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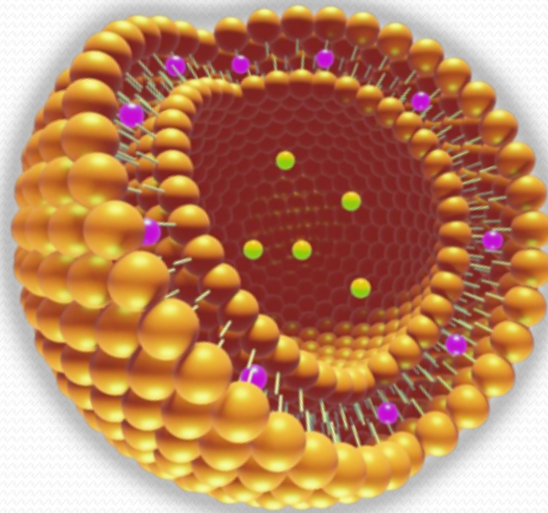
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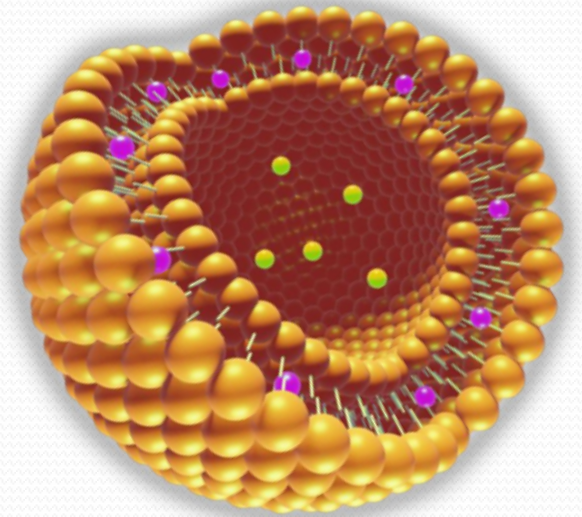


# Niosome Technology



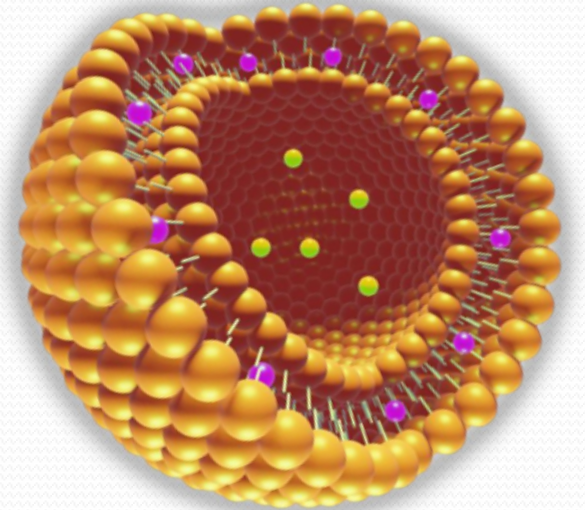
# What is Niosome...

ingredient is encapsulated in vesicles structurally similar to liposomes but with a bilayer composed **of non-ionic surface active agents rather than phospholipids**



# Why use Niosome....

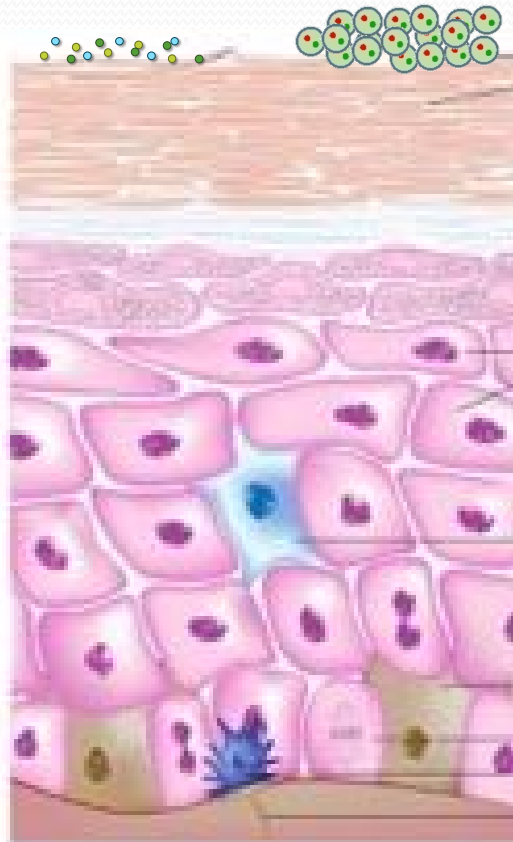
**to localize and concentrate the active ingredients**  
**in a skin compartment** of interest providing  
maximum efficacy of the cosmetic treatment



# ABSORPTION OF ACTIVE INGREDIENTS

ACTIVE INGREDIENTS

I.A. + DELIVERY SYSTEM



Stratum corneum  
No Metabolic Activity

Epidermis  
Cells with Active Metabolism

THE STRATUM CORNEUM LIMITS THE  
ABSORPTION OF ACTIVE  
INGREDIENTS

ACTIVE INGREDIENTS MUST REACH  
THE LIVING CELLS TO BE EFFECTIVE

# Why use a Delivery System?

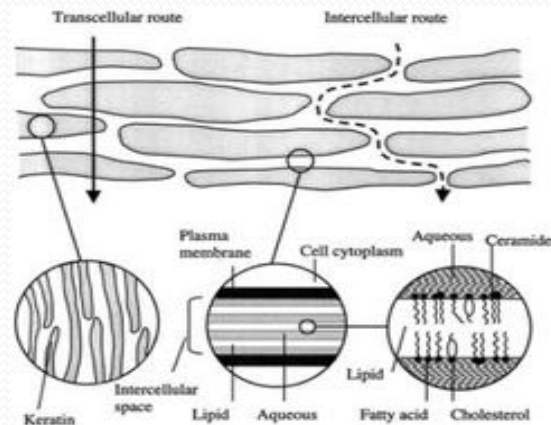
Skin care formulations should incorporate specific elements that improve the ability of active ingredients to overcome the stratum corneum



**DELIVERY SYSTEM or PENETRATION ENHANCER**



in order to partially disrupt and weaken the intercellular lipid lamellae in a reversible manner

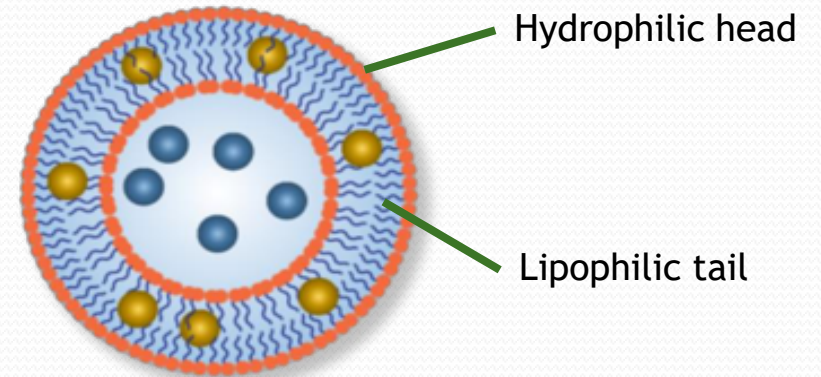


# Vesicle as Tool for Transdermal and Dermal Delivery

One approach is the use of vesicle as an active delivery system

Ø 150-250 nm

Composed of amphiphilic molecules



Their center consists of an aqueous cavity, which is surrounded by one or more bimolecular sheets of amphiphilic molecules

