

ENCAPSULATED POWER

Stabilisation | Retinol is considered to be one of the industry's gold standard ingredients for ageless skin. But how can this wonder-ingredient work even better? Dr Saher Duchi and Dr Danny Goldstein know how it can be shielded with micro encapsulation technology.

Dr Saher Duchi,
Chief Scientist, Tagra Biotechnologies, Israel, www.tagra.com

Dr Danny Goldstein,
VP R&D, Tagra Biotechnologies, Israel, www.tagra.com

Retinol is a derivative of vitamin A and is considered to be one of the industry's gold standard ingredients for ageless skin. Retinol helps users achieve younger, clearer, and healthier looking skin[1,2,3]. It does this by increasing cell turnover while enhancing collagen production – a combination that serves to decrease fine lines and wrinkles, unclog pores, combat acne and smooth and refine skin texture. Yet whilst Retinol is known for its powerful results, its efficacy can be easily compromised due to its **high sensitivity to oxidation**. It degrades in the presence of air, sunlight, acidic conditions, and heavy metals, which ultimately reduces its potency and limits its effectiveness.

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These challenges can be overcome with microencapsulated retinol[5]. By delivering the active ingredient in a stabilised, microencapsulated format, the innovative technology helps to improve the performance and shelf life of the final formulation. The polymeric shell ruptures only when the formulation is rubbed into the skin, releasing the encapsulated retinol over time. Until this moment, the microcapsule remains unbroken; a condition that serves to maintain retinol stability and eventually its efficacy.

Preparation of microcapsules

The microcapsules loaded with retinol were produced by the **solvent extraction method**[5,6]. The microcapsules were prepared by dissolving the polymer cellulose acetate butyrate, retinol, and other oil soluble additives in ethyl acetate.

The ethyl acetate was mixed with a water phase containing PVA to form an emulsion. The emulsion was then transferred into the extraction water phase. After complete sedimentation of the microcapsules, they were collected by filtration and washed with water to remove any impurities. The microcapsules were dried using lyophilisation to obtain free flow powder.

Microcapsules characterisation

Retinol was quantified by reverse-phase HPLC using a Jasco HPLC system equipped with variable ultraviolet detector. Separations were carried out using Ace 3, C18-PFP column (150 × 4.6mm), with isocratic mobile phase containing 85%v/v methanol and 15%v/v water, at a flowrate of 1.0ml/min. Retinol was detected at 325nm. The following parameters were evaluated: Content (percentage of concentration of retinol in the microcapsules) and entrapment efficiency (percentage of estimated content/theoretical content).

Microcapsules were analysed for their size and size distribution using laser diffraction particle size distribution analyser Horiba LA-350.

Studies and tests

The **stability** of the microcapsules was evaluated and compared to free retinol. The encapsulated and free retinol were incorporated in a water gel base formulation (pH 7.3) and incubated at 40°C in closed glass vessels protected from light. Their stability was evaluated by measuring retinol content (percentage of initial) by HPLC method after two and four weeks storage.

In-vivo efficacy test: A clinical study was performed to evaluate the anti-ageing activity of the microcapsules. Twenty subjects applied base night cream containing 1.% (equivalent to 0.1% of free retinol) twice daily for four weeks.

The efficacy of the treatment was evaluated via the Visa CR imaging system. Images were analysed by ImagePro software to determine changes in the appearance of facial skin texture[7,8].

At baseline and after four weeks of use, a trained technician took Cutometer measurements of each subject to measure the skin's firmness.

Antioxidant activity: The antioxidant activity compared to free Retinol was determined using 2,2-Diphenyl-1-picrylhydrazyl (DPPH) method. The reduction of DPPH was measured by spectrophotometer[9].

Results

Microcapsules characterisation: The obtained free flowing powder of microcapsules had an average retinol content of 8.6 ± 0.5% with mean entrapment efficacy of 90.1 ± 1.7%.

The mean size values of the microcapsules was about 14µm. The presence of one narrow peak indicates ▶

