bicosome®

Advanced lipid systems for skin drug delivery

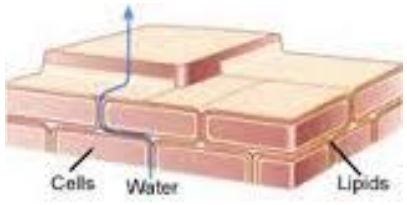


Rafael Bernad

THE CHALLENGE: SKIN DELIVERY

MARKET AND CUSTOMERS DEMAND PRODUCTS ABLE TO **PENETRATE GENTLY THE SKIN, REMAINING THERE, AND DELIVERING ITS BENEFITS** IN TARGET LAYERS.

Main barrier to skin penetration



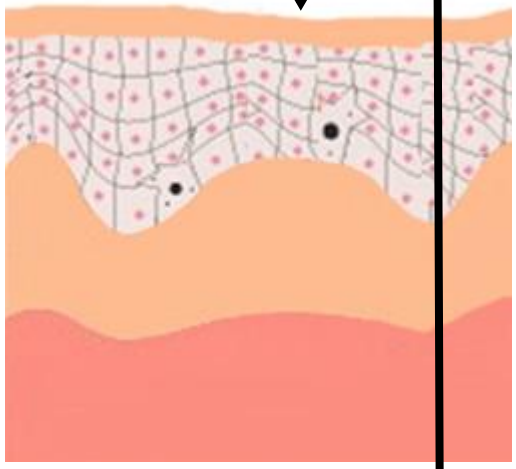
Stratum corneum

Epidermis

Dermis

Hypodermis

Superficial



* Skin layers representation

Aggressive systems

Many topical application products do not really penetrate the skin and disappear after just a single wash

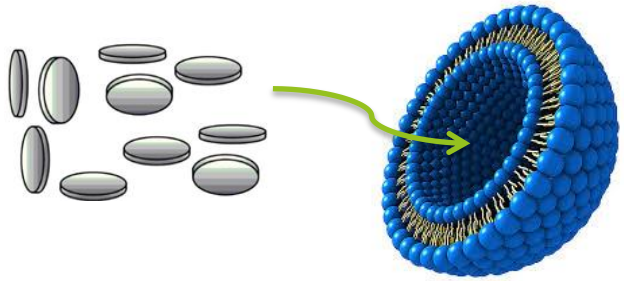
Other products penetrate aggressively the skin, promoting damages, and reaching the bloodstream

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BICOSOME TECHNOLOGY

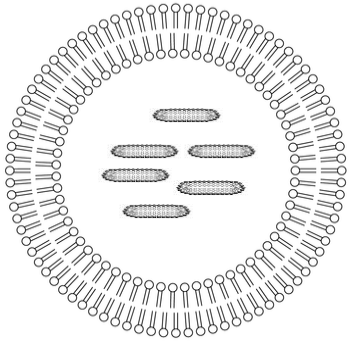
Bicosome is based on different lipid aggregates, smart structures enclosed in vesicles.

- Soft matter nanocarriers formed exclusively by lipids. High biocompatibility.
- Appropriate Size. Able to penetrate between the narrow intercellular spaces of the skin *stratum corneum.*
- Great morphological versatility, adopting different sizes and shape depending on composition and environment.



