Ultrafine Bubbles to Transform Water for the Sustainable Topical Delivery of Actives

Jan 3rd, 2025 | By Nick Jackowetz, Ph.D., and Carly Hanson, Ph.D., Hydrosome Labs, Westmont, IL USA | From Hydrosome Labs

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Editor's Note: This work examines the potential of water, treated via an ultrafine bubble technology, to deliver actives into skin. The penetration of niacinamide and carnosine (peptide) from a cosmetic formula is evaluated. Additional applications are proposed.

The cosmetics industry is rapidly evolving, driven by consumer demand for innovative, highly effective, natural and sustainable products.[1] Recent trends show a continued shift toward clean labels and natural ingredients, for which researchers are exploring novel active compounds from plant extracts, marine sources and biotechnology. These efforts have led to advancements in anti-aging, skin brightening and protective formulations, among others.

Amidst this innovation, water — the most prevalent ingredient in many cosmetic formulations — remains understudied. A search in major cosmetic science journals reveals a scarcity of research on water's role in cosmetic products, despite its

1. a high surface-to-volume ratio, which enhances surface activity, enabling efficient mass transfer and improved gas solubility;[3-5]
2. good stability due to negative electrostatic charge and reduced buoyancy, prolonging their lifespan in liquids;[6-8] and
3. improved penetration and permeability, thanks to their small size, which makes them ideal carriers for active ingredients.[9-11]

Researchers have proposed[12] an "attract and deliver" hypothesis for UFB-enhanced skin permeation. That is, the bubbles may attract and aggregate active ingredients through electrostatic and non-polar forces at the gas-liquid interface of the bubble, potentially shuttling these ingredients deeper into the skin. Such a dynamic could reduce reliance on exogenous chemical penetrating agents that may irritate sensitive skin.

The present work explores the potential of UFB-treated water[a] as an active delivery vehicle in cosmetic applications. Test formulas are prepared to examine its effects on the penetration of niacinamide and carnosine (peptide) into skin. Additional applications are also proposed.

Niacinamide Penetration and Skin Hydration Ex vivo

Skin permeation: Ex vivo testing of the UFB technology was conducted using confocal Raman spectroscopy to visualize the permeation of target molecules into the stratum corneum (SC) and viable epidermis. Skin samples (1 cm in diameter) were treated with 40 mg of two test formulas that were identical except for their water: one incorporated DI water and the other, UFB-treated water (see **Table 1**).

The formulas were massaged onto skin samples with a glass rod for 60 sec. These samples were placed in a Franz diffusion cell (filled with DI water) and incubated for 2 hr at 32°C. Excess formula was then removed via Kimwipe before Raman analysis (see **Figure 1** schematic).

Figure 2 shows the results of the niacinamide test, visualized via confocal Raman microscopy. These showed that Formula 1, with deionized (DI) water, was not successful in delivering niacinamide into the SC – the active remained on the skin surface. In contrast, Formula 2, with the UFB-treated water, showed significant penetration of the niacinamide through the SC and extending into the viable epidermis.

The mechanism by which the UFB water could enhance the dermal penetration of active ingredients such as niacinamide is still under investigation. It is likely via its function as a nano-scale carrier, considering the sub-200 nm size of the bubbles and characteristic Brownian motion kinetics. However, additional research is required.

Skin hydration: **Figure 3** shows the same niacinamide-containing formulations on the skin, but now focusing on the O-H frequency of water in the Raman spectrum to visualize skin hydration.

The Raman spectral band corresponding to O-H stretching vibrations (3350-3550 cm^{-1}) indicates the presence of hydroxyl-containing molecules. As water (H_2O) represents the predominant hydroxyl-containing species in biological tissue, the intensity of this band can be used to assess the relative water content and hydration status in skin. However, it should be noted that other hydroxyl-containing biomolecules may contribute to this spectral region, albeit to a much lesser extent than water, due to their lower relative concentrations.

Quantitative analysis of the water content within the skin samples showed that **Formula 2**, containing UFB-treated water, resulted in significantly higher hydration levels on the surface and viable epidermis in comparison with **Formula 1**, containing DI water.

What's more, Formula 2 was tested 26 months after initial analysis and the same niacinamide delivery benefits and increased hydration were observed, highlighting the stability of formulas incorporating UFB-treated water (not shown).

Carnosine Penetration Ex vivo

Ex vivo studies also were conducted using HPLC analysis to measure the permeation of the dipeptide carnosine into skin. Skin samples (1 cm in diameter) were treated with two identical test formulas except for their water – again, one included DI

Initial research of the UFB technology provides encouraging results and only recently has it been more widely incorporated into cosmetics and personal care applications.[10, 16] Active ingredient selection remains an ongoing area of study, especially in consideration of the structural moieties and functional groups that are well-tolerated by UFBs.

