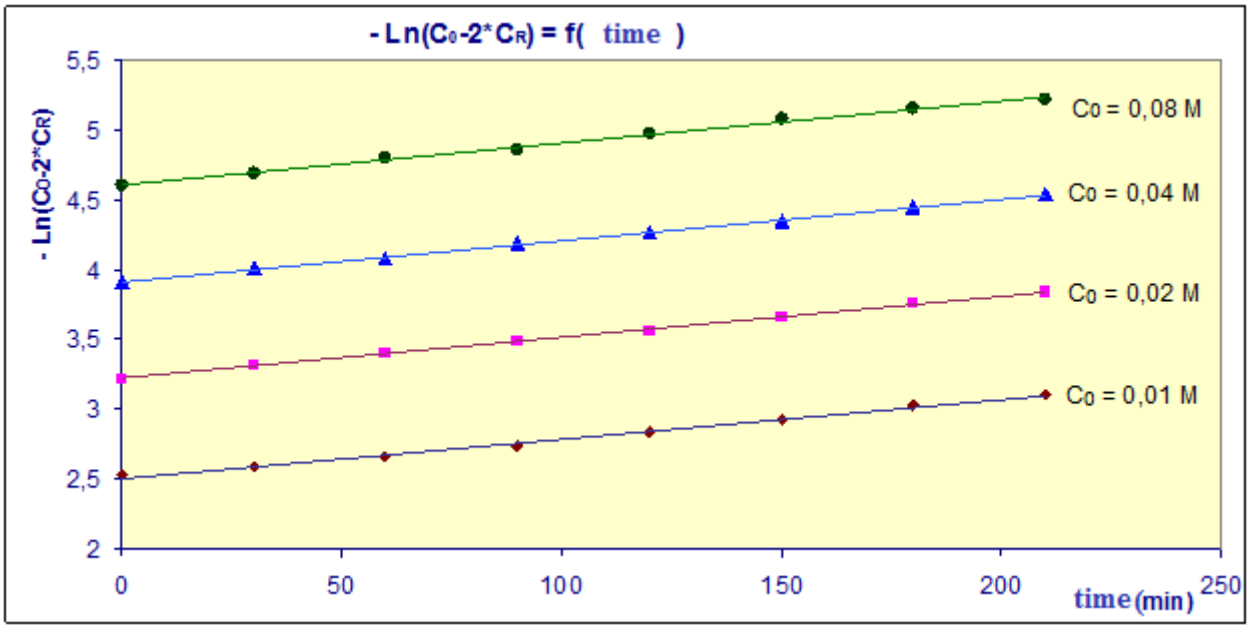

Fig 3: Representation of the straight -ln (C_0-$2C_r$) = f (time) paracetamol transport through the PVDF MLS and methyl cholate as a carrier to pH = 2 and T = 25°C

The slopes calculated from Fig. 3, according to equation 3, allow the determination of the permeability coefficients ***P*** and the initial flux $\boldsymbol{J_0}$.

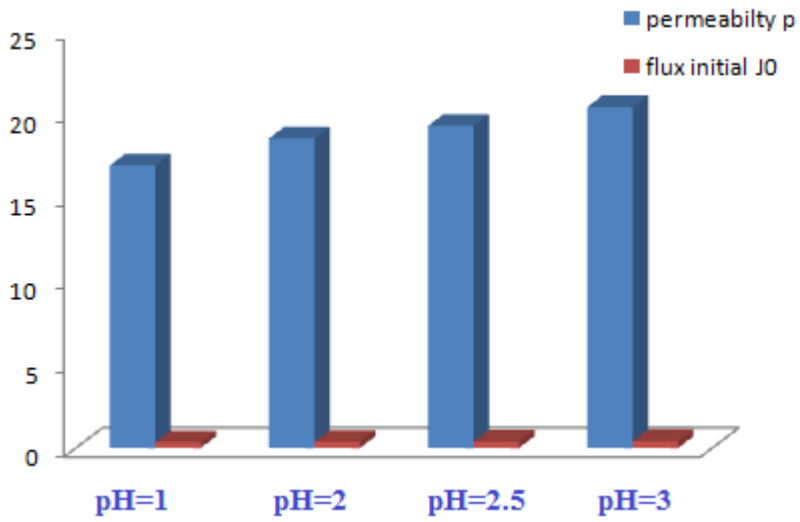

Fig 4 : permeabilty P and initial flux J_0

b) Determination of the macroscopic parameters:

