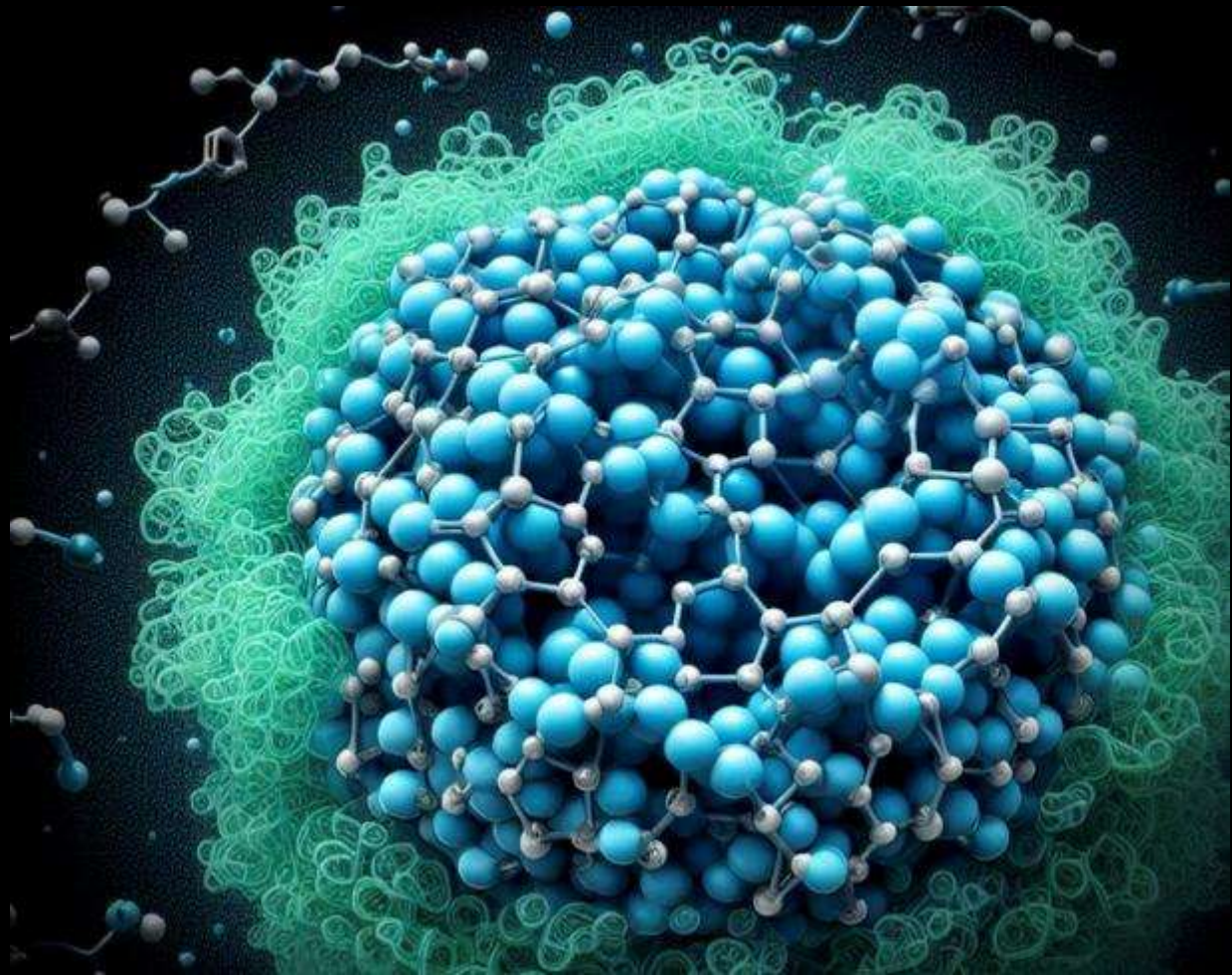
LIPODISQ®

Origins



Curiosity, Innovation.

Malvern Cosmeceutics Ltd, November 2024

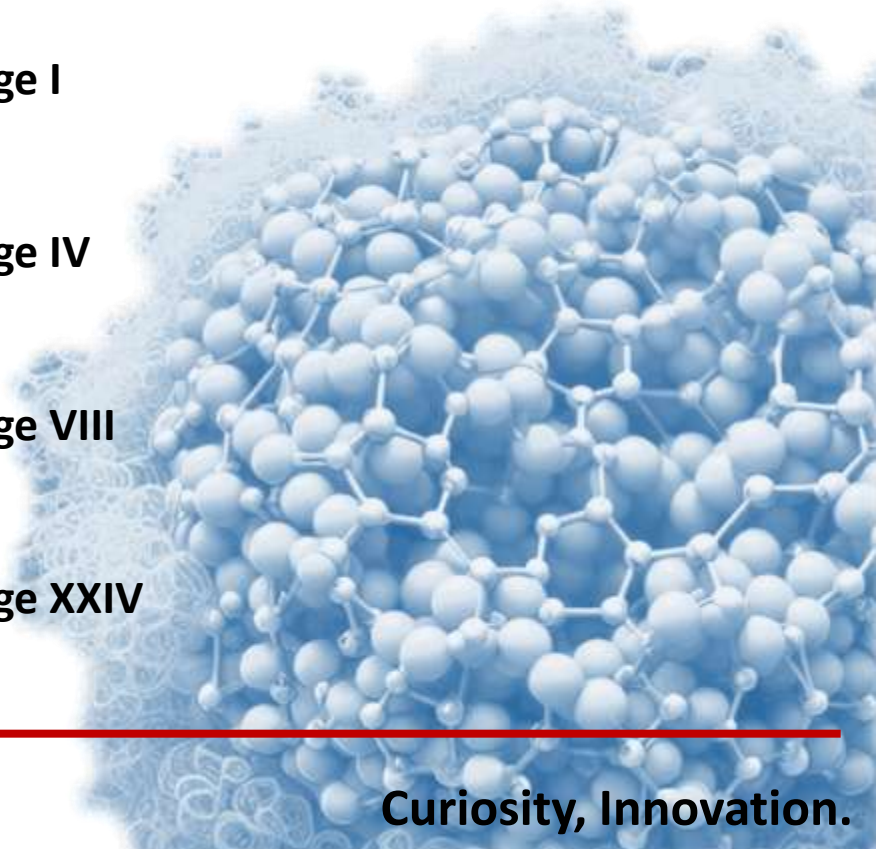
LIPODISQ® Origins

Introduction

In 2025 Malvern Cosmeceutics Ltd will be celebrating 20 years since incorporation and the continued advancement of our pioneering technology: Lipodisq®.

For two decades, we have been at the forefront of innovation, continuously evolving to meet the needs of our customers and the challenges of changing landscapes across multiple sectors. From our first product launch to our latest advancements, each step in our history reflects a commitment and passion for technology and innovation.

Content Highlights:



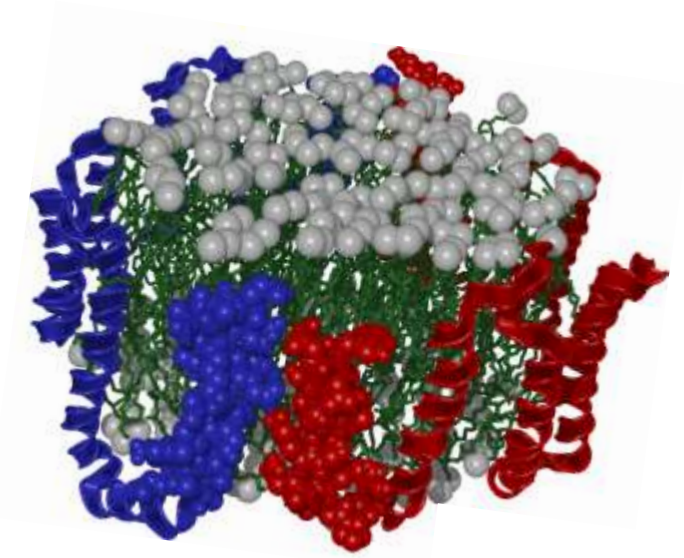
LIPODISQ® Origins

Nature Inspires

First described by Gofman and colleagues in the early 1950's, High Density Lipoproteins (HDLs), also known as "good" cholesterol, circulate in the bloodstream encapsulating aqueous insoluble cholesterol and lipids for transportation to the liver for excretion.

HDLs are a heterogeneous group of particles composed of an inner core of cholesterol ester and triglycerides surrounded by an amphipathic layer of free cholesterol, phospholipids and apolipoproteins.

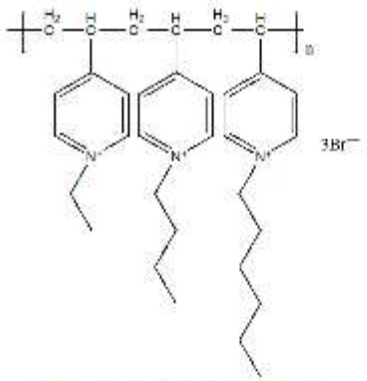
This naturally occurring nanoparticle (7 – 14nm), and in particular the structure and functional characteristics of apolipoprotein, is our inspiration.



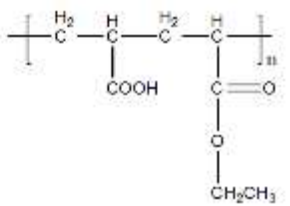
1950's

Biomimetic Polymers

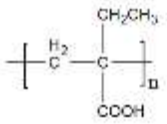
Aston University, UK: Dr Steve Tonge and Prof Brian Tighe (Biomaterials Group), inspired by HDL particle properties, initiate a research program to develop novel polymer architectures that mimic the natural apolipoprotein functionality, proposing such synthetic particles could be used as drug delivery vehicles.



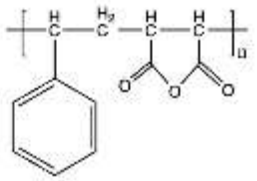
Quaternized poly(4-vinylpyridine)



Copolymer of acrylic acid and ethyl acrylate



Poly(2-ethacrylic acid)



Poly(styrene maleic anhydride)

A range of polymers that readily associate with hydrophobic species such as phospholipids were synthesised (including copolymers of acrylic or methacrylic acids with short-chain acrylates; copolymers of styrene or alkyl vinyl ethers with maleic anhydride and their corresponding hydrolysed maleic acid salts).

As part of this work, the 1:1 alternating Styrene Maleic anhydride copolymer [P(SMA)] was found to interact with phospholipids to form discoidal nanoparticles in aqueous solution at ~ pH 4 or below, successfully mimicking HDL properties, albeit in conditions outside of the usual physiological range.