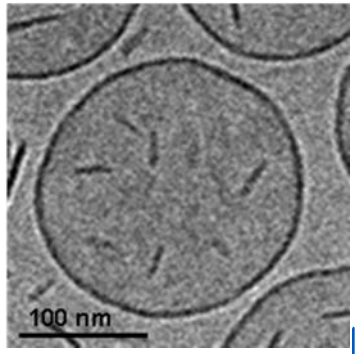
Smart structures

6-20 nm



Vesicles

150-250 nm

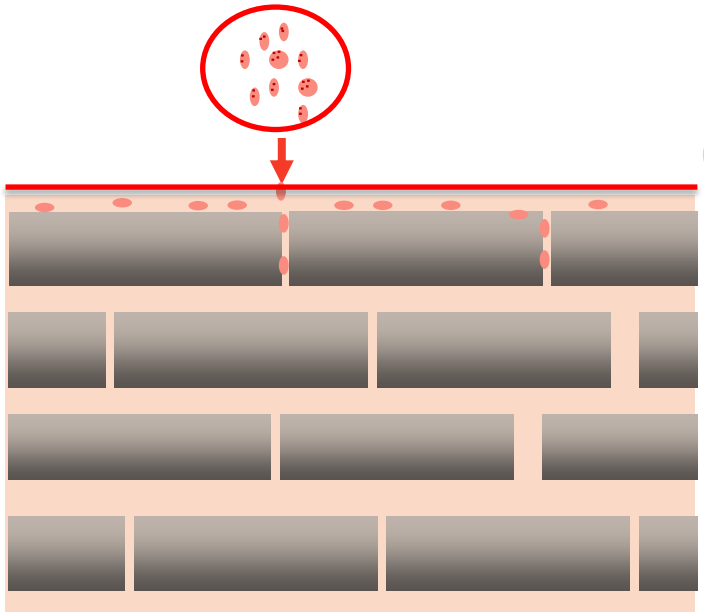


Cryo-TEM micrograph of bicosome® structures

bicosome®

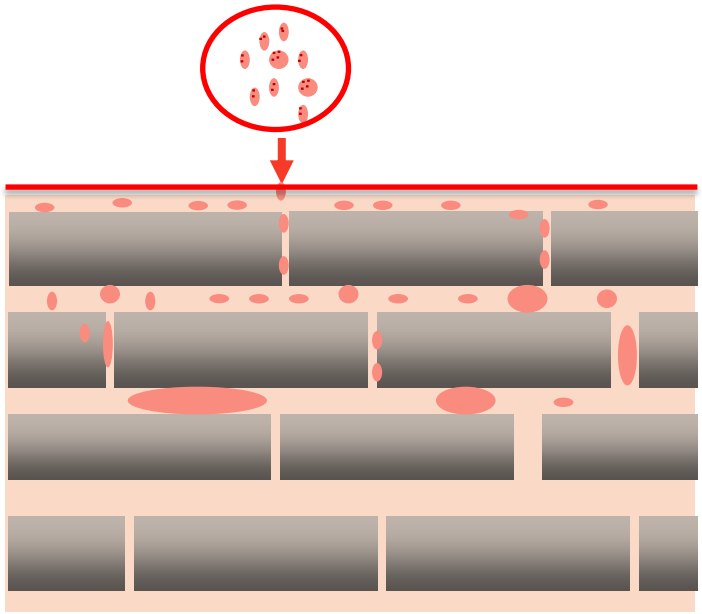
BICOSOME BIOMIMETIC MECHANISM

Bicosomes® modulate the skin barrier function without damaging the skin



1

BICOSOME BIOMIMETIC MECHANISM



1

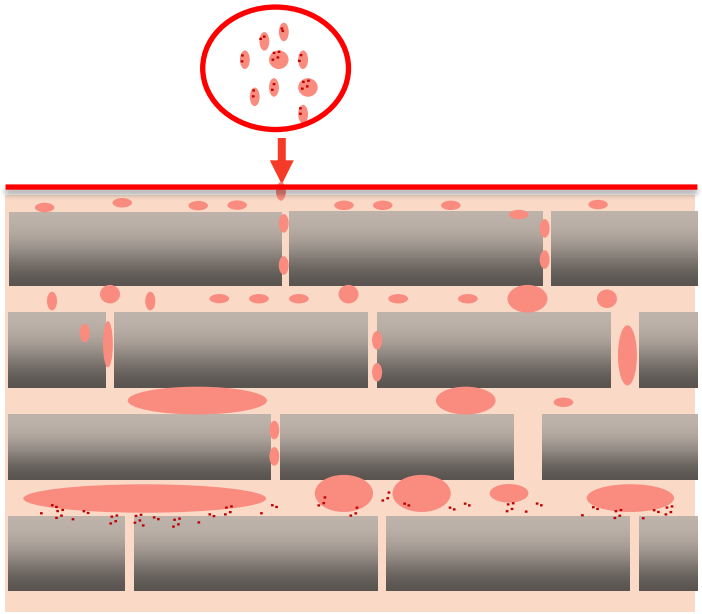
2

Bicosomes® modulate the skin barrier function without damaging the skin

Once inside the skin, Bicosome smart structures respond to the microenvironment of the internal layers and self-aggregate increasing their size

bicosome®

BICOSOME BIOMIMETIC MECHANISM



1

Bicosomes® modulate the skin barrier function without damaging the skin

2

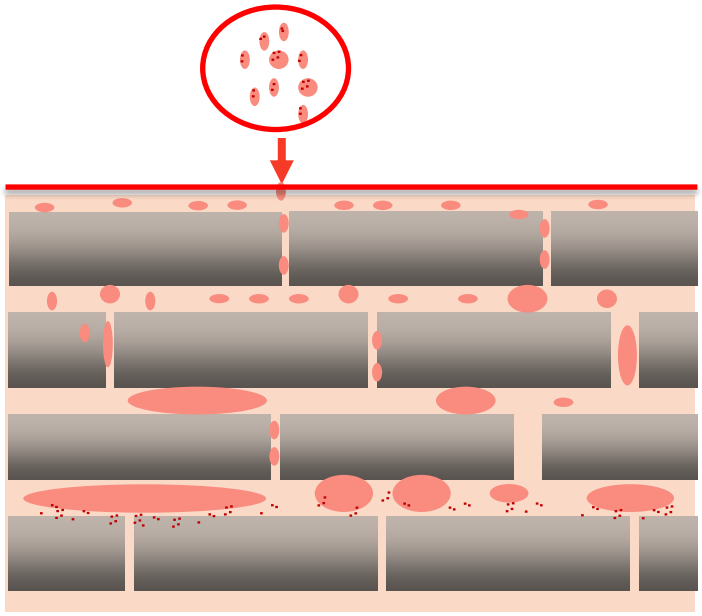
Once inside the skin, Bicosome smart structures respond to the microenvironment of the internal layers and self-aggregate increasing their size

3

This increase in size anchors them in the tissue and allows for the slowly delivery of its content, which results in higher efficacy and long lasting effects

bicosome®

BICOSOME BIOMIMETIC MECHANISM



1. Bicosomes® modulate the skin barrier function without damaging the skin
2. Once inside the skin, Bicosome smart structures respond to the microenvironment of the internal layers and self-aggregate increasing their size
3. This increase in size anchors them in the tissue and allows for the slowly delivery of its content, which results in higher efficacy and long lasting effects
4. Bicosomes® are freed following the skin renewal process (turn over process)

