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Transport and separation through bulk liquid membrane of some biologic active compounds

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Abstract Transport through liquid membranes of various chemical species is a viable method for different applications in analytical or technological domain. This paper presents the transport and separation results of two compounds of pharmaceutical importance: salicylic acid and aspirin, using bulk liquid membrane technique. We studied the effect of the feed source and receiving phase pH on the transport efficiency of the two compounds throught chloroform membrane. These results were correlated with speciation diagrams of salicylic acid and aspirin. The speciation diagrams shows that in these pH conditions, for aqueous phase of the membrane system, the two compounds are mostly undissociated form and therefore active for transport. In this system it can be achieve separation of the two compounds, salicylic acid and aspirin, using a suitable complexing agent in the feed source such as Fe^{3+}. In this way salicylic acid forms an inactive complex structure for transport while aspirin crosses the membrane and it is recovered in a percentage of 80% in the receiving phase membrane system.

Keywords: salicylic acid, acetylsalicylic acid, pertraction bulk liquid membrane

1. Introduction

Separation membrane enjoys a great success in separation techniques because it presents many advantages: efficiency and selectivity, as well as low cost price. Used at first to separate metal cations [1, 2], more recent research is oriented towards using membrane techniques to transport and separation of organic compounds [3, 4]. The main classes of organic compounds which are studied, in terms of transport and separation throught liquid membrane are: phenols and their derivates [5-7], organic amines [8], organic acids [9, 10], amino acids [11-13], and a significant number of drugs such as penicillin G [14], dopamine [15] and others.

Generally the transport studies of drugs were intended to simulate their transport through cell membranes.

Acetylsalicylic acid (aspirin) is one of the most popular drugs which can be synthesized using salicylic acid as raw material. Salicylic acid can be used as an ingredient in different pharmaceutical products.

The literature does not mentioned many studies related to the transport of the two compounds [16] through liquid membrane and almost no studies on the use of liquid membrane separation.

Therefore in this paper we proposed to study the behavior transport of salicylic acid and aspirin through organic liquid membrane well as the possibility of their separation using the salicylic acid complexing agent Fe^{3+}.

2. Experimental

All reagents used in transport experiments were of analytical grade. Salicylic acid and acetylsalicylic acid were Merck origin. Chloroform (Merck), used as membrane, was saturated with distilled water. Distilled water was previously saturated with chloroform and used in the preparation of feed source and receiving phase. Hydrochloric acid (Merck) and sodium hydroxide (Merck) were used to adjust feed source pH (pH = 2) and receiving phase pH (pH = 12). Ferric chloride was used as a salicylic acid complexing agent. Working

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temperature was 25 ±1°C and the transport time was 3 hours.

The membrane system applied to study the transport and separation of salicylic acid and acetylsalicylic acid consists of:

- Feed source (FS) – aqueous solution of salicylic acid and/or acetylsalicylic acid, each in a concentration of 10^{-3}, 10^{-4} mol/L. The separation experiments were realized as follows: in the feed source was added in excess than salicylic acid and aspirin concentration $FeCl_3$ (10^{-2} mol/L). The feed source was obtained acid pH with hydrochloric acid (pH = 1,7 – 2,2) and in a volume of 20 cm^3.
- Membrane (M) – consisted of chloroform with a volume of 50 cm^3.
- Receiving phase (RP) – sodium hydroxide solution 10^{-2} mol/L which provided a pH 12 to 12,3. The receiving phase volume was 7 cm^3.

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

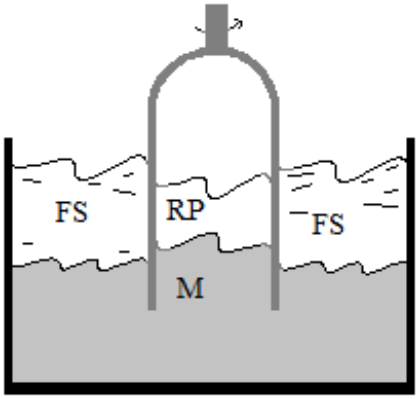


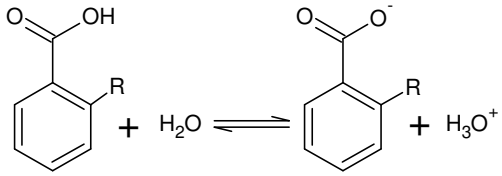
Fig. 1. Experimental device of transport

At the basis of cell membrane is chloroform. Feed source is above the membrane, between central and outer tube and receiving phase is in the central tube. Receiving phase having a volume less than the feed phase along with the organic substrate transport, from feed source in to receiving phase, takes place his concentration.