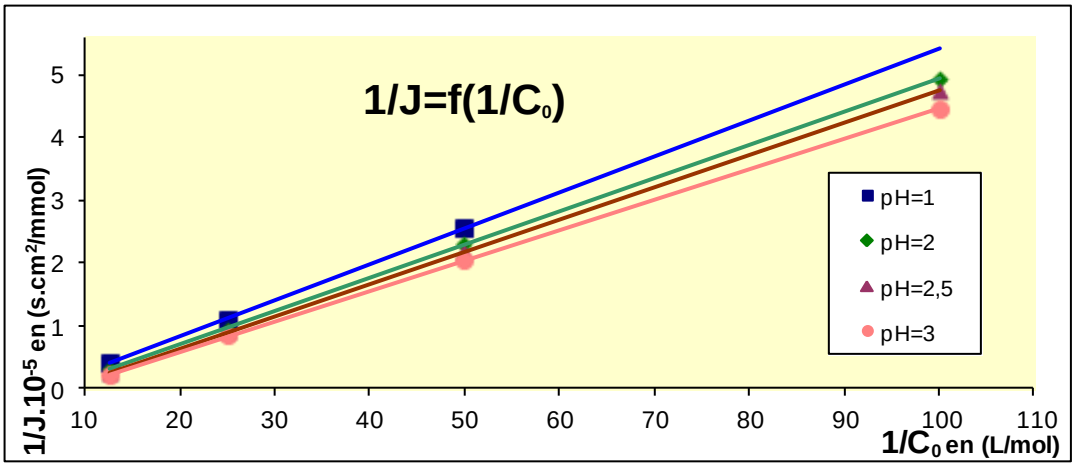

Fig. 5: The Lineweaver-Burk representation for the facilitated transport of pracetamol through the SLM, [MC] = 0.01 M, toluene phase and T = 298 K.

From these line segments (Fig. 5), slopes (*p*) and intercepts (*oo*) were calculated and using equation (5), the parameters ***D**** and K_{ass} were determined.

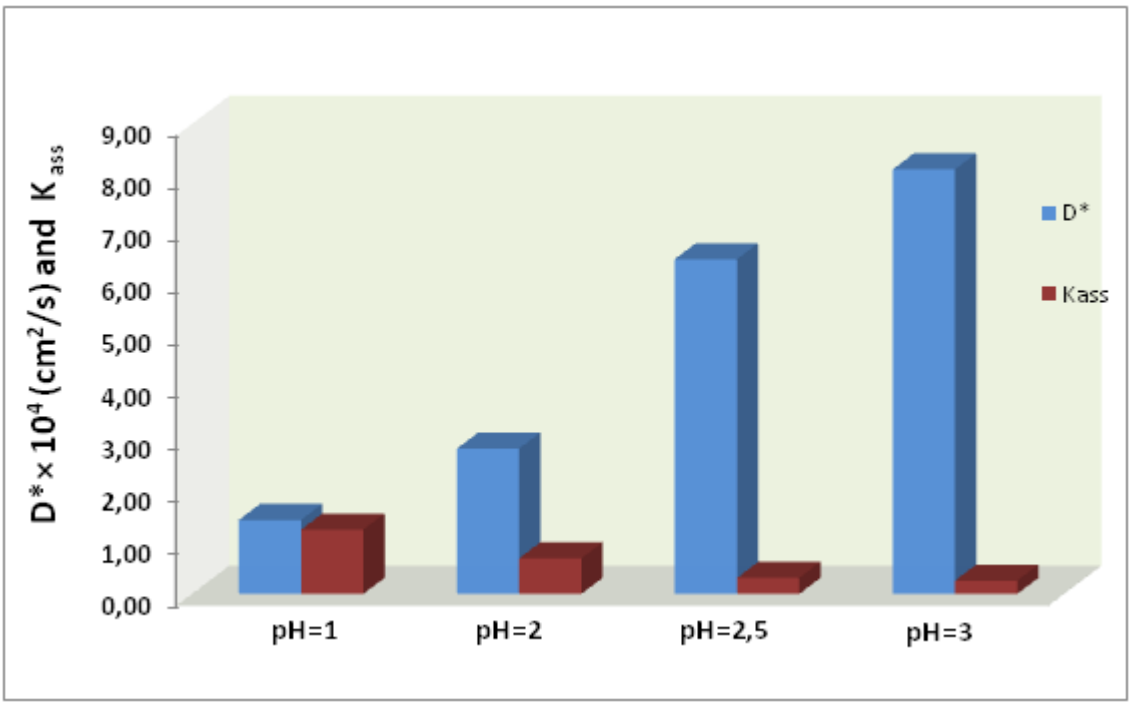

Fig (6): The representation of the evolution of microscopic parameters; the apparent diffusion coefficient ***D**** and the association constant K_{ass} to pH studied.

