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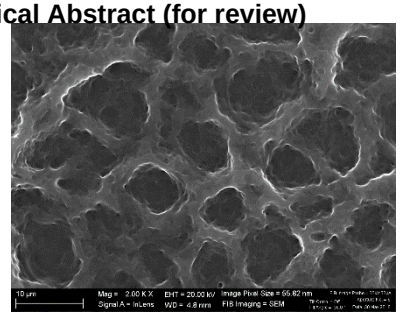
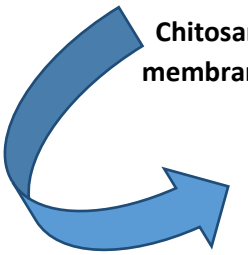
Abstract: A chitosan membrane composed by 60% (w/w) chitosan and 40% (w/w) Aliquat®336 has been proposed as a new biopolymeric support for electromembrane extraction. The new support has been characterized by Scanning Electron Microscopy, resulting a 30-35 □m thickness. Amoxicillin, nicotinic acid, hippuric acid, salicylic acid, anthranilic acid, ketoprofen, naproxen and ibuprofen have been successfully extracted using the proposed support. Better enrichment factors were obtained for the acidic polar analytes than for the non-steroidal anti-inflammatory compounds (ranging from 118 for hippuric acid and 20 for ibuprofen). Electromembrane extraction was developed applying a DC voltage of 100 V, 1-octanol as supported liquid membrane and 20 min of extraction. The target analytes have also been satisfactorily extracted from human urine samples, providing high extraction efficiencies. The chitosan membrane is presented as a promising alternative for supporting liquid membrane compared to commonly used materials for this purpose.

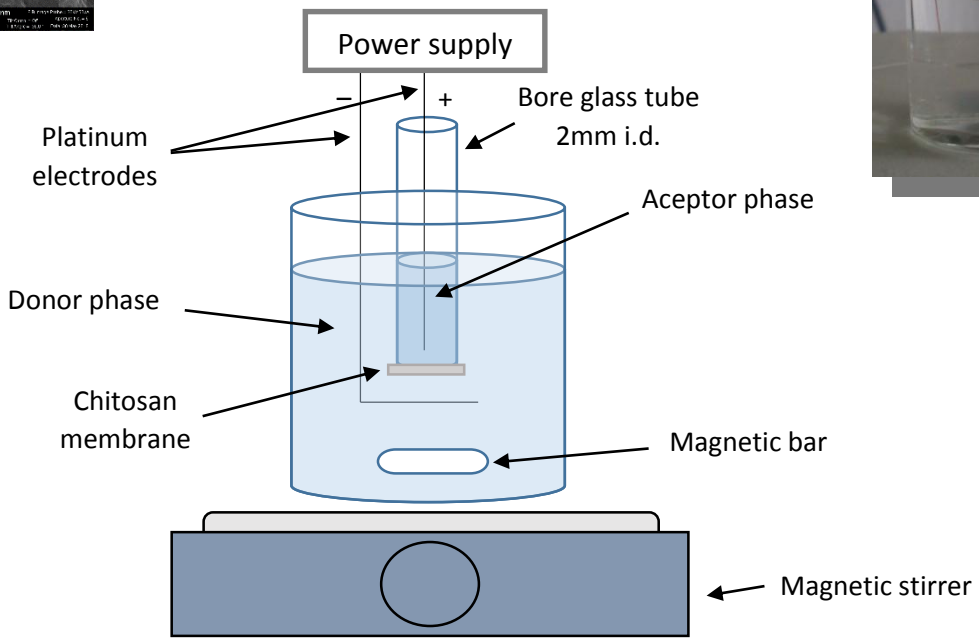
Highlights

- A new alternative biopolymeric support for electromembrane extraction is proposed
- The support consists in chitosan/Aliquat®336 (60:40% w,w) membrane, 35 µm thickness
- Non steroidal anti-inflammatory and polar acidic drugs have been extracted
- The validated EME procedure has been successfully applied in human urine samples

*Graphical Abstract (for review)







Chitosan tailor-made membranes as biopolymeric support for electromembrane extraction

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Abstract

A chitosan membrane composed by 60% (w/w) chitosan and 40% (w/w) Aliquat®336 has been proposed as a new biopolymeric support for electromembrane extraction. The new support has been characterized by Scanning Electron Microscopy, resulting a 30-35 μm thickness. Amoxicillin, nicotinic acid, hippuric acid, salicylic acid, anthranilic acid, ketoprofen, naproxen and ibuprofen have been successfully extracted using the proposed support. Better enrichment factors were obtained for the acidic polar analytes than for the non-steroidal anti-inflammatory compounds (ranging from 118 for hippuric acid and 20 for ibuprofen). Electromembrane extraction was developed applying a DC voltage of 100 V, 1-octanol as supported liquid membrane and 20 min of extraction. The target analytes have also been satisfactorily extracted from human urine samples, providing high extraction efficiencies. The chitosan membrane is presented as a promising alternative for supporting liquid membrane compared to commonly used materials for this purpose.

