Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

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Online publication date: 18 January 2011

To cite this Article Sadeghi, Susan , Jahani, Moslem and Ghiamati, Ebrahim(2011) 'Selective Transport of Cu^{2+} Ions through Bulk Liquid Membrane System Mediated by Erythromycin Ethyl Succinate', Separation Science and Technology, 46: 2, 215 — 223
To link to this Article: DOI: 10.1080/01496395.2010.507234
URL: http://dx.doi.org/10.1080/01496395.2010.507234

Separation Science and Technology, 46: 215–223, 2011

ISSN: 0149-6395 print/1520-5754 online
DOI: 10.1080/01496395.2010.507234

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Selective Transport of Cu^{2+} Ions through Bulk Liquid Membrane System Mediated by Erythromycin Ethyl Succinate

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The carrier mediated transport of Cu^{2+} ions from an aqueous medium has been examined. The ability of Erythromycin Ethyl Succinate (EES) as a carrier to form a complex with Cu^{2+} ions and transport them to the receiving phase is reported. The fundamental parameters influencing the transport of Cu^{2+} ions such as the pH in the source and receiving phases and concentration of the stripping agent in the receiving phase have been optimized and accordingly, the amount of Cu^{2+} transported across the liquid membrane after 5 h was 94.3 ± 1.8% in the presence of L-histidine as a suitable stripping agent. Moreover, the selectivity and efficiency of Cu^{2+} ions transport from aqueous solution over other cations in ternary and quaternary mixtures have been investigated. The results indicate that our fabricated membrane is very sensitive toward Cu^{+2} ions in the presence of heavy metal ions.

Keywords bulk liquid membrane; Cu^{2+} ions; erythromycin ethyl succinate; L-histidine; transport

INTRODUCTION

Membranes are perhaps the most important biological entity in ions transport, because most cellular processes including enzyme activities and active transport of substances occur across membranes (1–3). There are three-phase transport processes, where the carrier performs selective translocation. These methods have many advantages over two-phase extractions and are being widely employed in separation science involving bulk liquid, supported, and emulsion membranes (4). Bulk liquid membrane (BLM) systems consist of an organic solvent including a complexing carrier, separating a source solution containing the target species, and a receiving solution with a complexing agent for the target (3). BLMs are used to study ions transport mechanism in biological systems which mimics the cell's transport in the body (5). They are also utilized in analytical labs for the evaluation of various kinetic processes due to their ease of construction, conveniently determined mass transfer coefficients, and membrane thickness. Furthermore, BLMs are used as a sample pretreatment technique due to their ability to perform analyte enrichment as well as sample-matrix separation.

Considering environmental issues, heavy metal ions are not biodegradable and tend to accumulate into the environment causing various disorders. So, the development of new extraction techniques to remove heavy metal ions is of much interest. López-López et al., have presented an overview of recent developments in BLMs for trace-metal speciation and determination in natural waters (6). Recently, Chakrabarty et al. managed to perform elegant extraction and recovery of lignosulfonate in aqueous solution using BLM (7,8). They also conducted an effective simultaneous separation of mercury from aqueous solution (9,10).

Among heavy metal ions, copper is an essential trace element for fundamental biochemical processes, but it can be very toxic as well (11). Over the past few years, researchers have shown that upon transport into the cell, Cu^{2+} is delivered to specific molecules or sub cellular compartments by forming complexes with proteins. Thus it is likely that Cu^{2+} is able to displace metal ions in a number of catalytic or structural processes in many cellular proteins (11). BLMs have been also used for simultaneous extraction and recovery of Cu^{2+} ions from other heavy metal ions (12).

A survey of the literature on Cu^{2+} ions transport indicates that different lipophilic carriers have been conducted (12–18). Gunkel-Grillon and Buffle explored the speciation of Cu^{2+} ions through a permeation liquid membrane. They discriminated and selectively determined the free copper, labile, and inert Cu^{2+} complexes in natural water (13). Mendiguchia et al. reported preconcentration of Cu^{2+} ions from seawater by means of liquid membrane system employing di-(2-ethylhexyl) phosphoric acid (DEHPA) in kerosene as a membrane. Under optimum conditions, the preconcentration yield for real samples was 76.2% with copper preconcentration factor of 4.3 (12). Leon et al. probed the kinetics of Cu^{2+} ions transport facilitated by D2EHPA, CYANEX 272, and LIX 984N as carriers and protons as counter ions. The rate constants of the extraction and