1990 - 2000

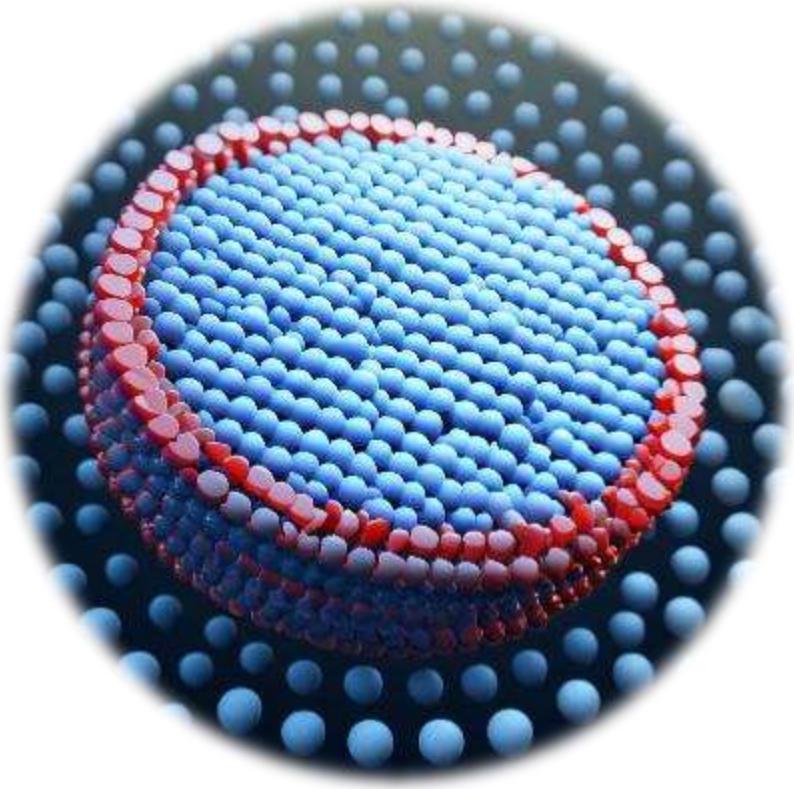
LIPODISQ® Origins

Malvern Cosmeceutics Ltd

Transforming industries with Nanotechnology:

Founded in 2005 by Dr Steve Tonge, Malvern Cosmeceutics Ltd (Malvern, UK) was incorporated to build upon the early academic research relating to P(SMA), with a primary aim to synthesise and modify related polymer structures capable of operating within the physiological range.

Since incorporation, Dr Steve Tonge and Andrew Harper have continued to innovate; engineering new generations of particle structures to create a proprietary platform termed Lipodisq® that delivers precision and efficacy in diverse applications.

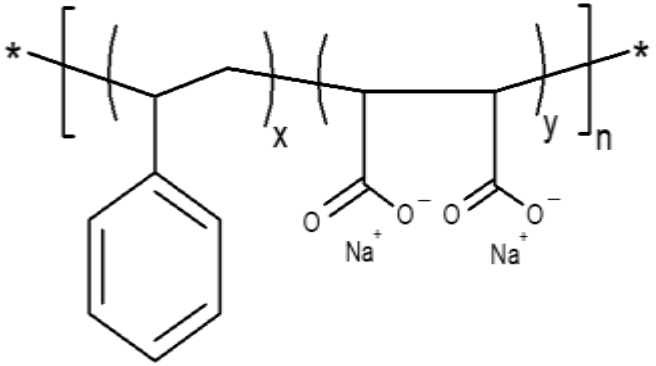


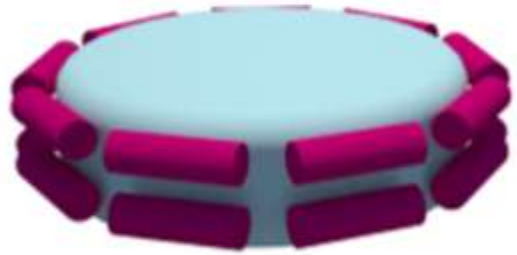
Today, Lipodisq® technology is utilised across multiple chemical industries. From protein chemistry and drug design to drug delivery development pipelines, while our core focus remains delivery of topical actives for the cosmetic and personal care sectors.

Our cutting-edge solutions are engineered to bring about transformative changes, offering unprecedented advancements in product development and manufacturing processes.

2005

Lipodisq® Generation α



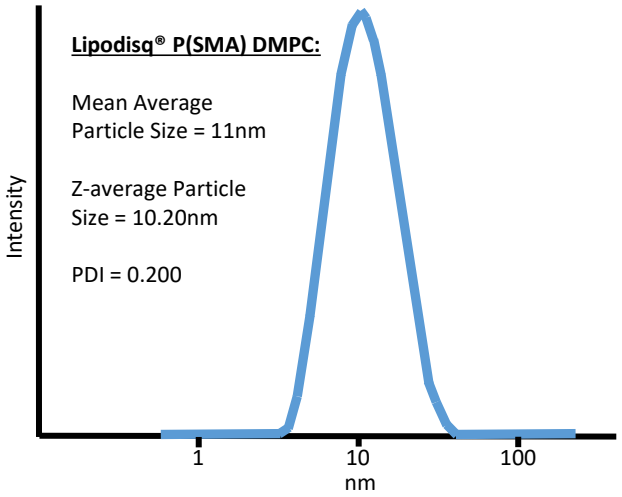


First generation Lipodisq® particles are constructed from novel polymers containing styrene and maleic acid monomer units. Precise control of the monomer ratios and molecular weight during polymerisation produces Poly(styrene-maleic anhydride) co-polymers, which, when hydrolysed to Poly(styrene-maleic acid) interact with phospholipids to form discoidal nanoparticles in aqueous solution, successfully mimicking HDL properties. The ratio of styrene and maleic anhydride/acid is tailored to produce Lipodisq® particles within the operational range of pH 3.50—10.50.

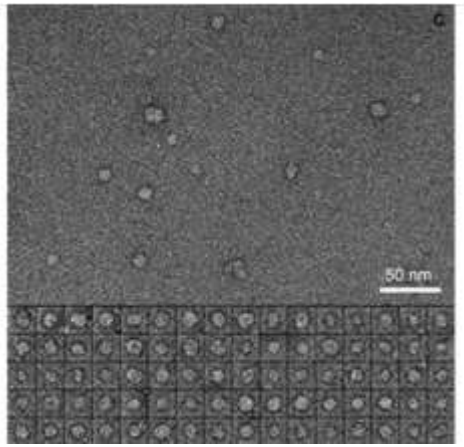
2005

LIPODISQ® Origins

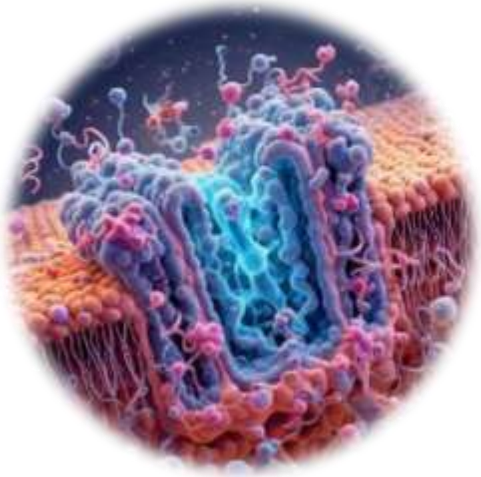
Lipodisq® Generation α



Commercial Lipodisq® P(SMA) products, containing 3:1 and 2:1 ratios of S:MA, in hydrolysed and non-hydrolysed form, were launched in 2007. When combined with phospholipids Lipodisq® nanostructures spontaneously form with a typical size of around 11 nm in diameter.



TEM image: Orwick, Judge, Procek,Lindholm, Graziadei, Engel, Gröbner and Watts (Oxford University) Angewandte Chemie 2012



Lipodisq® P(SMA) products are supplied to Industrial and Academic partners throughout the world. Utilised by a thriving community exploring the use of Lipodisq® for membrane protein research.

2007

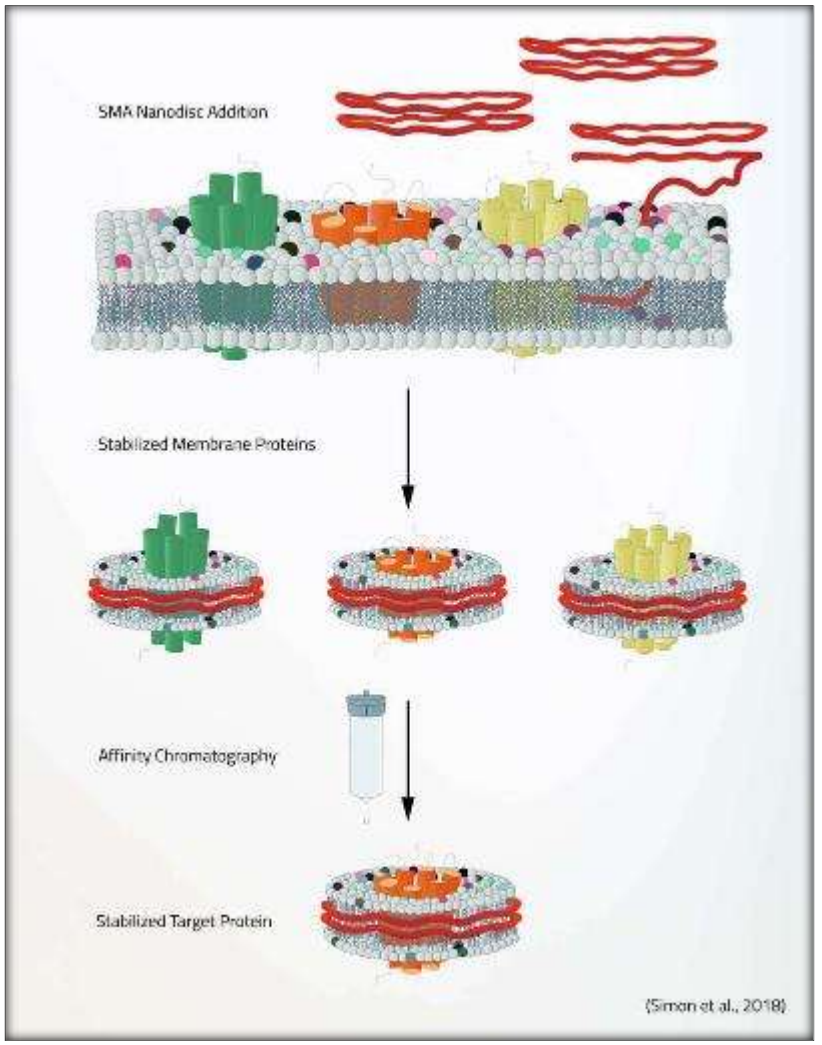
Curiosity, Innovation.