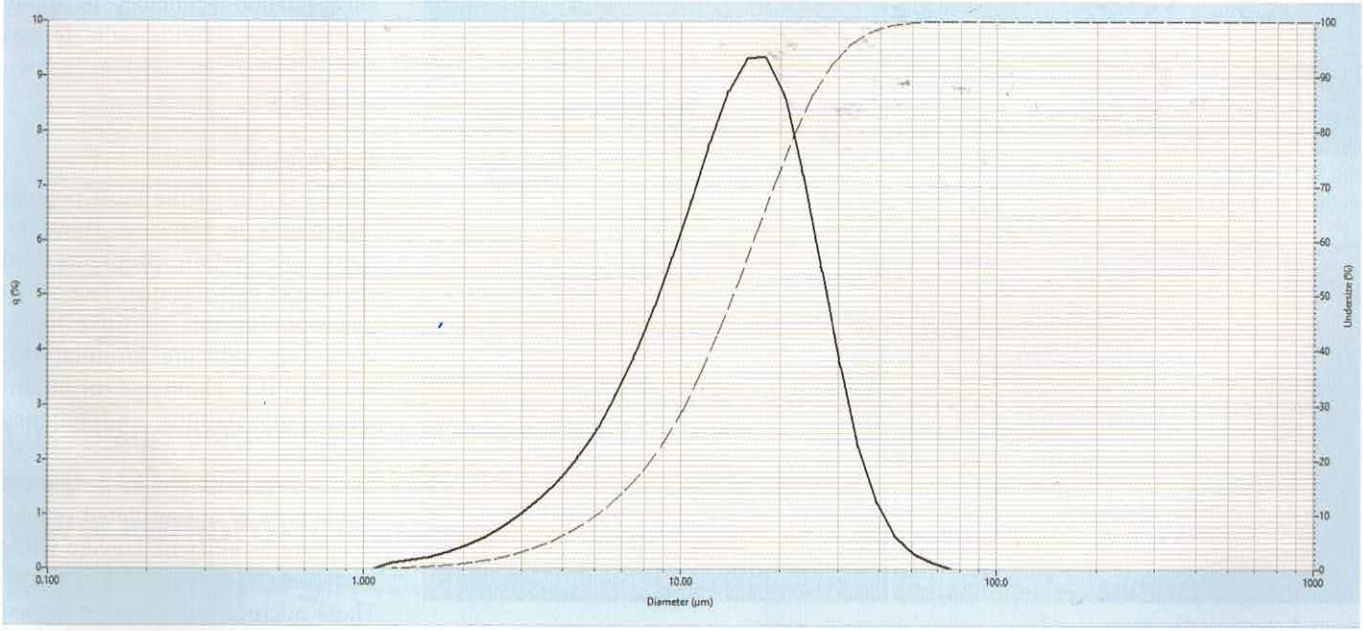


figure 1: Representative graph for the mean size and size distribution of the microcapsules.

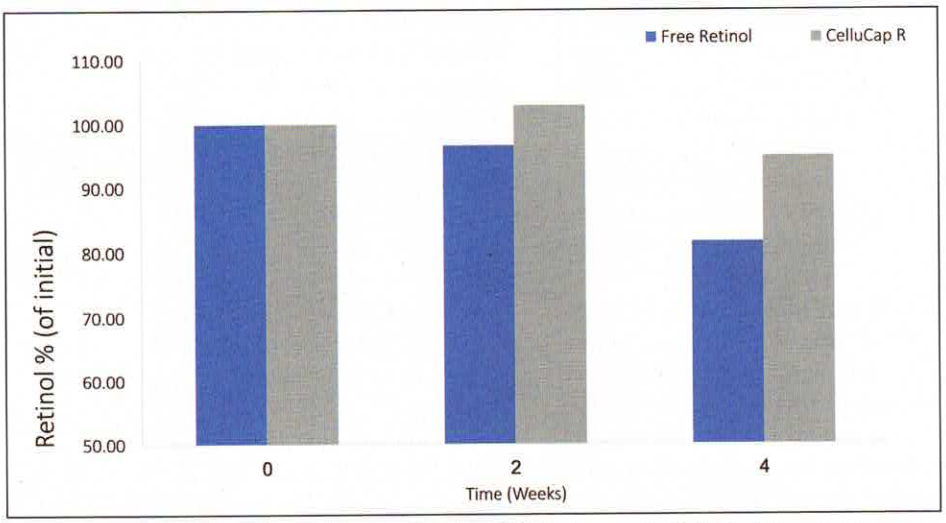


figure 2: Retinol stability in gel formulation incubated at 40°C for four weeks. CelluCap R (grey bar) compared to free retinol (blue bar). Data is represented as mean retinol content (percentage of initial).

that the microcapsules population is homogenous in size (figure 1).

The **stability** of encapsulated retinol compared to free retinol, both incorporated into a topical base gel formulation (pH 7.3), was evaluated over four weeks at 40°C.

The relative content of retinol (percentage of initial) in each sample (free retinol compared to encapsulate retinol) was measured as shown in figure 2.

The results show that the mean relative retinol content after four weeks at 40°C was significantly higher while formulating with the microcapsules compared to free retinol.

