



Delivering Retinol Efficiently

Encapsulation of a Powerful Active for Optimal Skin Performance

In vitro

In vivo

Technology

Agenda

Introduction

Conclusion

What is retinol?

- **Retinol** also known as **vitamin A1** is a liposoluble retinoid, used in ancient Egypt to treat night blindness.
- **Involved in many biological functions** such as embryogenesis, bone growth, immune system, reproduction, and vision.

Animal source – preformed vitamin A

Retinol and retinyl esters



Plant source – provitamin A

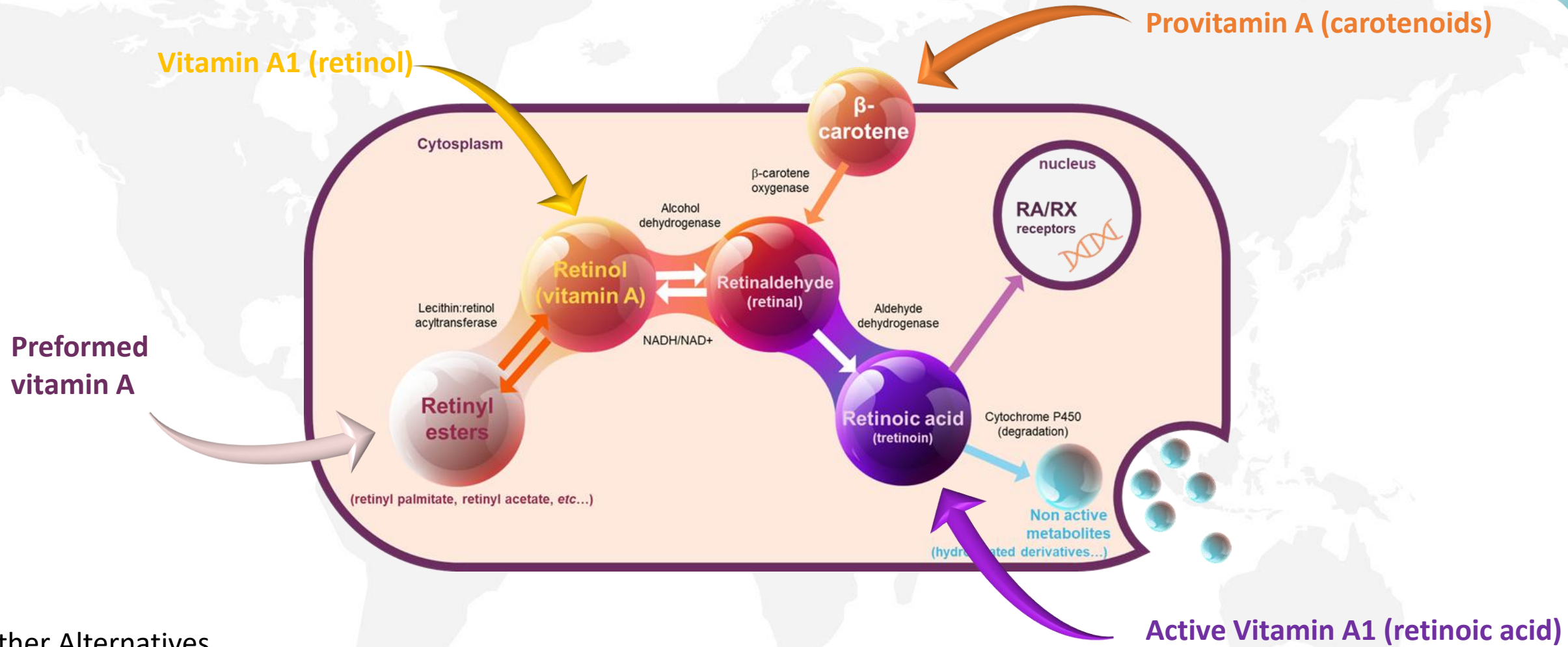
Carotenoids (β -carotene, α -carotene, and β -cryptoxanthin)



Lycopene, lutein, and zeaxanthin, are **non-provitamin A** carotenoids → not converted into vitamin A.

(Blaner WS., 2020)

Cutaneous metabolism of retinoids



Other Alternatives...

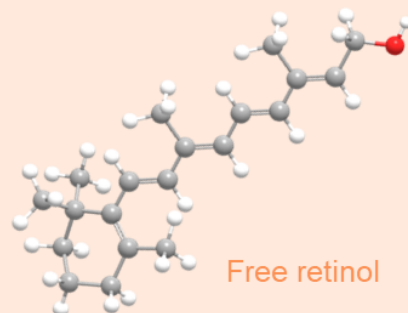
Hydroxy-pinacolone retinoate and retinol-like (*e.g.* bakuchiol)

Retinol is also a tricky ingredient!