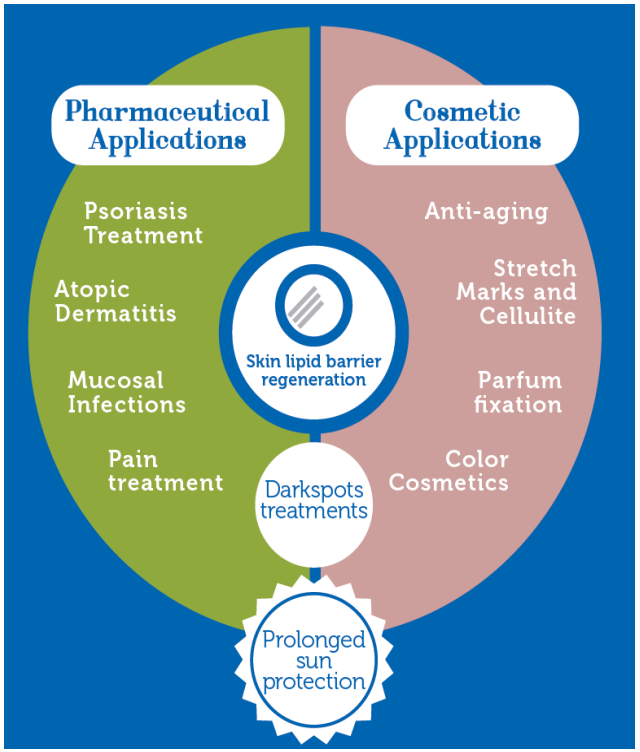
bicosome®

BICOSOME CLAIMS

- Modulation of skin penetration
- Lipid matrix reinforcement
- Retention in the skin
- Long lasting effects
- Target delivery
- Actives stabilisation

+

CLAIMS RELATED TO THE MOLECULE INCORPORATED AND THE IMPROVEMENT OF ITS EFFICACY

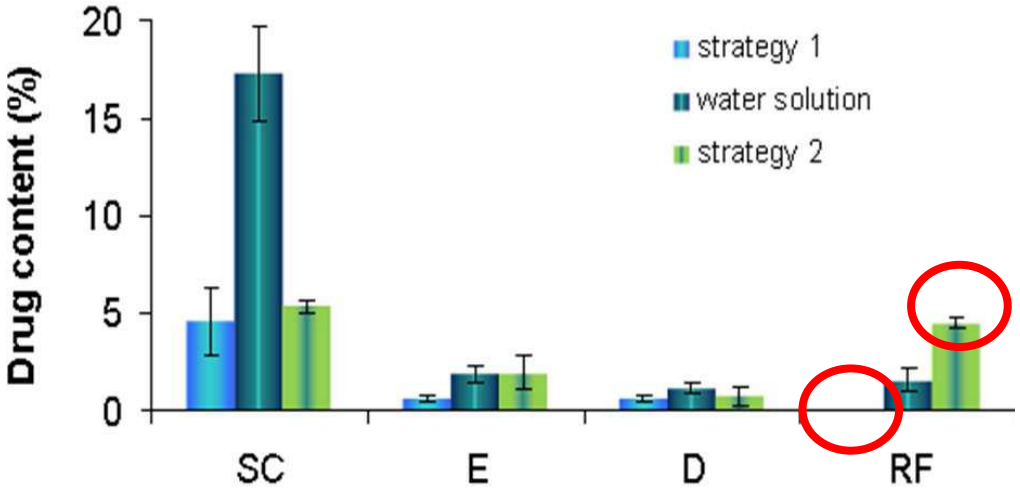


bicosome®

MODULATION OF SKIN PERMEATION

PERCUTANEOUS ABSORTION OF DICLOFENAC

- Strategy 1: A Bicosome system designed to retard DDEA penetration preventing or delaying the drug to reach the receptor fluid.
- Strategy 2: A Bicosome system designed to enhance DDEA penetration increasing the drug to reach the receptor fluid.



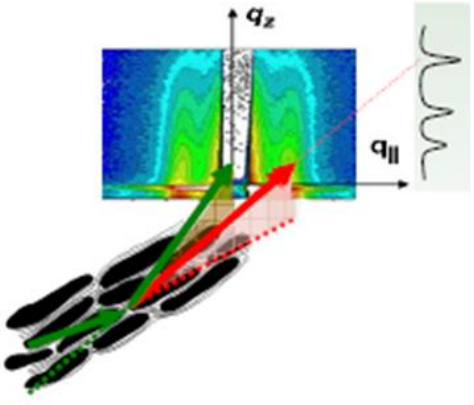
L. Rubio, G. Rodríguez, L. Barbosa-Barros, C. Alonso, M. Cócera, A. de la Maza, J.L. Parra, O. López, Colloids and Surfaces B: Biointerfaces, 2012, 92, 322