LIPODISQ® Origins

Lipodisq® Generation α

Protein Biochemistry Solutions:
Lipodisq® P(SMA) products assume a critical role in analytical processes and research applications enabling the extraction of native membrane proteins, including GPCRs, but also stabilizing them for in-depth analytical studies. This breakthrough technology, also referred to as SMALPs (**S**tyrene **M**aleic **A**cid **L**ipid **P**article**s**) in scientific journals is instrumental in advancing the design of novel drug molecules and drug/receptor interaction studies.

Lipodisq® technology has been propelled by a global community of academic and industrial researchers who have leveraged this technology, continually contributing to a deeper understanding of its capabilities. With over ***500 scientific publications***, dedicated conferences are held each year in the EU and US by enthusiastic members of the Lipodisq®/SMALP community.



2007

Curiosity, Innovation.

Lipodisq® Generation α

Licensees, Distributors and Highlighted Partners/Customers:

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AdipoGen® LIFE SCIENCES

syngenta

aurorium

SMALP

ORBISCOPE
Powered by Polyscope Polymers

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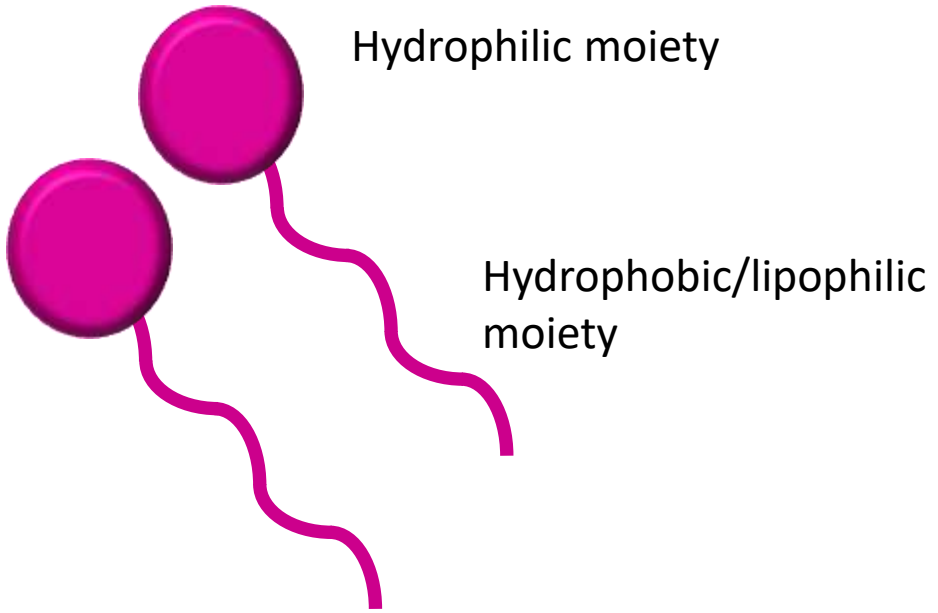
ucb Inspired by patients. Driven by science.

2007

Lipodisq® Generation β

Significant regulatory hurdles exist for the use of P(SMA) in drug delivery or personal care applications. To pursue the goal of developing particle mimics of HDLs for API delivery, a second phase of development of the Lipodisq® technology was required. This involved the reengineering of the particle to be constructed from raw materials that are conventionally used within Personal Care and Pharmaceutical markets.

An extensive program began to substitute P(SMA) polymers used to stabilise the phospholipid membrane with a surfactant based chaperone molecule. In order to function as a surfactant, a compound must necessarily include at least one hydrophilic moiety (polar or charged) and at least one hydrophobic/lipophilic moiety (non-polar).

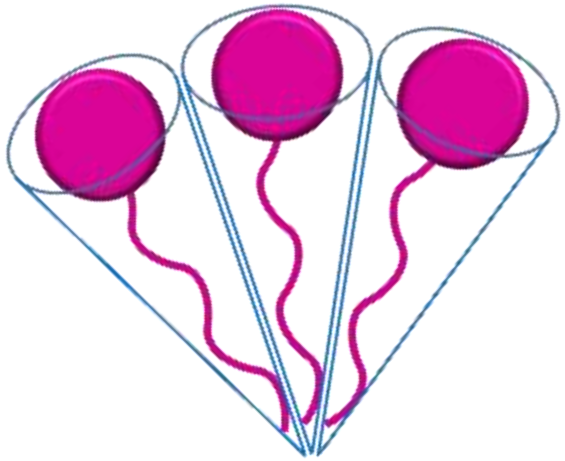


2007

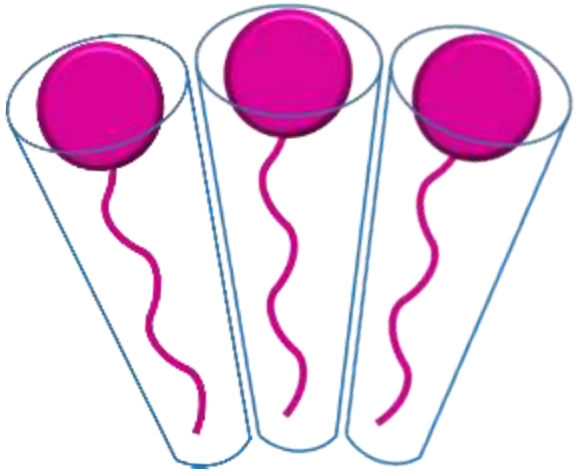
Lipodisq® Generation β

Surfactant Chaperones:

The HLB system provides an empirical parameter often assigned to a surfactant in order to characterise its hydrophilic/hydrophobic balance. Surfactants having higher HLB values are generally more hydrophilic, with those having lower HLB values generally being more hydrophobic. Surfactant molecules can be further defined by calculating their critical packing parameter which in turn defines the 'shape' of the surfactant assembly – cone, truncated cone, cylinder or inverted truncated cone.

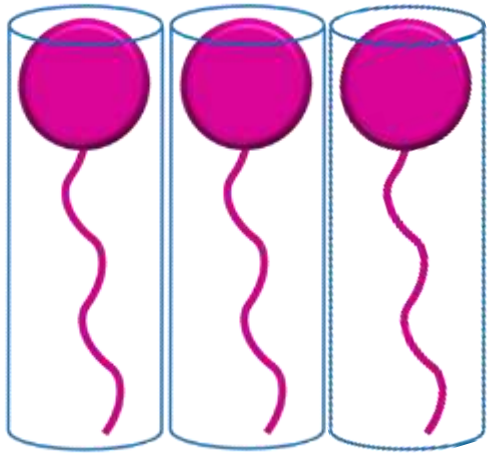


Cone Packing

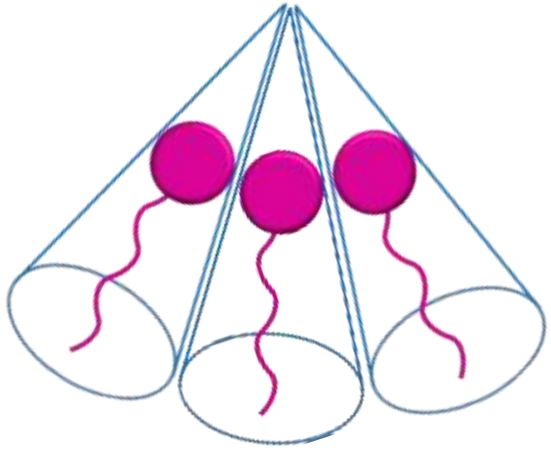


Truncated Cone Packing

2007



Cylindrical Packing



Inverted Cone Packing

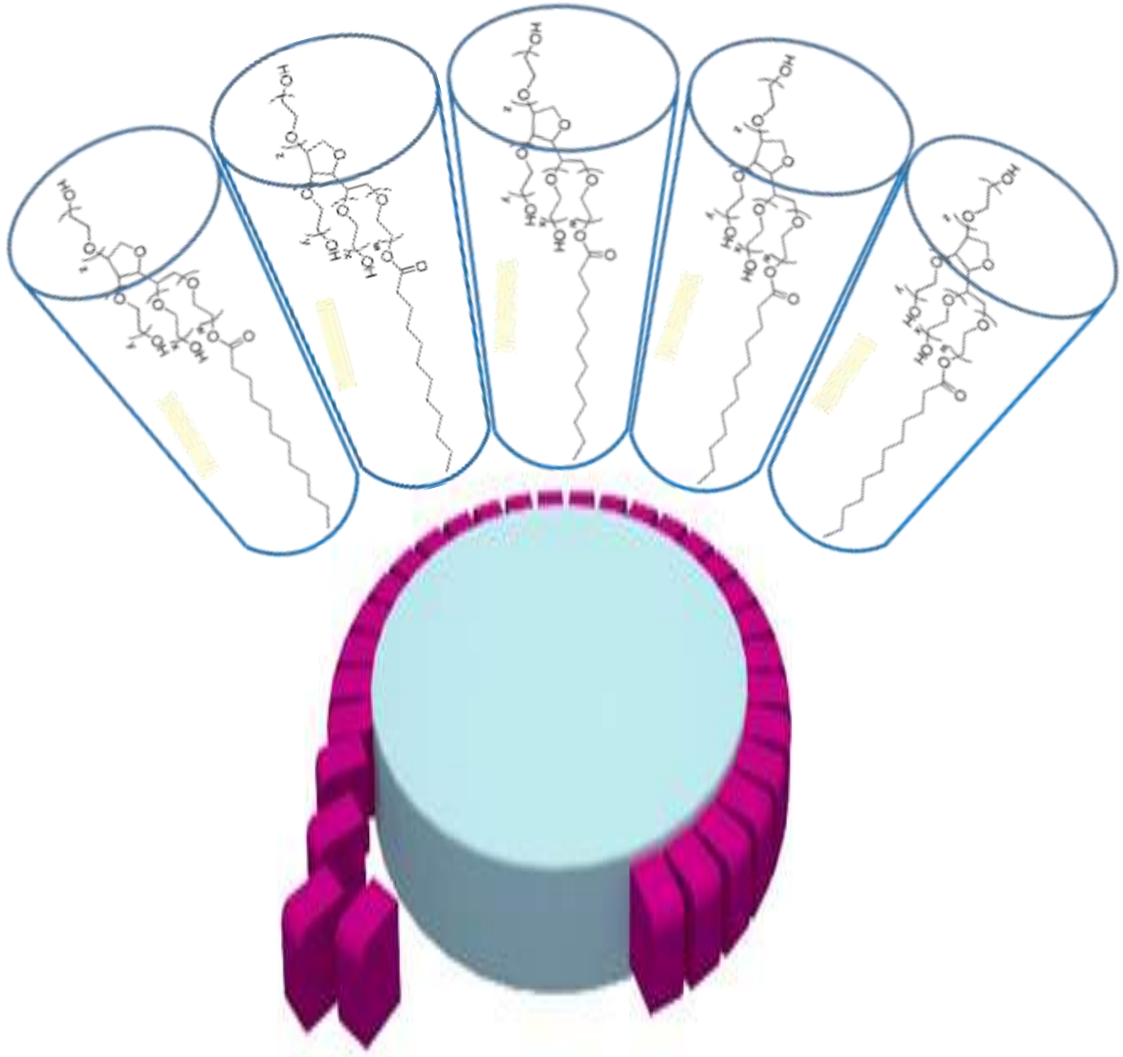
LIPODISQ® Origins

The packing parameter and molecular shape is essential to the formation of Lipodisq® particles of Generation β. The surfactant chaperone must be of optimum HLB and assume the necessary packing orientation to tightly pack around the perimeter of the phospholipid bilayer, burying its hydrophobic tails into the exposed fatty acid edge of the membrane.