Instability of retinol:

Due to its chemical structure, retinol as well as other retinoids, are highly subject to **various chemical changes** depending on environmental conditions (light, temperature, oxygen, pH, solvents...).

UV decomposition of retinol



Free radicals,
reactive oxygen
species
(ROS) and other
metabolites

Decrease of retinol
content in formulations.
**Product efficacy
is diminished.**



Retinol must be stored at **temperature less than - 4°C**
and **under inert gas.**

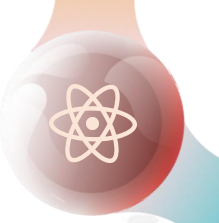
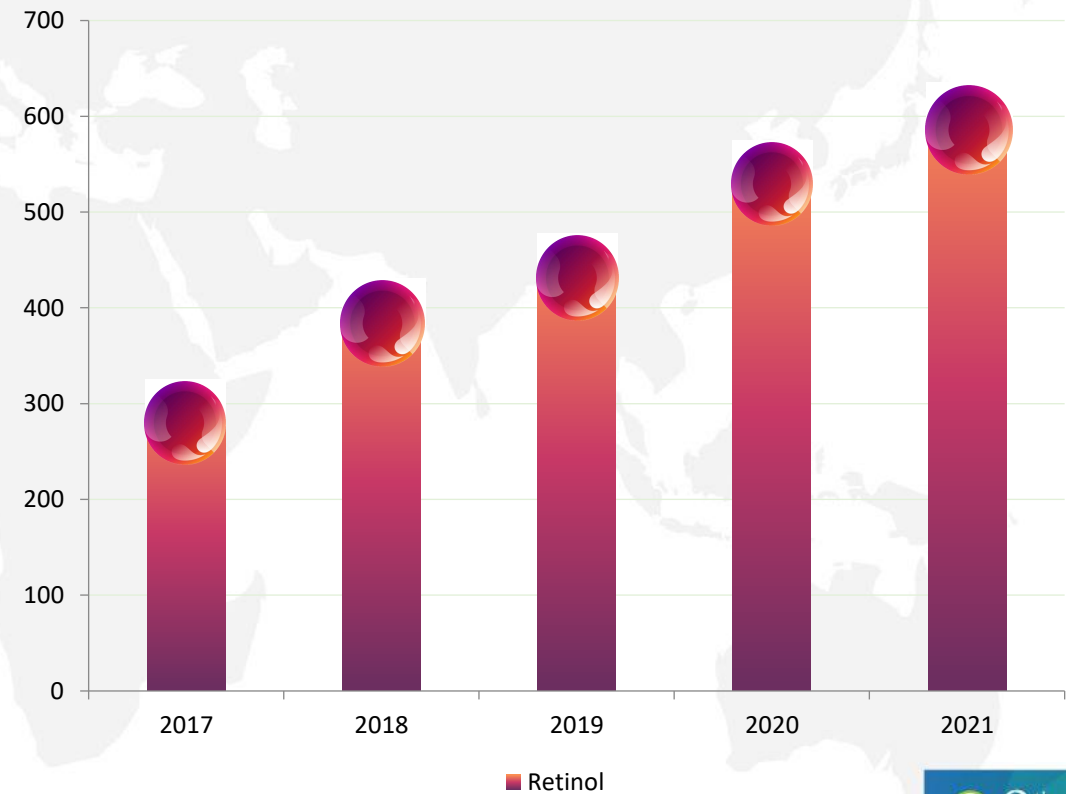


Market Dynamic

Retinyl palmitate is the most used vitamin A derivative in the last 5 years.
Products containing retinol represent the fastest growing market.

“More than 2.4K products in the last 5 last years in the beauty and personal care industry*”

Finished products that contain retinol



* Source: Mintel GNPD

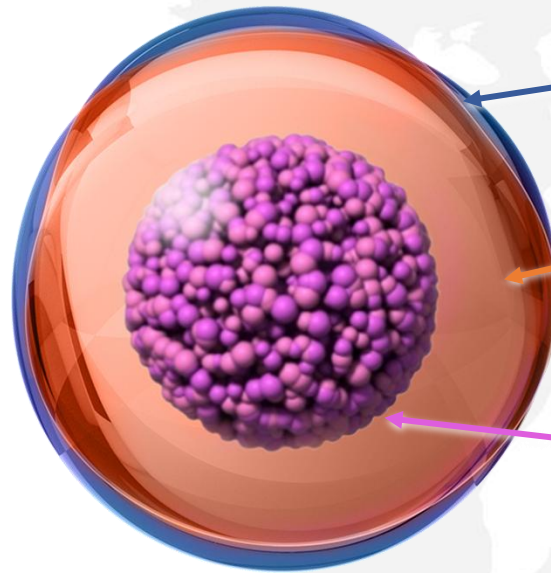
Technology

Characteristics, Encapsulation efficacy, Stability



Capsule technology

- **Pale yellow liquid (pH ~8.2)**
- **3 % encapsulated retinol**
- Capsules suspended in water
- spherical structures with visible and regular edges



