***Editor's Note:***
*Formulators and seekers of incredibly stable, almost monodisperse, "natural" emulsions, of all types, useful as delivery systems, will be delighted to read about the process described and the opportunities it offers.*

# Encapsulation and Controlled Release in Monodisperse Emulsions for Personal Care Applications

By David Palmer *

## Introduction

**Membrane Emulsification** is a technique of using microporous membranes to form emulsions in a controlled manner. It was initially developed in the late 1980s and primarily remained of academic interest until relatively recently.

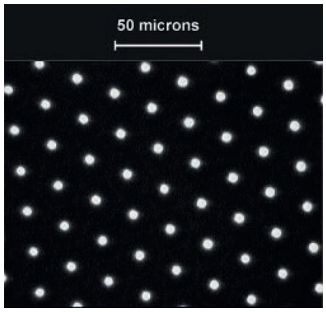
There was a tipping point in 2017 when the industrial community became aware of the opportunity it presented to overcome historical challenges of generating larger volumes of emulsified products in a variety of areas including cosmetics and personal care.

## Some Interesting History

In contrast to the current technology, early versions employed glass or ceramic membranes, with a random, disordered and variable pore size and structure. The tortuous path of ingredients through the pores meant that blockage of the pores was a constant issue, as were the materials of construction. Glass membranes in particular were unsuitable for food, pharmaceutical or personal care applications.

In recent years the technology has advanced and it is now possible to produce emulsions with controlled delivery activity at truly industrial scale.

As a spin out from Loughborough University in the UK, Micropore Technologies (2003) initially developed a small lab scale device (LDC-1) that used a disc shaped stainless steel membrane with laser drilled pores, to manufacture emulsions and then post-process them into various microcapsule or microparticle systems. These systems were often used for drug delivery, flavour or fragrance and other controlled release systems.




Stainless steel,
laser drilled membrane

The device allowed the manufacture of emulsions with well-defined droplet sizes. This breakthrough improved emulsion stability and reduced the concentration of emulsifiers that are required in traditional homogenized emulsions. By injecting the dispersed phase of the emulsion through the membrane at a steady rate, the stainless-steel membrane allows contained droplets to develop on its surface. As gentle shear forces are continually applied, when the droplet reaches a certain size the shear forces deform and detach the droplet. With this happening across the entire surface of the membrane, with many thousands of pores, it is possible to repeatably and reproducibly form consistent emulsion formulations of great value to formulators in the cosmetic industry.

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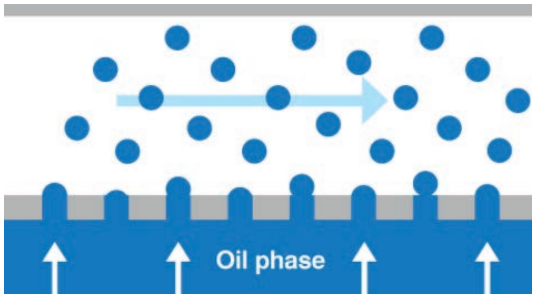



Schematic of droplet generation through the membrane pores

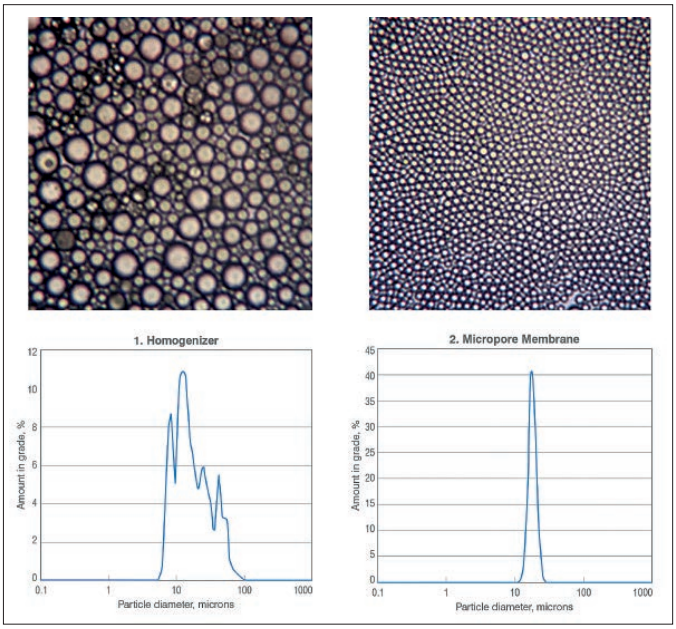
From academic roots, the device was primarily used by universities or companies looking at early stage R&D projects. As more clients embraced the technology, the requirement for larger capacity devices grew. Early attempts at continuous manufacture of emulsions, using an oscillatory membrane, resulted in a mechanically complex device which had outstanding results but remained technically challenging to scale up.

