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THE pH ROLE IN THE TRANSPORT OF ACTIVE PRINCIPLES OF DRUGS THROUGH AGITATED BULK LIQUID MEMBRANE

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Lucrarea prezintă un studiu de transport, axat pe influenţa pH-ului asupra transportului unor principii active, compuşi organici cu proprietăţi acide, des întalniţi în compoziţia medicamentelor: acid salicilic, acid acetilsalicilic. S-a studiat rolul pH-ului fazei sursă şi al fazei receptoare în procesul de transport prin membrana lichidă de cloroform.

Randamentele de transport cele mai bune s-au obţinut în următoarele condiţii de lucru: pH-ul fazei sursă egal cu doi şi pH-ul fazei receptoare egal cu doisprezece. Randamentele compuşilor organici studiaţi au fost: pentru acid salicilic, $\eta = 80\%$, acid acetilsalicilic, $\eta = 88\%$.

Rezultatele obţinute au fost corelate cu diagramele de speciaţie ale celor doi compuşi în funcţie de pH. Controlul analitic al procesului s-a urmărit spectofotometric, la lungimi de undă caracteristice celor doi compuşi.

This paper presents a study of the transport, focused on the influence of pH of active ingredients, organic compounds with acid properties, common in the composition of drugs: salicylic acid and acetylsalicylic acid. The role of pH in the receiving phase and feed source in the transport process through the liquid membrane of chloroform was studied.

The best transport efficiencies were obtained using the following working conditions: feed source pH equal to two and receiving phase pH equal to twelve. The transport efficiencies of studied organic compounds were: for salicylic acid $\eta = 80\%$ and for aspirin $\eta = 88\%$.

The results were correlated with the speciation diagrams of the compounds under study according to the pH. The content of active principle was measured by molecular absorption spectrometry in the UV region at specific absorption wavelengths.

Keywords: transport through liquid membranes, salicylic acid, acetylsalicylic acid

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1. Introduction

Organic compounds with acid properties, (phenolic structures or their acid derived) are products commonly found in industrial aqueous waste and are the most common forms of chemical pollutants from industrial wastewater. More than that, because of their toxicity to microorganisms in high concentrations (more than 3000 ppm), the state of degradation is limited. For this reason, one of the essential concerns consists of the treatment of wastewater that results from the production of active principles of drugs, chemical plants and others. These wastewaters contain a considerable amount of this type of compounds. [1].

Selective separation of organic compounds is and will remain a critical problem in the chemical industry. Conventional methods used for this purpose, such as fractional distillation, solvent extraction processes [2] and others, involves considerable costs of energy and large amounts of waste [3].

Over the years membrane science has won its place among the most important research subjects, membrane systems reporting sales of approximately $1 billion annually [4]. Among the processes that have shown enormous potential scope and are still developing are: emulsion liquid membranes and supported liquid membranes.[5 - 7]. The first type emulsion liquid membranes were made by N. N. Li, in 1968 [8]. Emulsions are obtained by the action of surfactant on a mixture of immiscible liquids. Emulsion liquid membranes allow multiple applications, both in the laboratory for analytical purposes but also at pilot or industrial scale for preparative and purification purposes. Among the many advantages that possess liquid membranes are numbered: specificity, minimal use of solvents and the fact that extraction and stripping are included in a single step [9]. Unfortunately in the literature are few large scale applications of emulsion liquid membranes and supported liquid membranes, mainly due to insufficient membrane stabillity [10, 11].

As a result, in this work we studied the behavior of bulk liquid membrane transport of active principles of drugs.

2. Experimental

The transport experiments were realised in a wall in wall type transport cell presented in fig.1.

Transport system was consists of: feed source (F.S.), solution of concentration 10^{-3} mol/L of studied compound, with volume equal to 20 cm^3. Experiments were performed using aqueous solutions of the studied compound with pH correction in the pH range 2 – 6. The pH value was determinated using hydrochloric acid (Merck) and sodium hydroxide (Merck). The receiving phase (R.P.) was a sodium hydroxide solution with a concentration ranging between 10^{-4}

– 10^{-2} mol/L, receiving phase volume being equal to 7 cm^3. The two terminal phases of the transport system were separeted by an organic membrane (M.) of chloroform with a volume of 50 cm^3. Working temperature was 25 ±1°C and the transport time was 3 hours. The reagents used were analytical grade and were used without further purification. There were used: acetylsalicylic acid and salicylic acid both having Merck origin. The chloroform (Sigma Aldrich) was saturated with distilled water. The distilled water was saturated with chloroform and used at the preparation of the feed source and of the receiving phase.