Hydrophilic outer face
(Lauryl glucoside)

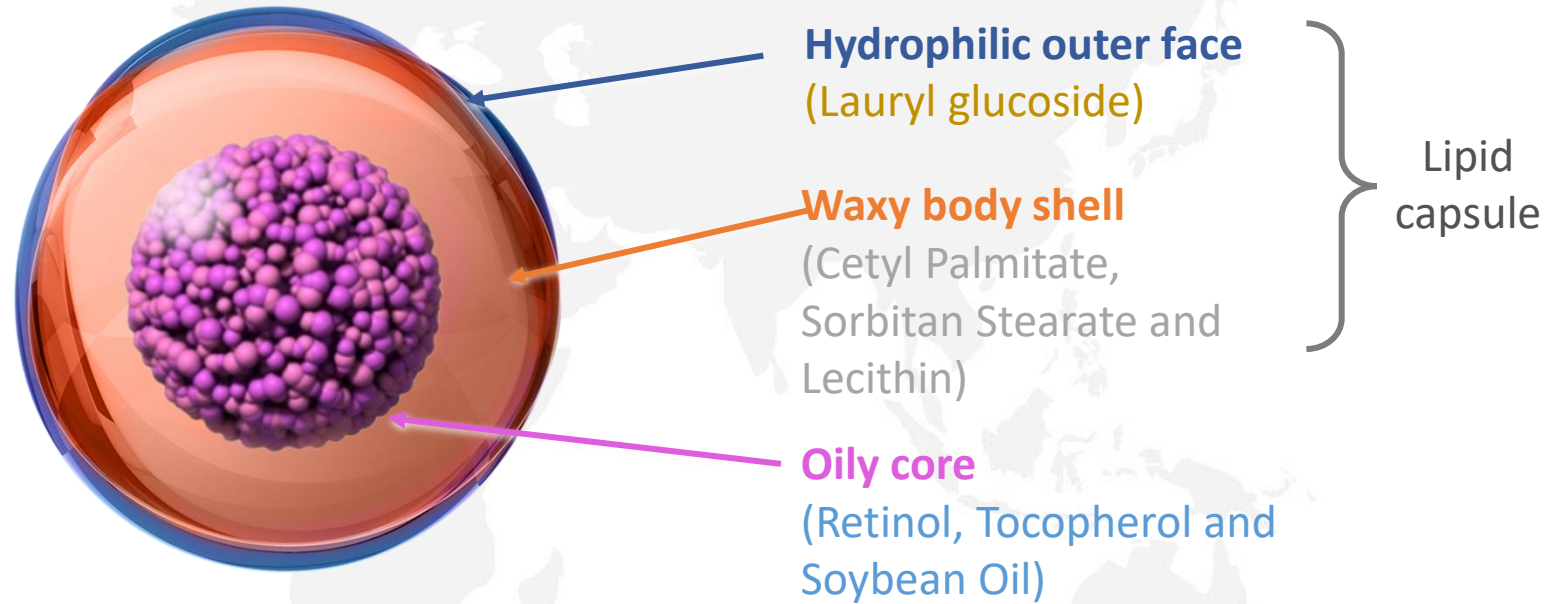
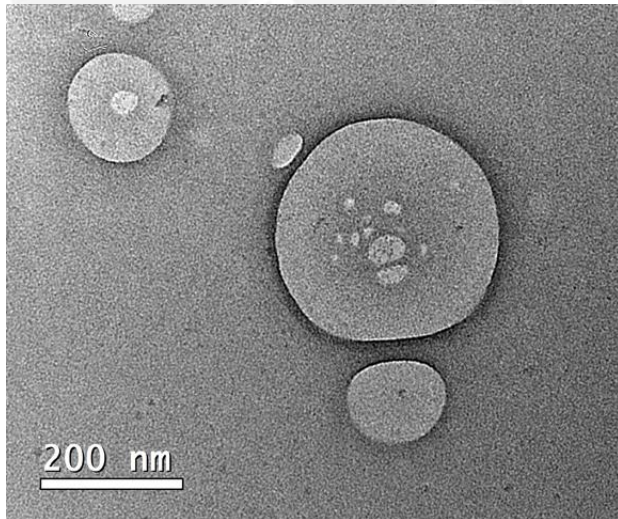
Waxy body shell
(Cetyl Palmitate,
Sorbitan Stearate and
Lecithin)

Oily core
(Retinol, Tocopherol and
Soybean Oil)