## Simplicity: a Key to Larger Things

As with many things in nature, simplicity is sometimes best. A rethink of the method to apply shear forces across the membrane resulted in a tubular membrane that used the flow of the continuous phase to deform and detach the droplets from the membrane. Referred to as **'crossflow membrane emulsification',** this removed the need to have moving mechanical parts, complex motor couplings and the like. With the Micropore AXF-1 there are no moving parts in the manufacturing process, apart from the dispersed phase and continuous phase pumps. Specifically designed to be used in aseptic industries, with continuous production of emulsion volumes up to 200l/hr now possible, industry uptake increased and new application areas became accessible.

Micropore AXF-1 continuous crossflow device – up to 200l/hr

The volume demand from some industry partners still exceeded what was possible with a single device. To resolve this issue, a multi-tube device was designed, enabling up to seven tubular membranes to be deployed in a modular fashion, giving a flexible route to scale up to volumes as high as 1400L/hr of emulsion, maintaining a low coefficient of variation (Micropore AXF-7).




Comparison of emulsion generated via homogeniser vs membrane emulsification

## Value of the Technique

The above figure demonstrates what has previously been unobtainable with techniques like homogenizers. An extraordinary narrowing of the particle size distribution is obtainable when membrane emulsification is used as compared to traditional rotor-stator homogenisers.

Membrane emulsification is a low energy consumption, gentle process. Thus, it is valuable when there is a need to minimise damage to sensitive ingredients. When handling sensitive biological materials, e.g. probiotics, the number of viable cells post-emulsification are considerably lower when homogenized than mixtures made by membrane emulsification.

In an independent study (ERDF/CPI 2017 Yeast Viability) it was shown that yeast cells dispersed in oil and emulsified by the two methods, 96% of membrane processed yeast remained viable as compared to 56% when homogenised. In an era of fermentation processes and use of biological extracts from natural flora, it is clear that a process that does not damage such valuable ingredients is of great value.

In addition, the near mono-dispersity of emulsions prepared by this method means that every droplet has the same buoyancy thereby reducing the emulsion's tendency to creaming or sedimentation. Any formulator working with the intention of designing and manufacturing a stable product is well familiar with this gargantuan task..

Furthermore, **this approach can also result in a reduction of the amount of surfactant or emulsifier that is normally required to stabilise emulsions.** Improvements in product shelf-life, skin feel and consistency are observed. Mathematical modelling of shear force and membrane configuration allows ease of scale up across all devices. For emulsions at high internal phase concentration, which frequently exhibit non-Newtonian (pseudo-plastic) behaviour, the rheological characterization of such systems is very important.

## Beyond "Simple" Emulsions

It is also possible to formulate with more complex systems. Multiple emulsions, whether water-in-oil-in water (w/o/w), or oil-in-water-in-oil (o/w/o), these multi-phase systems can be hard to handle on industrial scale.

One example which can be considered is the encapsulation of Vitamin C/Ascorbic acid, using an encapsulation technique known as 'complex coacervation'. Most encapsulation systems work best on hydrophobic actives and in this case, if the ascorbic acid is dispersed in an oil, it will drop out and dissolve in the aqueous phase and will disrupt the pH sensitive process. By forming a w/o emulsion with the acid in the water phase, it is possible to process this much like a "regular" oil.

Taking the vitamin C primary emulsion, and then processing it to form a w/o/w system using a homogenisation approach gives rise to processing issues. If stirred tank systems are used, every time a droplet is broken down there is an increased risk of the primary emulsion water phase, escaping into the bulk continuous phase, in all likelihood disrupting the formulation. Minimum droplet size is also limited by the speed of the stirrer, typically ~200 microns.

By contrast, by applying the membrane emulsification process to the same system, droplet formation on the membrane surface, and low shear detachment, both contribute to a more stable primary emulsion and an easier encapsulation process. A droplet size below 50 microns can readily be achieved.

## "Natural" Materials in Personal Care Formulations

While there is no formal definition of "natural" ingredients in personal care, there are a number of voluntary standards or certifications that companies can sign up to that indicate that the ingredients meet a certain standard. Each of these certifications have their own criteria, so the term "natural" is somewhat subjective. This subject has recently been discussed in detail in a prior issue of Eurocosmetics Magazine.

According to the FDA in the USA "FDA has not defined the term 'natural' and has not established a regulatory definition for this term in cosmetic labelling".