However, the technology has shown compatibility with most existing cosmetic formulations and stability under extreme high and low temperatures – down to 0°C[17] and up to autoclave sterilization cycles at 121°C under 15 psi for 15 min; it also tolerates high shear forces during mixing (not shown).

Since the mechanics of the UFB technology are still being explored, testing plays a crucial role in identifying the optimal concentration of UFBs for the given formulation, combination of active ingredient(s) and UFB parameters (i.e., size, concentration, gas composition, etc.) to maximize the desired benefits and outcomes of personal care formulations.

Interestingly, gas selection presents an exciting avenue for exploration. The current UFBs use ambient air (primarily nitrogen and oxygen), but future possibilities could incorporate gases chosen for their cosmetic benefits; oxygen, nitrogen, carbon dioxide, hydrogen and argon are being investigated.

Another area of focus is ensuring comfort for users. Notably, UFB formulations have been positively received by consumers without reported adverse reactions (not shown). To further ensure safety, the UFB technology has been self-GRAS certified through a third-party clinical research organization. In addition, studies exploring the interactions of UFBs with skin, their impact on skin health and their relationship with the skin microbiome are in progress to further optimize their benefits for skin care applications.

For example, UFBs could potentially enhance the delivery of hydrating ingredients such as hyaluronic acid or glycerin, or anti-aging actives like peptides, vitamins or antioxidants, amplifying their effects on skin renewal and collagen production.[13] Cleansers and makeup removers with UFBs may offer gentler yet effective cleansing by breaking down and lifting away impurities without the need for surfactants, potentially reducing skin irritation.[14]

Moreover, UFBs may help to stabilize emulsions and suspensions, reducing the need for additional stabilizers while extending shelf life.[15] This aligns well with the growing consumer demand for clean and minimalist formulations, contributing to more sustainable product development and potentially reducing waste. From a business perspective, the technology can also be integrated for on-site UFB water generation.

Conclusions

As shown here, ultrafine bubbles[a] present a novel opportunity for the cosmetics and personal care industry. They offer a unique combination of benefits that addresses many current industry challenges (i.e., actives delivery, stability) and consumer demands for more sustainable and green alternatives. Further research will uncover their greater potential.

Thus, the described UFB technology provides formulators with a new tool to create highly effective, environmentally friendly products that meet evolving consumer expectations. This technology shows great potential to be the next significant advancement in cosmetic science, enabling the development of cutting-edge products that combine performance, safety and sustainability.

[a] *Hydrosome H_2O is a patented technology of Hydrosome Labs.*

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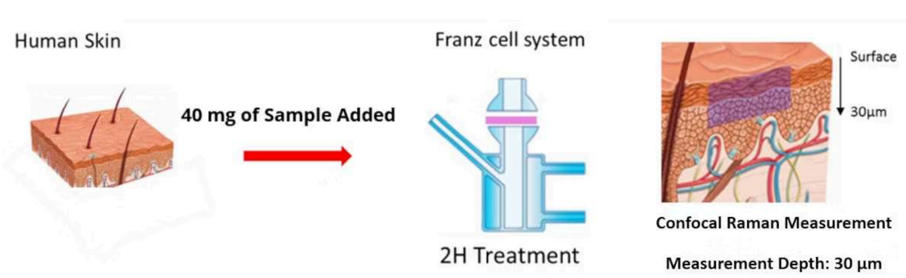
Figure 1. Schematic for experimental design of niacinamide permeation test



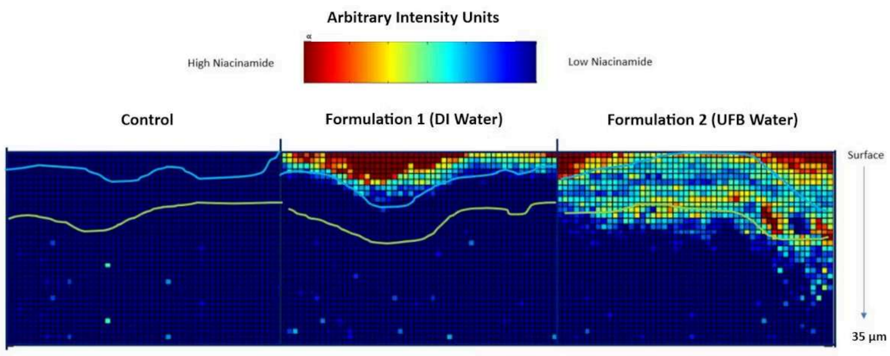


Image obtained from the integrated intensity of the 1597 cm^{-1} band normalized to the amide I band at 1650 cm^{-1}; blue line = surface of the SC; green line = boundary between the SC and viable epidermis