The pH was measured with a combined glass/AgCl, Ag electrode, using a HI 3220-02 pH-meter. The salicylic acid and acetylsalicylic acid content from the aqueous phase was measured through molecular absorption spectrometry in the UV region using a GBC Cintra 6 series V-3656 spectrometer. Compounds studied have absorption bands at the following wavelengths: salicylic acid at λ = 295 nm (in feed source and receiving phase), acetylsalicylic acid at λ = 273 nm (in feed source) and λ = 295 nm (in receiving phase) and the complex of salicylic acid and Fe^{3+} at λ = 523 nm (in feed source) and at λ = 460 nm (in receiving phase). The concentrations of salicylic acid and acetylsalicylic acid in the membrane phase were calculated from mass balance.

3. Results and discussions

Generally, in the case of the transport of organic compounds with acid or alkaline character, the active forms for transport are molecular forms easily soluble in organic membrane. Salicylic acid and acetylsalicylic acid in aqueous solution can participate in proton transfer pH controlled equilibrium.



R = OH, $OCOCH_3$

The degree of formation of active molecular transport species can be evaluated using speciation diagrams. Generally for a acid character compound H_nA formation level of a chemical species $H_cA^{(n-c)-}$ can be calculated using a relationship such as:

$$\alpha_c = \frac{\left[H_c A^{(n-c)-}\right]}{C} \quad (1)$$

where C is the initial concentration of H_nA

In the particular case of the two new compounds studied in this paper can be calculated with the equation:

$$\alpha_0 = \frac{1}{1+10^{pKa-pH}} \quad (2)$$

degree of formation of ionic species, and the relationship:

$$\alpha_1 = \frac{1}{1+10^{pH-pKa}} \quad (3)$$

degree of formation of molecular species.

Speciation diagrams obtained by applying these relationships are presented in **Fig. 2** and **3**:

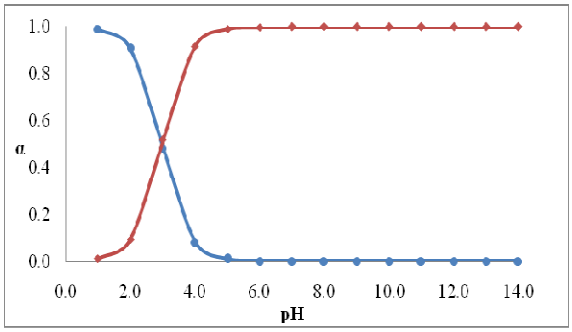


Fig. 2. Speciation diagram for salicylic acid

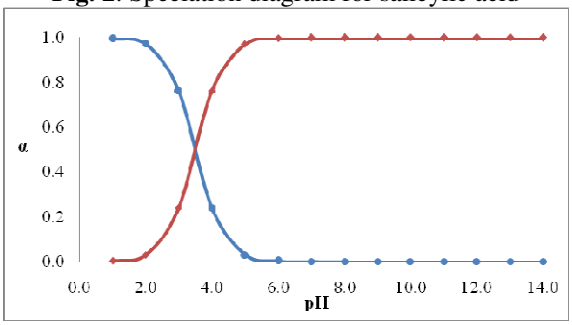


Fig. 3. Speciation diagram for acetylsalicylic acid

It is found that at pH = 2 salicylic acid in aqueous solution, the molecular form proportion is 98,9 % and aspirin at a rate of 99,6%. At pH = 12 salicylic acid and acetylsalicylic acid are in ionic form for more than 99%. Therefore the transport experiments were conducted at pH = 2 for feed source and pH = 12 for receiving phase. Optimal pH conditions were confirmed by [17].

Transport performance of the two compounds were evaluated using the relationship:

$$\%mol = \frac{C_i V}{C_{FS_0} V_{FS}} \quad (4)$$

C_i – the concentration of component "i" in phase membrane system, at the end of the process

V – phase membrane system volume

C_{FS0} – feed source initial concentration

V_{FS} – receiving phase volume

In these conditions the transport takes places in the receiving phase through a reaction and which mechanism is presented in **Fig. 4.**

Experimental data obtained from transport of two organic compounds show that they can be transferred from a acid feed source through a chloroform membrane in a alkaline phase with significant efficiency (see **Fig. 5.**). Transport efficiency is 80 % salicylic acid and acetylsalicylic acid 88 %. These results can be directly related to the chemical potential gradient within the membrane system.