Hydrophilic actives can be entrapped into the aqueous cavity  
Lipophilic actives can be associated with the bilayer

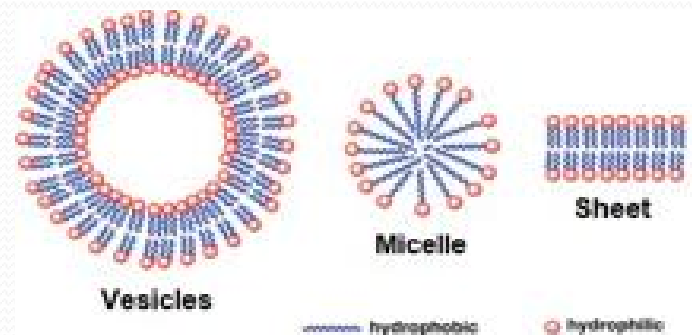
# Vesicle as Tool for Transdermal and Dermal Delivery

A wide variety of amphiphilic molecules can be used to prepare vesicles



Molecular structure can influence the type of colloidal aggregate and the physico-chemical characteristics such as, **size, charge, lamellarity and bilayer elasticity** and consequently the behavior of the vesicles

**Colloidal aggregate:**





# Vesicle as Tool for Transdermal and Dermal Delivery

In the last thirty years, many delivery systems have been developed

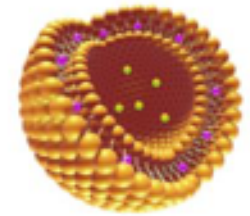
**Liposomes** - *Phospholipid bilayer* (1960s - 1970s)

**Conventional Niosome** - *Non-*

**Ethosomes** - *Phospholipid bilayer + ethanol* (1990s)

**Elastic Trasferosomes** - *Hybrid*

**Ultra-deformable Niosomes** - *Polyglycerol esters bilayer* (2008)



Vesicles as  
Delivery  
System

# Liposome Delivery System

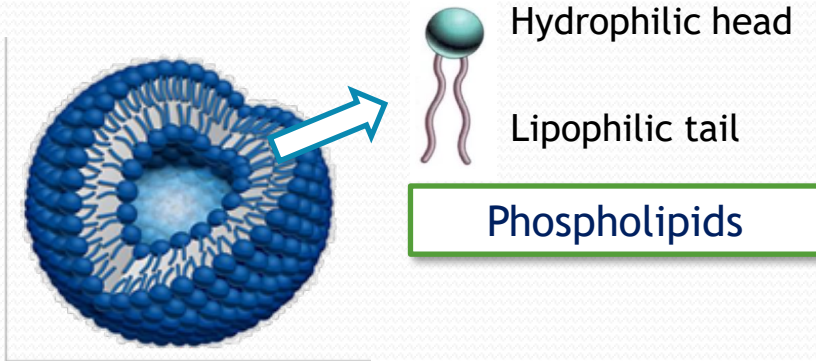
## *Advantages*

Reduce toxicity or irritation

Increase active stability

Increase **deposition** of active *in Stratum Corneum*

Liposome



## *Disadvantages*

Instability to **hydrolysis** of phospholipid molecules

Instability to **oxidation** of phospholipid molecules

Instability to **enzymatic degradation**

# Liposomes don't penetrate skin, but they may kick-start active ingredient delivery

By Andrew MCDUGALL [✉](#)

09-Mar-2016 - Last updated on 09-Mar-2016 at 11:23 GMT



RELATED TAGS: [Chemistry](#)

**Researchers in Denmark say that the way liposomes are perceived in beauty needs to change after showing that the vesicles, often praised by cosmetics companies for their alleged ability to transport active ingredients into the skin, cannot actually penetrate; but rather help the process get underway.**

From this study, [published in the journal PLOS One](#), they add that liposomes cannot penetrate the skin's barrier without breaking.

# Liposome Delivery System



RESEARCH ARTICLE

## Superresolution and Fluorescence Dynamics Evidence Reveal That Intact Liposomes Do Not Cross the Human Skin Barrier

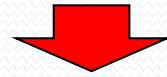
Jes Dreier<sup>1</sup>, Jens A. Sørensen<sup>2</sup>, Jonathan R. Brewer<sup>1\*</sup>

**1** Advanced bioimaging group/MEMPHYS Center for membrane biophysics, Department of Biochemistry and Molecular Biology, University of Southern Denmark, Odense, Denmark, **2** Department of reconstructive surgery, Odense University Hospital, Odense, Denmark

# Bilayer Elasticity: Deformable Vesicles

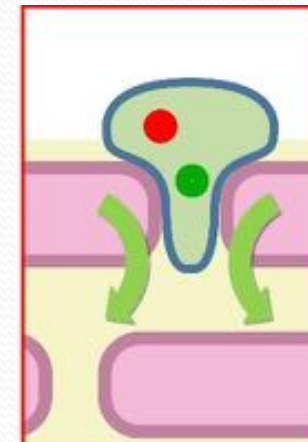
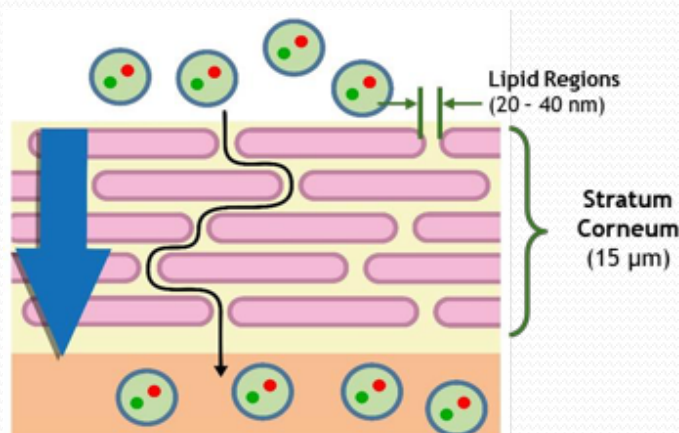
At the end of the 90s, Gregor Cevc demonstrated:

- 1) Bilayer elasticity represents a crucial factor in determining its ability to penetrate the skin
- 2) The liposome does not penetrate the skin as it has a bilayer too rigid and not deformable