Keywords: chitosan; polymeric support; electromembrane extraction; high polar compounds; pharmaceuticals

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Introduction

Chitosan is a polysaccharide derived from chitin, which can be obtained from natural sources. Some of them are aquatic organisms with hard skeletons like crabs, shrimps, lobsters or even from different microorganisms such as fungi. From a chemical point of view, it is obtained after a deacetylation process of chitin (N-acetyl-D-glucosamine units) [1]. This process is usually performed in alkaline media or by means of enzymatic reactions, obtaining a variable degree of deacetylation from 70 to 95% [2-4]. This is one of the most important features of the chitosan because it determines many of its physical and chemical properties as well as its biological activity [5]. It is also a hygroscopic pseudoplastic biopolymer which is able to interact through hydrogen bonding due to the presence of free hydroxyl and amine groups of its polymeric chain. It is soluble in inorganic acids (pH<6) and in several organic acids, being not soluble in water and alkali solutions. Therefore, it is usually prepared by dissolving it in aqueous acetic acid (1% v/v, pH 4). Chitosan solubility is highly affected by the molecular weight, the deacetylation degree, the temperature and concentration. The presence of free polar groups in the polymeric chain determines the chemical reactivity of the chitosan [1]. Other interesting properties such as biocompatibility, chelating or gelation ability and antimicrobial activity have also been described [6-8].

Many organic polymers have been described for preparing membranes with pharmaceutical applications and chitosan presents many advantages in this field [9]. On one hand, the hydrophilic nature of this biopolymer and on the other hand its ability of forming hydrogel structures with high water permeability, make chitosan an excellent candidate for preparing membranes with different applications such as immobilization of microorganisms, tissue engineering, human enzymes degradation or drug encapsulation [10,11].

The supports commonly used in electromembrane extraction (EME) (mainly polypropylene) play a role of passive porose supports of the liquid membranes. In the last years, an emerging trend consists in modifying the chemical structure of the classical inert supports as well as the addition of active substances for improving the efficiency of the extraction. Moreover, an emerging challenge implies the development of new materials having an active role in the EME procedure. Within this realm, new supports of different chemical nature have been recently introduced for carrying out EME experiments with satisfactory results. Polymer inclusion membranes [12-14], polypropylene hollow fiber reinforced with carbon nanotubes [15-16] or decorated with silver nanoparticles [17], nanostructred supports [18], agarose gels [19-20] or agar films containing silver nanoparticles [21] and polyacrilamide gels [22] have been valid alternatives for EME procedures to the classical polypropylene materials.

The synthesis of chitosan-based membranes seems to be a promising alternative as active support of supported liquid membrane (SLM), according to the previously

described characteristics of this biopolymer. In this work, a new chitosan-based membrane has been synthesized for the first time as support for SLM in EME. With this purpose, amoxicillin (AMX), nicotinic acid (NIC), hippuric acid (HIP), salicylic acid (SAL), anthranilic acid (ANT), ketoprofen (KTP), naproxen (NAX) and ibuprofen (IBU) have been used to test the feasibility of this new support. Besides, the EME procedure has been validated and satisfactorily applied to the extraction of the target analytes in human urine samples.

Experimental

Chemicals and reagents

All chemicals and reagents used in this work were of analytical grade. Chitosan of different molecular weights (low: 110-150 kDa, medium: 140-200 kDa and high:310-375 kDa) were purchased from Aldrich (Madrid, Spain). AMX, NIC, SAL, 1-octanol, dihexyl ether (DHE), nitro-phenyl-octyl-ether (NPOE) and Aliquat®336 were obtained from Fluka-Sigma-Aldrich (Madrid, Spain). ANT and HIP were obtained from Alfa Aesar (Karlsruhe, Germany). KTP, NAX, IBU, hydrochloric acid, acetic acid, sodium hydroxide, sodium acetate, ammonia, methanol, ammonium chloride and tris(2-ethylhexyl)phosphate were obtained from Merck (Darmstadt, Germany). Working solutions of NIC, AMX, HIP and ANT were prepared daily from stock aqueous solutions (400 mg L^{-1}). Aqueous solutions of SAL, KTP, NAX and IBU were also daily prepared from stock methanolic solutions of the same concentration. Ultrapure water from Milli-Q Plus water purification system (Millipore, Billerica, MA, USA) was used for preparing all solutions.

Chitosan membrane synthesis

The following procedure was used for the chitosan membrane preparation: 0.1 g of high molecular weight chitosan (310-375 KDa) was dissolved in 25 mL acetic acid 1% (v/v), being the pH of the resulting solution approximately equal to pH 3. Then, the pH was adjusted by carefully adding a solution of sodium hydroxide 1.0 M (drop by drop) until pH 5.0. On the other hand, 0.066 g Aliquat®336 was weighted and placed in a vial, where 25 mL of the chitosan solution was added under continuous stirring. Afterwards, this solution was poured onto glass Petri dishes (90 mm diameter), which were placed into a vacuum stove (35ºC) until complete evaporation of the solvent.

In order to neutralize acetic acid residues, synthesized membranes were washed with 10 mL of sodium hydroxide 0.1 M and 10 mL of water for 30 min. The washing process was repeated twice to ensure the complete elimination of acetic acid. Finally, the cleaned membrane was placed again in the vacuum stove until dryness and, subsequently, it was removed from the Petri dishes. The composition of the resulting

membranes was 60% (w/w) chitosan and 40% (w/w) Aliquat®336, with different thickness according to the solution volume added to the Petri dishes.

EME procedure

The electromembrane extraction of the target analytes was carried out using a self-made device, previously developed in our laboratory for the determination of NSAIDs by using agar films as support of the liquid membrane [21]. In the present work, the synthesized chitosan membranes described above were used as the support for SLM. It was cut into 5 x 5 mm pieces and each of them were glued to a bore glass tube (2.5 cm of lenght, 4 mm of external diameter and 2 mm of internal diameter) by using epoxy resin (Araldit Standard Ceys®, Barcelona, Spain).