Received 29 January 2010; accepted 6 July 2010.
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stripping reactions and the maximum transport fluxes of Cu^{2+} through the bulk liquid membrane were determined for the three carriers (14). Recently, the kinetics of the transport of Cu^{2+}, Cd^{2+}, and Ni^{2+} through a bulk liquid membrane containing pyridine-2-acetaldehyde benzoylhydrazone (2-APBH) as a carrier dissolved in toluene was studied by Galindo-Riaño et al. (15). They suggested a kinetic model involving two consecutive irreversible first-order reactions for metal extraction. Cleij and coworkers achieved efficient transport of Cu^{2+} ions by several structurally simple N-monoalkylated and N-dialkylated dipeptides through liquid membrane (16). They observed that the length of the *N*-alkyl chains and the hydrophobicity of the dipeptide moiety have quite a remarkable effect on transport efficiency of Cu^{2+}. Spreti et al. applied bulk liquid membrane containing 2,2′-bis(*p*-octyloxybenzyl)diethylenetriamine (bis-*p*ODET) as a carrier for selective removal of heavy metal ions from aqueous solutions through bulk liquid membrane (17). Sadeghi et al. used an inflammatory drug to extract Cu^{2+} ions from an aqueous solution in the presence of Cd^{2+}, Pb^{2+}, Zn^{2+}, Ni^{2+}, and Co^{2+} ions (18).

Up to now, there is no report on transport of Cu^{2+} ions by Erythromycin ethyl succinate (EES; Fig. 1). EES is an antibiotic that belongs to the macrolide group of antibiotics with poor solubility in water (19). It very rapidly absorbs and diffuses into most tissues and phagocytes and actively transports to the site of infection (20). It should be noted that some essential and trace element complexes have a role on the antibacterial activity of various macrolide antibiotics (21). Recent investigation demonstrates that antimicrobial activity of metal complexes of erythromycin on microorganisms increases with respect to parent erythromycin drug emphasizing the remarkable influence of the coordination of this class of antibiotics with metal ions on their bioavailability in blood plasma (22).

On the other hand, pharmaceutical compounds have been targeted as emerging environmental contaminants.

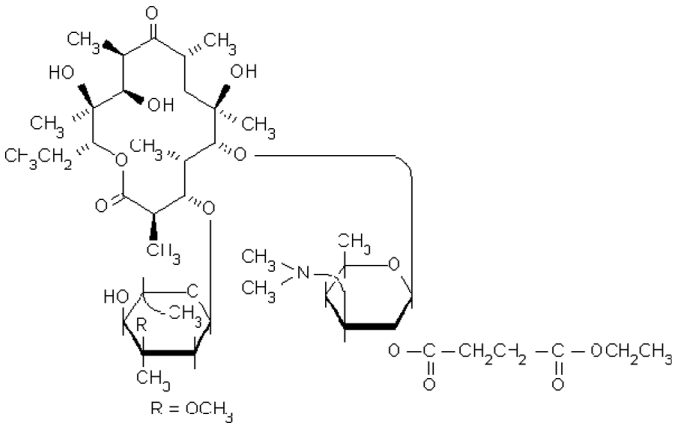

FIG. 1. Chemical structure of EES.

Among antibiotics, macrolides are one of the most prevalent species found in the environment and their residual concentrations in the aquatic environment have an impact on human health (20,23–25). Macrolides are known to bind strongly to soil particles because of their ability to form complexes with double-charged cations producing detrimental effects (26). Erythromycin as a human and veterinary medicine is expected to be preferentially adsorbed on solid environmental matrices as a contaminant (27). The objective of this work is a systematic investigation of the Cu^{2+} ions transport through liquid membrane mediated by using EES as a carrier which mimics the biological transport characteristics and provides a probe to evaluate potential metal-amino acid interactions. Moreover, this study may also expand our knowledge of general biocoordination phenomena to other chelating drugs and their applications to the biological and environmental sciences.

EXPERIMENTAL

Reagent and Chemicals

Organic compounds such as oleic acid (OA), palmetic acid (PA), stearic acid (ES), and the amino acids were purchased from Sigma and used without further purification. Organic solvents and inorganic compounds such as potassium thiocyanate, nitrate salt of the metals, sodium hydroxide, hydrochloric, and nitric acid solutions were purchased from Merck Company and used as received. Double-distilled water was used throughout the experiments. Erythromycine ethyl succinate (EES) powder was kindly supplied by Razi Pharmacy Company (Tehran, Iran) and used as received.

Apparatus

The BLM cell configuration used in this study is shown in Fig. 2. It is a concentric glass cell which consists of a cylindrical cell with inner diameter of 4.0 cm and another smaller glass cylinder open at both ends with an inner diameter of 1.5 cm fixed with some distance from the top inside the first cylinder. A Shimadzu 6300 atomic absorption spectrophotometer was used for the measurement of metal ions concentrations. pH measurements were made with a Corning 125 digital pH meter using a combined glass electrode. Conductivity measurements were carried out with a WTW LF 538 microprocessor conductivity meter using a cell constant of $1.0\,cm^{-1}$.