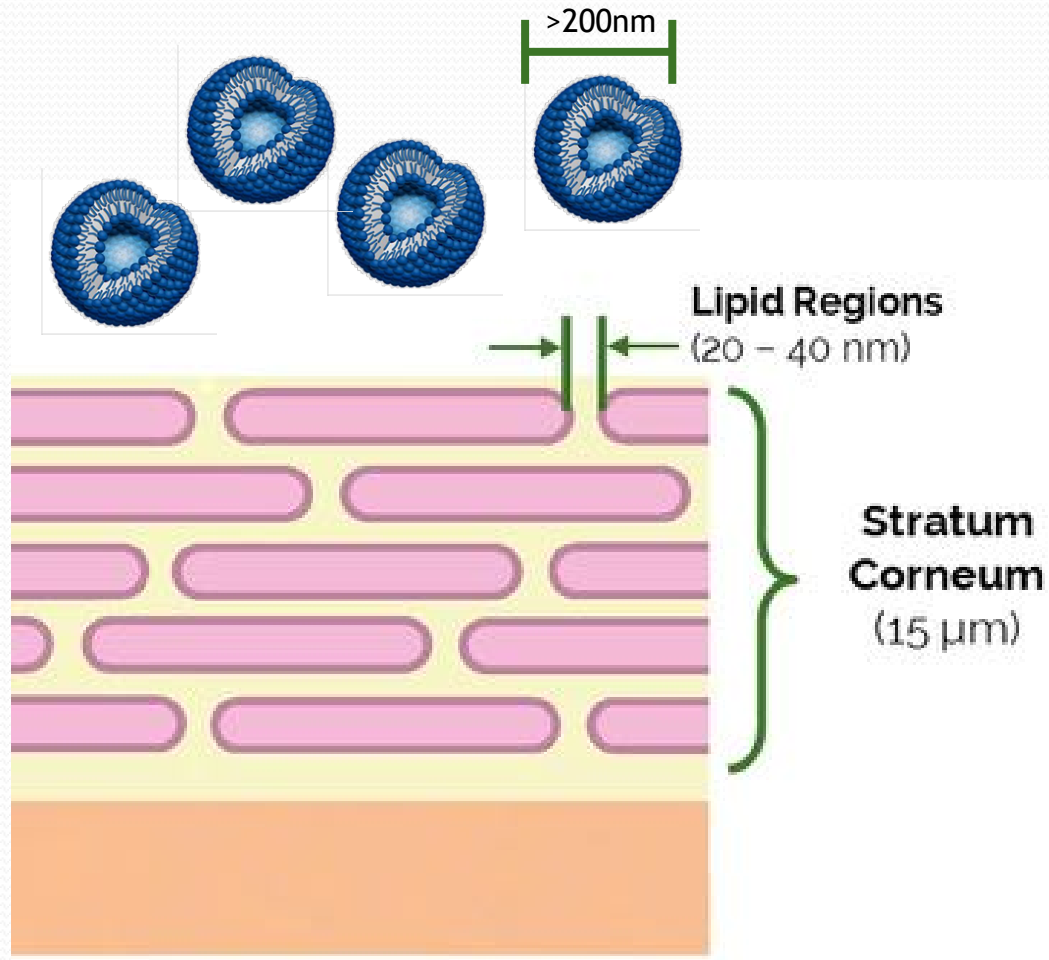
**Bilayer ELASTICITY** is the most important factor for a vesicular delivery system

If the vesicles are elastic, they can squeeze through the pores (20nm) in Stratum Corneum (these pores are less than one-tenth of the diameter of vesicles 200 nm)



# Old Generation Delivery Systems

*based on phospholipids*



## Two Limitations

### Instability into the *Stratum corneum*

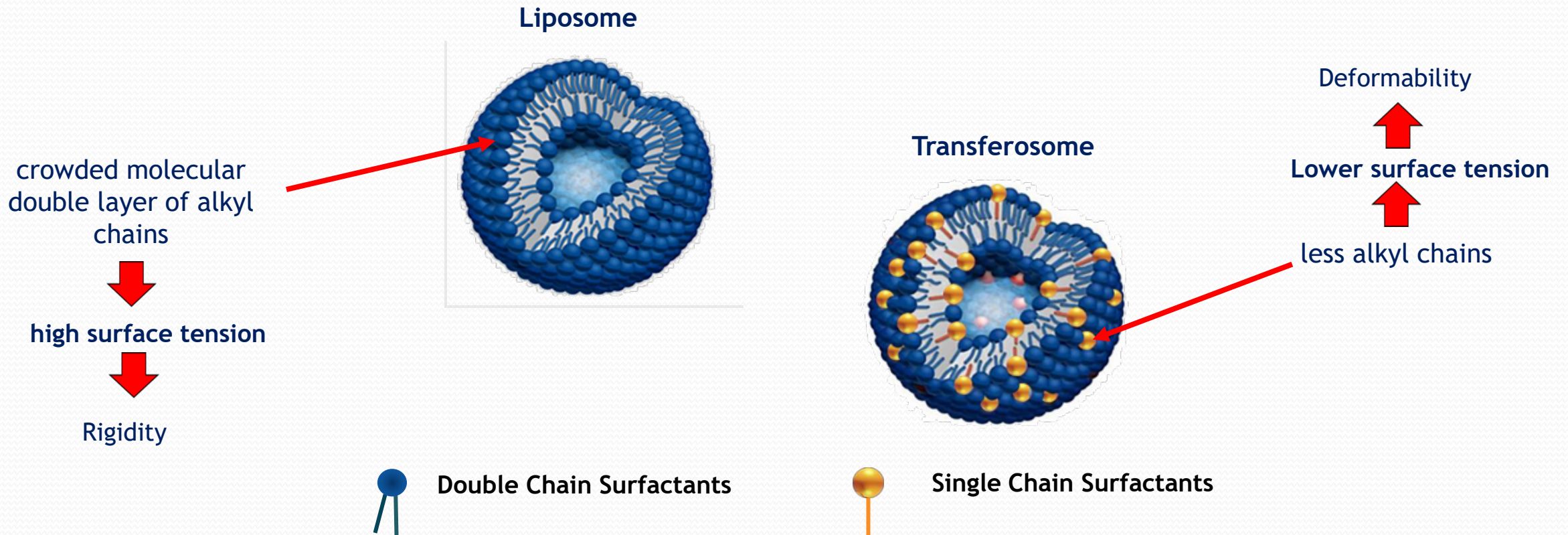
Phospholipids are sensible to enzymatic degradation and oxidation

### Liposome are rigid vesicles

High number of alkyl chains inside the membrane bilayer of the Stratum corneum made vesicles rigid

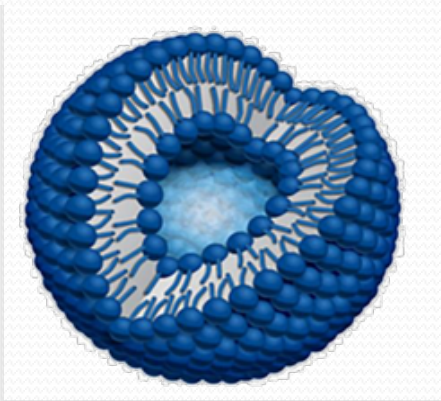
# Bilayer Elasticity: Deformable Vesicles