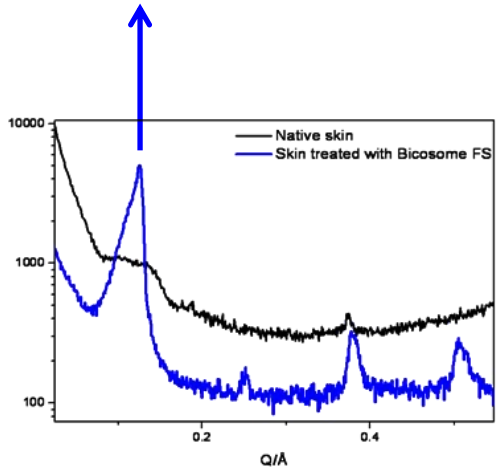
bicosome®

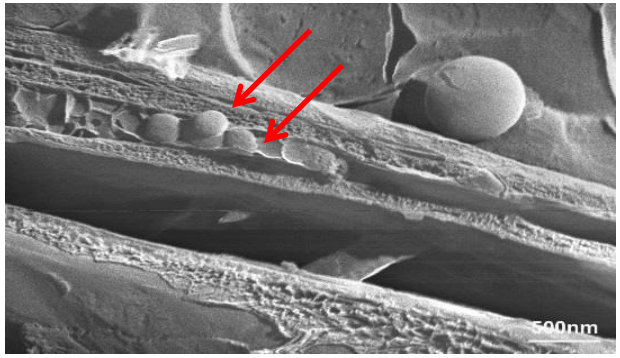
LIPID MATRIX REINFORCEMENT

Higher organization of the SC lipid structure of skin treated with Bicosome

GISAXS:







** Cryo SEM of Bicosomes anchored in the skin (Barbosa-Barros, L., 2008)*

Typical profile of non treated SC lipid structures

Bicosome reinforces the skin lipid structure by the incorporation of new lipids and by increasing the order in the lipid organization.

bicosome®

RETENTION

BICOSOME CONTAINING NYSTATIN

Percentage of drug permeated and retained in the mucosa tissue after treatment with Bicosome and commercial product.

Product applied	Drug content (%)
Nystatin in commercial product	17
Nystatin in Bicosome	73

Bicosome increases the retention of drug in the tissue.
The amount of nystatin retained in mucosa was higher when the drug was included in bicosome than when was formulated in the commercial product.