Procedure

Transport

All transport experiments were carried out at ambient temperature of about 25°C. The source phase (S) contained 5.0 mL of 1.0×10^{-4} mol L^{-1} Cu $(NO_3)_2$ and 1.0×10^{-2} mol L^{-1} of KSCN at pH 6.0. The receiving phase (R, 10 mL) consists of 5.0×10^{-2} mol L^{-1} of L-Histidine at pH

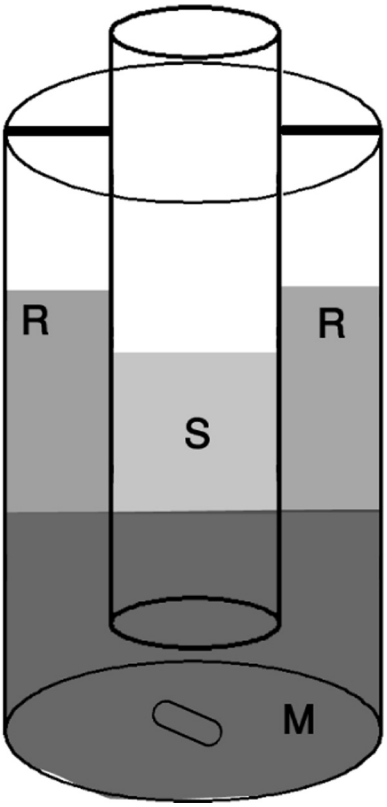

FIG. 2. Schematic of cell for Cu^{2+} transport.

7.0. A 20 mL chloroform solution containing 5.0×10^{-3} mol L^{-1} of EES and 5.0×10^{-2} mol L^{-1} oleic acid was placed at the bottom of the cell as a membrane phase (M). The cell was covered with aluminum foil to minimize evaporation. The organic layer was stirred by a teflon-coated magnetic bar for 5 hours. The stirring speed was 200 rpm. The metal ion concentrations in both the aqueous source and receiving phases were determined by an atomic absorption spectrophotometer (AAS). The pH value of the phases was adjusted with either sodium hydroxide or nitric acid solution.

Conductometry

In a typical experiment, 35.0 mL of 1.0×10^{-4} mol L^{-1} of metal salt solution in acetonitrile was placed in a dip–type conductivity cell and conductance of the solution was measured. Then, a known amount of 1.0×10^{-2} mol L^{-1} EES solution in acetonitrile was added to the cell solution in a stepwise manner until the EES–metal ions mole ratio reaches 4.0, using a micropipette, and the conductance of the solution was measured after each addition.

RESULTS AND DISCUSSION

The efficiency of the extraction of some transition metal ions by EES could be explained by the metals-EES complex formation constants which were determined by the conductometric method. The formation constant, K_f, of the resulting 1:2 of transition metal: EES complexes were evaluated by a computer fitting program of the molar conductance–mole ratio data to an appropriate equation (28). The results are shown in Table 1. It is worth mentioning that the stability sequence of the transition metals complexes with EES decreases in order of $Zn^{2+} < Cu^{2+} > Ni^{2+} > Co^{2+}$ nicely in agreement with the Irving–Williams order which holds for the equilibrium constants of transition metal ions. Further experiments were performed on two-phase extraction by using EES as a carrier in chloroform in order to choose the target ion. A test was conducted using 10 mL of 1.0×10^{-3} mol L^{-1} solution of the respective metal ions which was added to an equal volume of chloroform containing 1.0×10^{-3} mol L^{-1} EES. The mixture was then continuously shaken for about 1 h. Then the concentration of metal ions in the aqueous phase was determined by flame atomic absorption spectrophotometry. With reference to our obtained K_d values, Cu^{2+} ions possessed the most extraction efficiency in the organic phase. Based on the above findings, EES was selected as a carrier for the liquid membrane transport of Cu^{2+} ions in a three-phase separation.