Numerous classes of surfactant materials were investigated to determine the required structural characteristics to form nanoparticles of similar geometries to the original Lipodisq® assemblies based on P(SMA). It was essential that the surfactant components were approved for use within the Personal Care and Pharmaceutical industries and that the phospholipid membrane was formed from natural phospholipid sources rich in phosphatidylcholine, i.e. soy, sunflower.

Of the hundreds of surfactant structures reviewed, Polysorbate 20 was highlighted as the ideal material to meet the chemical needs of the particle and regulatory acceptance of the future products.

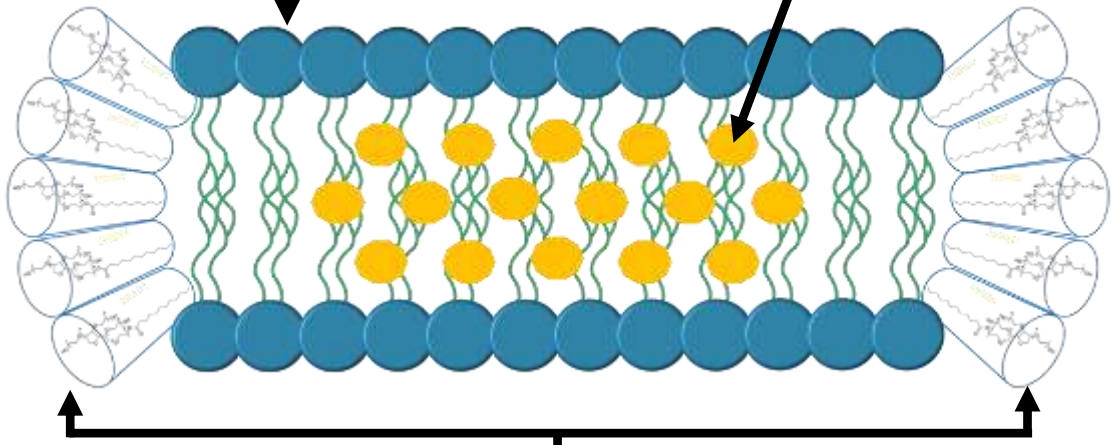
Lipodisq® Generation β



LIPODISQ® Origins

Phospholipid Membrane:
Phosphatidylcholine rich, sourced from Soy.
Non-GMO

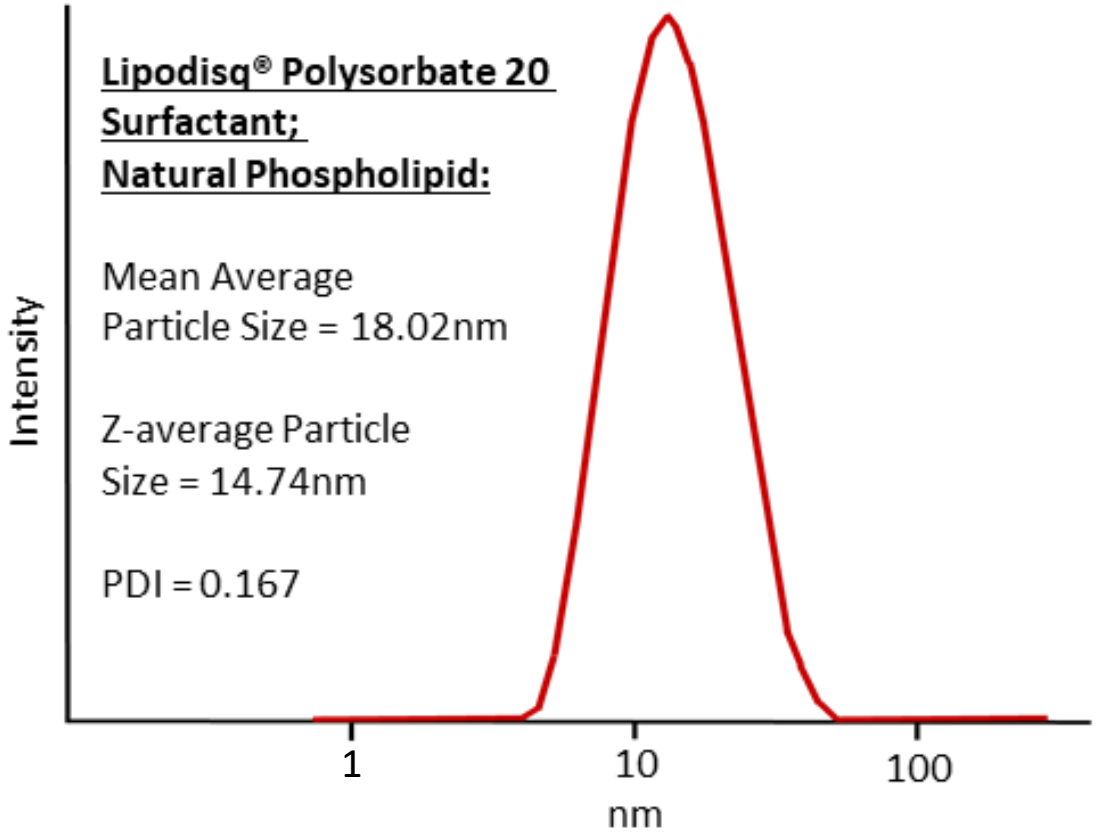
Lipophilic Active:
Encapsulated within hydrophobic core



Polysorbate 20 Surfactant:
RSPO MBAL Sourced

2007

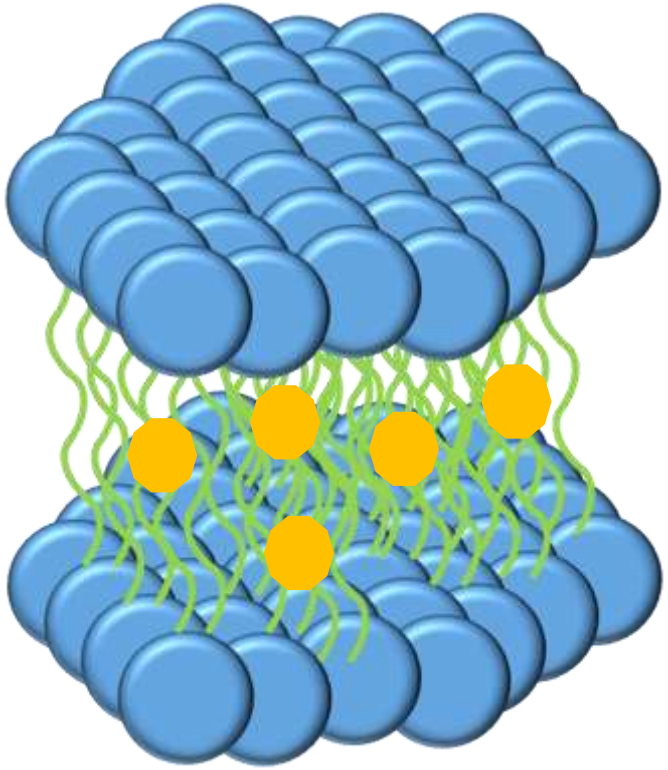
Lipodisq® Generation β



Curiosity, Innovation.

LIPODISQ® Origins

Personal Care Active Delivery:
The centre of a Lipodisq® is composed of a phospholipid bilayer with a defined high content of phosphatidylcholine. The lipophilic area is primarily made up of fatty acid tails of the phospholipids, which typically have a high log P value, ranging from 3 to 8 or higher, reflecting strong lipophilicity. This provides an optimal environment in which to solubilise and encapsulate **lipophilic/hydrophobic active agents**, rendering them **water soluble** and isolated from the surrounding aqueous environment.