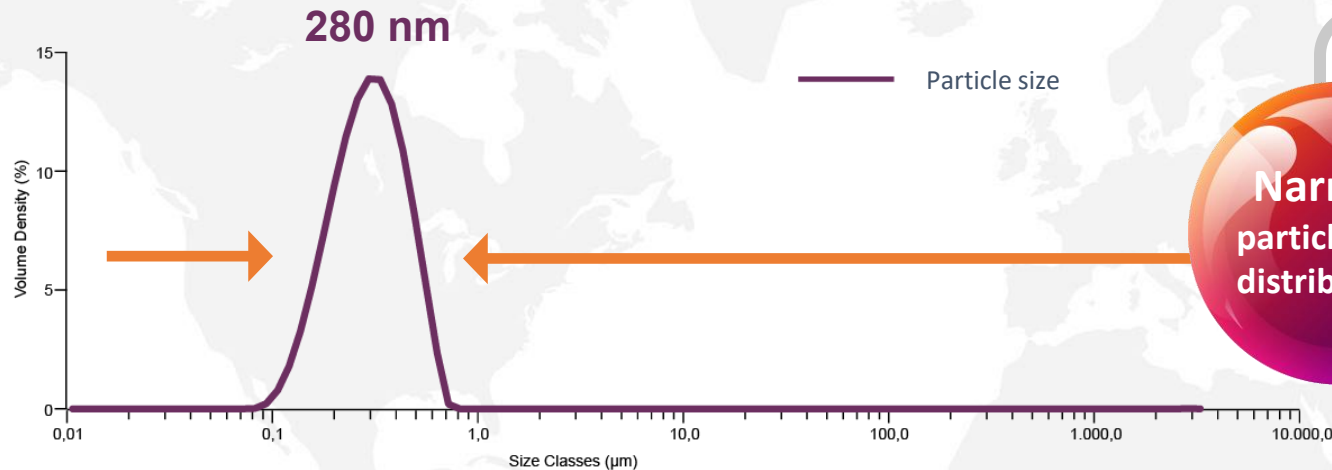
Lipid capsule

Capsule technology

Encapsulated retinol structure under microscope



Capsule characterisation



Polydispersity evaluation

Average particle size is ~280 nm.
Particle size is **homogenous**.

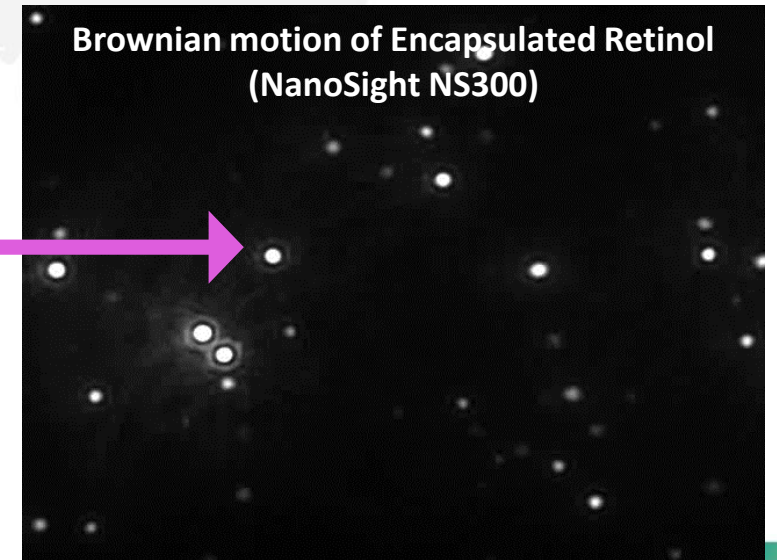
Narrow
particle size
distribution

Particle interaction evaluation

- Particles remain **stable in suspension**.
- No coalescence, no sedimentation, no crystallisation, no phase separation after preparation.

Perfectly
stable in
suspension

Brownian motion of Encapsulated Retinol
(NanoSight NS300)



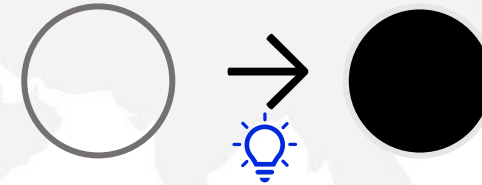
Proof of encapsulation *via* fluorescence

4 different samples were observed under fluorescent light:

1- Non encapsulated Retinol is fluorescent → will appear **blue** under fluorescent light



2- Placebo capsules (without retinol) non fluorescent → will appear **black** under fluorescent light