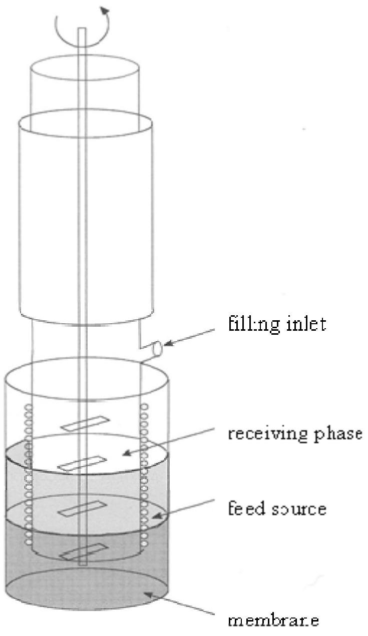


Fig. 1. Experimental device of transport

The organic compounds content from the aqueous phase was measured through molecular absorption spectrometry in the UV region using a GBC Cintra 6 series V-3656 spectrometer. The organic compounds present absorption bands in the UV region at the next wave lengths: acetylsalicylic acid at $\lambda = 273$nm (acid and neutral medium) and $\lambda = 295$nm (alkaline medium), salicylic acid at $\lambda = 295$ nm (acid, neutral and alkaline medium). The pH was measured with a combined glass/AgCl, Ag electrode, using a HI 3220-02 pH-meter. Calibration was performed with standard solutions oh pH: 4,12±0,02 and 9,18±0,02.

3. Results and discussions

The transport of a solute through a liquid membrane takes place when a chemical potential gradient or an external field acting on the system causing a state of disequilibrium. The organic compounds molecules with acid character can be transported through organic liquid chloroform membrane by a series of diffusion-extraction equilibriums that take place at membrane interfaces, concentrating them in alkaline receiving phase.

The transport studies followed the influence of feed source pH and the receiving phase pH.

The influence of feed source pH

The feed source pH was varied in the pH range 2 – 6 covering for an acid environment. Keeping the receiving phase pH equal to 12 for the two studied compounds the following transport were obtained efficiency according to feed source pH(fig.2 - 3)

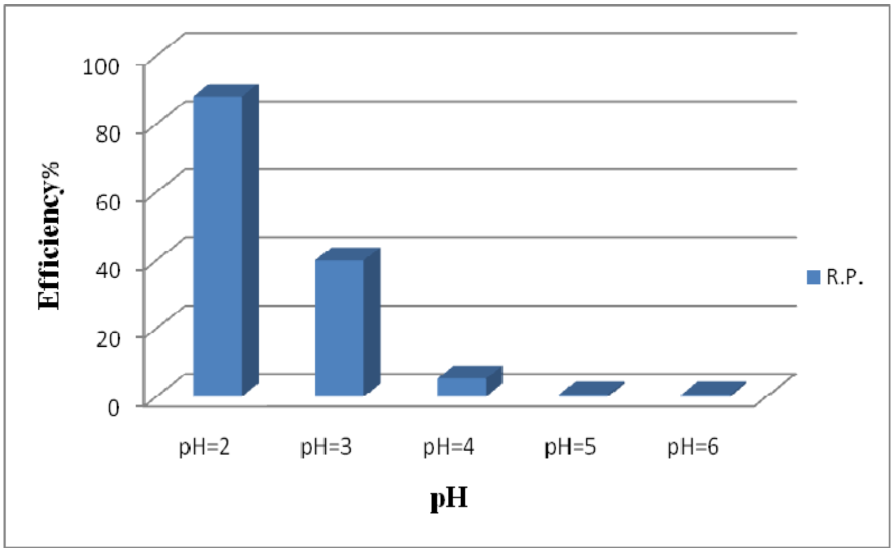


Fig.2. Transport of aspirin depending on the feed source pH
Feed source (F.S.)- acid solution of aspirin, the concentration 10^{-3}*mol/L membrane (M.)- chloroform, receiving phase (R.P.)- sodium hydroxide solution* 10^{-2} *mol/L*