2007

Lipodisq® Generation β

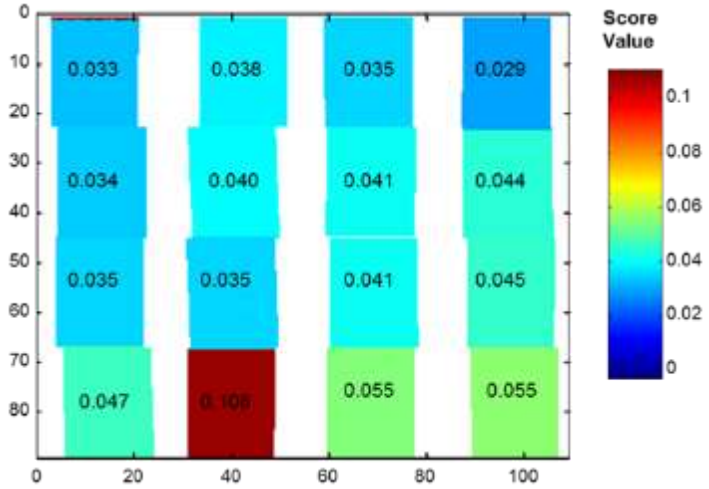
Key Features:

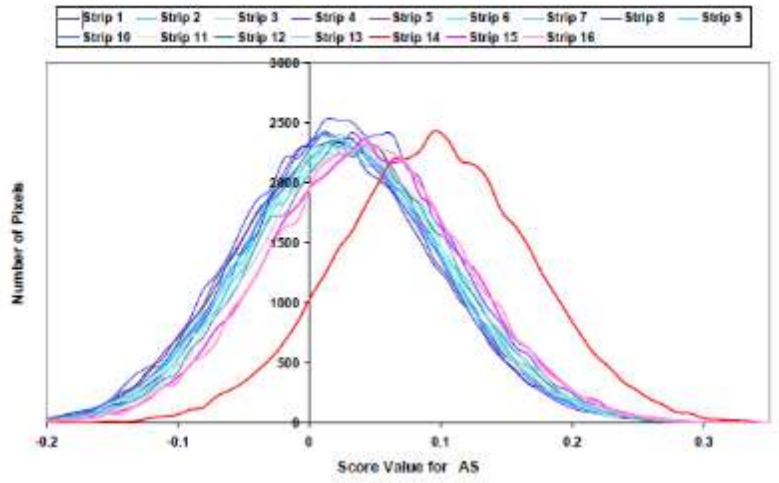
- Solubilise lipophililc/hydrophobic actives in water
- Small particle size (~10 – 40nm)
- Enables production of clear aqueous gels/solutions and also suitable for inclusion in conventional creams/serums
- Stable in aqueous solution upon dilution
- Facilitates skin absorption
- Sustained release of actives
- Improved stability of actives

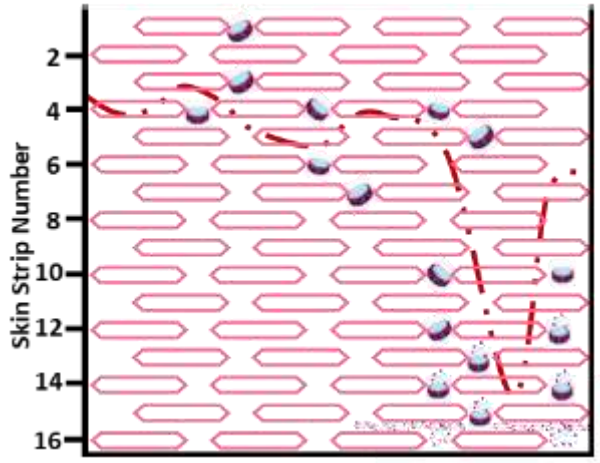
Lipodisq® Generation β

Transdermal Penetration:
The small size of Lipodisq® particles enables them to penetrate the upper layer of the epidermis, the stratum corneum. A high loading capacity for oil soluble agents, Lipodisq® have a far greater potential for delivering significant amounts of active agents, as compared to much larger particle systems such as liposomes/niosomes.

***In vivo* study:** Lipodisq® formulation containing a marker dye is applied to the outer layer of the skin for 20 minutes, the skin is washed and adhesive tape used to repeatedly strip layers of *stratum corneum*, the dye removed on each strip is then analysed spectrophotometrically using a near-infrared technique to assess the presence of the marker dye.







Results: Lipodisq® formulation facilitates penetration of the dye to the lower layers of the stratum corneum >16 consecutive skin strips, effectively overcoming the barrier function of the skin.

Lipodisq® Generation β

Active Stabilisation:

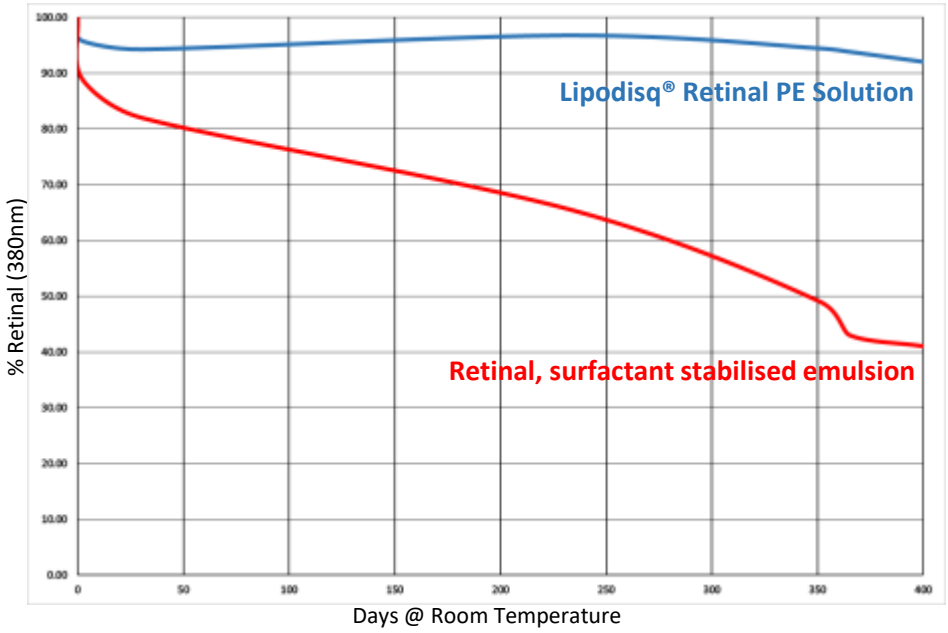
Whilst encapsulating hydrophobic or amphiphilic active agents within its phospholipid membrane and rendering them water soluble, Lipodisq® constructs also protect the active agent from oxidation and degradation. Lipodisq® formulated actives can exhibit superior stability, in concentrated formats as well as finished products, vs conventional product offerings. Providing both the consumer and product manufacturers with stable and efficacious products for the duration of their use.

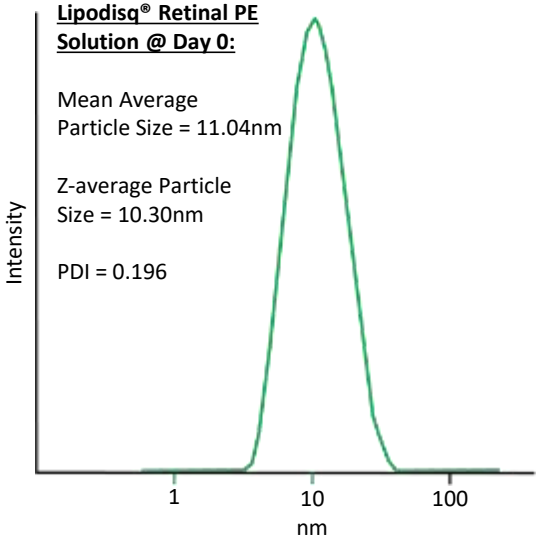
Case Study:

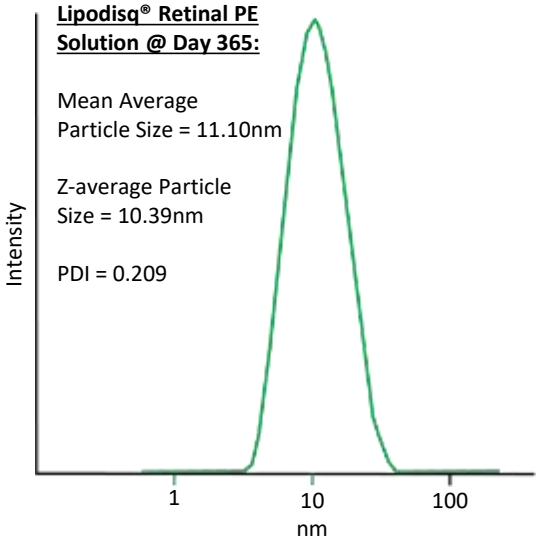
Lipodisq® Retinal PE Solution

After >**365 days** storage at room temperature, **93.80%** Retinal content retained within Lipodisq® sample (UV-Vis Spectrophotometer measurement @ λ 380nm) compared to **40.00%** Retinal content retained within a conventional formulation format.

Particle stability and size characteristics remain **unchanged**.







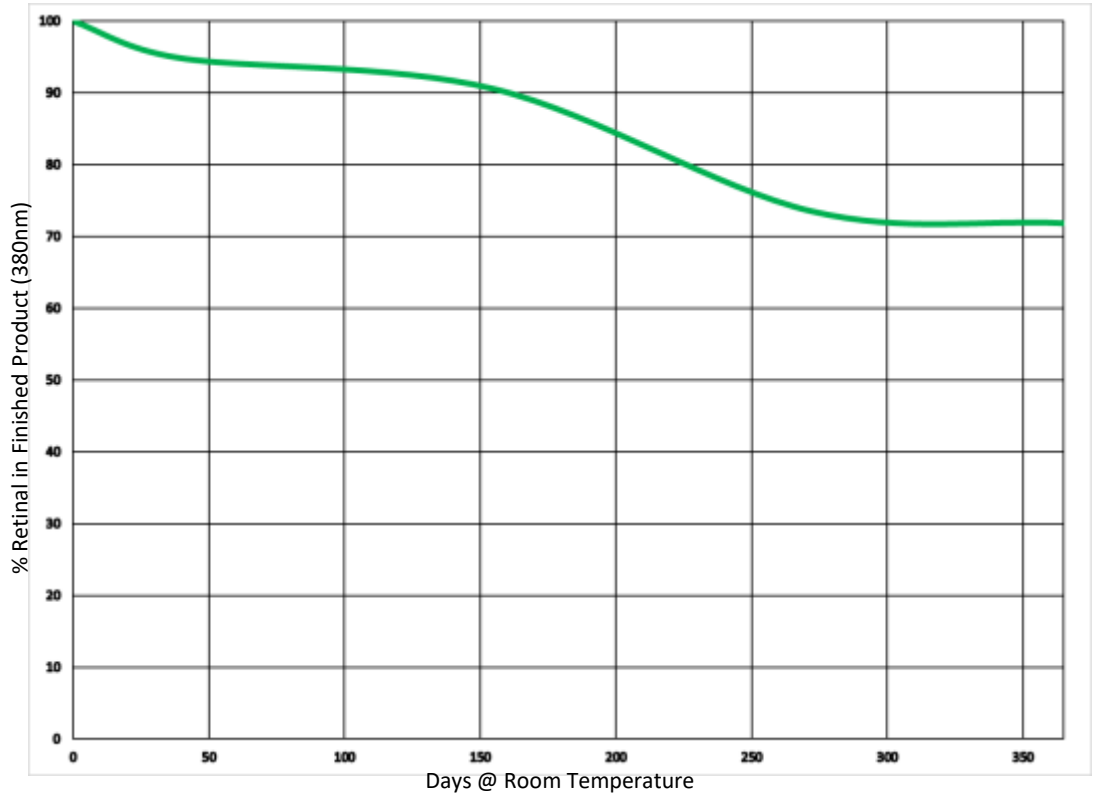
Lipodisq® Generation β

Formulation Stable:

Lipodisq® solutions for Personal Care, are compatible with most commonly used excipients. Lipodisq® are suitable for inclusion within aqueous gels, oil-in-water emulsion/creams, hydrogel patches and mask technologies. Stabilising performance of Lipodisq® encapsulated actives is retained during manufacturing and processing of finished products and throughout a product's shelf-life.