bicosome®

LONG LASTING EFFECT

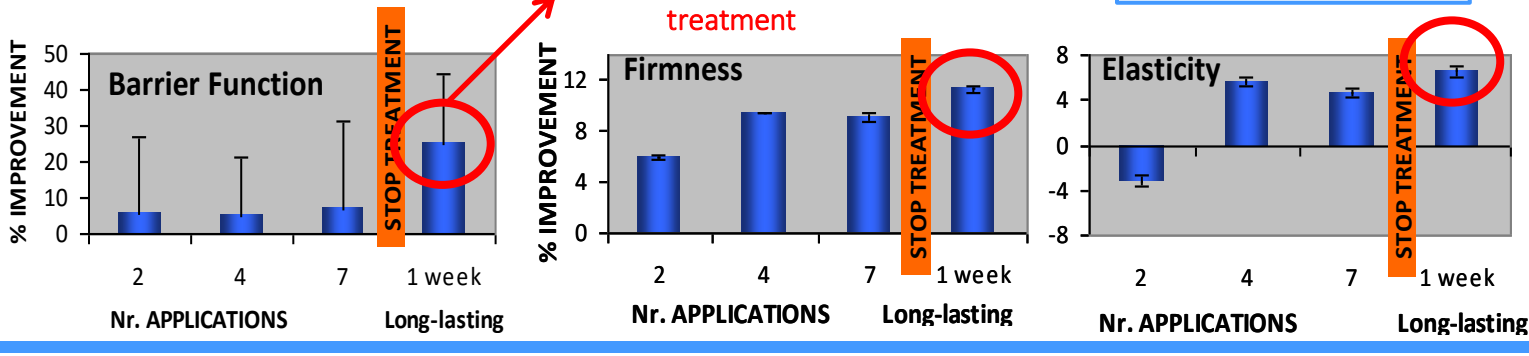
BICOSOME IN VIVO EFFICACY STUDIES

16 days of experiment
07 Applications (1 x day)
Volar forearm
14 measurements

20 volunteers
Female
Age 25-38
2% Bicosome

IMPROVEMENT OF SKIN CONDITIONS
SHORT AND LONG LASTING EFFECTS

25% of improvement seven days after stopping treatment



Bicosome <u>short-term effects</u>: Reinforces the barrier function (+6%), Skin Firmness (+9%) and Skin elasticty (+5%) after seven (07) applications.

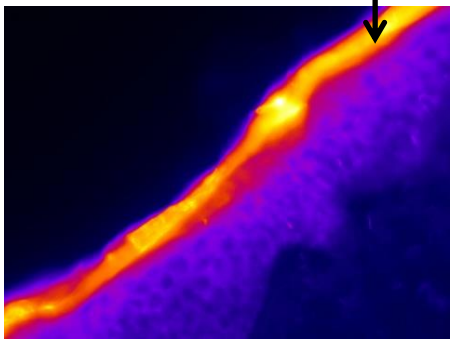
Bicosome <u>long lasting effects</u>: Bicosome kept treating the skin after stopping the treatment allowing an improvement in this period of **25% on skin barrier function**, **11% on Skin Firmness and 7% on Skin Elasticity after one week**.

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TARGET DELIVERY

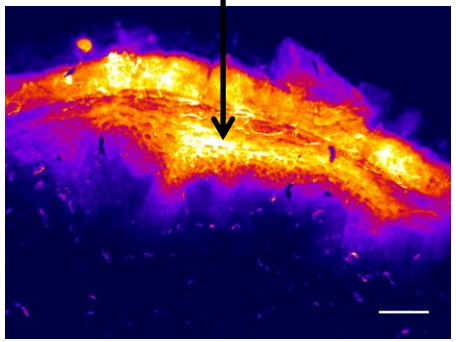
BICOSOME PROTOTYPE 1

Deepness of penetration and retention: *Stratum corneum*



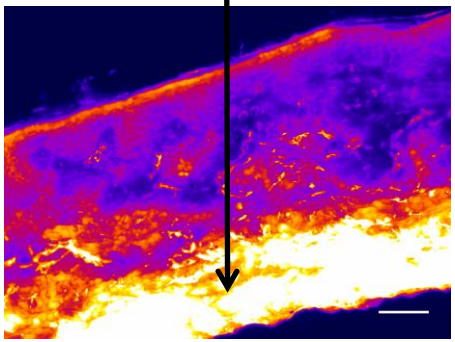
BICOSOME PROTOTYPE 2

Deepness of penetration and retention: Epidermis



BICOSOME PROTOTYPE 3

Deepness of penetration and retention: Dermis



* Fluorescence microscopy images of three different Bicosome systems encapsulating sodium fluorescein.