Effect of Thiocyanate Concentration

Recently, it has been proved that anions also have an important role in the transport of drugs (29). Regarding some preliminary experiments, we found out that thiocyanate as a complexing agent is needed for binding with Cu^{2+} in ionic form which in turn justifies the maximum transport of Cu^{2+} ions. In the presence of excess thiocyanate, Cu^{2+} ions exist as a relatively stable complex anion, $Cu(SCN)_4^{2-}$, which thereby increases the mass transfer at the interface of the source/membrane phases. This phenomenon occurs because of lower hydration energy of $Cu(SCN)_4^{2-}$ than that of nitrate ions which can move easily into the chloroform membrane containing EES. To understand the effect of thiocyanate concentration on transport efficiency, the optimum concentration of KSCN in the source solution was also investigated and found to be 1.0×10^{-2} mol L^{-1}. A further increase in KSCN concentration in the source

TABLE 1
Complex formation constant of some transition metal cations with EES

Cations	Complex formation constant Log K_f
Cu^{2+}	5.2
Co^{2+}	3.5
Zn^{2+}	5.1
Cd^{2+}	3.3
Ni^{2+}	3.8

phase resulted in a decrease in the percentage of Cu^{2+} ion transport. This is probably due to the competition of Cu^{2+} as $Cu(SCN)_4^{2-}$ and K^+ as KSCN with the EES for complex formation of $(K^+\text{-EES})_2Cu(SCN)_4^{2-}$ and K^+-EES-SCN^-, respectively.

In order to achieve the highest efficiency for Cu^{2+} ions transport across the membrane system, we optimized the effects of the experimental variables including the stirring speed, the pH of the source and receiving phases, the composition of the membrane, and the nature and concentration of the stripping agent.

Effect of Stirring

The influence of the stirring speed (100–350 rpm) on transport efficiency was studied with regard to stirring of both aqueous phases and minimizing the thickness of the membrane layer. It was found that the transport efficiency increased with elevated stirring speed and reached a maximum at 200 rpm, after which the rate of transport decreased. This is mainly attributed to the increase in contact between the aqueous and membrane phases. At higher speeds, some mixing of the source and receiving phases occurred. Thus, the stirring speed of 200 rpm was used in all experiments.

Effect of the Nature of Receiving Phase

A preliminary transport experiment was conducted using EES as carrier and water as receiving phase. It was found that in the absence of a complexing agent in the receiving phase, no significant transport of Cu^{2+} was observed. As expected, the permeability of the membrane system depends largely on the nature of the stripping agent in the receiving phase. The presence of a suitable amino acid in the receiving phase was believed to play an essential role in the metal ions releasing process via the formation of a ternary complex, carrier-metal ion- amino acid at the interface of membrane/receiving phase. As Kruck and Sarkar have suggested, such ternary complexes are important transient species in blood serum (30). Accordingly, various stripping agents including some amino acids were examined for obtaining the effective stripping of Cu^{2+} ions from the membrane phase. In the selection of amino acids, the structure and stability constant of Cu^{2+}- amino acid complexes were considered. Regarding these facts, some amino acids were chosen and the pH of the receiving solutions was adjusted to 7.0, compatible with biological pH, where the carboxylic acid and amine groups were deprotonated significantly but the phenolic group was only slightly deprotonated. This deprotonation is responsible for the coordination of the metal ions at these sites. As can be seen from Table 2, with histidine as stripping agent, the percentage of transport is higher than the other amino acids examined in this study. This is probably due to binding of histidine to Cu^{2+} ions via two nitrogen donor atoms of amine and imidazole groups in the coordination with the carboxylate weakly coordinated in the axial (31,32). Hence, histidine was used as a stripping agent in the next steps.

TABLE 2
Effect of receiving phase composition on the Cu^{2+} ions transport efficiency (Conditions: Source phase: 5 ml of 1.0×10^{-4} mol L^{-1} Cu^{2+} and 1.0×10^{-2} mol L^{-1} KSCN at pH 5; Membrane phase: 20 ml of 1.0×10^{-3} mol L^{-1} of EES and 5.0×10^{-2} mol L^{-1} oleic acid in chloroform; Receiving phase: 10 ml of 1.0×10^{-2} mol L^{-1} of stripping agent at pH 7

Receiving phase	% Transport to the receiving phase
Sulfuric acid	4.0
EDTA	0.0
L-Valine	0.0
L-Histidine	25.0
L-Phenyl Alanine	1.0
L-Serine	0.0
L-Leucine	1.0
L-Glutamine	3.3
L-Glycine	2.3
L-Methionine	2.5
L-Tryptophan	5.0
L-Cysteine	5.0

Effect of the pH of Source Phase

Among the factors involved in the transport process, the pH of the source phase could play a crucial role. The pH value in the aqueous solutions has to be adjusted to facilitate the ions transport towards the receiving solution. So, the effect of the pH of the source phase on the transport efficiency of Cu^{2+} ions in the presence of 1.0×10^{-2} mol L^{-1} SCN^- was examined. The results indicated that the maximum Cu^{2+} transport occurs in the pH range of 4.0–6.0. At lower pH values, there was a decrease in the percentage of Cu^{2+} transport due to the diminished complexing ability of the carrier for the protonated EES at the interface of the source phase/membrane phase. At higher pH values, Cu^{2+} ions precipitated. The subsequent experiments were carried out at pH 6.0 of the source phase.

