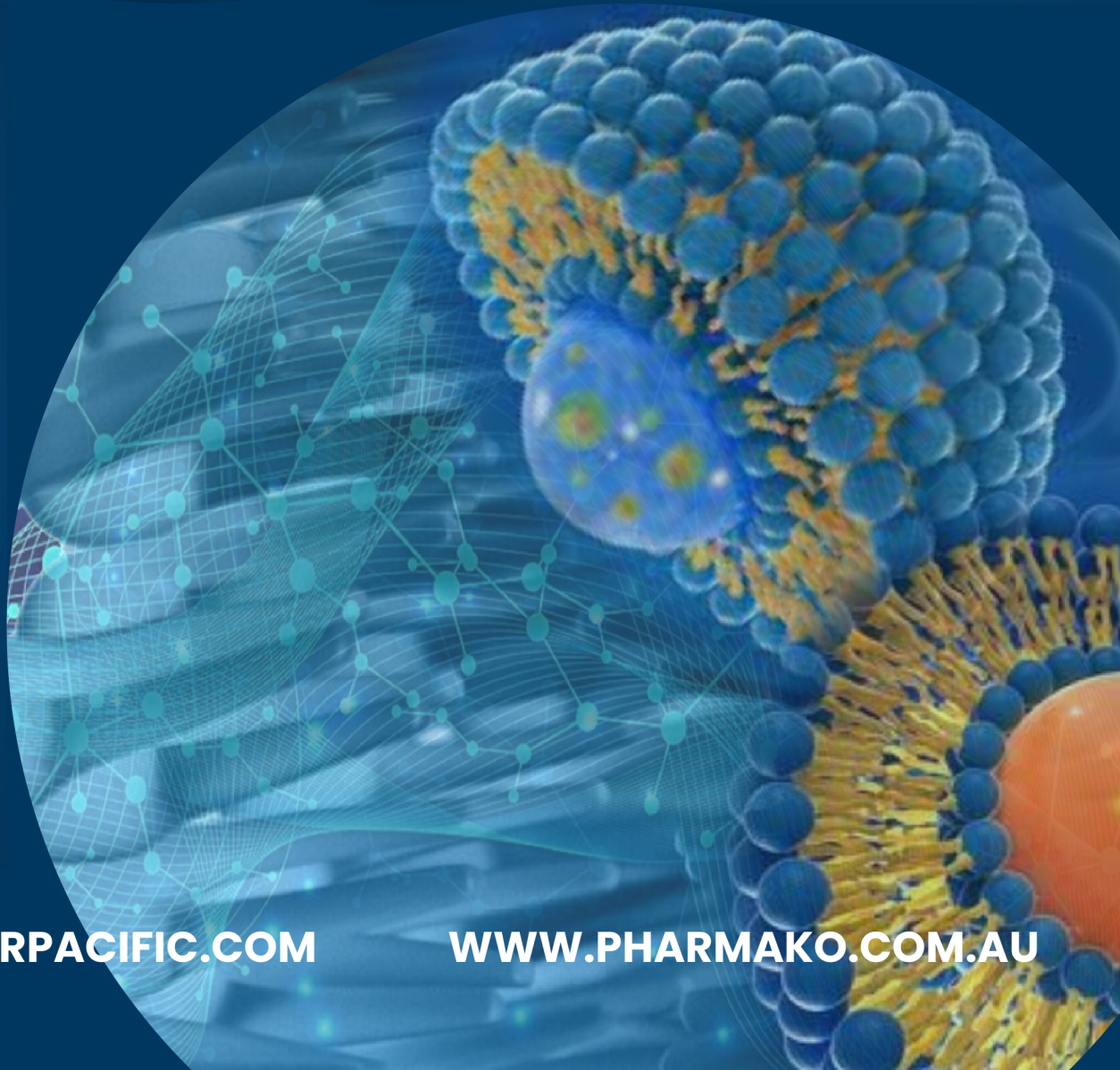




OPPORTUNITIES WITH DELIVERY FORMATS



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INTRODUCING INNOVATIVE DELIVERY TECHNOLOGIES

AquaCelle®

Award-winning, AquaCelle® is a customizable, self-micro-emulsifying delivery system (SMEDS).