Afterwards, the membrane was impregnated with 5.0 μL of 1-octanol. Once removed the excess of organic solvent with a wipe, 50 μL of ultrapure water (acceptor phase) were introduced inside the tubes using a microsyringe. Then, this arrangement was placed into a 10 mL vial containing an aqueous solution of the target analytes (donor phase). In order to develop the EME procedure, two platinum electrodes (0.25 mm diameter) were introduced into the donor and acceptor phases, keeping an average distance of 2 mm between them. A three channels Laboratory DC Power Supply (Benchtop Instrument, Pennsylvania, USA) with programmable voltage in the range 1-120 V was used for connecting both electrodes. In order to register the measured current during the extraction process, a digital multimeter was employed. Data acquisition were performed with an automatized system controlled by a personal computer during all the extraction time. Supplementary Figure 1 shows the described device used for carrying out EME.

A DC potential of 100 V was applied during 10 min with constant stirring at 600 rpm of the donor phase. The average current registered during the extraction time was in the range of 95-460 μA. Once EME finished, the acceptor phase was collected with a microsyringe and 20 μL were injected in the HPLC system.

The assembly of the EME device is simple, fast and low cost, being possible to make several devices at one time without special requirements. For obtaining the best performance, it is recommended do not reuse the device to ensure a high efficiency on the separation procedure.

HPLC-DAD determination

The HPLC separation of the target analytes were carried out using a LabChrom® VWR-Hitachi (Barcelona, Spain) liquid chromatograph, equipped with a quaternary L-7100 pump and a L-7455 diode array detector (DAD). Sample injection (20 μL) was done using a L-2200 autosampler. The chromatographic column was a LiChroCART® 75-4 Purosphere® STAR RP-18e 3 μm (75 mm×4.0 mm i.d) (VWR, Darmstadt,

Germany), with a Kromasil® 100 Å, C18, 5 μm (15 mm×4.6 mm i.d.) (Schrarlab S.L., Barcelona, Spain) guard column. During elution, column was thermostated at 20°C.

The chromatographic separation was performed using a mobile phase consisting of a mixture of 0.05% (v/v) formic acid aqueous solution (component A) and acetonitrile (component B) at 0.8 mL min^{-1} flow rate. A gradient elution was applied from 99% to 90% (v/v) of the A component during 3 min. Subsequently, those conditions are held during 1 min. Afterwards, the component A is decreased linearly until 60% (v/v) in 0.1 min maintaining these conditions during 12 minutes and finally, the composition of A decreased until 0% in 7 minutes. The initial conditions are restored waiting for 5 min before the next injection.

DAD detection was employed to quantify the selected analytes, by using the following monitoring wavelengths for each compound: 230 nm for AMX, 260 nm for NIC, 235 nm for HIP, 235 nm for SAL, 224 nm for ANT, 255 nm for KTP, 224 nm for IBU and 230 nm for NAX

Results and discussion

In order to carry out preliminary EME assays, 10 mL of a standard aqueous solution of the target analytes (200 μg L^{-1}) was used as donor phase and 50 μL of an aqueous solution was used as acceptor phase.

Composition and thickness of chitosan membrane

The final thickness and composition of the synthetized membrane can be mainly affected by three factors: a) the molecular weight of the biopolymer, b) the chitosan/Aliquat®336 ratio and total volume of the chitosan/Aliquat®336 poured in the Petri dish and c) the medium pH during the membrane synthesis. The influence of each factor has been investigated separately to achieve the best performance in the EME procedure. Scanning Electron Microscopy (SEM) using a Zeiss Auriga (Carl Zeiss Microscopy, Oberkochen, Germany) was used for characterizing membranes in terms of thickness and homogeneity.

a) Chitosan molecular weight

For this purpose, 0.1g of chitosan of three different molecular weights (low, medium and high, respectively) were dissolved in 25 mL of acetic acid aqueous solution 1% (v/v). This solution were poured out into 90 mm diameter Petri dishes and dried as described in Experimental Section. SEM images as well as EME tests revealed that high molecular weight chitosan membranes presented a more homogeneous surficial distribution of the biopolymer, leading to more reproducible EME results. Thus, chitosan of high molecular weight were chosen for the following steps.

b) Chitosan/Aliquat®336 ratio and total volume

Different chitosan/Aliquat®336 w/w ratios (90:10; 60:40 and 30:70) were tested, obtaining membranes with variable flexibility. After developing EME, it was observed that the amount of Aliquat®336 only affected to the physical properties of the membrane, but not to the efficiency of the extraction. From these results, it is interesting to point out that Aliquat®336 mainly plays a plasticizer role instead of effective carrier. For this reason, the optimal ratio was 60:40 (w/w) for an easier manipulation and insertion of the membrane in the experimental device.

The total volume of the mixture chitosan/Aliquat®336 is responsible of the membrane thickness. To test the influence of the total volume on the thickness of the membrane used different volumes of mixture (10, 15, 25 mL) were poured out into the Petri dishes. When 10 and 15 mL were added, the synthetized membranes were very fragile showing little consistency, complicating their subsequent manipulation to place it in the experimental device. When using 25 mL, the obtained membranes had a suitable consistency facilitating their handling, having a thickness of 30-35 μm, estimated from SEM micrograph images.