4-2 Influence of the temperature factor:

From the representation $Ln(J_0)$ versus 1/T (Figure (7)) we calculated the activation parameters in the facilitate extraction process of paracetamol through this membrane.

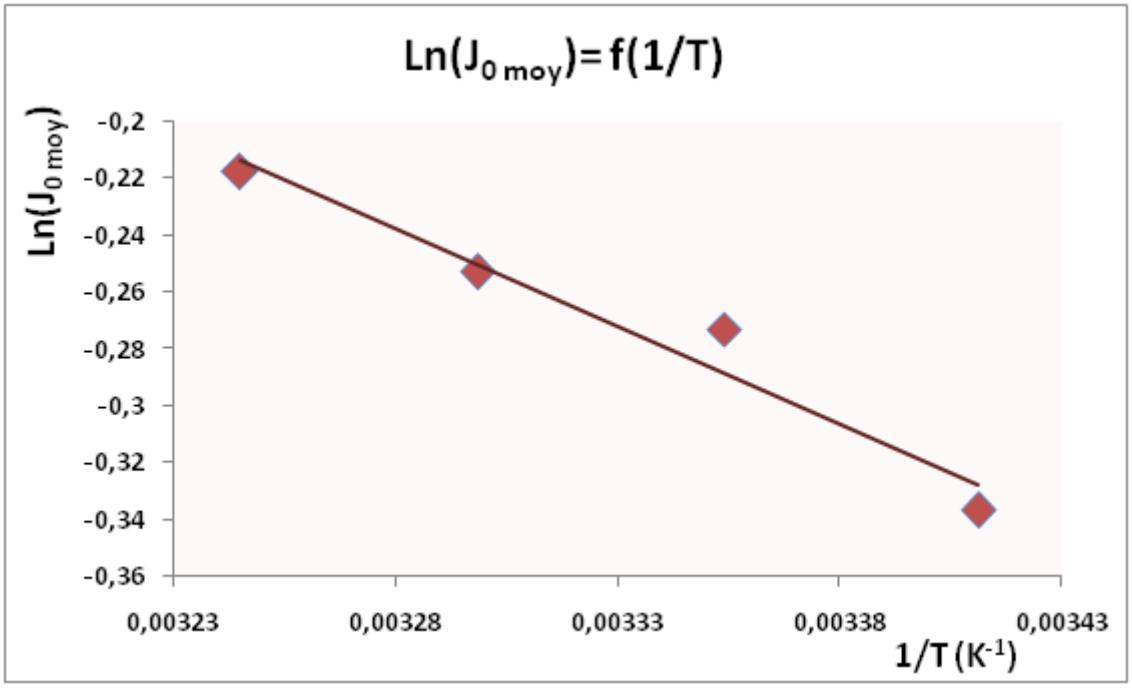

Fig. 7: Dependence of paracetamol fluxes on temperature obtained in facilitated extraction across the SLM**.**

- The activation energy: ***Ea***= 5,69 KJ/mol

-The activation enthalpy: $\Delta H^{\#}$ = 3,215 KJ/ mol

- The activation entropy: $\Delta S^{\#}$ = - 236 $J.mol^{-1}\ K^{-1}$

The low values E_a and $\Delta H^{\#}$ indicate that the transition state on the formation-dissociation reaction of the complex (*ST*) requires low energy. The negative value of $\Delta S^{\#}$ expresses a gain of order and therefore a real association between substrate and carrier in this transition state. (…)

5. Conclusion:

These studies showed that the lipophilic agent methyl cholate is very effective for the facilitated extraction process of paracetamol and the prepared SLM is very permeable for of the substrate for this oriented process (high values of macroscopic parameters ***P*** and J_0). The proposed mechanism allows the determination of the microscopic parameters ***Kass*** and ***D**** relating to the movement of paracetamol substrate through the membrane organic phase.. The obtained values show that the stability and diffusion of the substrate-carrier complex (*ST*) are closely related to the movement nature of the substrate in the organic phase of the SLM. The increase in

temperature rised the values of ***P, J_0*** and ***D****. Furthermore, this study identified the activation parameters (***E_a***, ***$\Delta H^{\#}$*** and ***$\Delta S^{\#}$***) that characterize the formation and the dissociation reactions of the complex (*ST*) at interfaces. The obtained values confirm the high permeability of the SLM and allow the determination of the mechanism of the substrate movement through the organic phase of the membrane. The diffusion of the substrate through the SLM is due to a series of reactions (formation/dissociation) and to successive jumps of substrate molecules from one carrier to another (T. ELJADDI)

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