A Novel Approach for the Extraction of Selected Pharmaceuticals From Water using Liquid-Core Microcapsules

M. Whelehan[1], V. Vojinovic[2], V. Breguet[2] and I.W. Marison[1*]

[1] DCU, Glasnevin, Dublin, Ireland.
[2] EPFL, Lausanne, Switzerland.
E-mail: micheal.whelehan2@mail.dcu.ie

Introduction:

The presence and fate of pharmaceuticals in ground and surface water is now been recognized as an emerging issue in environmental science (Heberer, 2002). Pharmaceuticals are used extensively in human and veterinary medicine and can enter the aquatic environment following manufacture, application or ingestion/excretion (Hilton, 2003). Many of the more commonly used drug groups (antibiotics) are used in quite similar amounts to those of many agrochemicals and other organic micro-pollutants but they are not required to undergo the same rigorous testing for environmental fate and effects (Jones 2002).

Treated wastewater is one of the main pathways for enter of pharmaceuticals into the aquatic environment. This is attributed to the inability of sewage treatment plants (STP's) to adequately remove these compounds from sewage influent. Pharmaceuticals not readily degraded in STP's are being discharged as changed or unchanged forms, usually forming complex mixtures of many compounds in treated effluents. This results in the contamination of rivers, lakes, estuaries and rarely, groundwater and drinking water (Fent, 2006).

The ecotoxicological effects of pharmaceuticals accumulating in the aquatic environment on the wildlife and on humans are largely unknown. Although, severe cases of the accumulation of drugs in the environment have been reported in recent years, none of which were seen in hindsight. Oaks *et al* (2004) reported how residues of the anti-inflammatory drug diclofenac in the Pakistan and Indian environment caused the rapid decline of the vulture population. The oriental white-backed vulture has seen a population decline of > 95% since the 1990's and in recent times more catastrophic declines have been seen in other vulture species.

A novel approach to recover herbicides/pesticides from water using liquid-core microcapsules has been reported (Wyss, 2004) and has been verified to successfully and efficiently extract a range of pesticides and herbicides on lab-scale from aqueous solutions. This methodology termed capsular perstraction involves the encapsulation of an organic solvent within an alginate hydrogel. Similar types of capsules have also been used as extraction aids in ISPR-fermentation processes (Stark, 2002).

In this study liquid-core microcapsules having a diameter of 0.5 mm are used as a novel approach to recover four pharmaceuticals from aqueous solutions. The four model pharmaceuticals chosen were sulfamethoxazole (antibiotic), furosemide (diuretic), carbamazepine (neuroactive) and warfarin (anti-coagulant). A solvent, suitable for the extraction of the drugs is first chosen, and is elected based on the partition coefficient of each drug between an aqueous phase and the solvent. Subsequent experiments resulted in the encapsulation of the solvent in a porous hydrogel membrane

composed of alginate, which is used to extract the drugs from aqueous solutions. This study examines the feasibility of extracting pharmaceuticals from water using liquid-core microcapsules.

Materials and Method:

Preparation of Liquid-Core Microcapsules:
Full details of the procedure used to make liquid-core microcapsules has been described elsewhere (Wyss, 2004). Briefly, mononuclear microcapsules were produced by using the prilling technique preformed on an Inotech encapsulator (IEM). The encapsulator was fitted with a concentric nozzle with internal diameter of 200 µm and external diameter of 300 µm. Spherical microcapsules were obtained by the application of a set vibrational frequency with defined amplitude to the co-extruded liquid and collect in gelling bath consisting of $CaCl_2$. Size and size distributions of capsules was determined using a video camera attached to a light microscope interfaced to a PC operating with Cyberview image analysis software. Samples containing up to 200 capsules where taken and the mean size and standard deviation was determined.

Liquid-Liquid Extraction (LLE) and Capsular Perstraction (CP):
LLE and CP were carried-out with a constant volume of organic phase extractant (0.5 ml) and aqueous-phase containing the pharmaceuticals (50 ml), which enabled results to be directly compared. Agitation of the two phases was preformed at 250 rpm. Temperature was controlled at 25 ^{0}C. Samples from the aqueous phase were analyzed for the presence of the pharmaceuticals.