The SEM micrograph images (Figure 1a) show that the outer side of the membrane has a different morphology that the internal one, probably due to the last stage of the solvent evaporation process. Therefore, the thickness measurements were made at two different distances, corresponding to the inner (H2) and outer (H1) regions of the membrane. A micrograph image showing the pore size homogeneity in the thicker chitosan membrane can be observed in Figure 1b.

c) The influence of medium pH

The chitosan contains ionizable amine groups in its chemical structure showing a pk_a value in the range of 6.1-6.5 depending on the degree of N-deacetylation [9, 23]. At pH > 6.5, chitosan solutions become hydrogels, being this process irreversible. Thus, the pH of solutions in which the polymer is solved (pH 4.0, acetic acid 1% v/v) could have a great influence in the posterior extraction of the target analytes. For this purpose, the pH of the chitosan solutions was investigated between 4.0 and 6.4 and subsequently chitosan membranes were synthetized, as it is mentioned above. EME of the target analytes were developed using these membranes as support of SLM. The highest enrichment factors were obtained for those membranes prepared at pH 5, being these conditions chosen for subsequent experiments.

Organic solvent for SLM

Dihexyl ether (DHE), 1-octanol, nitrophenyl-octyl ether (NPOE) as well as solvent mixtures (50:50 v/v) were also tested as SLM, developing the extraction at a potential of 50 V during 10 min. When using DHE, lowest enrichment factors were obtained for all the target analytes (from 60 for NIC to 10 for NAX). The addition of NPOE slightly improved the enrichment factors (10% higher), as well as the mixture 1-octanol-NPOE. However, when 1-octanol was used as SLM, compounds poorly extracted with the previous solvents substantially improved their enrichment factors (around 50%).

The effect of Aliquat®336 was previously studied as a component of the synthetized chitosan membrane playing mainly a plasticize role. However, it is well known that Aliquat@336 is an anion carrier, so it could have an active role in the EME process when it is added to the SLM. Thus, mixtures of 1-octanol/Aliquat®336 5% (v/w) and 10% (v/w) were used as SLM without any improvement in the extraction efficiency. This fact concludes that EME was not a carrier mediated extraction.

Influence of pH of acceptor and donor phases and applied voltage

An important variable for the EME efficiency is the pH of acceptor and donor phases. Under determined conditions, electrolysis can occur generating H^+ and OH^- which can affect to the pH of the involved phases, affecting to the extraction development [24-26]. The acceptor phase was studied at a pH 5 (aqueous water solution), 6 (adjusted using a 100 mM acetate/acetic buffer), 10 (adjusted with 100 mM ammonium chloride/ammonia buffer) and pH 12 (10 mM sodium hydroxide solution) while the donor phase was kept fixed at pH 4.6 (aqueous analytes solution). EME was performed for 10 min at 50 V. The highest enrichment factors were obtained for all compounds at pH 5 (see Figure 2) and it is remarkable that this pH value does not changed substantially during EME.

The influence of the donor phase pH was evaluated within the range 2-12, fixing the acceptor phase at pH 5. It can be noticed that in the case of NSAIDs, higher enrichment factors were obtained at pH 4.6, decreasing these ones as the pH was increased (Figure 3). Polar compounds showed high enrichments in the 4.6-7 pH range. Consequently, pH of donor phase was set at 4.6 for further experiments.

Finally, the influence of applied voltage was studied in the range of 10-120 V. The obtained results showed that enrichment factors increased up to 100 V, excepting for IBU and SAL (Supplementary Figure 2). IBU showed the higher enrichment factors at 30 V, decreasing it slightly until 50 V and keeping it constant up to 120 V. SAL showed a high enrichment between 50 and 80 V, maintaining it constant until 120 V. Accordingly, 100 V was selected as applied voltage during EME process.

Influence of time of extraction

Time of EME was studied at 5, 7, 10, 15 and 20 min under optimal conditions obtained in previous sections (pH 4.6 as donor solution, pH 5 as acceptor solution and 100 V). Best results (in terms of enrichment factors) were achieved at 10 min, not observing any high improvement with longer times of extraction.

Using the optimized EME procedure, enrichment factors for the target compounds were as follows: 116 for NIC, 33 for AMX, 118 for HIP, 49 for ANT, 113 for SAL, 43 for KTP, 30 for NAX and 20 for IBU. Taking into account the obtained values, it can be assessed that chitosan membranes are an efficient support for extracting NSAIDs as well as polar drugs by means of electromembrane extraction.

Validation of the EME procedure

The validation process involved the calculation of the following quality parameters: linearity, sensitivity and precision. Supplementary Table 1 shows the calibration data of the chromatographic method, including linear range, limit of detection (LOD) and limit of quantitation (LOQ) for all the analytes. For calculation of LOD and LOQ three times signal to noise ratio and ten times signal to noise ratio, respectively, were considered [27]. It was observed a good linearity in all cases. The values of the linearity were in the range between 98.9% for NIC and 94.0% for AMX. LOD values were within 1.0 μg L^{-1} for KTP and 7.0 μg L^{-1} for IBU. LOQ ranged between 3.0 μg L^{-1} for KTP and 22.0 μg L^{-1} for IBU. In the case of AMX, two linear ranges were obtained at different concentrations, from 9 to 20 μg L^{-1} and from 21 to 80 μg L^{-1}.