Effect of Carrier Concentration

Metal ions extraction in a liquid membrane system can be accelerated by a carrier mediated transport. Thus, the effect of EES on the transport efficiency of Cu^{2+} ions in the concentration range of $0.0 - 1.0 \times 10^{-2}$ mol L^{-1} has been investigated and the results are illustrated in Fig. 3. Evidently, in the absence of EES in the membrane phase, no significant movement of Cu^{2+} ions through the chloroform was observed. The transport efficiency of Cu^{2+} rises

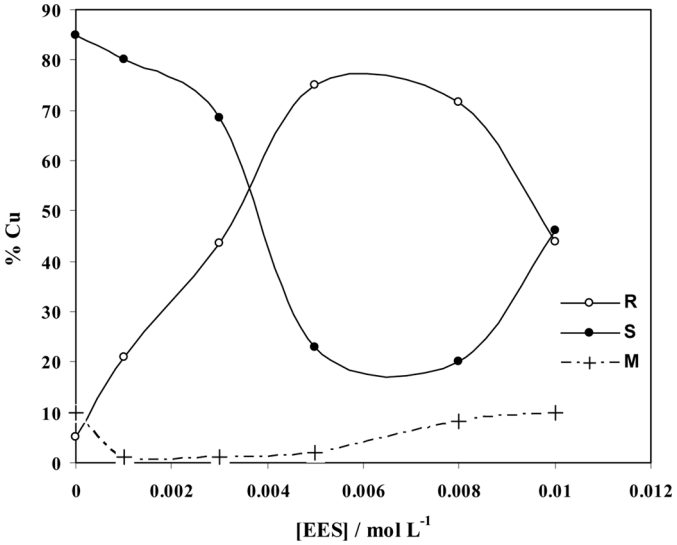

FIG. 3. Effect of carrier concentration on Cu^{2+} ions transport efficiency (Conditions: Source phase: 5 mL of 1.0×10^{-4} mol L^{-1} Cu^{2+} and SCN^- 1.0×10^{-2} mol L^{-1} at pH 5; Membrane phase: 20 mL of EES at different concentrations in chloroform; Receiving phase: 10 mL of 1.0×10^{-2} mol L^{-1} of L-histidine at pH 7; Time: 5 h).

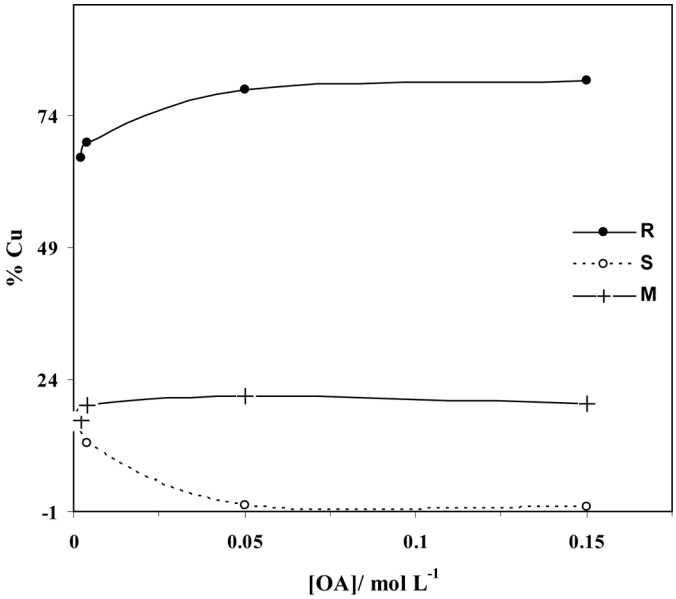

FIG. 4. Effect of OA concentration on Cu^{2+} ions transport efficiency (Conditions: Source phase: 5 mL of 1.0×10^{-4} mol L^{-1} Cu^{2+} and 1.0×10^{-2} mol L^{-1} KSCN at pH 5; Membrane phase: 20 mL of 5.0×10^{-3} mol L^{-1} of EES and OA at different concentration in chloroform; Receiving phase: 10 mL of 1.0×10^{-2} mol L^{-1} L-histidine at pH 7; Time: 5 h).

with increasing carrier concentration in the organic phase up to 5.0×10^{-3} mol L^{-1}. Further increase in carrier concentration shows a declining trend in the transport efficiency. This may be attributed to the strong binding of Cu^{2+} to the carrier and difficulty in delivering the Cu^{2+} ions into the receiving phase or increasing in viscosity of the membrane and a longer diffusion path of the complex. Thus, 5.0×10^{-3} mol L^{-1} of the carrier concentration was selected for the next steps.