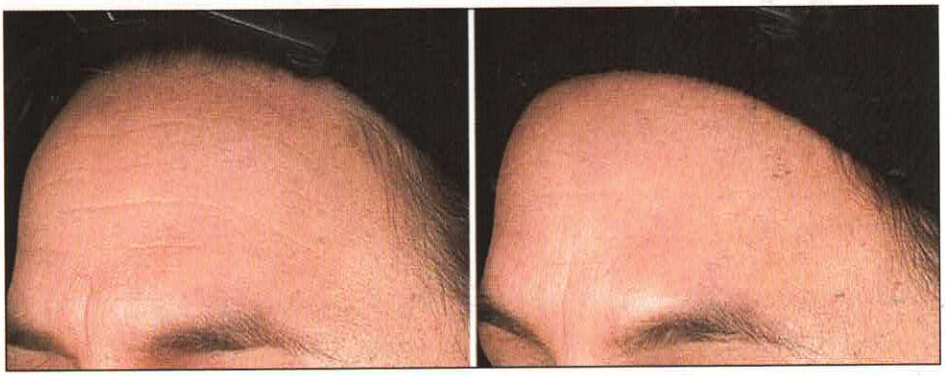


figure 3: representative image of reduction of the appearance of forehead wrinkles at (left) Baseline and 28 days treatment with CelluCap R (right).



figure 4: representative image of visible softening of marionette lines at baseline (left) and 28 days treatment with CelluCap R (right).

It was also clearly shown that by formulating with the microcapsules the discoloration of the gel formulation was prevented over time.

In-vivo efficacy results: For the efficacy evaluation of a formulation containing 1.1% of the microcapsules (0.1% of free retinol) on skin, the Visa CR imaging system was used. The firmness of the skin was measured on each subject using Cutometer. The images were analysed to determine changes in the appearance of facial skin texture.

After four weeks of treatment twice daily, the results showed a 55.2% increase in skin firmness and an 11.2% improvement in the appearance of fine lines and wrinkles (statistically significant difference from baseline, $p < 0.05$) as shown in figure 3 and 4.

In addition, 90% of participants agreed that the appearance of their fine lines and wrinkles were reduced and a full 100% agreed their skin felt firmer and looked younger, healthier, clearer, softer, smoother, and more even.

The **antioxidant activity** of the microcapsules compared to free retinol was evaluated by DPPH assay by determining the percentage inhibition of DPPH radicals. After the encapsulation of retinol by encapsulation technology, its ability to "scavenge" DPPH radicals was significantly increased as shown in figure 5.

Conclusions

Retinol is one of the most popular ingredients in skincare. However, there are certain problems and challenges that scientists face when incorporating this sensitive ingredient into skincare formulations; namely, the challenge of maintaining its stability and potency over time.

But it was possible to develop a **stable form of encapsulated retinol**, to ensure its efficient delivery while preserving its potency and efficacy. These microcapsules were designed to **release the retinol following**

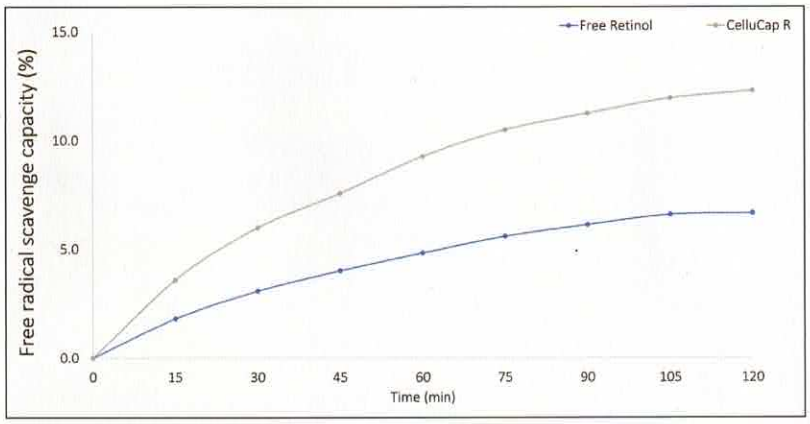


figure 5: Antioxidant activity of CelluCap R microcapsules compared to free retinol (the final concentration of retinol in both tested samples was equal).

mechanical pressure, which results in breakage of the polymeric shell. Upon application, while rubbing the formulation into skin, the polymeric shell collapses and the microcapsules begin to fracture, releasing the encapsulated retinol. Microcapsules breakdown into invisible particles, but still retain a portion of the payload to continue and deliver over time.

The results of this study clearly show that **retinol microcapsules are significantly more stable than the freeform of retinol.**

In addition, the in-vivo clinical clearly shows that the encapsulation process preserves the dermatological activity of retinol as an anti-ageing/wrinkle agent with fast-acting results. □

References

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4 CelluCap R, INCI: Retinol, Cellulose Acetate Butyrate, Tricaprylin, Pentaerythrityl Tetra-di-tbutyl Hydroxyhydrocinnamate

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