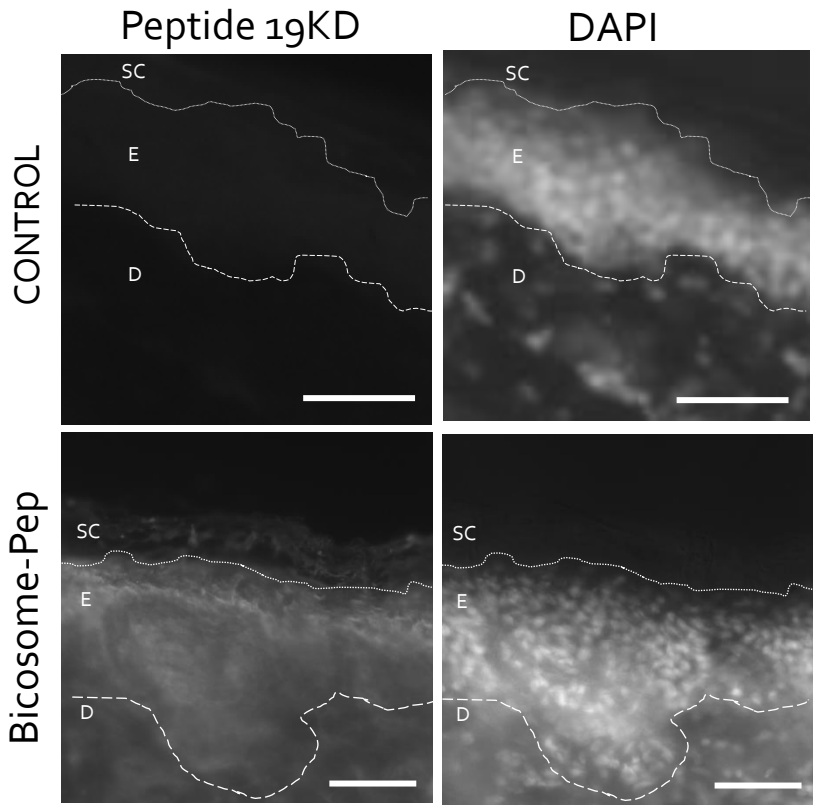
MODULATION OF SKIN PENETRATION
Technique: FLUORESCENCE MICROSCOPY

bicosome®

TARGET DELIVERY

BICOSOME 19kD peptide PROTOTYPE

Deepness of penetration Dermis



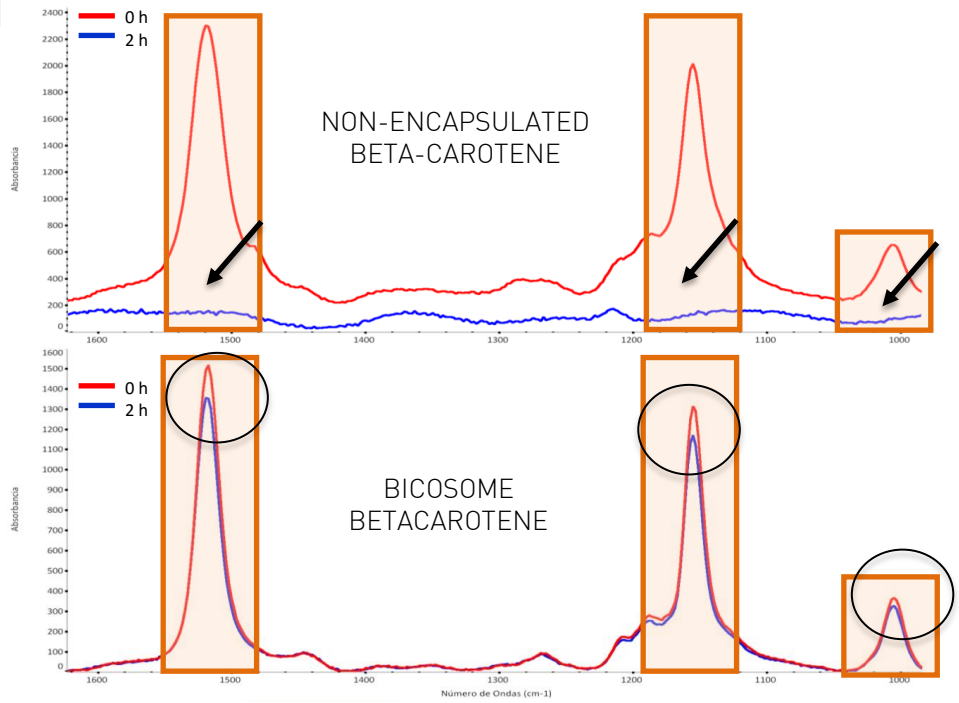
* Fluorescence microscopy images of skin treated with Bicosome systems encapsulating peptides

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MODULATION OF SKIN PENETRATION
Technique: FLUORESCENCE MICROSCOPY

ACTIVES STABILISATION

BICOSOME CONTAINING BETACAROTENE



Without protection, Beta-carotene peaks completely disappear after 2hs of UV irradiation.