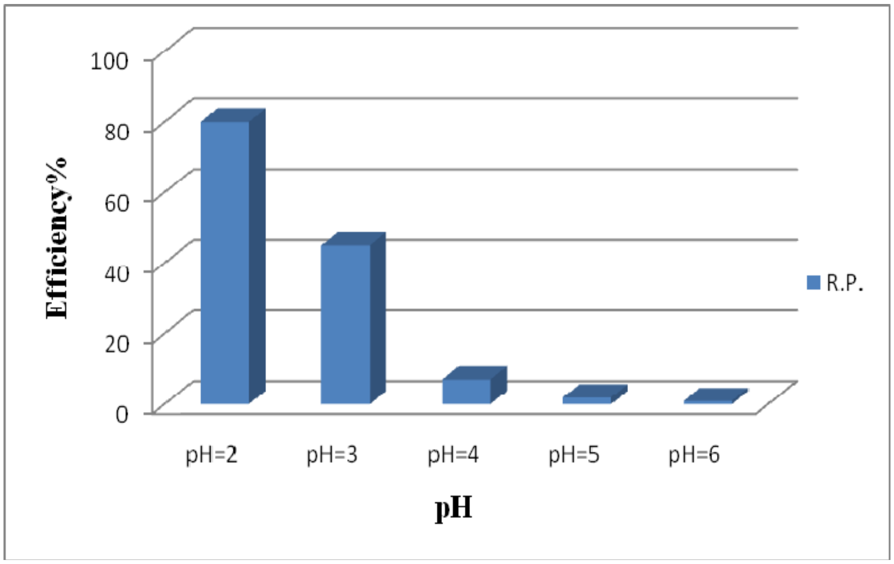


Fig.3. Transport of salicylic acid depending on the feed source pH
Feed source (F.S.)- acid solution of salicylic acid, the concentration 10^{-3}*mol/L, membrane (M.)- chloroform, receiving phase (R.P.)- sodium hydroxide solution* 10^{-2} *mol/L*

The experimental results obtained show that the transport of the two compounds studied takes place with high effeciency in condition of acid feed source pH. Maximum yields of the transport are obtained at pH = 2 and greatly decrease at pH = 4 and pH = 5.

The influence of receiving phase pH

Due to the fact that the transport of active principles through a chloroform membrane is a transport with reaction in receiving phase, we studied the influence of NaOH concentration of the receiving phase on the concentration range 10^{-2} – 10^{-4} mol/L. Laboratory experiments have been performed for the feed sources consisting of salicylic acid solution and aspirin solution, each in concentration of 10^{-3}mol/L at pH = 2, obtained with hydrochloric acid. The experimental results obtained are presented in fig. 4 – 5.

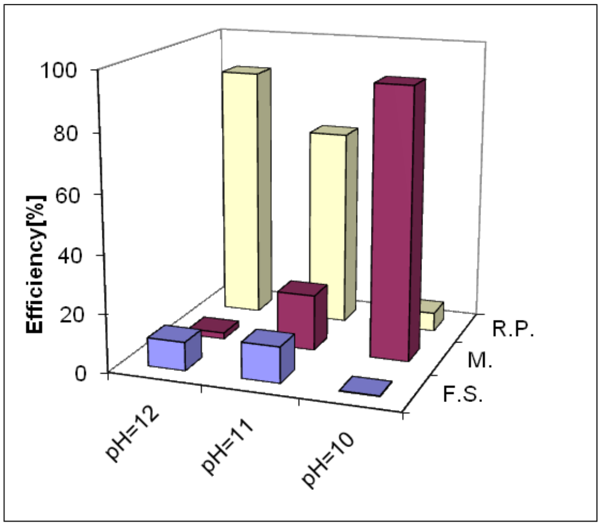


Fig.4. Distribution of aspirin in phase membrane sistem depending on the receiving phase pH at the end of transport process