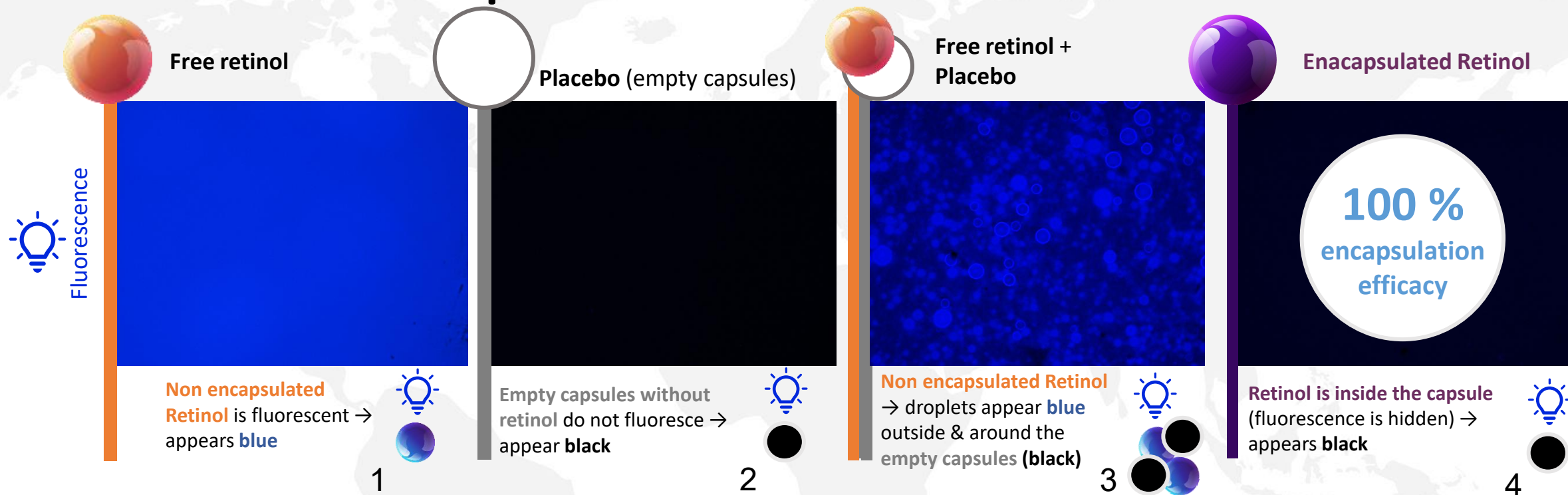
3- Mixture of Free retinol and **Placebo capsules** (without retinol) → should appear **blue** and **black**



4- Retinol inside the **Encapsulated Retinol** capsule (fluorescence is hidden) → should appear **black**



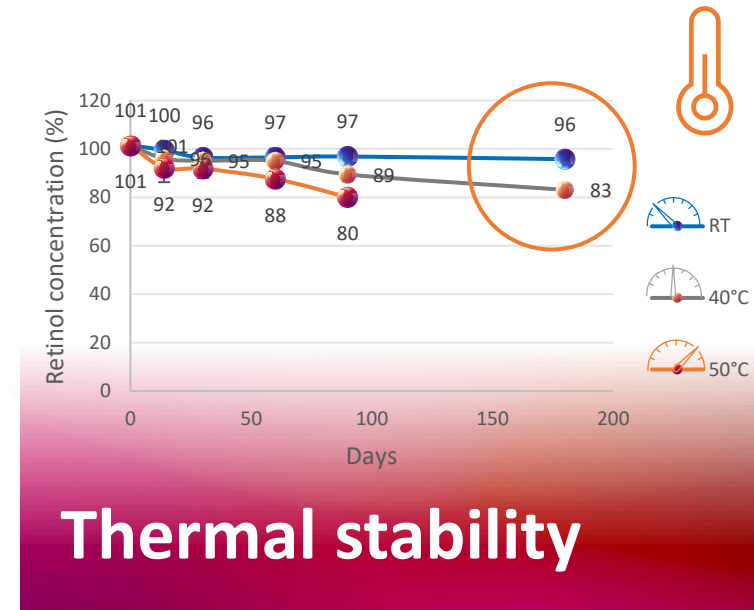
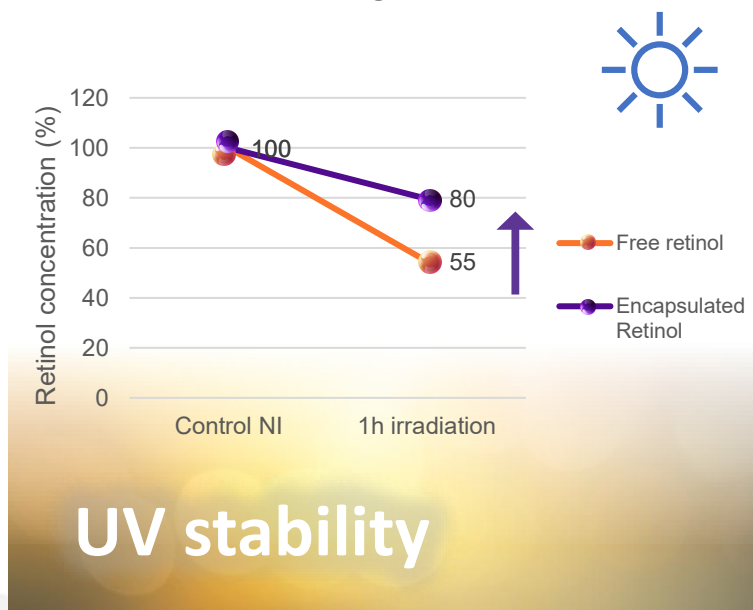
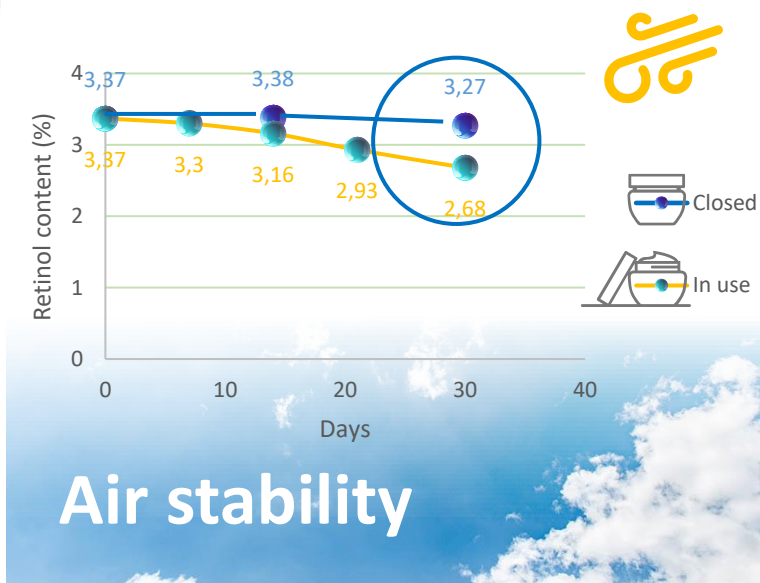
Proof of encapsulation – *results*



