O8-4	**Liquid-core microcapsules: A novel mechanism for compound recovery and purification**	

Whelehan M.[#] and Marison I.W.[*]
Dublin City University (DCU), Glasnevin – Dublin, Rep. of Ireland
[#]micheal.whelehan2@mail.dcu.ie

INTRODUCTION

Liquid-core microcapsules (Figure 2) can be described as miniature sized spherical structures usually < 1 mm in diameter. They consist of one or more liquids (cores) completely enveloped within a defined porous or impermeable membrane(s) (Whelehan 2010a). These particles can be manufactured from a wide range of natural and/or synthetic materials using numerous techniques. Since the 1950's these capsules have been applied successfully to a diverse range of industrial fields such as chemical, pharmaceutical, cosmetics and printing, where they have become well developed and accepted.

Our research group is focused on producing liquid-core microcapsules to a specific criteria, from a range of pre-selected porous membrane (alginate, cellulose sulphate gelatin) and core materials (oleic acid, dibutyl sebacate, vegetable oils), using the concentric jet break-up (vibrating-nozzle) technique (Whelehan 2010a).

In our laboratory these capsules have been effectively used to recover and purify a large range of compounds from a diverse range of environments. The novel and innovative methodology has been applied to a number of areas including water treatment, enzyme technology, bioprocessing, cell culture and downstream processing (Whelehan 2010a, Whelehan 2010b and Wyss 2004), whereby they have helped overcome existence limitations adherent to all these processes.

This short paper will give a brief description of some of the results obtained in our lab when liquid-core microcapsules were applied to the aforementioned areas.

MATERIALS AND METHODS

Production of microcapsules

Liquid-core microcapsules were prepared using the vibrating nozzle technique performed on an Inotech Encapsulator IE-50R (Now EncapBioSystems). From Figure 1: Two liquids, one for the membrane and the liquid-core, are co-extruded together through a concentric nozzle using syringe pumps. This results in a co-extruded concentric jet, which is broken up into spherical monocentric droplets by oscillating the nozzle, which applies a set vibrational frequency with defined amplitude to the jet. The droplets are subsequently hardened by falling into a stirred gelling bath, forming the liquid-core microcapsules. A stroboscopic lamp enables the droplets to be monitored during breakup of the liquid jet. An electrostatic voltage system prevents droplet coalescence by inducing a strong negative charge onto the surface of the droplets, enabling the formation of mono-dispersed microcapsules of equal size, shape and volume (Figure 2).

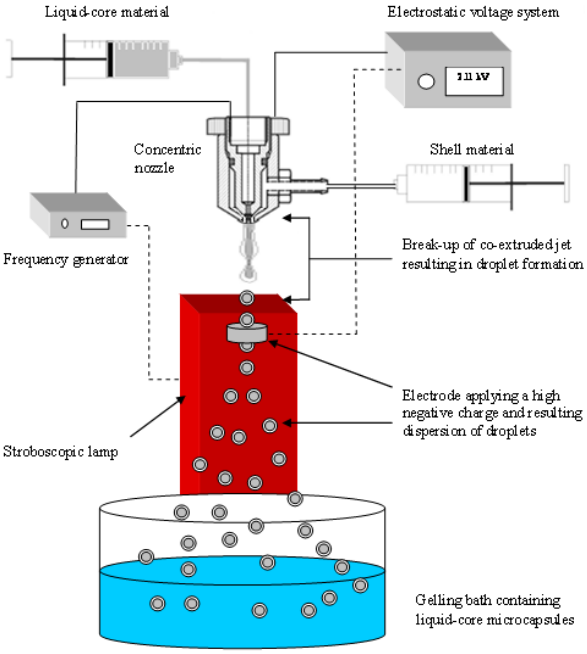

Figure 1: Schematic of vibrating concentric nozzle technique used to produce liquid-core microcapsules.

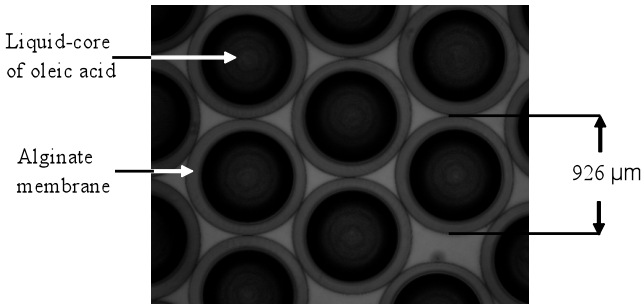

Figure 2: Light microscope image displaying liquid-core microcapsules produced from the setup in Fig. 1.

RESULTS AND DISCUSSION

Removal of pharmaceuticals and herbicides/pesticides

The presence in surface, ground and drinking water of commonly used medications for human health and wellbeing, and herbicides/pesticides used in agriculture, may now represent a serious health issue. Their presence is attributed to the inability of standard water treatment plants to remove them (Whelehan 2010a). In this study the feasibility of using liquid-core microcapsules as novel approach to remove seven pharmaceuticals and four herbicides/pesticides commonly found in environmental

waters was investigated. From the results (Figures 3 and 4) it can be seen that microcapsules containing a liquid-core of either dibutyl sebacate or oleic acid, are capable of rapidly extracting (< 40 min in most cases) between 15-100% of the pharmaceuticals (initial conc. of 20 mg/l), and 25-75% of the herbicides/pesticides, when only a 4 and 3.5% liquid volume ratio of capsules was used. Higher amounts of the compounds can be extracted by simply increasing the amount of capsules, which will also result in a faster removal rate.