*Why do phospholipids form very rigid liposome vesicles?*

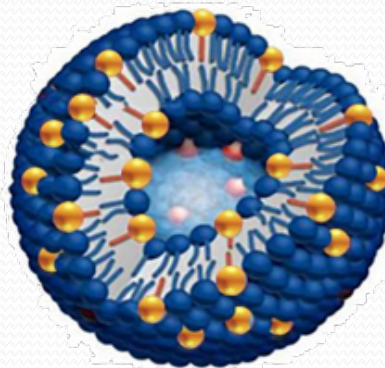


# Evolution of Vesicular Delivery Systems

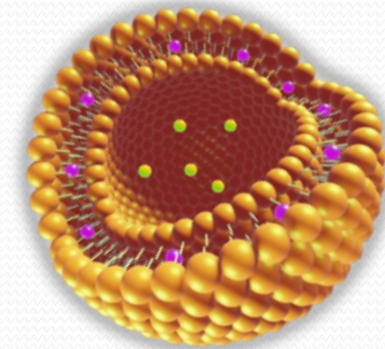
Liposome



Transfersome



Ultra-Deformable Niosome



● Double Chain Surfactants

● Double Chain Surfactants  
● Single Chain Surfactants

● Single Chain Surfactants

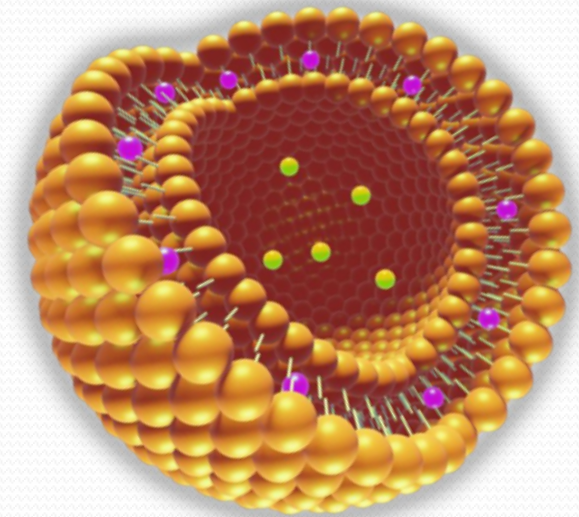
Prof. Gregor Cevc (1996)  
introduced Hybrid Liposome (Transfersome)

Prof. Honeywell and Prof. Bouwstra (2006)  
introduced Ultra-Deformable Niosome



# DELIVERY SYSTEM FOR A BETTER SKIN PENETRATION

## NIOSOME



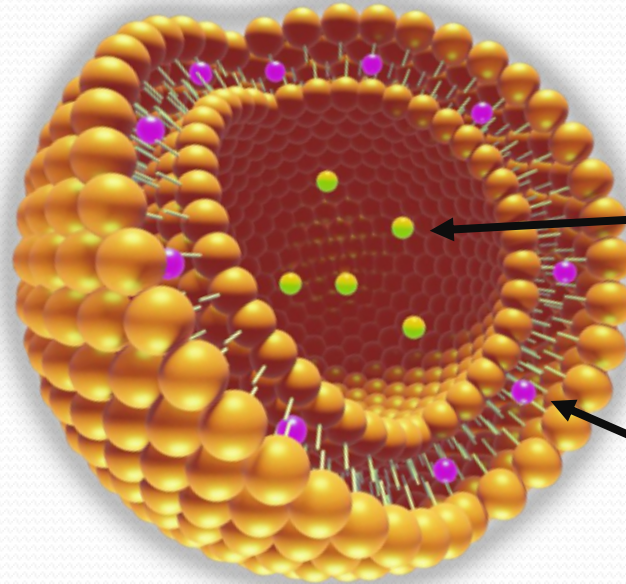
Last Generation of Vesicular Delivery System  
for Active Ingredients

# NIOSOME: Ultra-Deformable Vesicles

Ø Diameter ~ 150 - 250 nm

*Bilayer composition:*

Polyglycerol Esters



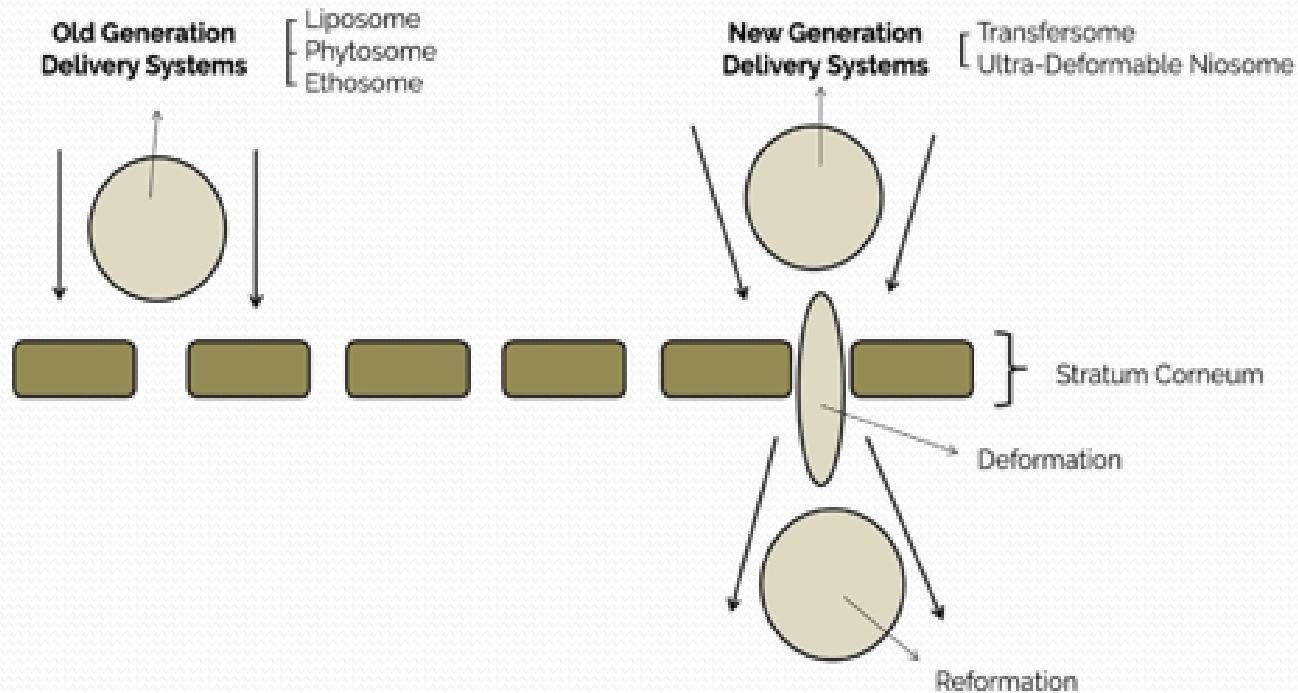
*Core of the Vesicles*  
Hydrophilic Molecules