Specifically designed and clinically proven to optimize the bioavailability of oily lipophilic active ingredients such as ubiquinol, omega-3s, lutein, and resveratrol whilst maintaining product stability. Clinically tested with improved bioavailability by up to **700%**.

LipiSperse®

Multi-award-winning LipiSperse® is an advanced cold water dispersion technology (CWD).

Allowing solid/powder lipophilic active ingredients such as curcumin, resveratrol, palmitoylethanolamide (PEA), and quercetin, with otherwise relatively low bioavailability and poor solubility in water, to be easily dispersed in cold water, thereby increasing their bioavailability and uptake in the body. Superior performance means only 10% LipiSperse® is required with an impressive **90%** active load, the largest active/nutrient ratio in a water-soluble formulation.

CPO®

Compressible Powdered Oils (CPO®) is an innovative oil conversion technology specifically designed to overcome the challenges of formulating with oily lipid-based ingredients.

CPO®s overcome formulation challenges, addressing the problem of product spoilage from oils. This ingenious material development allows oily active ingredients to be included in stable tablet and powder formulations without leaching the oils.

Newest Targeted Delivery Innovation

Liposomes are not new, but can you tell the difference between real and "fake" liposomal technology? Are you getting the real deal that ensures your DS is efficacious and effective? The following paper explains our new liposome technology - PlexoZome® - real liposomes and 100% customizable!

PlexoZome® is a scientifically proven complex genuine liposomal technology, verified through TEM and Cryo-TEM imaging, Zeta potential, and DLS testing.



A 3D rendering of liposomes, which are spherical vesicles with a phospholipid bilayer membrane. One liposome is shown in a cross-section, revealing a central orange sphere representing a drug payload. The background is a blue-toned molecular structure with glowing nodes and connecting lines.

TARGETED DELIVERY WITH GENUINE LIPOSOMES

This White Paper looks at PlexoZome®, a scientifically proven complex liposomal technology. These genuine liposomes are verified through TEM & Cryo-TEM imaging, Zeta potential and DLS testing.

Stable liposomal technology developed and made in Australia

 **PlexoZome®**

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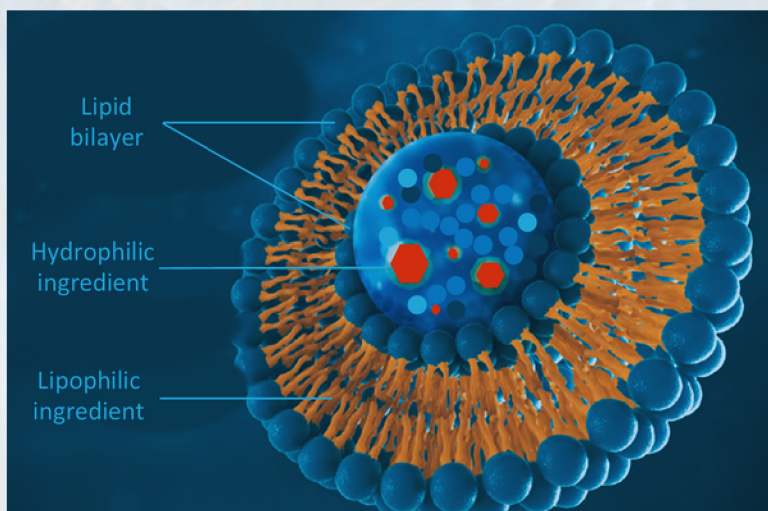
LIPOSOMES

In the dietary supplement industry, many ingredients in the formulator's toolbox have been around for at least a decade or more. While a plethora of ingredients have matured in the sense that they have good levels of consumer awareness and well-established benefits that have been validated by clinical research, how can brands continue to innovate and differentiate from existing products on the market with these ingredients?

One way to innovate and differentiate is by using technology to enhance absorption and bioavailability. A 2016 survey consisting of 200 consumers revealed that most supplement users (approximately 75%) were willing to pay a premium for vitamins/supplements with improved absorption.[1]

Until recently, most approaches to improving bioavailability focused on adding other botanical ingredients that may have synergies for improving a specific compound's absorption, such as adding piperine (a component of black pepper [*Piper nigrum*]) to curcumin (a component of turmeric [*Curcuma longa*]) formulas.[2]

However, a limitation of this route to improving bioavailability is that it is combination specific. The benefits of a compound such as piperine may not extend to all other ingredients widely used on the market.