Effect of the Nature and Concentration of Additive

It should be mentioned that the addition of a long-chain fatty acid like oleic acid, as an additive to the membrane phase, enhances the transport efficiency thereby causing an increase in the lipophilicity of the membrane (33,34). Another possibility is that the fatty acids can form an inverse micelle (35,36) inside the organic phase, trapping the carrier molecule and its Cu^{2+} complex together, so, ions transport occurs easily across the membrane. Thus, three fatty acids, i.e., oleic, palmetic, and stearic acids were selected and their effects on the Cu^{2+} ions transport were investigated. The outcomes revealed that OA resulted in a higher transport percentage of Cu^{2+} ions than the other chosen fatty acids. It should be noted that neither EES nor OA alone can quantitively transport Cu^{2+} ions through the liquid membrane. A synergistic effect in transport efficiency of Cu^{2+} ions could be observed by using EES in the presence of oleic acid. The optimized concentration of OA was found to be 5.0×10^{-2} mol L^{-1}(Fig. 4).

Effect of the Stripping Agent Concentration

The relation between the histidine concentration and the transport efficiency of Cu^{2+} ions into the receiving phase was examined in the concentration range of

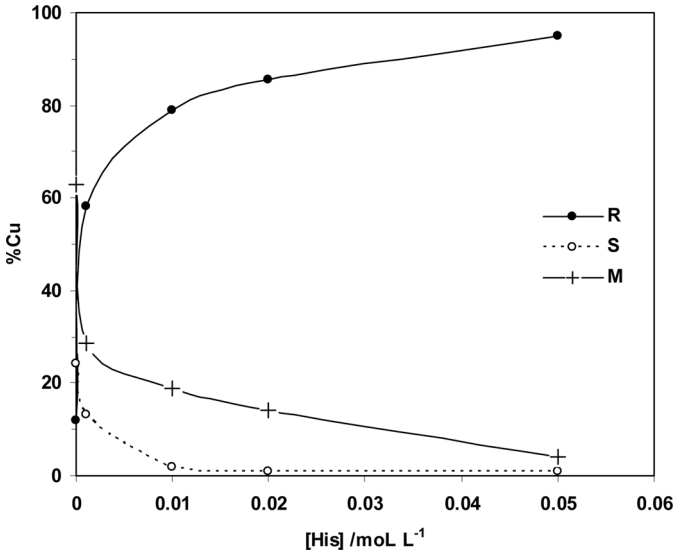

FIG. 5. Effect of L-histidine concentration in receiving phase on Cu^{2+} ions transport efficiency (Conditions: Source phase: 5 ml of 1.0×10^{-4} mol L^{-1} Cu^{2+} and 1.0×10^{-2} mol L^{-1} KSCN at pH 5; Membrane phase: 20 mL of 5.0×10^{-3} mol L^{-1} of EES and 5.0×10^{-2} mol L^{-1} OA in chloroform; Receiving phase: 10 mL of L-histidine at different concentration at pH 7; Time: 5 h).

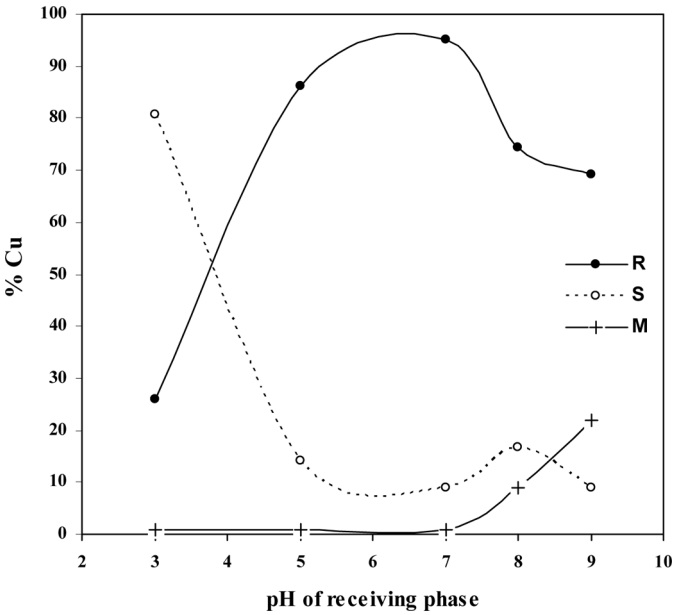

FIG. 6. Effect of pH of receiving phase on Cu^{2+} ions transport efficiency (Conditions: Source phase: 5 mL of 1.0×10^{-4} mol L^{-1} Cu^{2+} and 1.0×10^{-2} mol L^{-1} KSCN at pH 5; Membrane phase: 20 mL of 5.0×10^{-3} mol L^{-1} of EES and 5.0×10^{-2} mol L^{-1} OA in chloroform; Receiving phase: 10 mL of L-histidine 5.0×10^{-2} mol L^{-1} at different pH; Time: 5 h).