Working on the assumption that "natural" materials are "from nature" is not helpful either. Nearly all materials have gone through a refinement or purification step, to remove toxins or undesirable colours, odours, or other contaminants.

It is for today's consumers to decide what is acceptable to them, or which brands and corporate ethics resonate most strongly. Some will not use any animal-derived raw materials at all, even if it is not part of the animal itself (e.g. beeswax), others will tolerate small amounts of animal derived raw materials but describe by it's INCI name, "E" number or synonym.

With attention increasingly on the impact of microplastics on the environment and the recent bans to adding them to personal care formulations, formulators now search for alternate systems. In respect of exfoliant effects, microplastics can easily be replaced by natural materials such as ground walnut shell, or pumice. However, these materials can cause a brown or grey colour to the finished formulation, which is not aesthetically pleasing. **Microencapsulation can be a way to formulate with problematic materials while masking colour, odour or unwanted interactions with other components within the formulation.**

Microencapsulation was initially deployed commercially in the 1950s. Its primary use was carbonless-copy paper. Tiny microcapsules, containing droplets of colourless dye, coated onto the back of a sheet of paper, as part of a multi-sheet set. When pressure was applied by the tip of a pen, the capsules would rupture and the ink transferred to the coated surface of the next sheet, which caused the dye to colour and present a duplicate image from the pen-strokes.

The most commonly deployed chemistry was "complex coacervation", a technique that worked on the electrostatic charges of two water soluble biopolymers. Taking gelatin, an amphoteric biopolymer, for example, and dissolving it at elevated temperature and a pH above its iso-electric point, so that the charge on the polymer would remain negative. Another useful approach included dissolving anionic gum Arabic/gum acacia in the correct proportions, to act as the counter-anion.

At this point the material to be encapsulated, a hydrophobic liquid, in our current example a solution of leuco dyes, can be added which is emulsified to the desired droplet size. Once emulsified to the correct size, a pH adjustment alters the charge on the gelatin polymer, causing electrostatic interaction, or "complex" with the gum Arabic. Together they form a viscous polymer-rich phase, known as the "coacervate". The temperature of the system is carefully controlled and more coacervate comes out of solution and begins to coat the surface of the oil droplets, eventually forming a continuous wall or shell. At this point the capsule walls can be chemically stabilized and the batch is ready for post-processing and eventually coating. The technology has since evolved to encapsulate a whole range of different actives, such as flavours, fragrances and the like. Many of these actives are well known adjuvants for cosmetic products and of high interest to formulators.

The essential raw materials are "natural", gum Arabic is the powdered sap from a tree that grows in a specific region in Africa, whereas gelatin is denatured collagen typically obtained from pig-skin or cold-water fish-skin. Both materials are widely used in food and some pharmaceutical applications and have some really useful technical properties that are hard to replicate with other raw materials.

Other encapsulation methods began to be developed, and together with a more "industrial" chemistry, removed some of the uncertainty around using naturally derived materials. Batch-to-batch variation could be minimized, and processes behaved more predictably. Systems like melamine formaldehyde, acrylates, polyurethanes, isocyanate chemistry took over from coacervation in number of industrial applications.

Various other industries started to see the benefits of microencapsulation, including crop protection, fragrance delivery, functional foods, drug delivery. **Over the years, controlled delivery systems have made their way into almost every industry including Cosmetics and Personal Care.** We note, in passing, we have included in this article a variety of "non-cosmetic" applica-

tions. This is not mere meandering as our experience has shown that cross fertilization of ideas can lead to novel products. We are thinking of how cosmetic scientists study the properties of carpets when developing ideas for hair care products.

## Fragrance Product Applications

One of the many applications for encapsulation in the personal care industry is fragrance delivery. The majority of fragrance houses have in-house encapsulation capabilities. Fragrances are complex blends of many different chemistries, each with their own solubilities and volatilities, their influence on formulation stability can be unpredictable. The act of encapsulating fragrances brings many benefits, such as preventing the unwanted interaction between the formulation and the fragrance, being able to release a potent release of fragrance upon application e.g. rubbing on a cream or lotion. In the same way, long lasting fragrance delivery in laundry products is achieved by microencapsulation.