GENUINE LIPOSOMES

However, new technology can be formulated specifically to the nature of each ingredient's properties to provide functional benefits for inclusion in liquid formulations. Pharmako Biotechnologies, an Australia-based company, has developed a unique liposomal technology, PlexoZome®.

Liposomes have been described as a "...vessel with a spherical structure that comprises one or more bilayer lipids in the aqueous part of a shell."[3] Liposomes can carry both lipophilic (able to dissolve in fat) and hydrophilic (able to dissolve in water) ingredients. The lipophilic ingredients can be stored within the lipid bilayer, while the hydrophilic ingredients can be stored within the aqueous core. Advantages of liposomal delivery can include increased absorption/bioavailability[4] and easier ingestion compared to capsules or tablets for those with difficulties swallowing. In a survey of 369 consumers, it was found that 16.5% of participants described difficulties swallowing.[5]

The liposomal technology by Pharmako Biotechnologies has been authenticated to create true liposomes through Transmission Electron Microscopy (TEM) and cryo-TEM. Transmission electron microscopy allows for the visualization of individual particles as well as their inner structure.[6] Cryo-TEM is considered amongst the best methods to visualize liposomes[6] and is a method by which the particles are frozen in place to allow for better observation under an electron microscope.



Furthermore, the liposomes' stability is confirmed by measuring their zeta potential (ZP). The higher the ZP, the greater likelihood that the particles can resist aggregation[7] or clumping.

Even the particle size of these liposomes can be customized. The size distribution of these materials can be measured using dynamic light scattering (DLS), which is a measurement of the "...intensity of the light scattered over time".[8]

As liposomes are generally below the visible wavelength of light (380 to 700 nm[9]), it is impossible to see them using a standard light microscope. So, how do you confirm that you have actually made liposomes and not a 'soup' of ingredients?

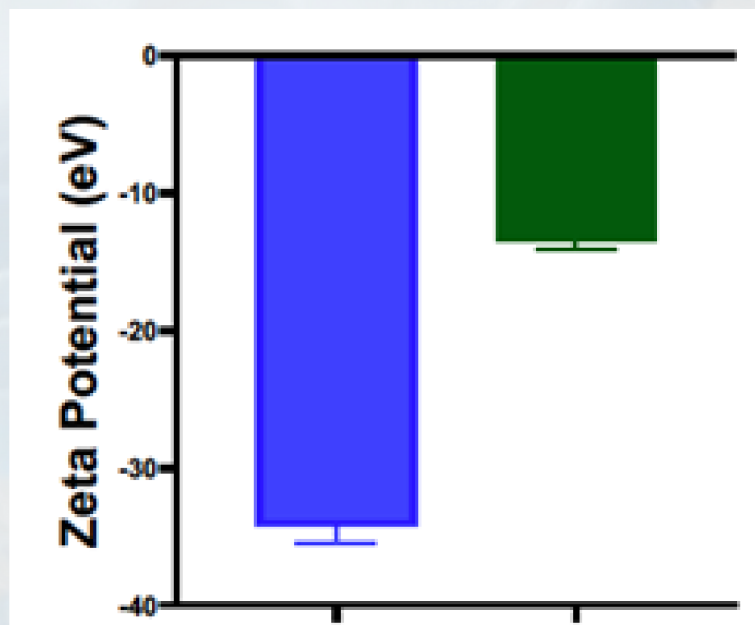
Besides particle size and distribution, two important tools around the characterization and presence of liposomes are zeta potential and transmission electron microscopy imaging.

ZETA POTENTIAL

Zeta potential is the electric potential at the interface of the lipid bi-layer and the water surrounding it.