1.0×10^{-3} –1.0×10^{-1} mol L^{-1} and the results are shown in Fig. 5. As can be seen, an increase in the histidine concentration causes the transport efficiency of Cu^{2+} to increase, but further elevation in histidine concentration levels above 5.0×10^{-2} mol L^{-1} results in no improvement in the efficiency of Cu^{2+} transport. So, the concentration of 5.0×10^{-2} mol L^{-1} was selected as an optimum concentration and was used for further studies.

Effect of the Receiving Phase pH

The acidity of the receiving phase was varied to achieve maximum transport. The results are illustrated in Fig. 6. It is apparent that the transport efficiency of Cu^{2+} ions increases accordingly with the pH up to 7.0 but then decreases. Hence, pH 7.0 was chosen for further studies. At lower pH values, a decrease in transport efficiency of Cu^{2+} ions may be due to low complexing ability of the amino acid of histidine. At higher pH values, Cu-His-OH species (with the log k_f of 2.7 vs. Cu $(His)_2$ species with log k_f of 18.0) is formed and the transport efficiency decreases (32).

Time Dependence of Cu^{2+} Transport

Time dependence of Cu^{2+} transport through the liquid membrane containing EES under the optimized experimental conditions was also examined. Figure 7 shows a gradual increase in metal concentration in the receiving phase along with a sharp decrease in Cu^{2+} concentration of the source phase during the 3 hours of transport, meaning that 30% of Cu^{2+} remains in the organic phase but 10% will be left over in the source phase. The fluxes (number of mmole diffusing per unit area per unit time) at the interfaces between the source and membrane phases; and the membrane and receiving phases were found to be 5.3×10^{-9} and 3.2×10^{-9} mmole $cm^{-2} s^{-1}$, respectively, indicating that the transport kinetics is controlled by the stripping of Cu^{2+} ions from the membrane to the receiving phase. Under the optimum conditions, about 94% of the total Cu^{2+} ions were transported into the receiving phase after 5 h. Beyond 5 h, a slight decrease in transport efficiency is seen most probably due to back extraction of Cu^{2+} into the membrane phase. The reproducibility of Cu^{2+} transport

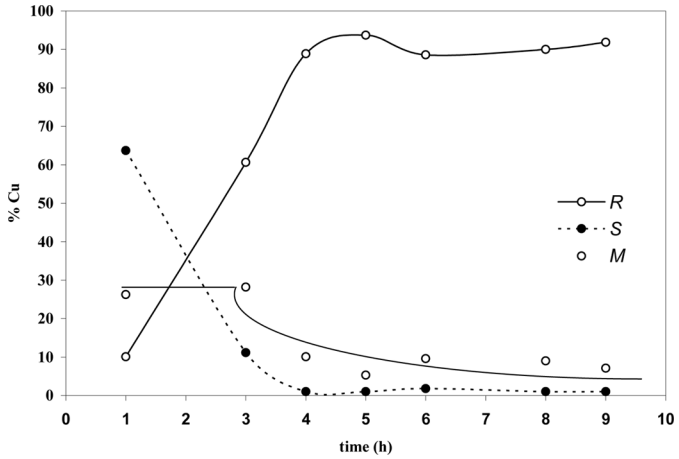

FIG. 7. Effect of time on Cu^{2+} ions transport efficiency under optimum condition.

from eight replicated measurements under optimum condition was found to be ±1.8%.

Mechanism of Ion Transport

Based on our findings, a mechanism is proposed for the transport of Cu^{2+} ions across the bulk liquid membrane. Attracting OA from the bulk organic solvent to the interface of source phase/membrane by $Cu(SCN)_4^{2-}$ favors the appearance of Cu^{2+}-oleate complex, a more stable association of $(K^+\text{-EES})_2Cu(SCN)_4^{2-}$ is formed and distributes preferentially into the organic membrane. At the interface between the membrane and receiving phases, the stripping agent that is, histidine, constitutes a stable Cu^{2+} complex and removes Cu^{2+} from its anionic complex. The released carrier diffuses back across the membrane and will be available at the membrane–source interface maintaining its presence and continues the transport of Cu^{2+} ions until its concentration becomes too low and unable to form Cu^{2+}-EES complex.