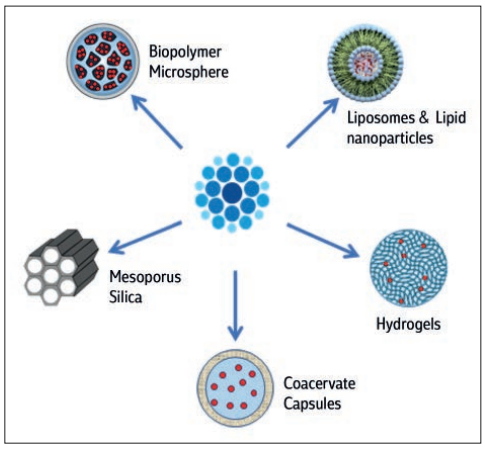
In terms of product differentiation, encapsulation opens the way to a multitude of novel product designs. Large aesthetic particles containing beneficial vitamin blends in shower gels. Anti-ageing actives in faux-caviar particles. "Two-tone" flavour lip-balm, colour changing hand-soaps. Lavender pillow spritz, with motion activated fragrance release. All these and more can be achieved using microencapsulation.

For personal care products, proximity to skin limits the type of chemistry that can be used for microcapsule systems, but many other applications continue to spread tiny, non-biodegradable particles into the wastewater, waterways and fields.

For the informed consumer, the choice between a functional product and polluting the Earth's oceans should not have to be an issue. There are alternative approaches that avoid adding non-degradable microplastics to the environment.

## Green chemistry

Whilst the current state-of-the-art allows for biodegradable options, the animal derived aspect of some of the raw materials can mean that it is not suitable for every formulator. There are a range of alternate chemistries and particle morphologies that can be used to solve almost any controlled release challenge.



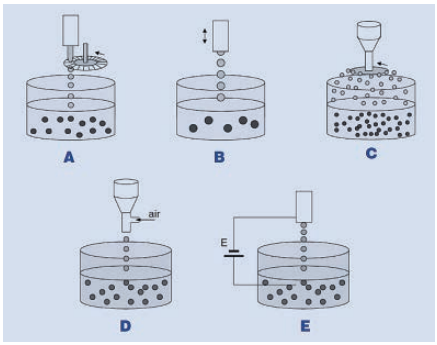

Various particle morphologies

Typically, microparticles offer two modes of release; binary, as-in, it is broken or it isn't, or diffusive release, where the active can diffuse out over time. Each of these systems can be tailored to have specific triggers, such as pressure, pH change, dilution, etc. The binary particles are often core/shell microcapsule systems, where there is a physical barrier around the active preventing any interaction with the external environment. Microbeads have a more diffusive or porous structure, allowing small molecules to pass in/out of the structure.

## Natural Microbeads

There are many naturally derived polymers that can be used to manufacture beads, prills or particles, the majority involve some kind of dripping mechanism to form the particles.

Many dripping techniques are available, ranging from a) jetcutter b) oscillatory nozzle c) spinning disk d) pulsed airflow e) electrostatic. Although each of these approaches are more efficient than just using gravity alone, they are all limited in terms of the minimum droplet size possible (~200µm+) and control of the particle size distribution. In addition, deformation of the droplets on impact with the collection bath, can cause undesirable morphologies.




Methods for generating droplets

Membrane emulsification sidesteps these challenges by forming hydrogel droplets directly as a w/o emulsion. Precise size control can be achieved, with perfectly spherical droplets in sizes less than 50µm.

Thermal gelation is the simplest curing mechanism, materials like agar-agar, carrageenan and gelatine can be processed at elevated temperature and cooled in a controlled manner. Ionic gelation or precipitation is relatively straightforward when using a dripping technique, however with membrane emulsification an alternate approach is required.

The preparation of a fine emulsion or dispersion of the relevant curing solution (w/o) is prepared and added to the w/o hydrogel system. The relative proportions of curing agent and polymer concentration is an important consideration. As the hydrogel droplets encounter the fine dispersion of curing agent, surface curing takes place, without significant absorption of additional aqueous phase, therefore the droplet volume is not significantly increased, maintaining the initial favoured size distribution. This allows for generation of sub-200µm hydrogel microspheres with a consistent particle size distribution. **This, in turn, has an influence on consistent delivery of active component,** mechanical

stability of the particle. Alginate, chitosan, carrageenan, agar-agar, systems are naturally derived hydrogels, used in an array of delivery systems. Knowledge of each polymer's relative stability or weakness helps to design a system that is stable long-term in the formulation but will then release under the desired conditions.

There are a range of marine biopolymers that can be extracted from marine sources that can be used to form interesting particles. Probably the best known is sodium alginate, commonly used to form a gel in air-freshener blocks. Mixing an active ingredient into a solution of sodium alginate and then dripping this solution into a bath of Calcium Chloride, the calcium ion displaces the sodium ion and calcium alginate is formed, which is insoluble in water. This results in spherical particles containing the active that will slowly permeate out over time. This can also be used for entrapping a high loading of pigment particles, for aesthetic effect. Recent successful commercialization of sea-grown biopolymers in Israel is thought to add to the list of natural ingredients useful with the process described in this article.