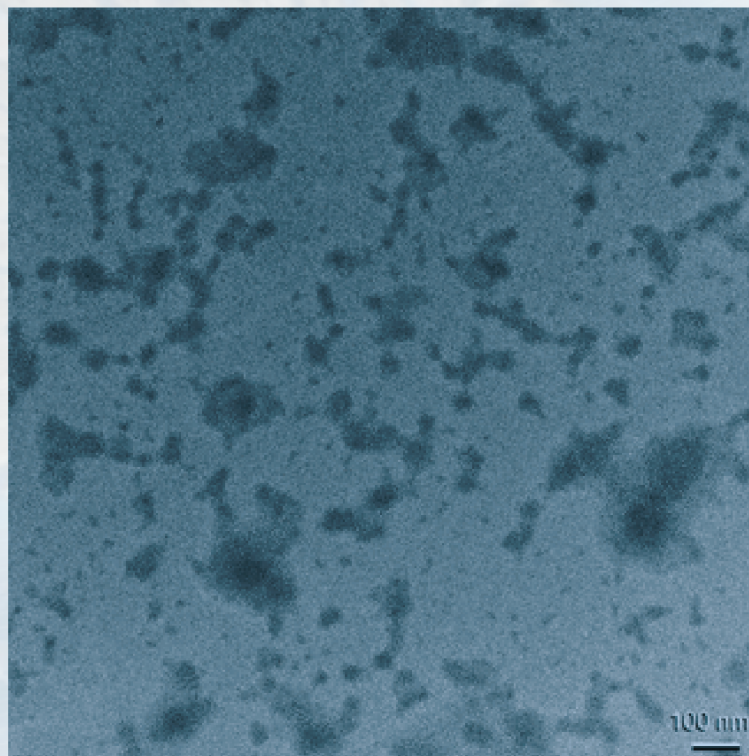
Colloidal dispersions (e.g., liposomes in water) with a medium to high zeta potential (negative or positive charge greater than 20 eV) are electrically stable, while those with a low zeta potential (anything below 20 eV) are unstable and tend to coagulate or flocculate (clump).

Also, zeta potential is one of the available tools to characterize a double layer, such as that in a liposome. The below chart shows the difference between a particular formulation made by two manufacturers using different manufacturing methods.



Pharmako Biotechnologies PlexoZome® D3 – high zeta Potential (negative charge) means more stability and no coagulation.

Competitor Liposomal D3 – low zeta potential means less stability and high coagulation



Picture 1. Negative staining TEM of competitor D3 with 2% uranyl acetate. Liposomes are not clearly visible and, whatever structures are there, appear to be clumping, due to their very low zeta potential.

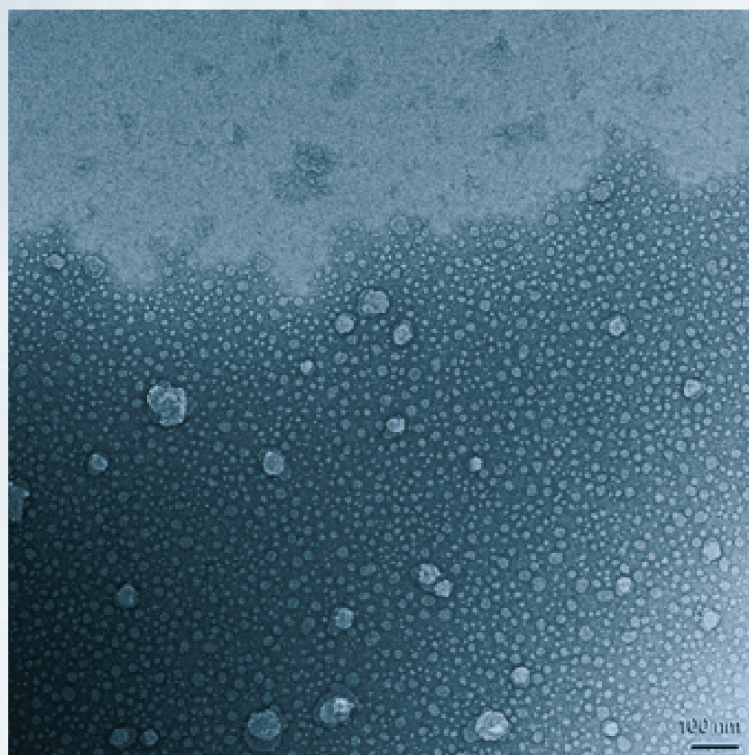
TEM (Transmission Electron Microscopy) IMAGING

TEM imaging technique uses an electron beam to image a nanoparticle sample. It provides much higher resolution than is possible with light-based imaging techniques.