Selectivity of the Bulk Liquid Membrane

The selective extraction is a key point when mixtures of different metal species having the same valence are involved. In this study, ternary or quaternary mixtures of the metal ions in the presence of Cu^{2+} ions in the source phase were used to probe the selectivity of the membrane system. The results for the competitive transport of 0.5 mmol of Cu^{2+} ions and equimolar of some foreign cations in the source phase are summarized in Table 3. We found that there are no significant interferences from other studied metal ions on Cu^{2+} ions transport efficiency. Although Zn^{2+} ions form a strong complex with EES, the percentage of transported Zn^{2+} ions were minor. In addition, EES has the ability to extract Ni^{2+} from the

TABLE 3

Selectivity of the membrane phase (Conditions: Source phase: 5 ml of 1.0×10^{-4} mol L^{-1} Cu^{2+} and equimolar of other cations and 1.0×10^{-2} mol L^{-1} KSCN at pH 6; Membrane phase: 20 mL of 5.0×10^{-3} mol L^{-1} of EES and 5.0×10^{-2} mol L^{-1} oleic acid in chloroform; Receiving phase: 10 ml of L-Histidine 5.0×10^{-2} mol L^{-1} at pH 7. Time: 5 h)

Cation	% Metal in S	% Metal in R	Cation	% Metal in S	% Metal in R
Mixture 1			Mixture 2		
Cu^{2+}	0.0	93.1	Cu^{2+}	0.0	95.7
Zn^{2+}	96.1	0.0	Zn^{2+}	96.0	0.0
Co^{2+}	98.1	0.0	Cd^{2+}	93.5	0.0
Mixture 3			Mixture 4		
Cu^{2+}	0.0	96.3	Cu^{2+}	8.7	91.8
Cd^{2+}	95.3	3.5	Cd^{2+}	97.0	7.0
Co^{2+}	98.6	0.0	Ni^{2+}	83.5	1.0
Mixture 5			Mixture 6		
Cu^{2+}	8.0	92.5	Cu^{2+}	11.0	91.1
Co^{2+}	96.2	1.7	Ni^{2+}	92.0	0.0
Ni^{2+}	90.9	0.0	Zn^{2+}	95.0	4.0
[a]Mixture 7			[b]Mixture 8		
Cu^{2+}	9.5	94.6	Cu^{2+}	6.1	95.6
Ni^{2+}	99.5	1.0	Ni^{2+}	99.8	1.0
Co^{2+}	99.0	2.0	Co^{2+}	99.2	3.0
Mixture 9			Mixture 10		
Cu^{2+}	0.0	92.9	Cu^{2+}	10.2	90.5
Cd^{2+}	96.5	0.0	Ni^{2+}	94.1	0.0
Co^{2+}	99.2	0.0	Co^{2+}	91.0	5.0
Zn^{2+}	95.0	3.0	Zn^{2+}	95.0	7.2
Mixture 11					
Cu^{2+}	8.8	92.4			
Ni^{2+}	97.5	0.0			
Cd^{2+}	89.0	7.0			
Zn^{2+}	94.0	6.0			

[a]Source phase, 10 mL of 1.0×10^{-4} mol L^{-1} Cu^{2-}, 1.0×10^{-3} mol L^{-1} of other cations.
[b]Source phase, 10 mL of 1.0×10^{-4} mol L^{-1} Cu^{2+}, 5.0×10^{-3} mol L^{-1} of other cations.

source phase, but its concentration in the receiving phase at the end of the process was low and most of the Ni^{2+} remained in the organic phase. We concluded that thermodynamic equilibrium and ion transport kinetics from the aqueous source phase to the organic membrane dictate the membrane selectivity. Thus, the difference in the kinetics behaviors of the components can explain the degree of selectivity.

CONCLUSIONS

Erythromycin ethyl succinate could be used as a carrier to selectively transport Cu^{2+} ions. By maintaining the pH of the source phase at 6.0 and receiving phase at 7.0, the maximum transport efficiency of Cu^{2+} ions was $93.5 \pm 1.8\%$ in 5 hours. This study showed that the EES can transport Cu^{2+} ions and deliver them to L-histidine much better than other transition metal ions. Our method can be used as a wastewater treatment. Additionally, interaction of Cu^{2+} ions with EES will affect the performance of EEs in living systems. Such study is important in drug administration, and could be extended to other chelating drugs and their applications in the biological and environmental sciences.

ACKNOWLEDGEMENTS

The support of this work by the Research Council of the University of Birjand is gratefully acknowledged. The authors are thankful to Razi Pharmaceutical Company for providing authentic Erythromycine ethyl succinate.

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