“ No blue signal for **Encapsulated retinol** under fluorescent light confirming **active retinol is fully encapsulated**. ”

Retinol's stability within the capsules

Measured retinol content over time after exposure to light, air, or heat of the **Encapsulated Retinol** capsules.



Encapsulated Retinol is more stable to air, UV and heat than **free retinol**.
It can be used repeatedly **up to 15 days after opening at room temperature**.

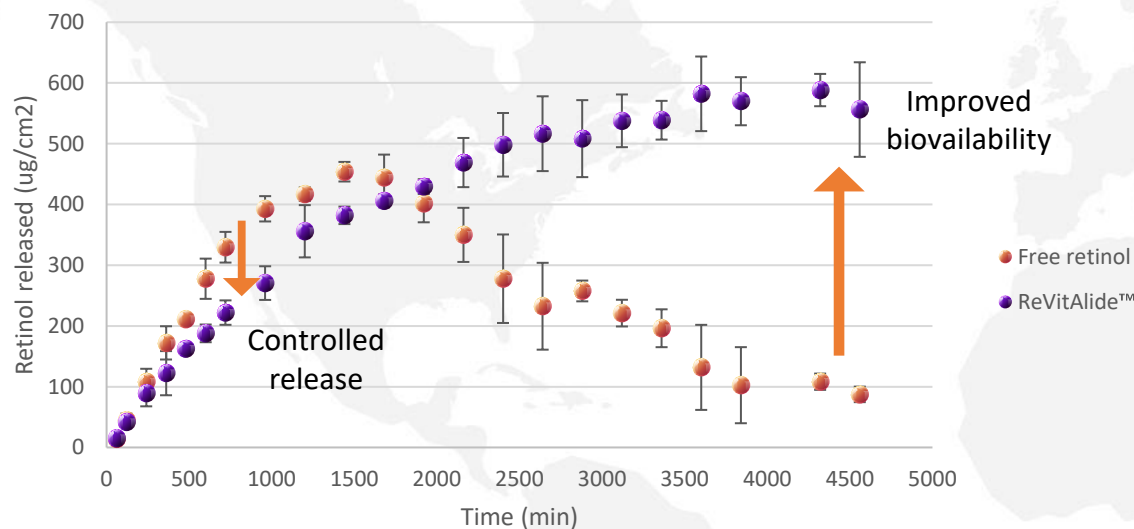
In Vitro & Ex Vivo

Skin release, Cutaneous penetration and Bioavailability

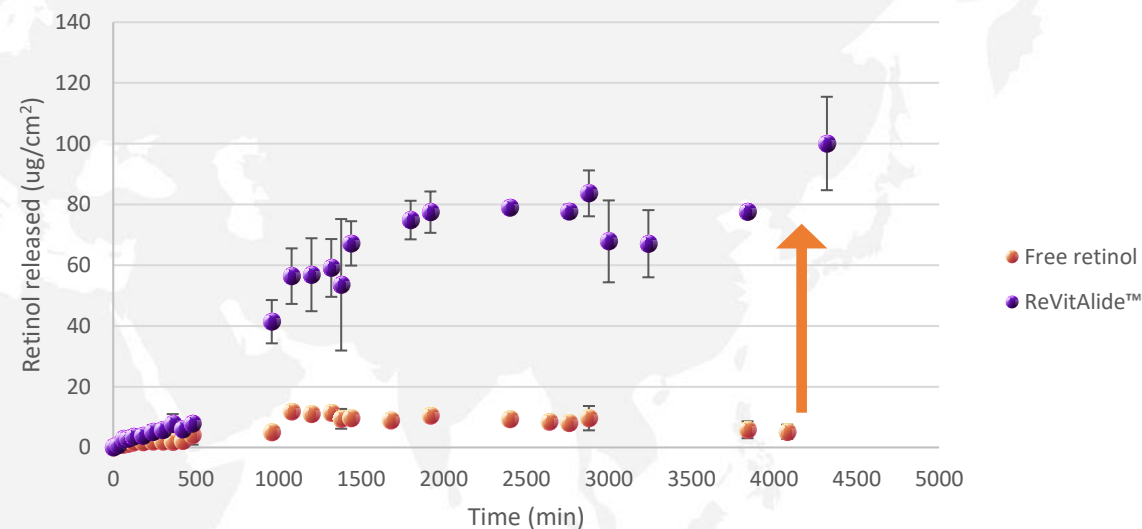


Skin release profile – *results*

Skin release profile of active ingredients



Release from finished products

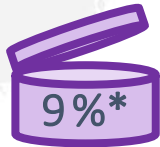


Encapsulated retinol promotes controlled and prolonged retinol release resulting in higher bioavailability compared to free retinol.

Skin penetration evaluation – *method*

Complementary studies via Raman spectroscopy performed by BIO-EC (France) on skin explants (abdomoplasties from a 46 and 40-year old female donors)

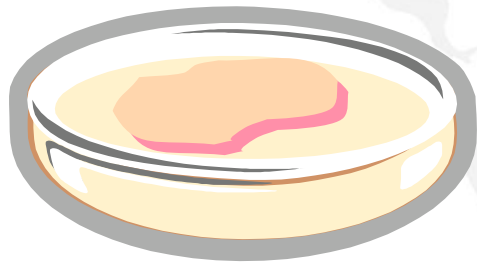
Encapsulated retinol



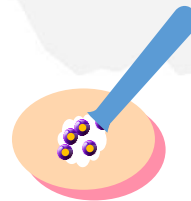
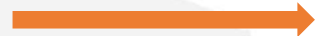
Free retinol



Control



Skin explants kept alive under physiological conditions



Topical application of a cream containing **Encapsulated Retinol** or free retinol