Feed source (F.S.)- acid solution of aspirin, the concentration 10^{-3}*mol/L membrane (M.)- chloroform, receiving phase (R.P.)- sodium hydroxide solution* $10^{-2, -3, -4}$ *mol/L*

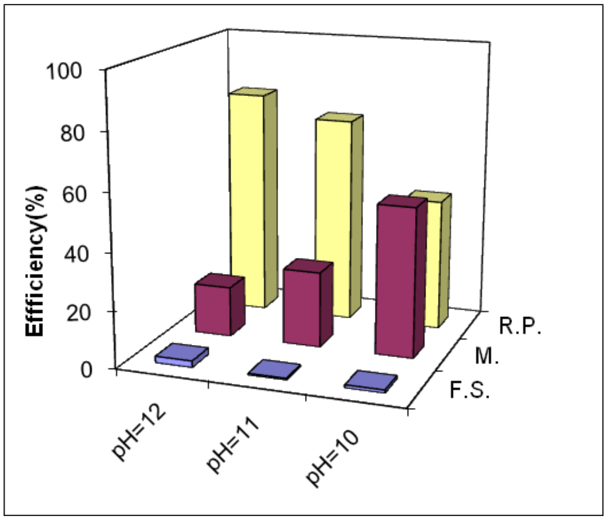


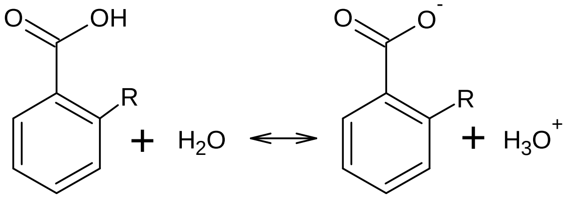
Fig.5. Distribution of salicylic acid in phase membrane sistem depending on the receiving phase pH at the end of transport process

Feed source (F.S.)- acid solution of salicylic acid, the concentration 10^{-3}*mol/L,membrane (M.)- chloroform, receiving phase (R.P.)- sodium hydroxide solution* $10^{-2, -3, -4}$ *mol/L*

As for aspirin and for salicylic acid, transport efficiency shows the highest values at pH = 12 and decreases significantly along with lower the concentration of NaOH in receiving phase. At the pH = 10 (concentration of NaOH = 10^{-4} mol/L) transport process becomes insignificant.

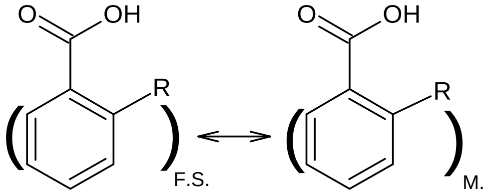
These results can be correlated with the equilibriums that take place in three-phase system studied.

In the feed source (F.S.) equilibrium take place with proton exchange:



R = OH, $OCOCH_3$

This equilibrium is controlled by pH. At the pH<pK_a, R'-COOH predominate undissociated form of the organic compounds which is distributed between the feed source and membrane according to equilibrium distribution:



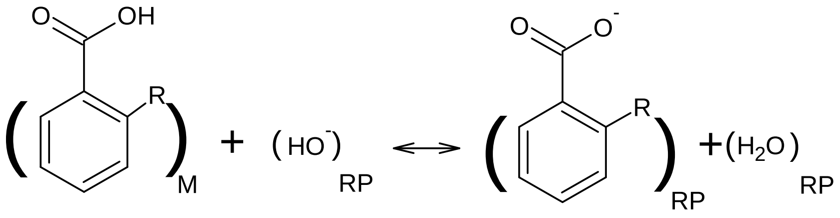
R = OH, $OCOCH_3$

in a proportion that depends of distribution constant expressed by the relation:

$$R_{R'-COOH} = \frac{[R'-COOH]_M}{[R'-COOH]_{F.S.}}$$

where M. is the membrane and F.S. is the feed source.

The molecular form of the organic compounds (phenolic derivate) crosses the membrane and at the membrane | receiving phase interface a chemical equilibrium takes place:



R = OH, $OCOCH_3$

Is established therefore that the pH is an operational parameter that can play a significant role in optimizing the transport process of the studied organic compounds.