Membrane emulsification can be used to prepare mono-dispersed microbeads in a smaller range than that which can be achieved by dripping technologies. Forming a w/o emulsion with the alginate solution and then either adding a calcium solution or having an insoluble form of calcium in the alginate solution and dissolving it with acid, so that the calcium is available to react and solidify the droplets.

Carrageenan is also a seaweed derived material, by heating and forming droplets of a carrageenan solution and active, a thermosetting mechanism can provide solid particles of dispersed active. Various other materials can be used to manufacture microbeads using thermosetting, such as agar-agar, butters, waxes or fats.

Porous silica particles can be manufactured, with control over the final pore sizes, allowing active materials to be diffused in at a future point. It is also possible to post-coat the particles, giving a particle that has a binary "trigger" but then a diffusive release. This means it is possible to engineer some advanced particle behaviours, using relatively inexpensive natural raw materials.

Similarly, chitosan is soluble in water at acidic pH but not alkali, so forming droplets into an alkali environment can provide precipitated chitosan microparticles, depending on the source of the chitosan, potentially giving formulators a non-animal option.

## Natural Microcapsules

Although complex coacervate capsules have been discussed previously, the focus was on the "traditional" approach. Recent development work has looked at replacing the gelatine with a number of alternative raw materials, in a slightly modified process. Whey protein isolates can be induced to form coacervate, with gum Arabic, it will even form capsule walls. The capsules can be isolated and washed but when added to most formulations, the performance was poor and the wall integrity quickly compromised. Gelatin complexing with sodium carboxy-methyl-cellulose, provides different wall properties but does not escape from the use of an animal derived component.

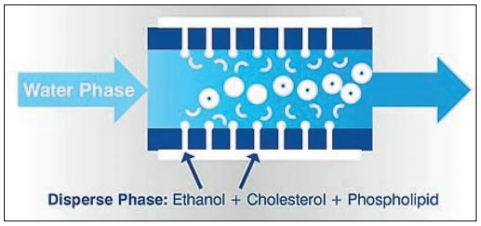
Marine chitosan, one of the world's most abundant biopolymers, which is an extract from the chitinous shells of crustaceans, can form coacervate with gum Arabic but has the double impact of being animal derived and also concerns some people, who may be wary of shellfish allergies.

In recent years the availability of chitosan from non-animal sources have allowed investigations into whether it behaves in the same way as marine chitosan. Chitosan being an umbrella terms for de-acetylated chitin, so matching the molecular weight and degree of deacetylation are key parameters. The woody stems of some mushrooms can be processed and treated in such a way as to obtain a natural, non-animal grade of chitosan which can be used as a replacement for marine chitosan, providing a vegan/vegetarian alternative to traditional gelatin/gum Arabic encapsulation systems.

Finally, whilst liposomes appear to have a core shell morphology, they are typically a nano-scale phospholipid bi-layer with internal hydrophobic and hydrophilic areas, typically utilised in pharmaceuticals for the delivery of drug actives.

They are formed from biological ingredients and have similar structures to materials found in the human body. The amphiphilic phospholipid bilayer of liposomes has close resemblance to the mammalian cell membrane, enabling efficient interactions between liposomes and cell membrane and, subsequently, effective cellular uptake. They can be used as a delivery mechanism in areas such as topical administration of beneficial skin agents.

Traditionally hard to manufacture in large quantities, these have been niche materials for personal care. Recent developments, using membranes as micromixers have shown that liposomes can be manufactured to the quality of drop-by-drop microfluidics but on a much larger and faster scale.




Membrane used as a micro-mixer for liposome production

## Conclusion

To summarize, most encapsulation processes require a droplet formation stage, whether as an emulsion (w/o, or o/w) or as a precise method of micro-mixing (liposomes). Membrane emulsification can provide superior control in both respects and allows the design and consistent manufacture of a variety of engineering microparticles. Having spent many years making microparticles with "brute force" emulsification systems, the overwhelming consistency obtained by making every droplet the same size, results in a predictable and controllable release profile, is a clear benefit.

Working closely with clients to bring advantages to their formulations, using novel aseptic manufacturing methods is a successful marriage of chemistry and processing equipment. Whilst membrane emulsification is compatible with both synthetic and natural chemistries, as part of our ethos, Micropore is involved in a number of projects to replace synthetic systems with more natural, biodegradable approaches. We welcome the opportunity to be of service!