For comparison purposes, Table 1 shows the enrichment factors data obtained with polypropylene supports, agarose films, nano-structured supports (Tiss-OH), PIMs and the new proposed support. It is remarkable that high polar acidic compounds as NIC, AMX, HIP, ANT can be only extracted when using Tiss-OH, PIMs and the proposed chitosan membranes. However, enrichment factors obtained using chitosan membranes are higher in all cases. Besides, it also improves the efficiency of the extraction in the case of NSAIDs.

In order to check the suitability of the proposed method for urine analysis, blank human urine samples were spiked at three concentration levels (according to their corresponding linear ranges) of the target analytes. Following, the samples were diluted with ultrapure water (1:1000, v/v) and submitted to the EME/HPLC-DAD procedure. The obtained recoveries are depicted in Table 2. As can be noted, the obtained values were in good agreement with the expected for all the compounds at the different concentration levels. One single day measurements (repeatability) as well as weekly

measurements (three days per week) (intermediate precision) were carried out showing %RSD values between 1-11% and 5-14%, respectively.

Application to real urine samples

Urine samples from volunteers subjected to a single dosage (500 mg) of acetylsalicylic acid (ASA) or IBU (600 mg) were diluted with ultrapure water (1:1000, v/v) and submitted to the EME/HPLC procedure. The corresponding chromatograms are shown in Supplementary Figure 3. Table 3 shows the measured contents of IBU, SAL and HIP at different excretion times after the dosage ingestion, as well as the spiked levels.

The level found for SAL (20.1 mg L^{-1}) was lower than the expected one, being a possible explanation the fact that urine sample was collected only 2h after the intake of ASA. SAL is generated by hydrolysis from ASA being 100% excreted as SAL in a period of time ranging 2-4h after administration [28] with usual levels of hundreds μg mL^{-1} [29]. This urine sample also showed an intense HIP peak. It must be considered that HIP is one of the main human urinary endogenous metabolite, and in certain cases very high urine levels could be correlated to children diabetes, possible toluene intoxication or renal failures [30-32]. It has also been reported that HIP levels in urine can be increased due to the consumption of aspirin or by fruit rich diet [33], which was the case of the volunteer.

It is well known that the complete elimination of IBU occurs after 24h of ingestion, being approximately excreted 10% through urine between 6-8h after intake. The measured IBU content is in agreement with this because the urine sample was collected 7 hours after the dosage. The rest of the IBU is excreted in form of metabolites, mainly as hydroxylates and carboxylates compounds and its conjugates [34-35].

Conclusions

The proposed EME procedure using a new biopolymeric support (chitosan/Aliquat®336 membrane) has been demonstrated to be useful for the electromembrane extraction of polar acidic compounds and non-steroidal anti-inflammatory drugs. It has also been satisfactorily applied to the analysis of human urine samples. The proposed support showed a better performance compared to previously described EME supports.

The obtained results suggest that tailor-made membranes such as the proposed ones could be used as a suitable alternative supports for SLM in EME devices, allowing future structural modifications on demand of the nature of the extracted compounds.

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Captions of Figures

Figure 1. SEM images of chitosan thicker membrane (For details, see text). (1a) Thickness measurement (1b) Homogeneous distribution of the chitosan membrane structure

Figure 2. Influence of the acceptor phase pH at 50V during 10 minutes

Figure 3. Influence of the donor phase pH at 50V during 10 minutes.

Captions of Tables

Table 1. Comparison of enrichment factors using different supports.

Table 2. Recoveries (%) of the target analytes using EME/HPLC procedure from spiked human urine samples.

Table 1

Table 1. Comparison of enrichment factors using different supports.

Analyte	**PP 6S/2**	**PP 1E**	**AgNPs agar films**	**Tiss®-OH**	**PIMs**	**Chitosan membranes**
NIC	*	*	*	25.7	27	116
AMX	*	*	*	20	17.3	33
HIP	*	*	*	20.7	26	118
ANT	*	*	*	*	11.3	49
SAL	0.1	0.2	15.3	28.3	16.7	113
KTP	0.1	0.6	3.4	*	11.7	43
NAX	0.1	0.7	2.5	*	16	30
DIC	0.2	0.6	2.7	*	*	*
IBU	0.2	0.7	2.6	*	12.3	20

Table 2

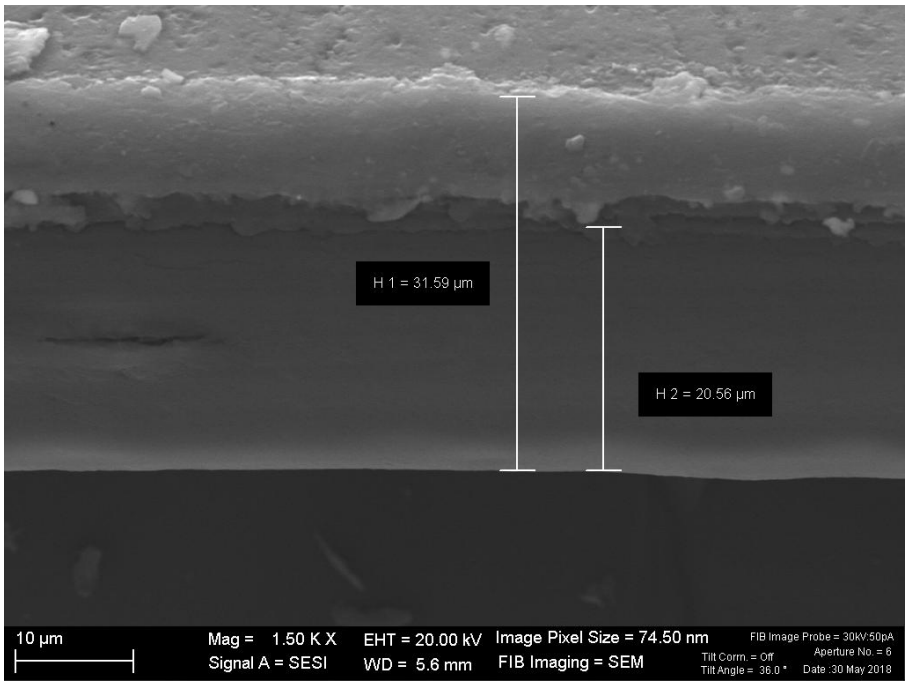
Table 2. Recoveries (%) of the target analytes using EME/HPLC procedure from spiked human urine samples.