*Membrane Bilayer*  
Lipophilic Molecules

The Bilayer Composition of Single Alkyl Chains  
Guarantees the **Elastic Properties of the Vesicles**

# NIOSOME: Ultra-Deformable Vesicles

Conventional Liposome



Ultra-Deformable Niosome



# NIOSOME: Ultra-Deformable Vesicles

Vesicles visualized after 1 h non-occlusive application using Freeze-Fracture Electron Microscopy (FFEM)

Electron microscopy

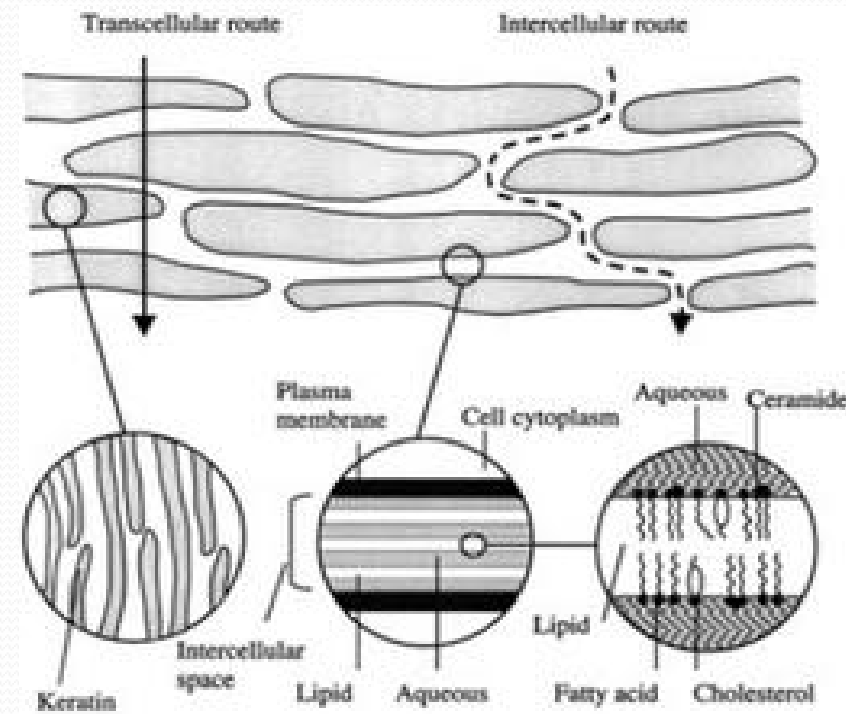
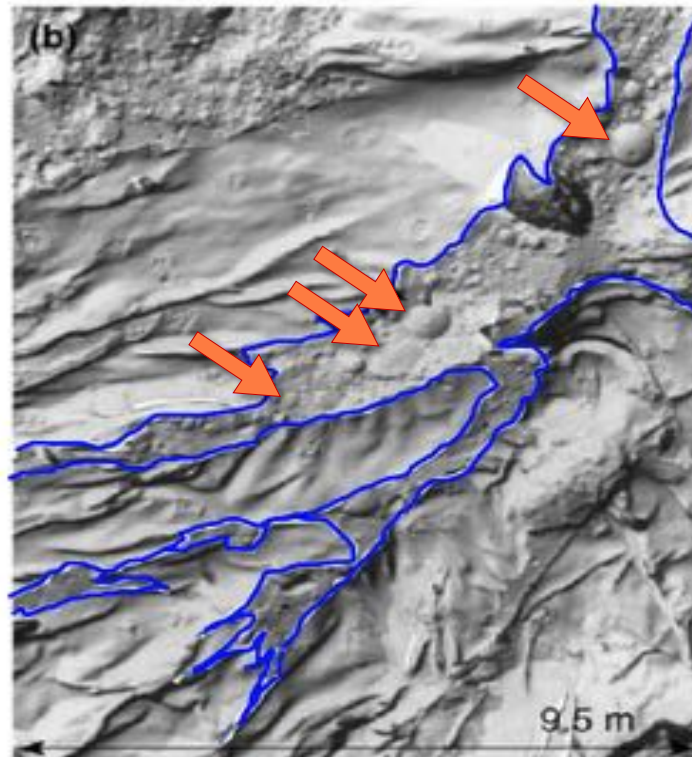
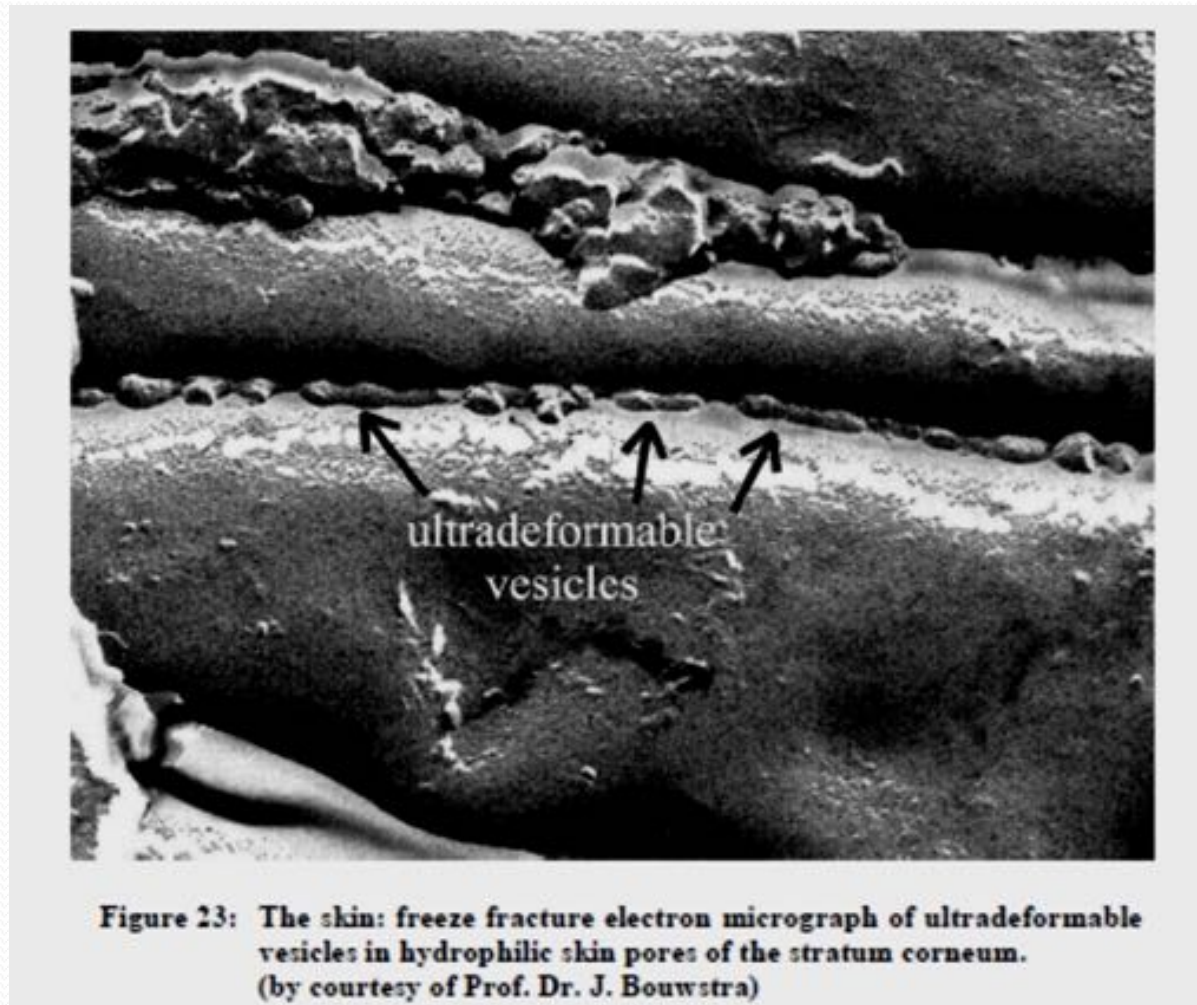