Bicosome preserves the Beta-carotene molecules. After 2h of UV irradiation the peaks of beta-carotene are practically identical.

Technique: RAMAN SPECTROSCOPY

E. Fernández, et al., RCS Advances, 2014, 4, 53109-53121.

Carotene PROTECTION
Technique: Raman Spectroscopy

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API EFFICACY IMPROVEMENT

BICOSOME CONTAINING NYSTATIN

MIC determination:

	Candida albicans ATCC 10231	Sacharomyces cerevisae ATCC 9763
Free nystatin	3.125 µg/ml	3.125 µg/ml
Nys-com (Mycostatin)	0.781 µg/ml	0.781 µg/ml
Nys-Bicosome	0.390 µg/ml	0.197 µg/ml

2 x more active against *Candida albicans*

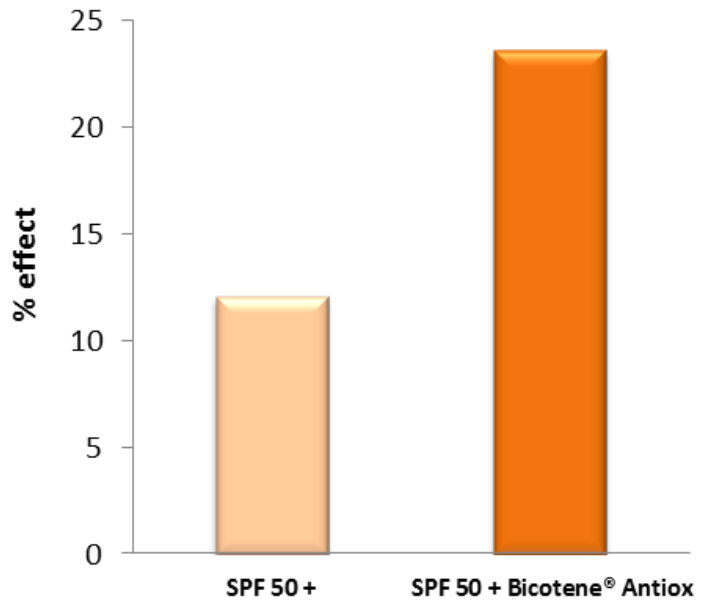
4 x more active against *Sacharomyces cerevisae*

Bicosome increases the effectiveness of Nystatin.
The system allows a reduction of the concentration of nystatin in pharmaceutical formulations without affecting antimicrobial efficacy.

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PRODUCT EFFICACY IMPROVEMENT

BICOSOME CONTAINING BETACAROTENE



* % compared with native skin (in *vitro*)

Bicosome containing betacarotene was able to double the FR protection of a sunscreen SPF 50 + during UV exposure

Technique: ELECTRON PARAMAGNETIC RESSONANCE (EPR)

bicosome®

THE ORIGIN





Research group: Biophysics of lipids and Interphases

iQAC

INSTITUTE OF ADVANCED CHEMISTRY OF CATALONIA

CSIC
CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS

SPANISH RESEARCH COUNCIL (CSIC)

GOBIERNO DE ESPAÑA
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

UNION EUROPEA
FONDO SOCIAL EUROPEO
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GOBIERNO DE ESPAÑA
MINISTERIO DE INDUSTRIA, ENERGÍA Y TURISMO

Programa Torres Quevedo
Convocatoria financiada por el FONDO SOCIAL EUROPEO

INNCORPORA

ENISA

CDTI
INICIATIVA neotec

bicosome®

DEVELOPING HIGH PERFORMANCE SKIN CARE INGREDIENTS

THANK YOU

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