	Urine spiked concentration (mg L^{-1})		
Analyte[a]	**10**	**25**	**50**
NIC	80.0	96.1	97.3
AMX	91.2	89.7	95.3
HIP	86.9	103.5	94.6
ANT	85.1[b]	103.2	92.7
SAL	92.4	99.9[c]	–
KTP	93.1[d]	89.8[e]	90.9[c]
NAX	99.1[b]	89.9	80.2
IBU	–	92.8	98.3

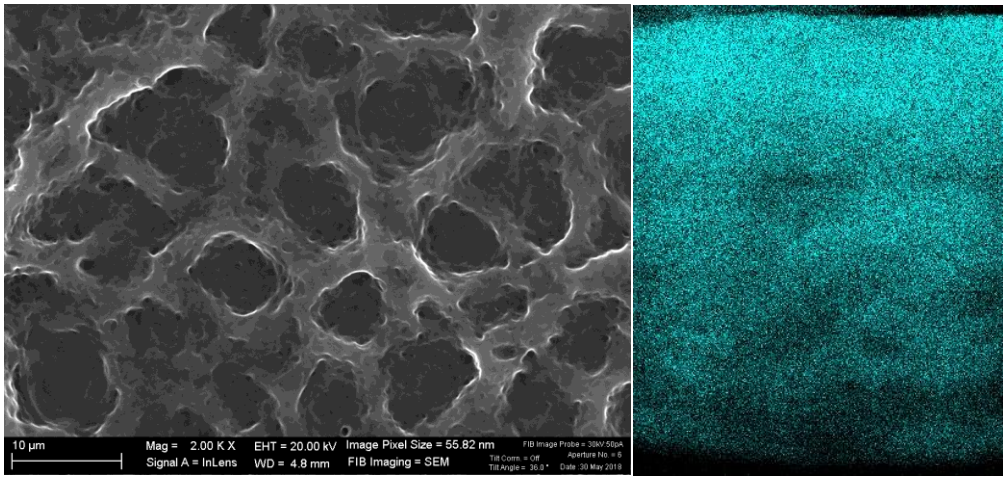
[a]Average of three determinations (RSD < 6%)
[b]15 mg L^{-1}
[c]20 mg L^{-1}
[d]5 mg L^{-1}
[e]10 mg L^{-1}

Figure 1

Figure 1.



(1a)



(1b)