Case Study:
Aqueous gel containing Lipodisq® Retinal PE Solution (Retinal content 0.05%)

Post production processing and **>365 days** storage at room temperature, **72%** Retinal content retained in the finished product (UV-Vis Spectrophotometer measurement @ λ 380nm). No Secondary anti-oxidants or stabilisers have been included.



LIPODISQ® Origins

Lipodisq® Generation β

Personal Care Market Entry:

In September 2012, Curcu Nano Serum launches in Japan, the first formulation to be developed utilising Lipodisq® for the stabilisation and delivery of proprietary hydrophobic extracts of Japanese White and Spring Turmeric, to effectively combat hyperpigmentation for users throughout Japan and SEA. Marketing campaigns of brand owner Veritas focused on the use of a Nano-Technology, highlighting the penetration and efficacy benefits it provides. By May 2013, Curcu Nano Serum was a regular 'Best Seller' on television shopping network: 'Shop Channel Japan'.

In October 2012, Lipodisq® Solutions for Personal Care are launched in the UK in collaboration with our long standing distribution partner, Adina Cosmetic Ingredients Ltd.

Lipodisq™ Technology
Curcu

ADINA
COSMETIC INGREDIENTS

2012

Curiosity, Innovation.

Lipodisq® Generation β

Lipodisq® Products for Personal Care:

Lipodisq® Retinol PE Solution
(INCI: Aqua, Polysorbate 20, Retinol, Lecithin, Phenoxyethanol, Ethylhexylglycerin, BHT, BHA)
Anti-ageing, skin lightening/brightening, stimulates collagen production, thickens dermal layer and has a plumping effect.

Lipodisq® Retinal PE Solution ***NEW for Q4 2024***
(INCI: Aqua, Polysorbate 20, Retinal, Lecithin, Phenoxyethanol, Ethylhexylglycerin)
Anti-ageing, skin lightening/brightening, stimulates collagen production, thickens dermal layer and has a plumping effect. Just one step metabolic conversion needed to form retinoic acid within the skin.

Lipodisq® Ascorbyl Palmitate PE Solution
(INCI: Aqua, Polysorbate 20, Lecithin, Ascorbyl Palmitate, Phenoxyethanol, Ethylhexylglycerin)
Stimulates collagen production, anti-oxidant and radical scavenging, with anti-ageing, anti-pigmenting effect, reverses skin damage and protects against environmental aggressors.

Lipodisq® Hyaluronate PE Solution
(INCI: Aqua, Sodium hyaluronate, Polysorbate 20, Lecithin, Phenoxyethanol, Ethylhexylglycerin)
Sodium Hyaluronate: Selected low molecular weight (<10,000Da) grade to provide efficient moisturising and hydration, plumping, anti-aging and skin restructuring effects.

Lipodisq® Generation β

Lipodisq® Products for Personal Care:

Lipodisq® Skin Brightener PE Solution
(INCI: Aqua, Niacinamide, Sodium ascorbyl phosphate, Polysorbate 20, Lecithin, Phenoxyethanol, Ethylhexylglycerin)
Promote even skin tone and reverses age-spot related pigmentation.

Lipodisq® Escin SAP PE Solution
(INCI: Aqua, Polysorbate 20, Extract of Aesculus hippocastanum, Sodium ascorbyl phosphate, Lecithin, Phenoxyethanol, Ethylhexylglycerin)
Vasoconstrictive and brightening properties to address skin surface redness, promote micro-circulation and lymphatic drainage under eye, combat cellulite in the leg/thigh.

Lipodisq® Niacinamide PE Solution
(INCI: Aqua, Niacinamide, Polysorbate 20, Lecithin, Phenoxyethanol, Ethylhexylglycerin)
Promote even skin tone and reverses age-spot related pigmentation.

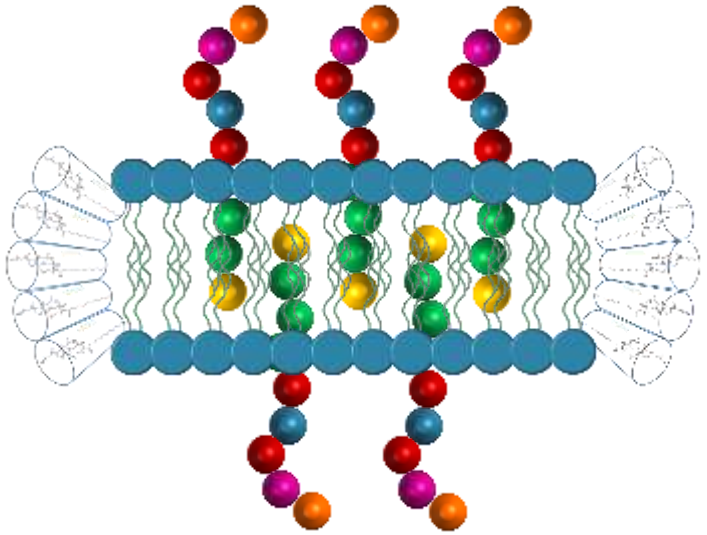
Lipodisq® Oxyresveratrol PE Solution
(INCI: Aqua, Polysorbate 20, Dipotassium Glycyrrhizate, Lecithin, Oxyresveratrol, Phenoxyethanol, Ethylhexylglycerin)
Skin brightening/lightening properties via inhibition of tyrosinase. Potent anti-oxidant for ROS scavenging, anti-ageing and anti-inflammatory activity.

Lipodisq® Generation β

Lipodisq® Products for Personal Care:

Peptides:

With extensive experience of stabilising membrane proteins with Generation α, Lipodisq® technology is well suited to the encapsulation and delivery of therapeutic proteins, protein fragments and peptides. Lipodisq® technology is used to deliver conventional, commercially available peptides and exclusive peptide structures for personal care applications.



Proprietary actives and exclusivity:

Exclusive Lipodisq® products are developed with brand owners based on both proprietary and market available active principles. Exclusive options can be based on market or territory, as well as active agent.

Regulatory:

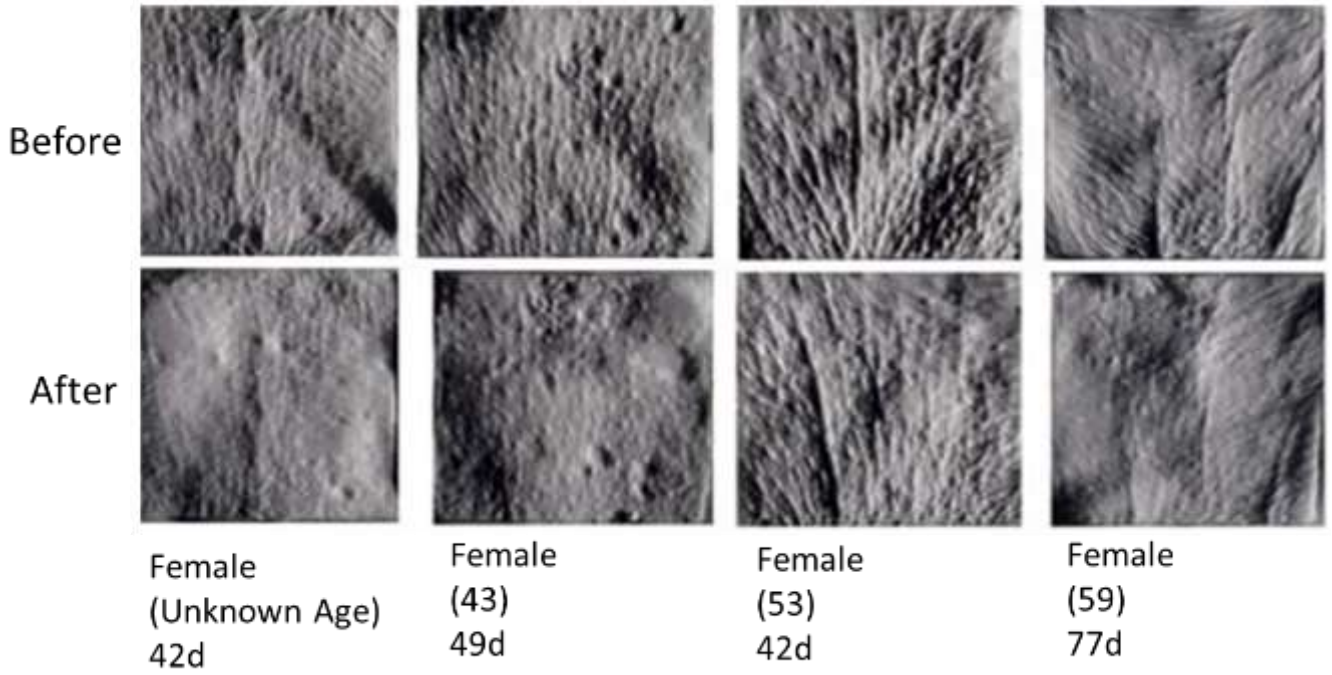
Lipodisq® components are approved for use worldwide. Regulatory status of component active principles should be confirmed locally. Lipodisq® formulations have been approved for inclusion within 'Quasi-Drug' recognised products in Japan.

Lipodisq® Generation β

Example Consumer Product Efficacy:

NIP+FAB

Nip + Fab
Retinol Fix Blemish Gel Treatment 10%
[10% Lipodisq Retinol PE Solution] Acne Care



VERITAS

Veritas Ltd
Curcu Nano Serum
[8% Lipodisq Turmeric Extract Solution] Anti-wrinkle

LIPODISQ® Origins

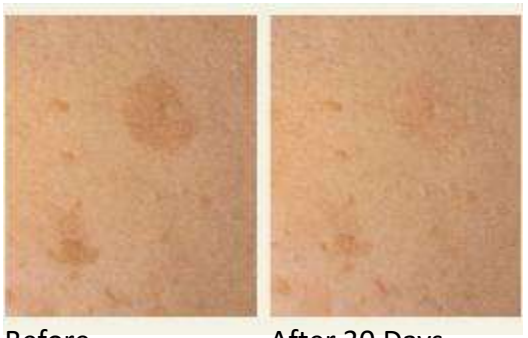
Lipodisq® Generation β

Example Consumer Product Efficacy:

Sunspots:

Before After 30 Days

Even Skin tone:



Before After 30 Days

RE:ERTH

RE:ERTH Pte Ltd

Illuminating Concentrate

[12% Lipodisq Oxyresveratrol PE Solution] Hyperpigmentation

Sunspots on hands:

Lipodisq® Technology Curcu

Veritas Ltd

Curcu Nano Serum

[8% Lipodisq Turmeric Extract Solution] Hyperpigmentation

Curiosity, Innovation.