8 and 24 hours

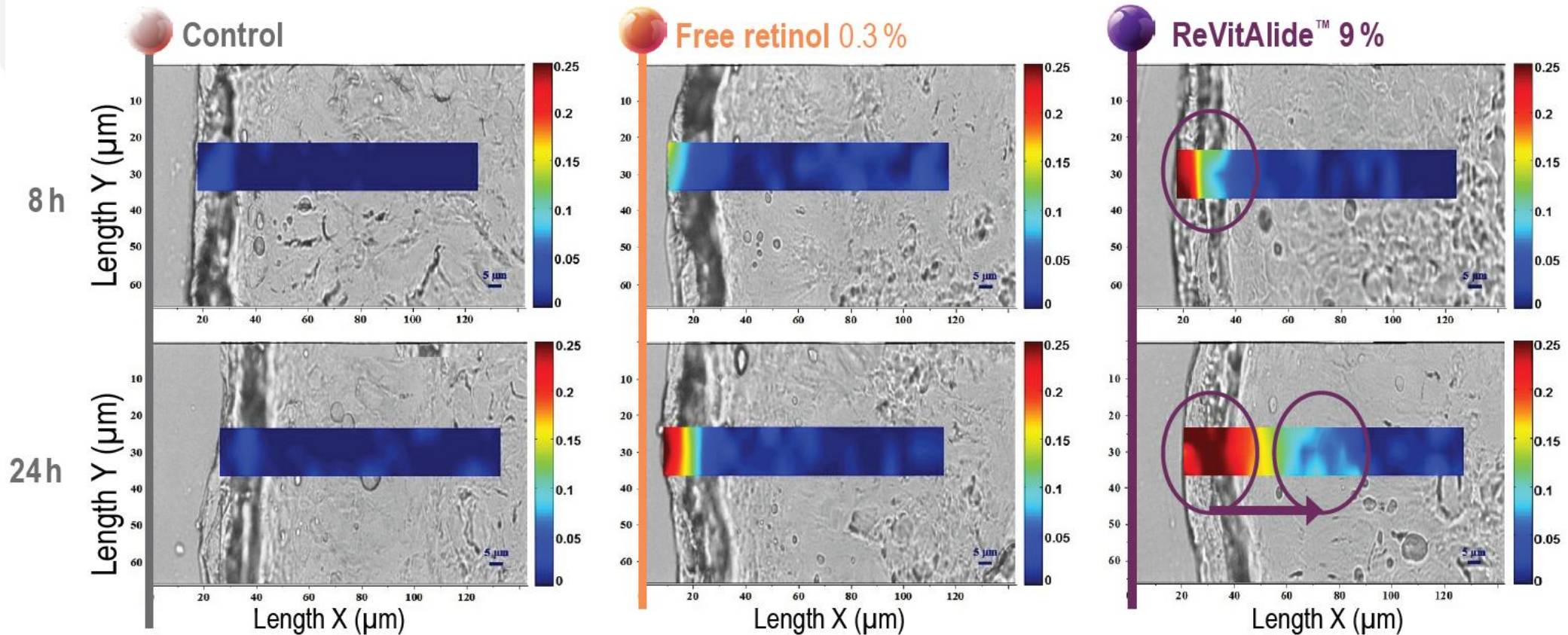
later



Evaluation of the penetration kinetic and tissue distribution of **Encapsulated Retinol** using **Raman spectroscopy** after tissue fixation

* 0.27 % active retinol

Skin penetration kinetic — *results*



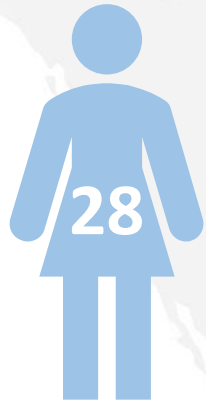
Compared to free retinol, **Encapsulated retinol** highly promotes skin penetration of retinol.

In Vivo

Skin tolerance and Anti-wrinkle efficacy

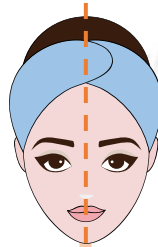


Anti-wrinkle efficacy evaluation – *protocol*



Mean age: **61**
55 to 68 years old
With crow's feet wrinkles

APPLICATION



Cream containing
3* % Encapsulated Retinol
or placebo

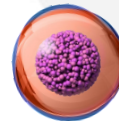


Twice daily
on half-face



2 month-application

(*): 0.09 % active retinol



TOLERANCE

: no adverse effect observed during the study



PRIMOS® 3D Skin Measuring
Visia® CR (pictures)

T0



T2 months



Wrinkle prevention – *results*

Placebo
(right side of the face)



#56



T0



T2 months



Increase of wrinkle appearance.



Decrease of wrinkle appearance.

Encapsulated Retinol 3 %*
(*) 0.09 % active retinol
(left side of the face)

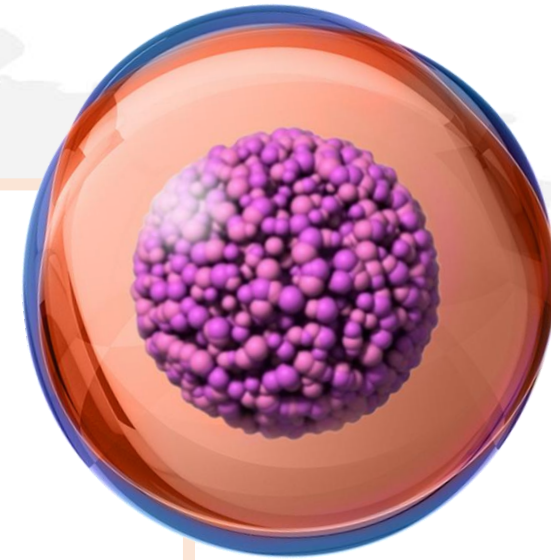


Conlclusion



Conclusion

- Retinol as well as other retinoids, are highly subject to various chemical changes
- Encapsulating the retinol preserves its chemical structure
- **3 % encapsulated retinol** in suspension in water
- It is a **stable, highly bioavailable** and **well-tolerated retinol** solution
- Technology proved through via **Particle size, Raman fluorescent microscopy** and **stability testing**



In Vitro and Ex Vivo

- **Good skin release profile**
- **Transcutaneous delivery** of retinol proved from skin penetration kinetics testing
- **Slow** and **controlled release** of retinol
- Increased **bioavailability** of retinol into the skin
- **Modulation** of retinol content

In Vivo

- **No reaction** or **irritation from tolerance** and **sensitisation testing**
- **Improved skin tolerance**
- **Very good skin compatibility**
- **High Anti-wrinkle efficacy** after 2 months

Questions?