Figure 2

Figure 2

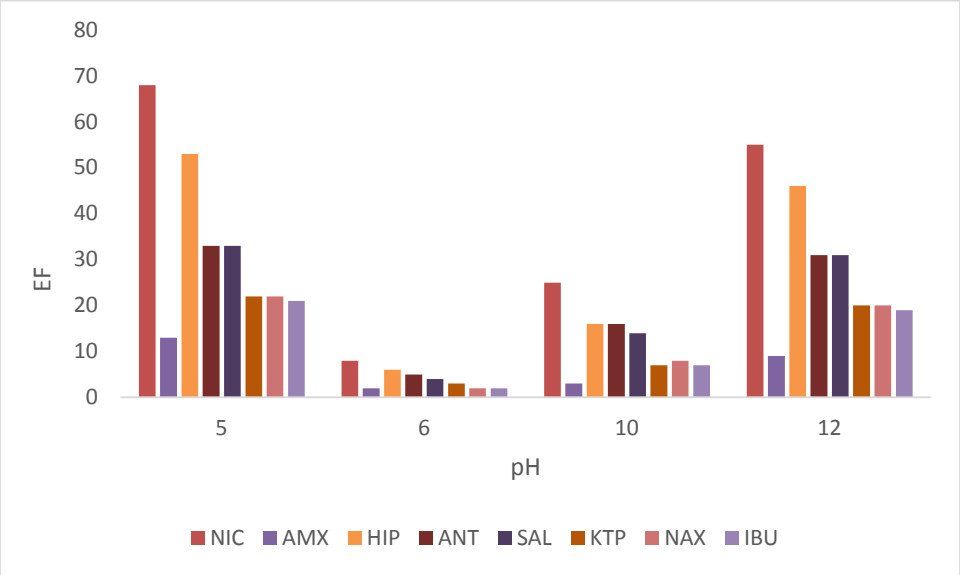
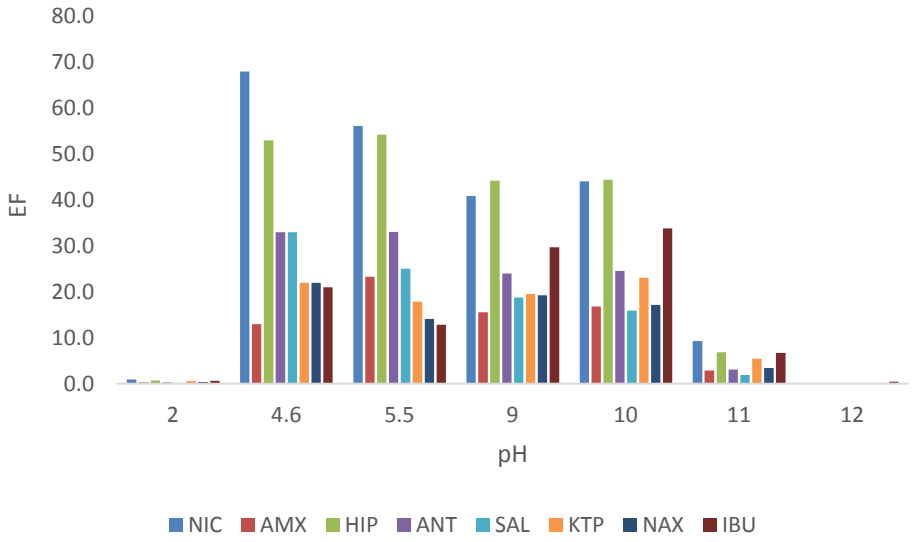
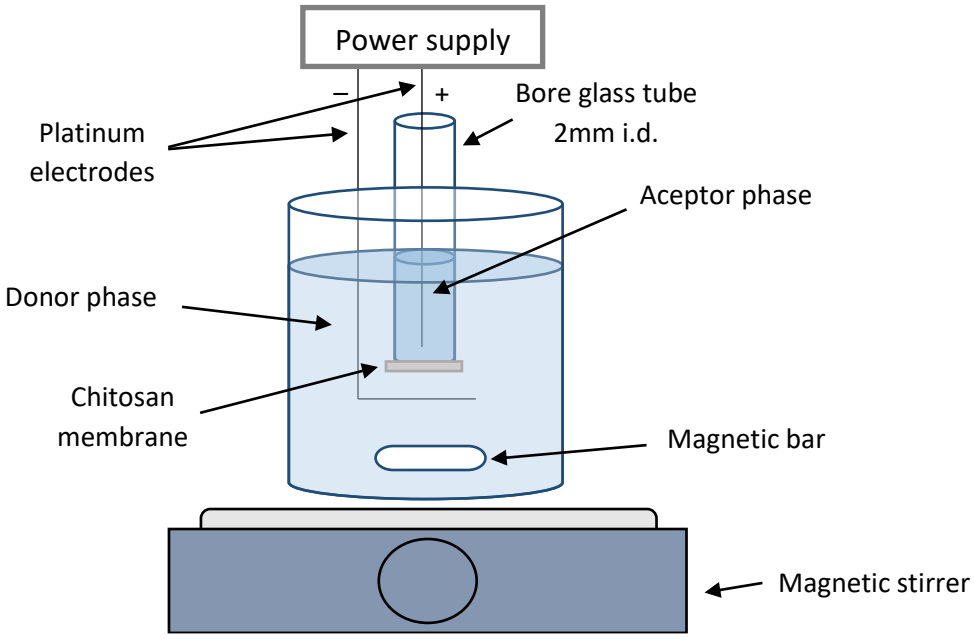