Partition Coefficient and Mass Transfer:
The partition coefficient of the pharmaceuticals between the solvent and organic phase was calculated using Eq. 1, where C_b is the organic concentration and C_{aq} is the aqueous concentration. The concentration of pharmaceutical inside the oil core of the microcapsule is calculated using Eq. 2, where V_{aq} is the aqueous phase volume and V_b is the capsule volume.

$$P = \frac{c_b}{c_{aq}} \qquad [1] \qquad V_{aq}^0 c_{aq}^0 - V_{aq} c_{aq} = V_b \left(c_b - c_0^b \right) \qquad [2]$$

Results and Discussion:

Choice of Organic Phase Extractant (Liquid-Liquid Extraction):
The partition co-efficient is a measure of the solvents capacity for the product, and is defined as the ratio of the product concentration in the solvent to the product concentration in the aqueous phase, at equilibrium. Table 1 below highlights the partition coefficient values for the four drugs between the aqueous and organic phase. Dibutyl sebacate (DBS), oleic acid (OA) and migloyl (MG) where chosen as the organic solvents, based on there high degree of hydrophobicity, with dibutyl sebacate and oleic acid possessing log P_{oct} of 6.2 and 7.7 respectively (Stark, 2003). This high level of hydrophobicity ensures that the mutual solubility between the oils and water at equilibrium is very low.

Table 1. Partition Coefficient of sulfamethoxazole (SMX), furosemide (FM), carbamazepine (CMZ) and warfarin (WF) between water and one the oils, DBS, OA and MG.

	DBS	OA	MG
SMX	17	1.82	3.3
FM	60	15	1.5
CMZ	25	71	5.5
WF	182	35	60

DBS showed the highest level of extraction for most of the drugs, with WF possessing the highest partition for the solvent. The higher rate of extraction compared to the other compounds reflects the considerably higher hydrophobicity of WF (log P_{oct}, 3.5) compared to SMX (log P_{oct}, 0.89), FM (log P_{oct}, 2.03) and CMZ (log P_{oct}, 2.45). From the results it was decided to encapsulate DBS within an alginate membrane for further extraction experiments

Liquid-Liquid Extraction and Capsular Perstraction:

Extraction efficiencies of LLE and CP were compared to each other by incubation of the four test compounds into one solution containing DBS (0.5 ml) and a second solution containing microcapsules with an equal volume of the solvent. Samples were removed from the aqueous phase of both solutions every 10 min so that the level and rate of extraction of both could be compared.

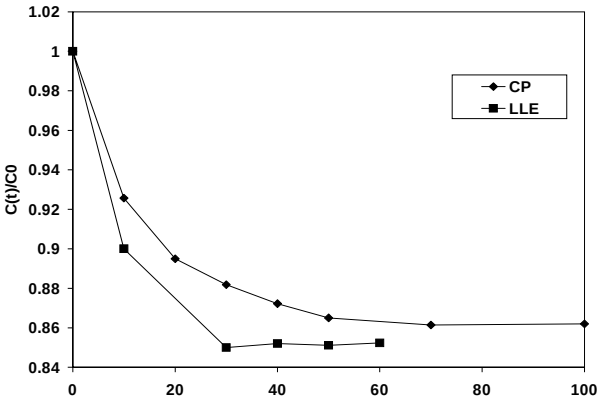

Figure 1. Comparison of LLE and CP extraction efficiencies for SMX in water. Symbols: c(t)/c0. Ratio of concentration at time t to initial concentration.