Image by courtesy of Prof. Honeywell-Nguyen PL

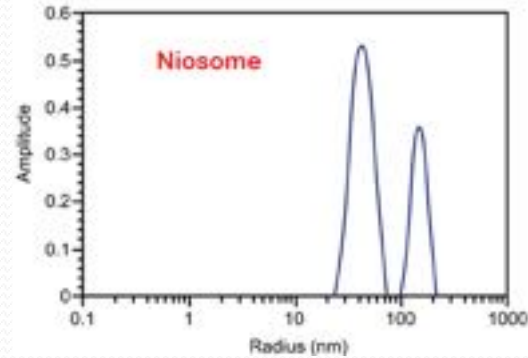
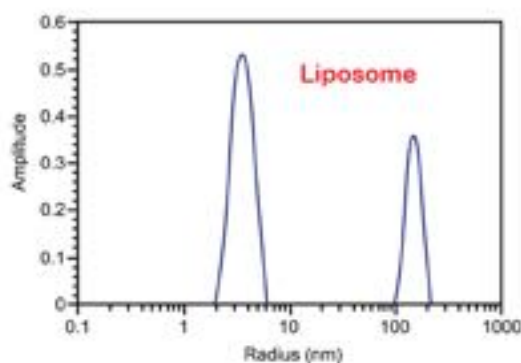
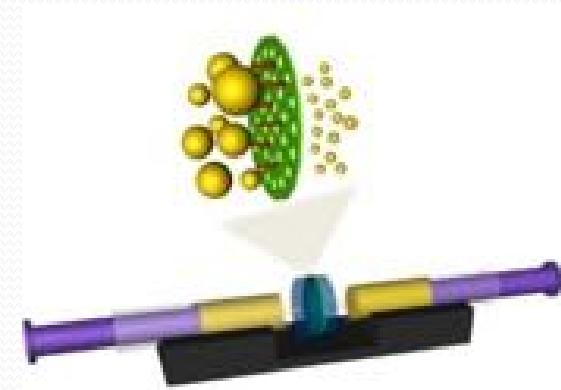
# NIOSOME: Ultra-Deformable Vesicles



# Deformability Index

Evaluations of elasticity of deformable vesicles can be carried out by **extrusion measurement**.

The vesicles are extruded through a polycarbonate membrane filter with a specific pore size at constant pressure.



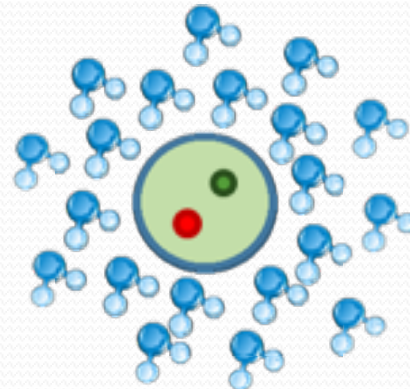
More rigid the vesicles smaller the size after the extrusion when compared to the starting point.

This phenomenon is caused by the breaking of the more rigid vesicles during the passage through the membrane pores.

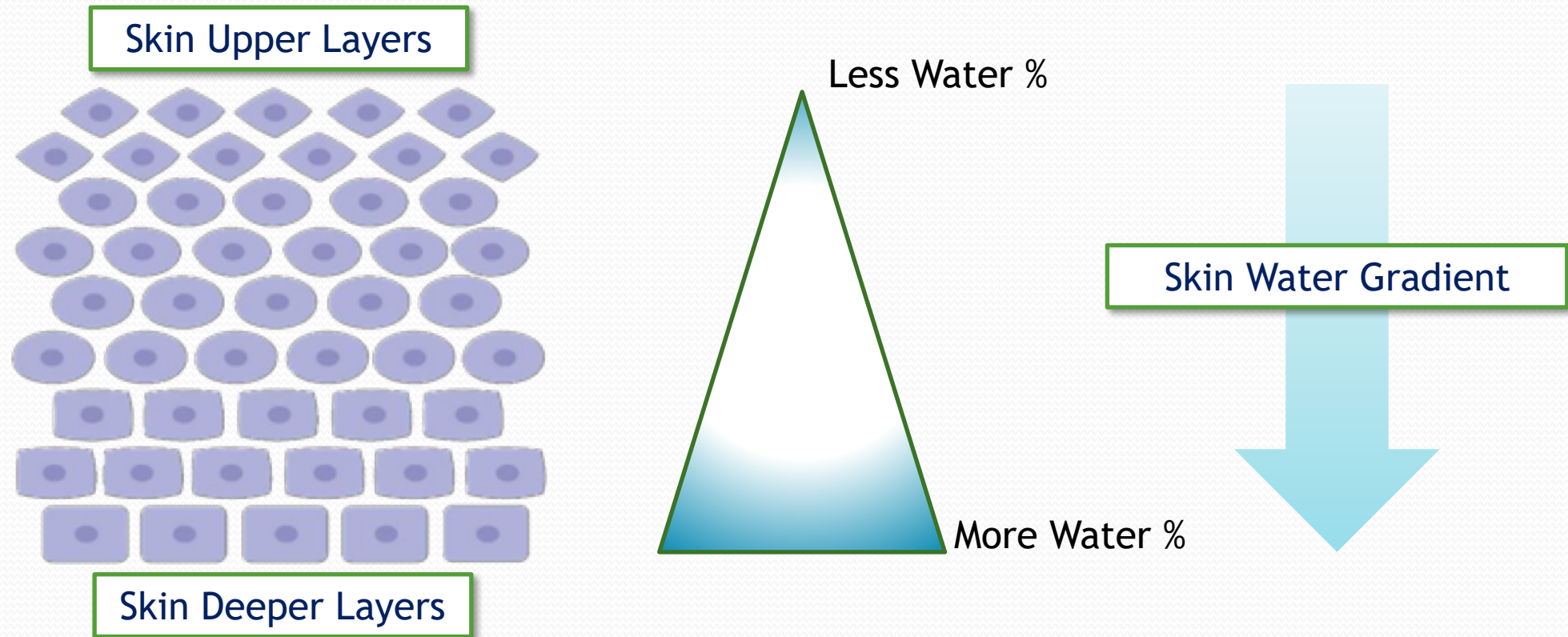
# NIOSOME: Mechanism of skin penetration

The deformability of the vesicle is a necessary but not sufficient condition to ensure optimal penetration through the skin

The polarity and the ability of the vesicle to be solvated by a shell of water molecules is another important condition.