Lipodisq® Generation β

Example Consumer Product Efficacy:

Day 0

Day 28

Anti-wrinkle Gel Formulation
(Custom Finished Product, Malvern Cosmeceutics Ltd)

[5% Lipodisq Retinol PE Solution]

Lipodisq® Generation β

Licensees, Distributors and Highlighted Partners/Customers:

VERITAS

Rodial

RE:ERTH

Mature
Beauty is Continuous
～続いていく美しさ～

ADINA
COSMETIC INGREDIENTS

bioscope
HEALTHCARE INNOVATION

Lipodisq™ Technology
Qurcu

The Organic Pharmacy

NIP+FAB

HALSKIN

Mybestie®
Skincare with Cosmeceuticals

MYDAYBE®

COWSHED

SUPER FACIALIST

Dr.Anmytas

KUARAL

skin Chemists
LONDON

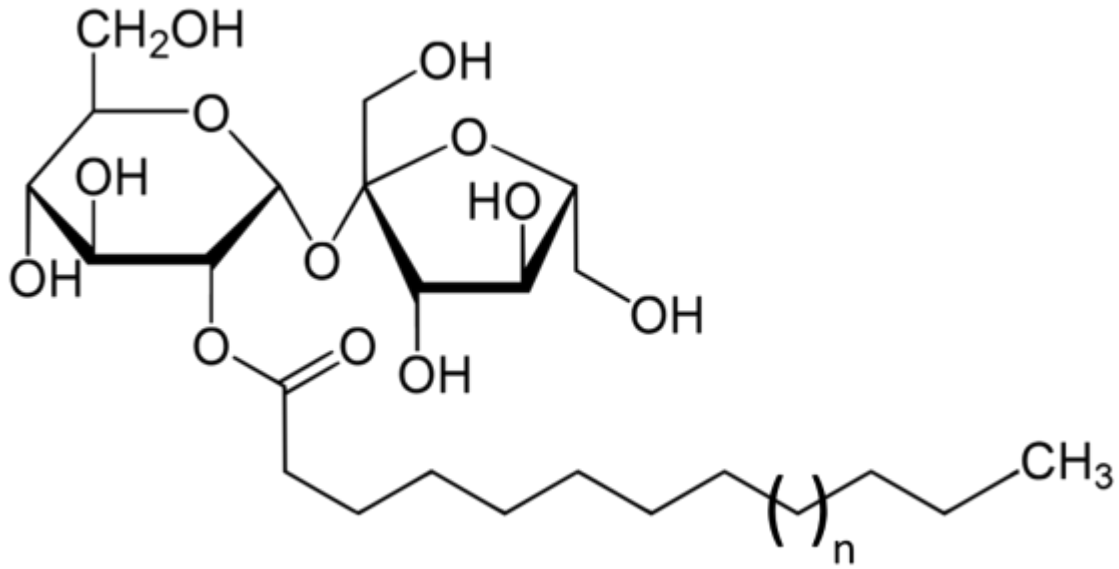
Lipodisq® Generation γ

Closer to Nature:

In 2021, we launched the final phase of Lipodisq® Green particle development, Generation γ, to support personal care manufacturers in achieving naturality claims for their products. Lipodisq® was re-engineered to replace the Polysorbate 20 surfactant with one derived from natural components.

By leveraging the theory and insights gained from generation β development, we were able to hypothesize the essential surfactant structures and molecular shape needed for Lipodisq® Green particle formation. Suitable candidate molecules were identified within the surfactant classification: Sucrose esters.

Sucrose esters are non-ionic surfactants derived from the esterification of sucrose with fatty acids and are commonly used in food, cosmetics, and pharmaceuticals. Their natural origin and biodegradability make them popular choices for products emphasizing sustainability and naturality.

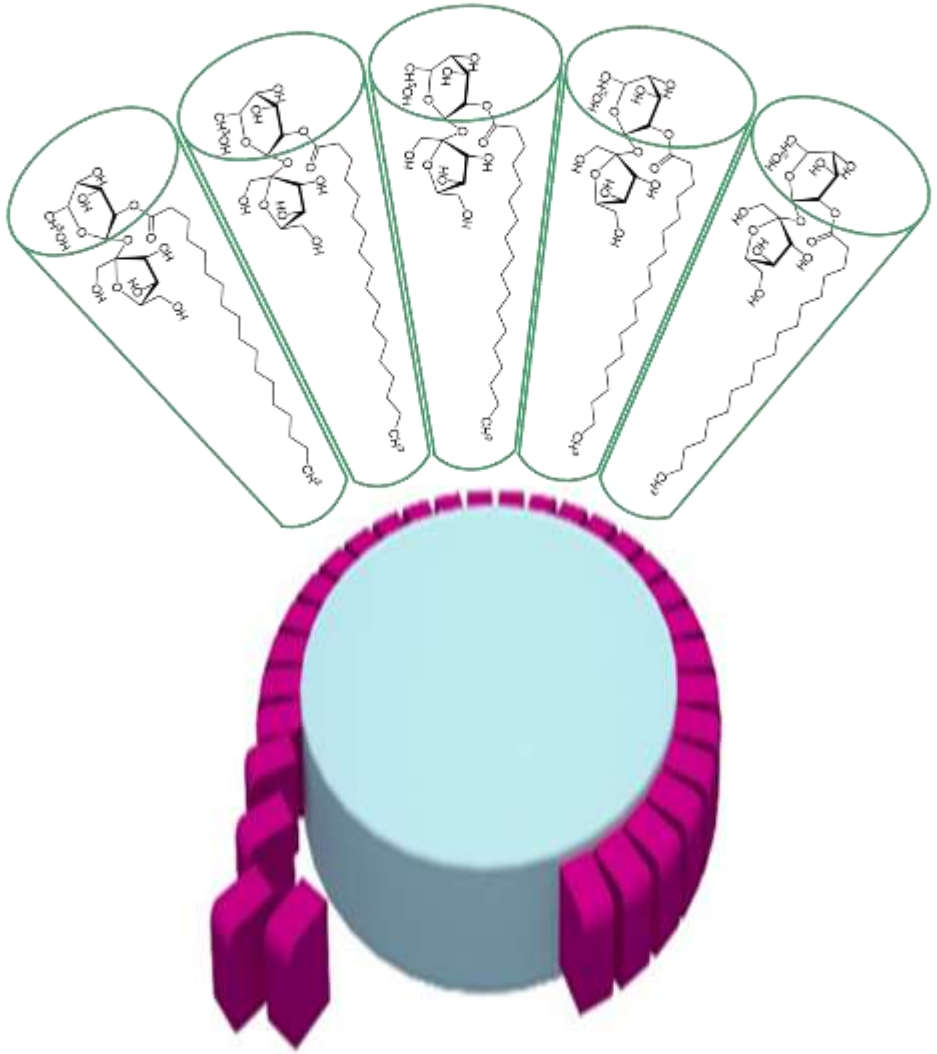


2021

Lipodisq® Generation γ

Naturality:
Depending on the chemical type and/or source of active ingredients, Lipodisq® Green solutions can be offered with a 100% naturality claim.

The fully biodegradable particles, now made from food approved materials, also pave the way for oral nutraceutical delivery, enhancing product efficacy through the stabilizing effects of nano-encapsulation.