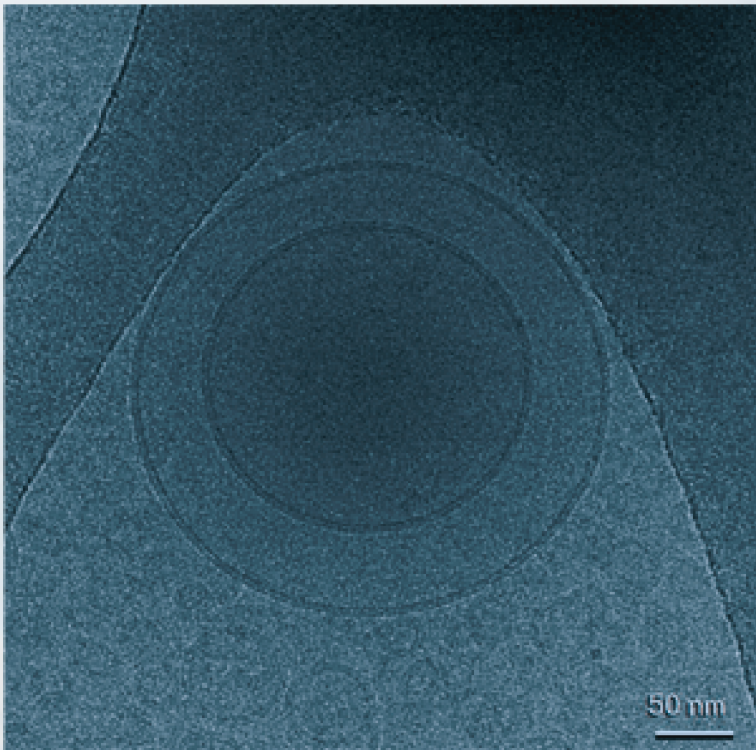
TEM is an essential method for the characterization of the presence, size, and shape of liposomes. It can directly visualize single particles (at the low-end nanoscale) and even detail their inner structure, e.g., lipid bi-layer. There are two distinct methods for TEM visualization. One is cryo-electron microscopy (cryo-TEM), and the other is negative staining TEM.

Liposomes must be preserved for the electron microscope to visualize them best close to their native structure. As such, cryo-TEM is best suited for this application. Cryo-TEM uses thin films of suspensions that are plunged and frozen to create vitrified ice films that can be imaged directly in the electron microscope under liquid nitrogen temperature. This requires costly equipment, detailed methods, and experienced operators;^[10] hence it is not readily commercially available.

The other method is negative staining TEM (usually with uranyl acetate). Liposomes must be stained to distinguish their features, as they do not have enough contrast. Negative staining TEM is faster and simpler than cryo-TEM. It also requires less advanced equipment and methods and is more readily available.



Picture 2. Negative staining TEM of Pharmako Biotechnologies PlexoZome® D3 with 2% uranyl acetate. Liposomes are clearly visible and are freely distributed in the liquid medium.



Picture 3. Cryo-TEM of Pharmako Biotechnologies Plexozome® D3. Liposomal bilayer membrane is clearly seen.

While Pharmako Biotechnologies offers its customers the ability to evaluate and customize any ingredient, they are interested in formulation into a PlexoZome® product. The company has already pre-validated several available ingredients for purchase. These include:

- Vitamin B12 (methylcobalamin)
- Vitamin D3
- Vitamin D3 & K2-7
- Vitamin C
- Glutathione
- Hyaluronic Acid
- Phospholipids-Phosphatidylcholine
- Collagen
- Nicotinamide Riboside (NR)

If you're interested in incorporating PlexoZome® technology into your next product, Pharmako Biotechnologies can customize any ingredient, so don't hesitate to get in touch with us or our global distributor, GENCOR.



FOR FURTHER INFORMATION ABOUT PLEXOZOME® OR TO DISCUSS
HOW PLEXOZOME® TECHNOLOGY CAN BENEFIT YOU CONTACT:

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