# NIOSOME: Mechanism of skin penetration



TEWL creates a decreasing gradient of water as we reach the superficial layers of the skin



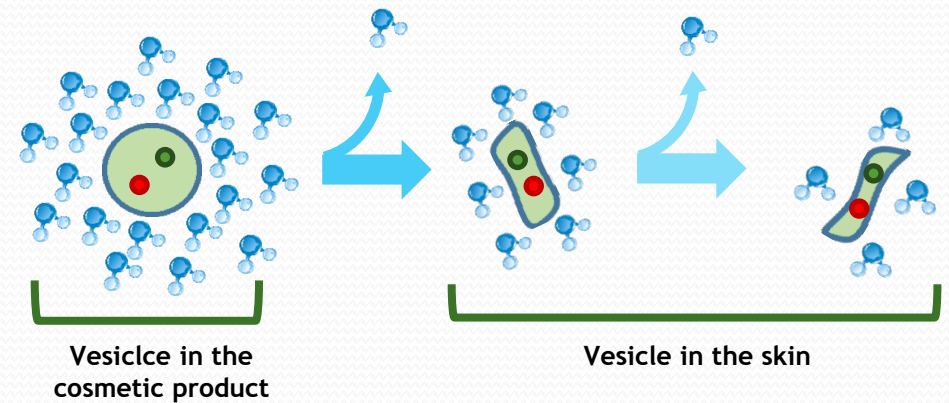
# NIOSOME: The Osmotic Gradient

As Niosome vesicle always seek to avoid dehydration...

Vesicles applied on skin loses part of the water shell and for that tends to penetrate skin squeezing through minute pores and migrate into the water-rich deeper strata to secure its adequate hydration.

Skin Penetration is driven by the water concentration gradient.

From the horny layer surface (relatively dry) to the wet viable tissues

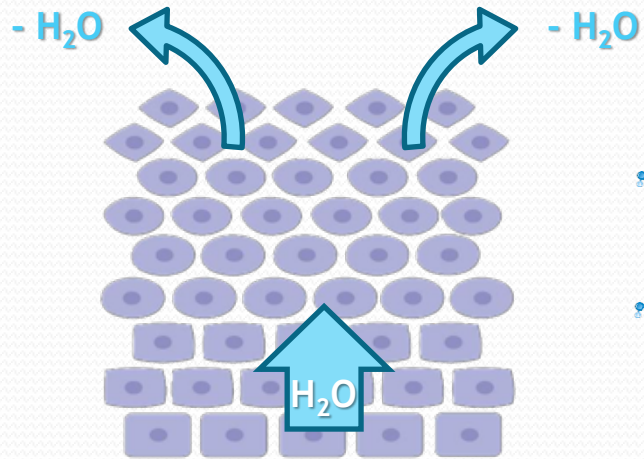


The transport of these elastic vesicles is thus independent of concentration

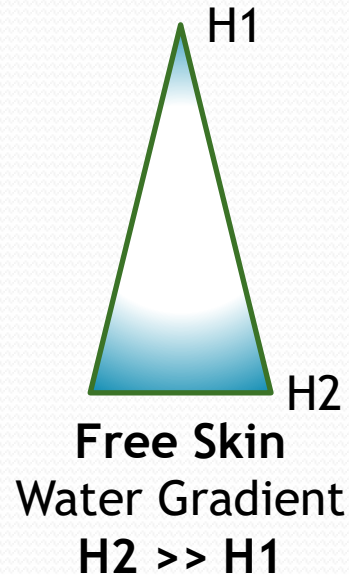
# NIOSOME: The Osmotic Gradient

## FREE SKIN

Water gradient is created by TEWL

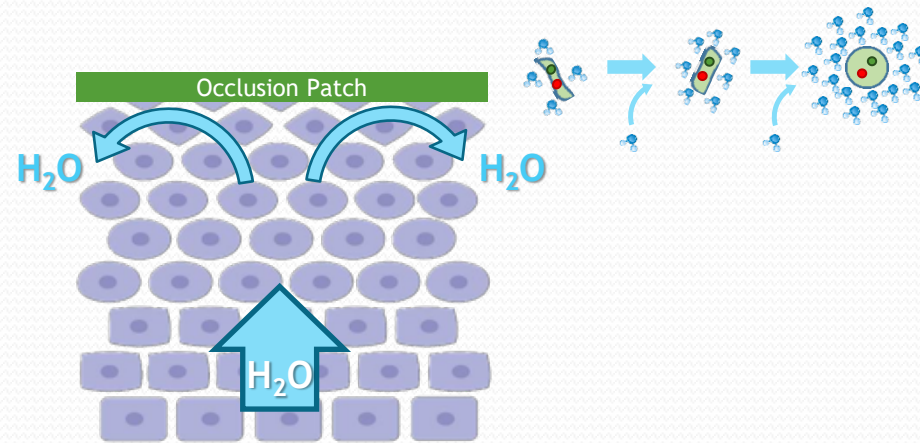


Dehydrated vesicles can squeeze between Stratum Corneum Gaps and penetrate deep in the skin actively attracted by the water gradient