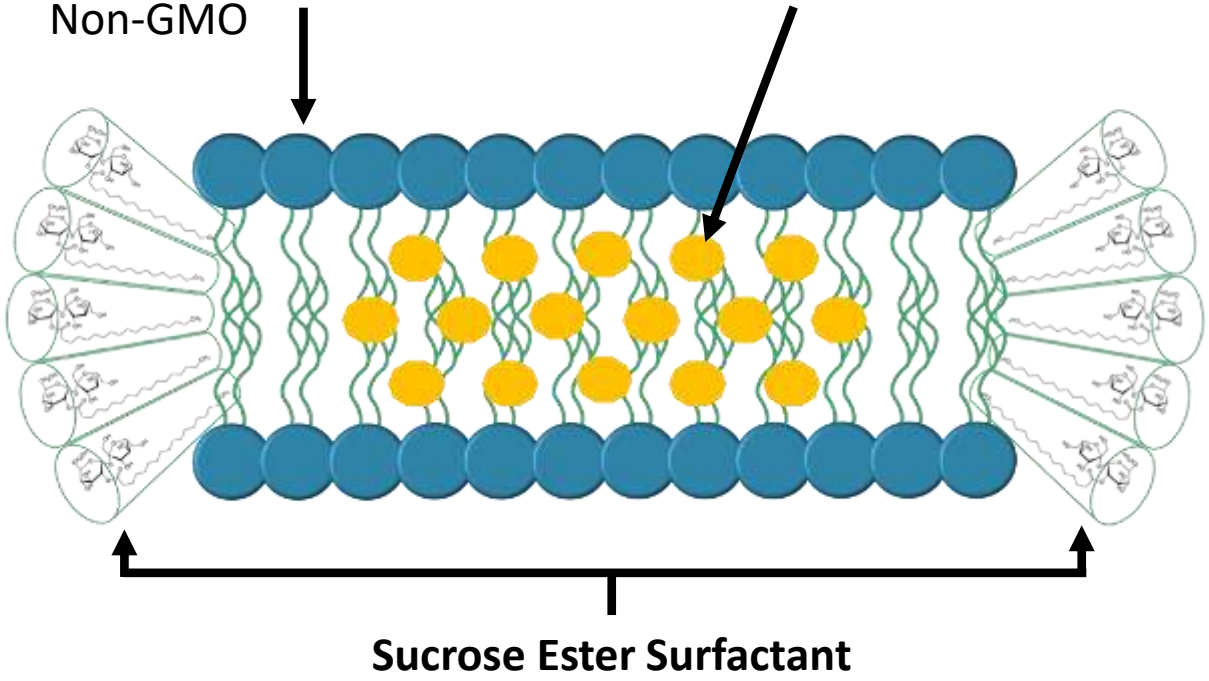
LIPODISQ® Origins

Lipodisq® Generation γ

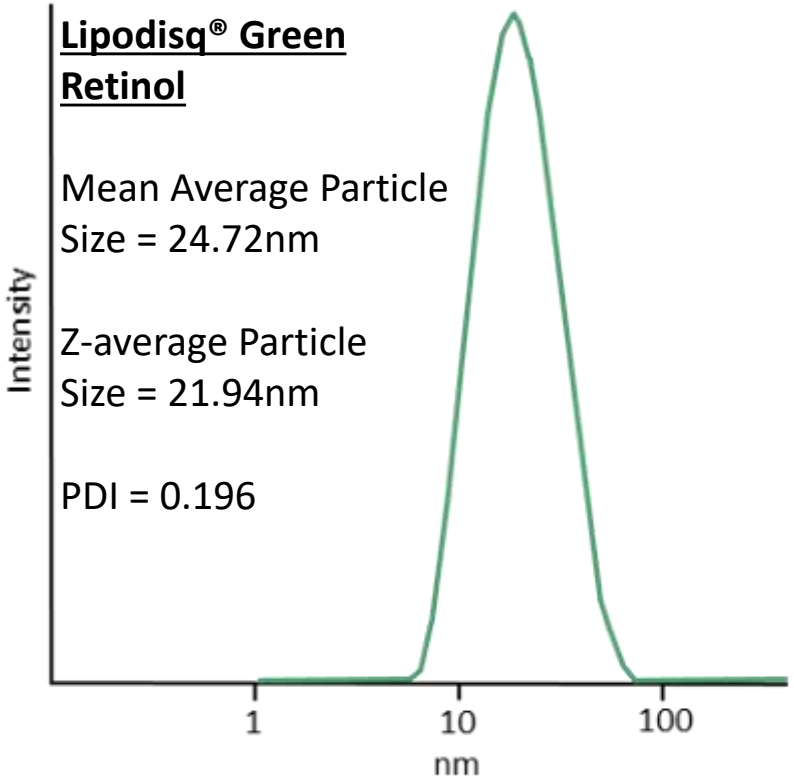
Key particle properties remain the same:

Phospholipid Membrane:
Phosphatidylcholine rich, sourced from Soy.
Non-GMO

Lipophilic Active:
Encapsulated within hydrophobic core



Sucrose Ester Surfactant



Lipodisq® Green Retinol: 99% Naturality Score

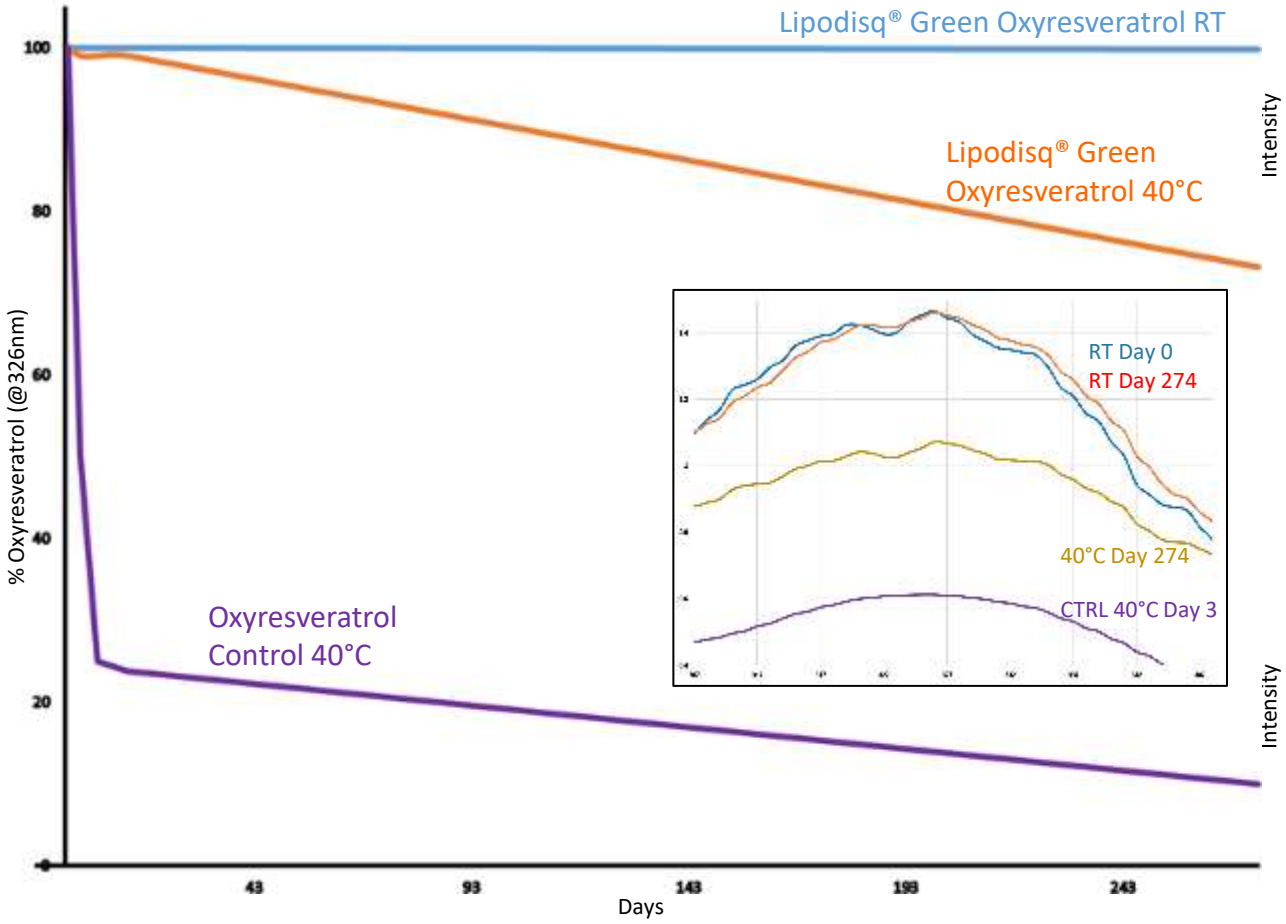
Curiosity, Innovation.

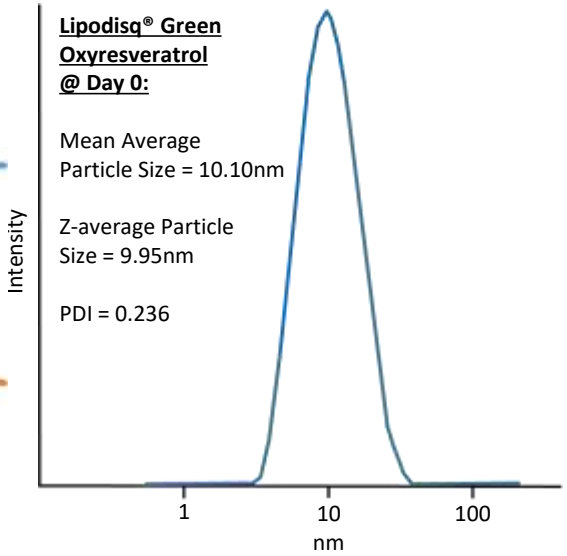
Lipodisq® Generation γ

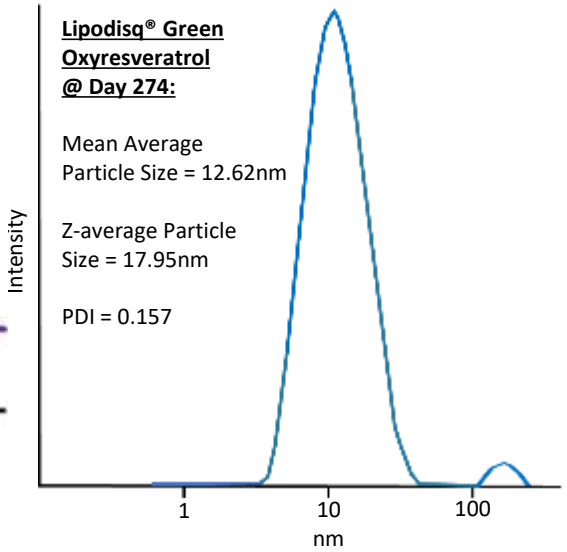
Active Stabilisation:

Case Study: Lipodisq® Green Oxyresveratrol Solution

After >**270 Days** storage at room temperature, **99.79%** Oxy-resveratrol content retained within Lipodisq® sample (UV-Vis Spectrophotometer measurement @ λ 326nm).
Sample stored at 40°C, **73.17%** Oxyresveratrol content retained, compared to control sample (conventional stabilised emulsion), **50.00**% after 3 days, **25.00%** after 7 days, degrading to **<10.00%** by 274 Days.
Particle and size characteristics remain **stable**.







Lipodisq® Generation γ

Lipodisq® Green Solutions for Personal Care **NEW for 2025:**

Lipodisq® Green Retinol Solution
(INCI: Aqua, Sucrose ester, Retinol, Lecithin, Undecane, Pentylene glycol, Caprylyl glycol, Tridecane, Bioflavonoids, Tocopherol)
Anti-ageing, skin lightening/brightening, stimulates collagen production, thickens dermal layer and has a plumping effect.

Lipodisq® Green Niacinamide Solution
(INCI: Aqua, Niacinamide, Sucrose ester, Lecithin, Pentylene glycol, Caprylyl glycol, Bioflavonoids)
Promotes even skin tone and reverses age-spot related pigmentation.

Lipodisq® Green Oxyresveratrol PE Solution
(INCI: Aqua, Sucrose ester, Dipotassium Glycyrrhizate, Lecithin, Oxyresveratrol, Pentylene glycol, Caprylyl glycol, Bioflavonoids)
Skin brightening/lightening properties via inhibition of tyrosinase. Potent anti- oxidant for ROS scavenging, anti-ageing and anti-inflammatory activity.

Lipodisq® Green Hyaluronate PE Solution
(INCI: Aqua, Sodium hyaluronate, Sucrose ester, Lecithin, Pentylene glycol, Caprylyl glycol, Bioflavonoids)
Sodium Hyaluronate: Selected low molecular weight (<10,000Da) grade to provide efficient moisturising and hydration, plumping, anti-aging and skin restructuring effects.

2025

Lipodisq® IP

Lipodisq® technology is covered by one or more of the following patents owned by Malvern Cosmeceutics Limited:

AU 2006253886
CA 2,611,144
CN ZL200680018957.2
EP 1890675
GB 2426703
JP 5142898
IN 261468
US 8623414
WO/2021/005340A1 pending

AU2007327054
CN ZL200780044148.3
GB2464393
JP6567575
JP5142989
SA2009/02939

LIPODISQ®

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Curiosity, Innovation.