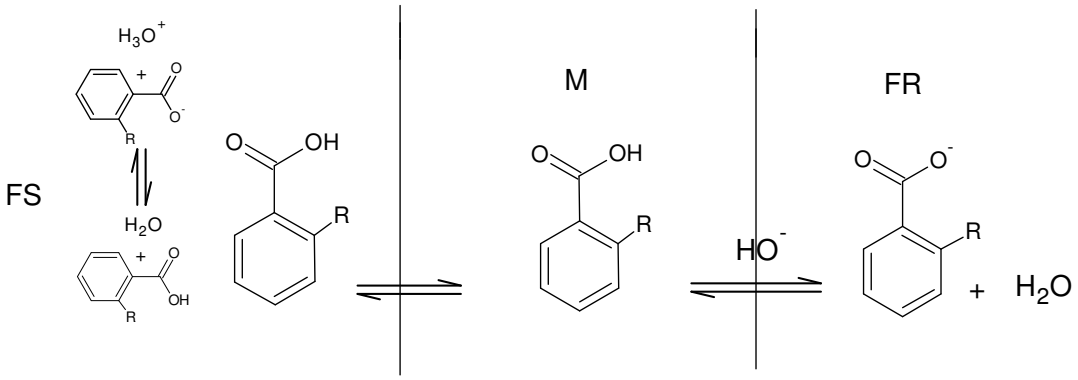


Fig. 4. Transport mechanism

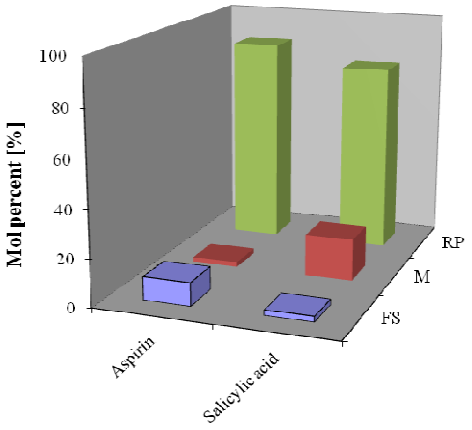


Fig.5. Results transport salicylic acid and acetylsalicylic acid (aspirin) through organic liquid membrane. Feed source: salicylic acid and acetylsalicilic acid solution each at a concentration of 10^{-3} mol/L in the presence oh HCl concentration 10^{-2} mol/L; Membrane: chloroform; Receiving phase: NaOH solution at a concentration of 10^{-2} mol/L.

By introducing cation Fe^{3+} in the feed source, they can form inactive electrical charge carriers transport complexes with salicylic acid. This hypothesis was confirmed by experimental data presented in **Fig. 6.**

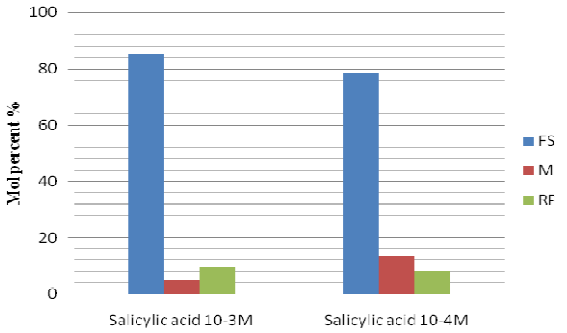


Fig.6. Results transport of salicylic acid and acetylsalicylic acid in the presence of Fe^{3+} through organic liquid membrane. Feed source: salicylic acid and acetylsalicilic acid solution in a concentration of 10^{-3}, 10^{-4}mol/L in the presence of Fe^{3+} concentration 10^{-2} mol/L and HCl concentration 10^{-2} mol/L; Membrane: chloroform; Receiving phase: NaOH solution at a concentration of 10^{-2} mol/L.

Transport results in a mixture of salicylic acid and acetylsalicylic acid in the presence of Fe^{3+} cations exclusively reveal the blocking effect of transport through chloroform membrane of salicylic acid compared with acetylsalicylic acid (**Fig.7.**). Aspirin cross the membrane and recovered in 80 % membrane system receiving phase.

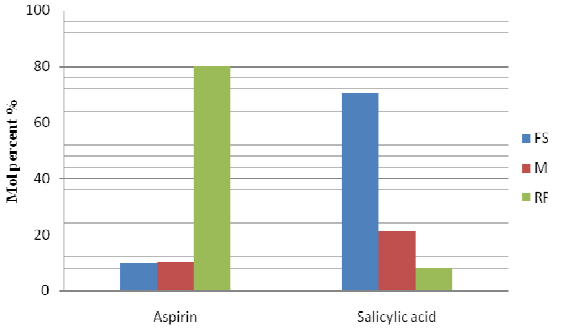


Fig.7. Results transports of a mixture consist of salicylic acid and acetylsalicylic acid in the presence of Fe^{3+} through organic liquid membrane. Feed source: salicylic acid and acetylsalicilic acid solution in a concentration of 10^{-4}mol/L in the presence of Fe^{3+} concentration 10^{-2} mol/L and HCl concentration 10^{-2} mol/L; Membrane: chloroform; Receiving phase:NaOH solution at a concentration of 10^{-2} mol/L.

4. Conclusion

The experimental results presented in this work reveal the possibility of transport with significant yields of two compounds with biological importance through a chloroform liquid membrane. The transport efficiency of salicylic acid was < 10 % and of the acetylsalicylic acid was 80%. In this system it can be achieved the separation of the two compounds using a suitable complexing agent form salicylic acid such as Fe^{3+}. In this way salicylic acid form an inactive transport complex while aspirin crosses the membrane and recovered in a percentage of 80% in the membrane system receiving phase.

5. Acknowledgments

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6. References

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