Depending on pH, in the feed source undissociated forms, active for transport predominate. Their degree of formation can evaluated by the relationships:

$$\alpha_0 = \frac{1}{1+10^{\mathrm{pKa-pH}}} \qquad (1)$$

$$\alpha_1 = \frac{1}{1+10^{pH-pKa}} \qquad (2)$$

where:

α_0 = degree of anion formation

α_1 = degree of undissociated acid formation

With these relationships were calculated speciation diagrams for the compounds studied presented in fig.6 - 7:

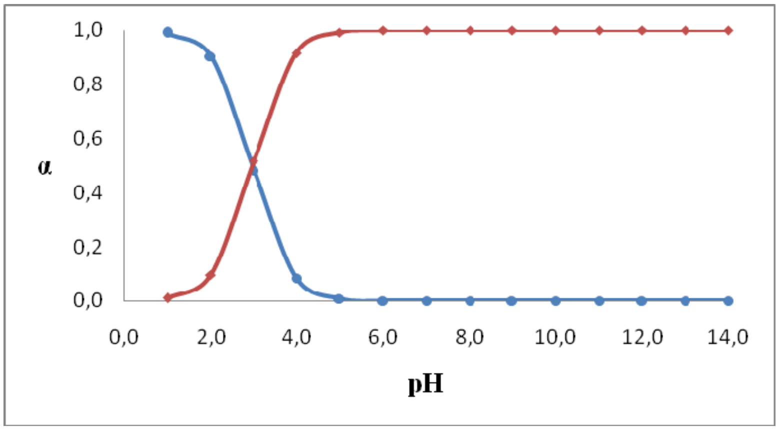


Fig.6. Speciation diagram for salicylic acid

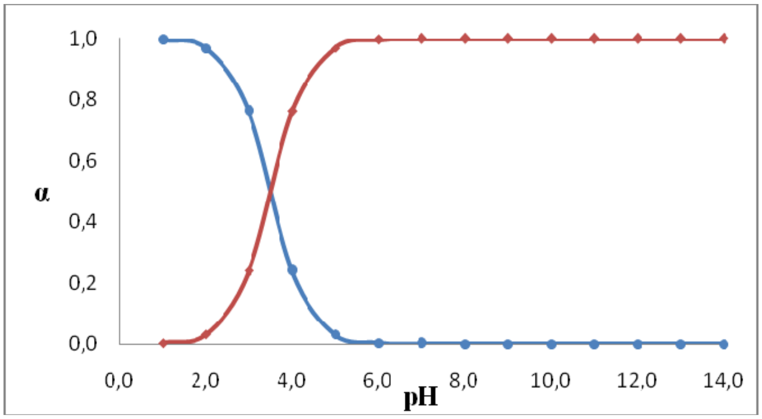


Fig.7. Speciation diagram for acetylsalicylic acid

It can be observed that an acid pH promotes a maximum degree of formation of active molecular species in chloroform organic membrane transport. From the analysis of speciation diagrams, in the case of aspirin and salicylic acid, we can observe that the pH has the greatest influence in the formation of molecular species.

At pH = 2 the formation degree of undissociated compounds is 99,6% for acetylsalicylic acid and 98,9 % for salicylic acid. At pH = 4 this decreases significantly and reaches 75% for aspirin and at 48% for salicylic acid. It can be said then that the feed source pH is a very important parameter in the development of the transport of these two compounds through bulk organic membrane.

4. Conclusion

This paper presents experimental data obtained at transport through agitated bulk organic membrane of active principles of drugs: acetylsalicylic acid, salicylic acid.

The operational parameters which can significantly influence transport efficiency: feed source pH, receiving phase pH were studied. The results were correlated with equilibriums that take place in phases and at the membrane system interfaces and chemical speciation diagrams of the two studied compounds. The best efficiencies of transport were obtained for the feed source at pH = 2 and for receiving phase at pH = 12, transport efficiency for studied compounds were above 80%.

Unlike supported liquid membrane technique and the emulsion liquid membrane technique, the alternative agitated bulk liquid membrane remove disadvantages related to the stability or breaking of the emulsion. Therefore we can consider the agitated bulk liquid membrane technology is a viable option for recovery of organic compounds with acid properties.

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