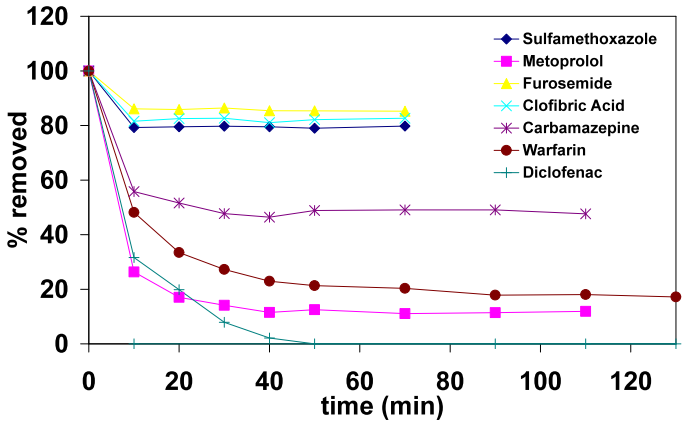

Figure 3: Extraction of seven pharmaceuticals from water using microcapsules with a liquid-core of dibutyl sebacate and oleic acid (Whelehan 2010a).

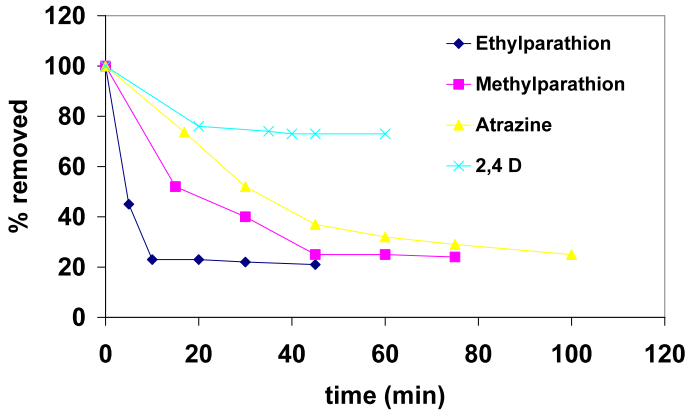

Figure 4: Extraction of herbicides and pesticides from water using microcapsules with a liquid-core of dibutyl sebacate (Wyss 2004).

Recovery and purification of geldanamycin

The anti-tumour antibiotic geldanamycin (GA) is produced as a secondary metabolite by *S. hygroscopicus* in submerged fermentations. Accumulation of the antibiotic in the culture environment can result in the rapid decline of the GA to negligible concentrations (Figure 5), due to by-products produced by the cells in the stationary phase of growth (Whelehan 2010b). To alleviate this problem, liquid-core microcapsules were added to cultures to recover the antibiotic in-situ from its detrimental fermentation environment, and also to facilitate its subsequent purification. Figure 5 displays how capsule addition improved net production of GA by 30% compared to control fermentations (143 mg/l to 110 mg/l). More important, the immediate in-situ extraction of the antibiotic resulted in the recovered material being stable in the culture environment for over 24 days.

In addition to increased production levels, the microcapsules served as a platform for the subsequent purification of the antibiotic using a very straightforward procedure (Whelehan 2010b). This was achieved by back-extracting the GA from microcapsules into another solvent (acetonitrile), followed by crystallization (solvent evaporation) of the antibiotic from this phase. This significantly reduced the complexity and number of downstream processing steps required to obtain large quantities of highly a purified product, and enabled the recovery of > 53% of the antibiotic extracted from the fermentation, which had a purity > 97%.

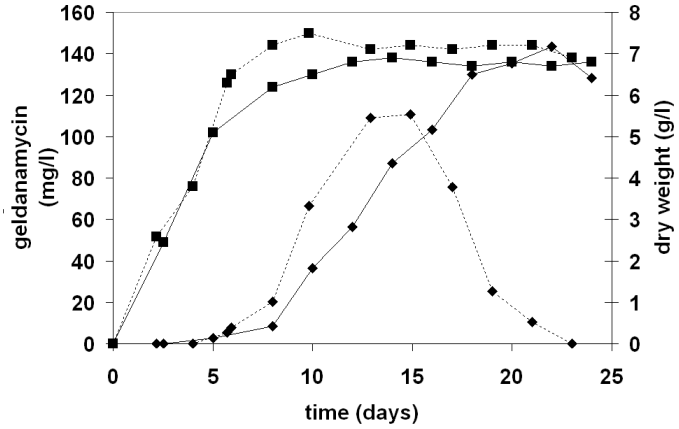

Figure 5: Comparison of the overall net production of GA and growth of *S. hygroscopicus* between cultures containing microcapsules (full lines) and cultures having no capsules (dashed lines). Symbols: cell dry weight [squares] and GA concentration [diamonds] (Whelehan 2010b).

CONCLUSIONS

This short paper has clearly shown the potential that exists for applying liquid-core microcapsules as a simple, innovative and successful extraction and purification methodology in chemical and biological processes.

REFERENCES

- Whelehan M. et al. (2010a) *Removal of pharmaceuticals from water: Using liquid-core microcapsules as a novel approach.* Water Research 44 2314-2324
- Whelehan M. et al. (2010b) *Successful application of capsular perstraction as a novel in-situ product recovery technique.* Process Biochemistry (in press article no PRBI-D-10-00443)
- Wyss A. et al. (2004) *A novel approach for the extraction of herbicides and pesticides from water using liquid-core microcapsules*. Biotechnology and Bioengineering 87 (6) 734-742