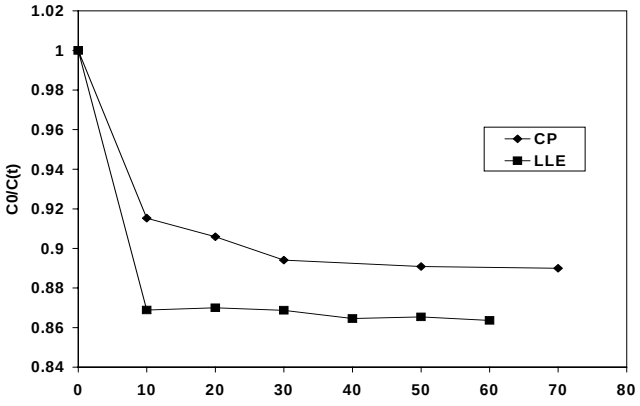

Figure 2. Comparison of LLE and CP extraction efficiencies for CMZ. Symbols: c(t)/c0. Ratio of concentration at time t to initial concentration.

SMX declines to only 14% in the aqueous phase, using both LLE and CP, which is similar to the CMZ result for LLE. In both cases LLE removes the greater amount of pharmaceuticals at a quicker rate. The faster extraction using free oil could be explained by the resistance to mass transfer which can be present in microcapsules as explained by Wyss, 2004. These resistances can be as follows: (1) the aqueous diffusion layer around the capsule; (2) the resistance within the polymer membrane, and

(3) the resistance in the organic-phase core. The low extraction quantity of 14% could be enhanced by increasing the oil volume ratio, which for the present experiment is only at 1%.

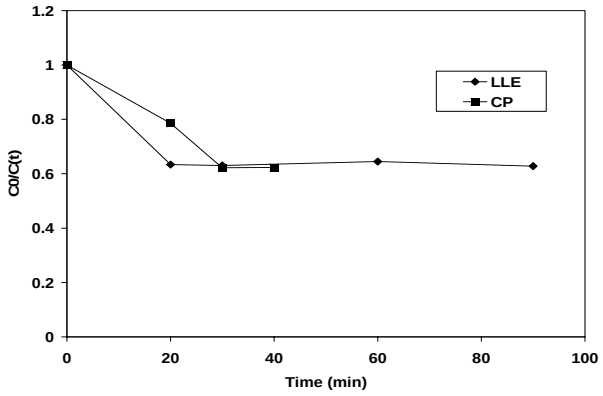

Figure 3. Comparison of LLE and CP extraction eficiencies for FM in water. Symbols: c(t)/c0. Ratio of concentration at time t to initial concentration.

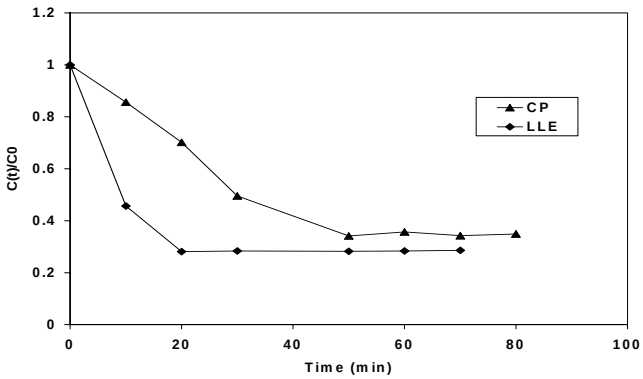

Figure 4. Comparison of LLE and CP extraction efficiencies for WF in water. Symbols: c(t)/c0 Ratio of concentration at time t to initial concentration.

The WF concentration in the aqueous phase rapidly declined to reach an equilibrium of 30% (LLE) and 35% (CP) of its original aqueous phase concentration. Again LLE had a quicker rate of extraction due to mass transfer resistances adherent to capsules. FM reached its equilibrium after only 20 minutes. Complete removal could be achieved very quickly by increasing the oil volume ratio. The greater amounts of WF extracted again can be related to its considerably higher log P_{oct} value compared to the other test compounds.

Conclusions:

The goal of this study was to assess the feasibility of using liquid-core microcapsules to extract pharmaceuticals from water. Although results show that liquid-liquid extraction removed greater amounts of test compounds at faster rates, it is still susceptible to many problems which are overcome by microcapsule use. These drawbacks include the formation of stable emulsions which affect the recovery of product and the re-cycling of the solvent for future use. Also, relatively large quantities of solvent are required, and a system has to be used which involves vigorous agitation to provide a high surface contact between the two phases and thus achieve a high mass transfer.

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