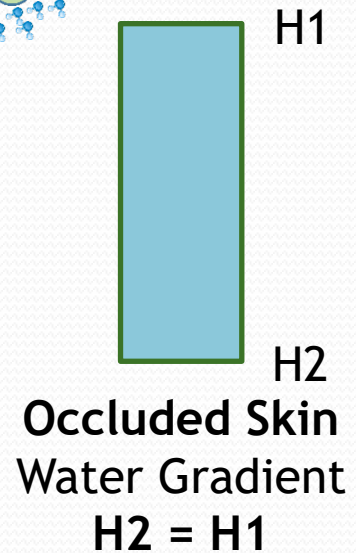


## OCCLUDED SKIN

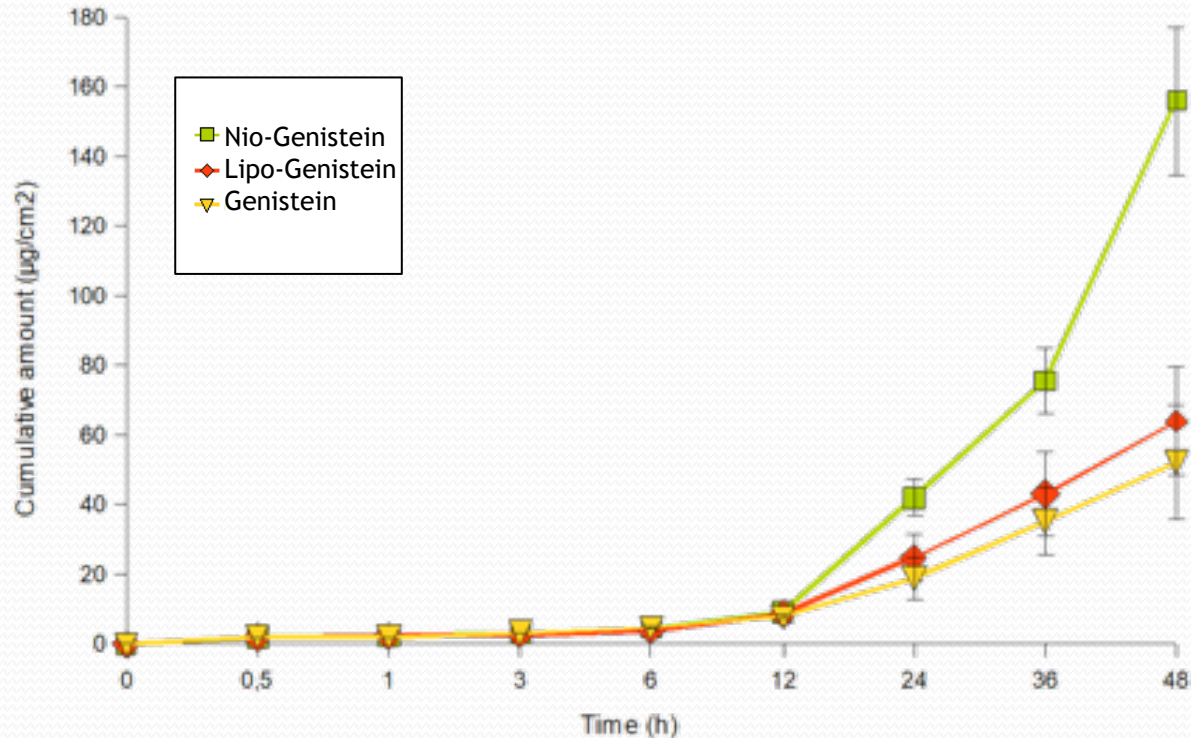
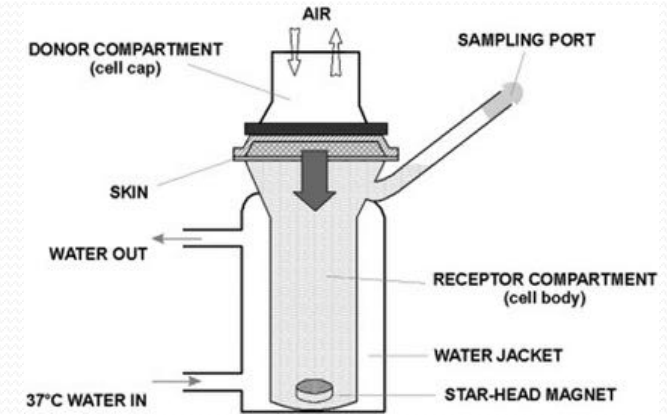
Penetration is blocked by Rapid Re-Hydration



Dehydrated vesicles absorb superficial water without penetration



# Skin Penetration Study by Franz Diffusion Cell



Both Liposome and Niosome permeate  
Stratum Corneum

Formulation with Niosome  
demonstrated a higher skin permeation  
and stability after 48 h incubation  
compared to Liposomes

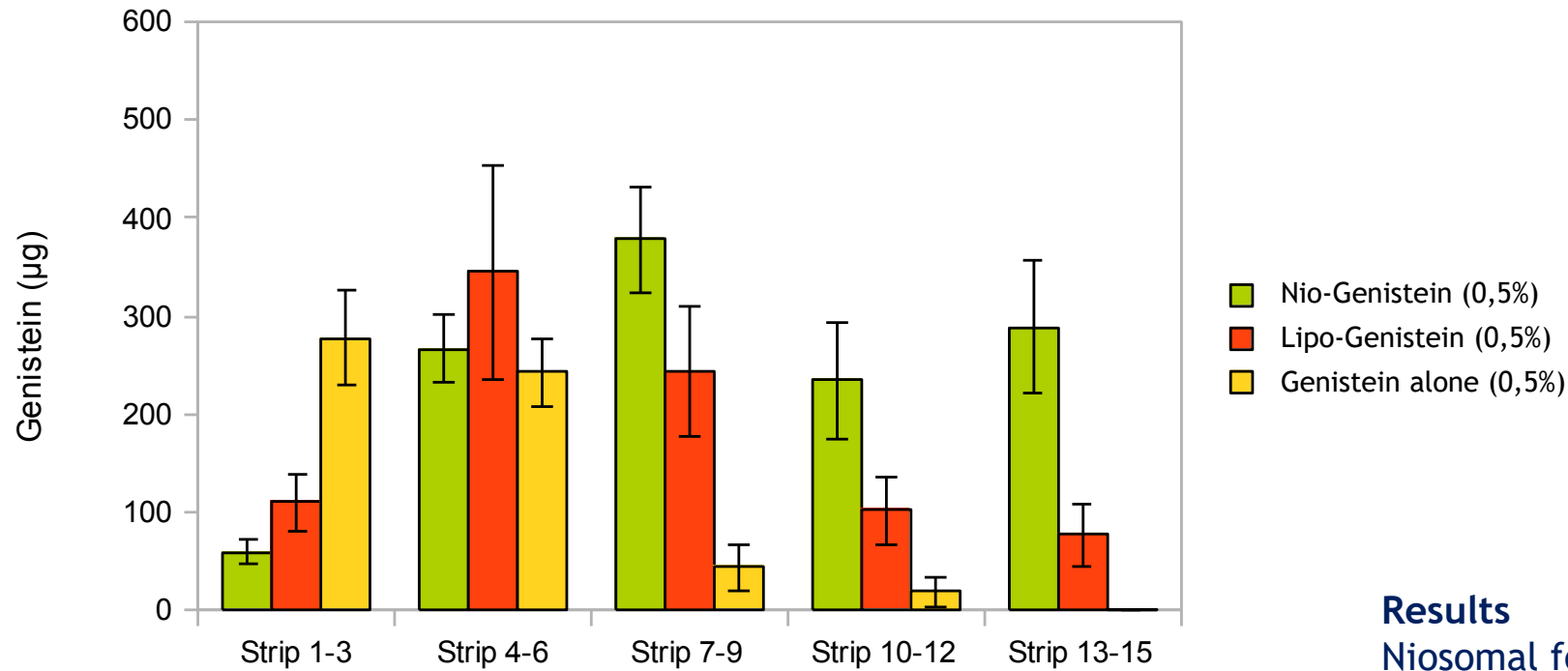
# Skin Penetration Study by Tape Stripping Technique

## Experimental procedure



(Tesafilm 2 x 3,0cm Beiersdorf,  
Germany)

# Skin Penetration Study by Tape Stripping Technique



## Results

Niosomal formulation markedly enhanced, when compared with Liposomal formulation, the delivery of the entrapped active agent: Genistein



*Thank You*