Figure 3

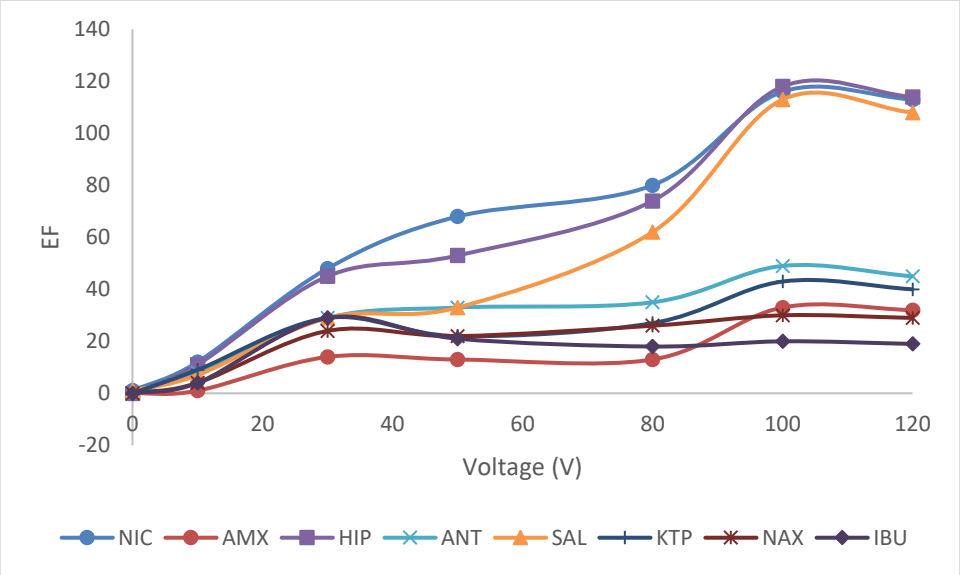
Figure 3



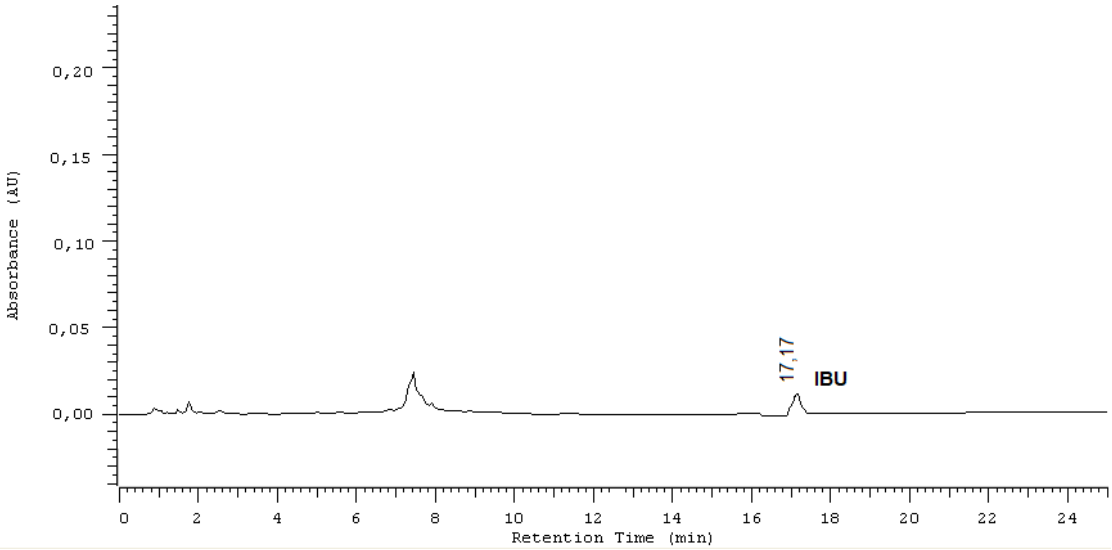
Supplementary Figure 1. EME experimental device.



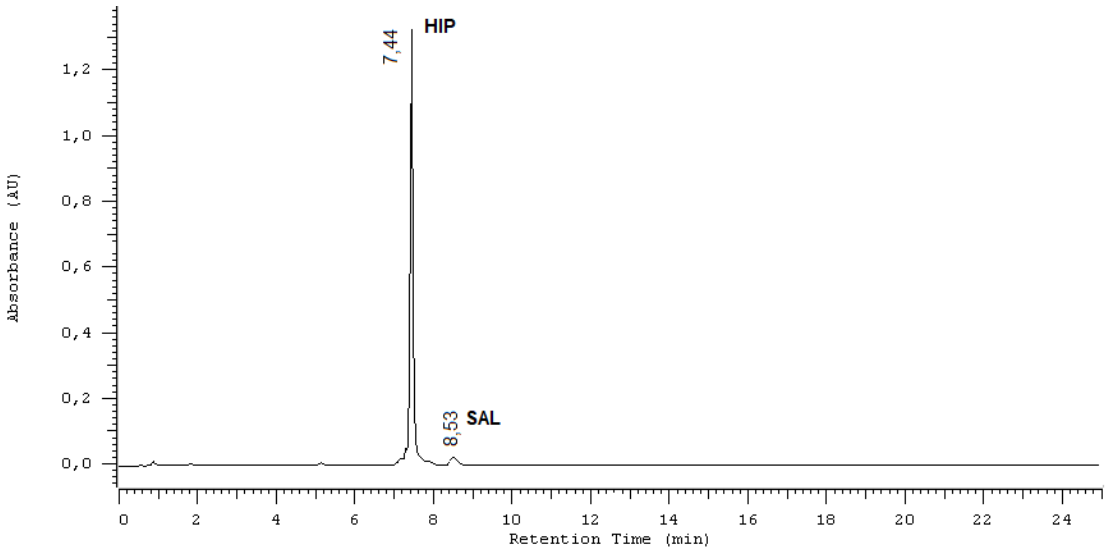
Supplementary Figure 2. Influence of the applied voltage in the efficiency of EME.



Supplementary Figure 3. HPLC chromatograms of human urine samples submitted to the EME procedure. (a) human urine sample collected 7h after an oral administration of 600 mg of ibuprofen (b) human urine sample collected 4h after an oral administration of 500 mg of acetylsalicylic acid.



(a)



(b)

Supplementary Table 1. Calibration data, Limit of Detection (LOD), Limit of Quantitation (LOQ), enrichment factor (EF) and recovery (%) for the analytes.

Analyte	**Linear range ($\mu g\ L^{-1}$)**	**Linearity**		**LOD ($\mu g\ L^{-1}$)**	**LOQ ($\mu g\ L^{-1}$)**	**EF**	**Recovery (%)**
		(%)	**(R^2)**				
NIC	7-100	98.9	0.9987	2.0	7.0	116	58
AMX	9-20 21-80	94.0 96.7	0.9964 0.9989	3.0 6.0	9.0 21.0	33	17
HIP	8-90	98.3	0.9978	2.0	8.0	118	59
ANT	14-100	97.0	0.9956	4.0	14.0	49	25
SAL	6-20	95.8	0.9965	2.0	6.0	113	57
KTP	3-25	98.2	0.9993	1.0	3.0	43	22
NAX	15-100	97.3	0.9978	5.0	15.0	30	15
IBU	22-100	97.1	0.9975	7.0	22.0	20	10