CLICK TO VIEW FIGURE

Figure 3. Hyperspectral images of the control skin (untreated) and Formula 1 (with 3% niacinamide and DI water) and Formula 2 (3% niacinamide and UFB water) treated skin

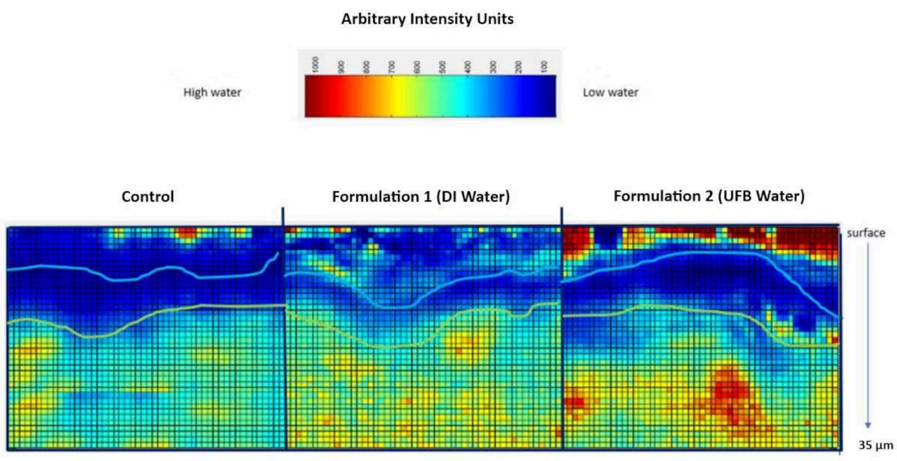
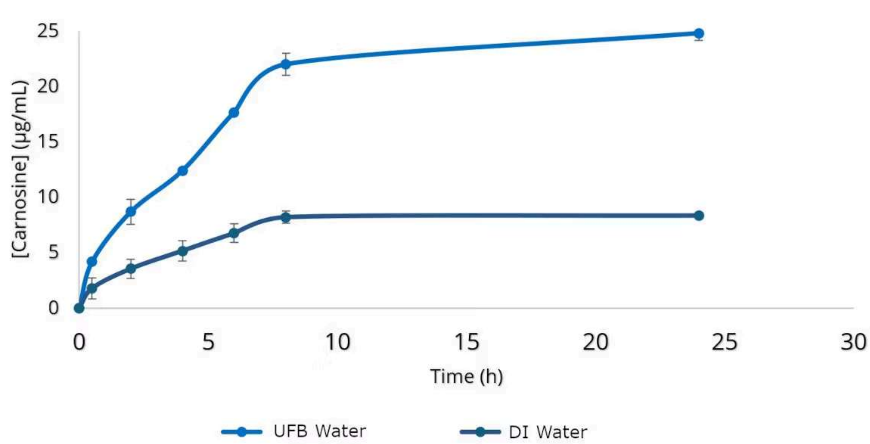


Image obtained from the integrated area of a portion of the O-H stretch (3350 - 3550 cm^{-1}) normalized to the protein amide I band at 1650 cm^{-1}; blue line = surface of the SC; green line = boundary between the SC and viable epidermis

CLICK TO VIEW FIGURE

Figure 4. HPLC results comparing carnosine penetration with UFB water vs. DI water in ex vivo skin samples



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Formula 1 (DI Water)	Formula 2 (UFB Water)
Deionized Water	UFB Water
Caprylic/Capric Triglyceride (MCT oil)	Caprylic/Capric Triglyceride (MCT oil)
Polyglyceryl-2 Stearate (and) Glyceryl Stearate (and) Stearyl Alcohol (Polyaquol 2W, Innovacos)	Polyglyceryl-2 Stearate (and) Glyceryl Stearate (and) Stearyl Alcohol (Polyaquol 2W, Innovacos)
Glycerin	Glycerin
Niacinamide	Niacinamide
1,2-Hexanediol (and) Caprylyl Glycol (Symdiol 68, Symrise)	1,2-Hexanediol (and) Caprylyl Glycol (Symdiol 68, Symrise)
Pentylene Glycol (Hydrolyte 5 Green, Symrise)	Pentylene Glycol (Hydrolyte 5 Green, Symrise)

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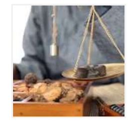

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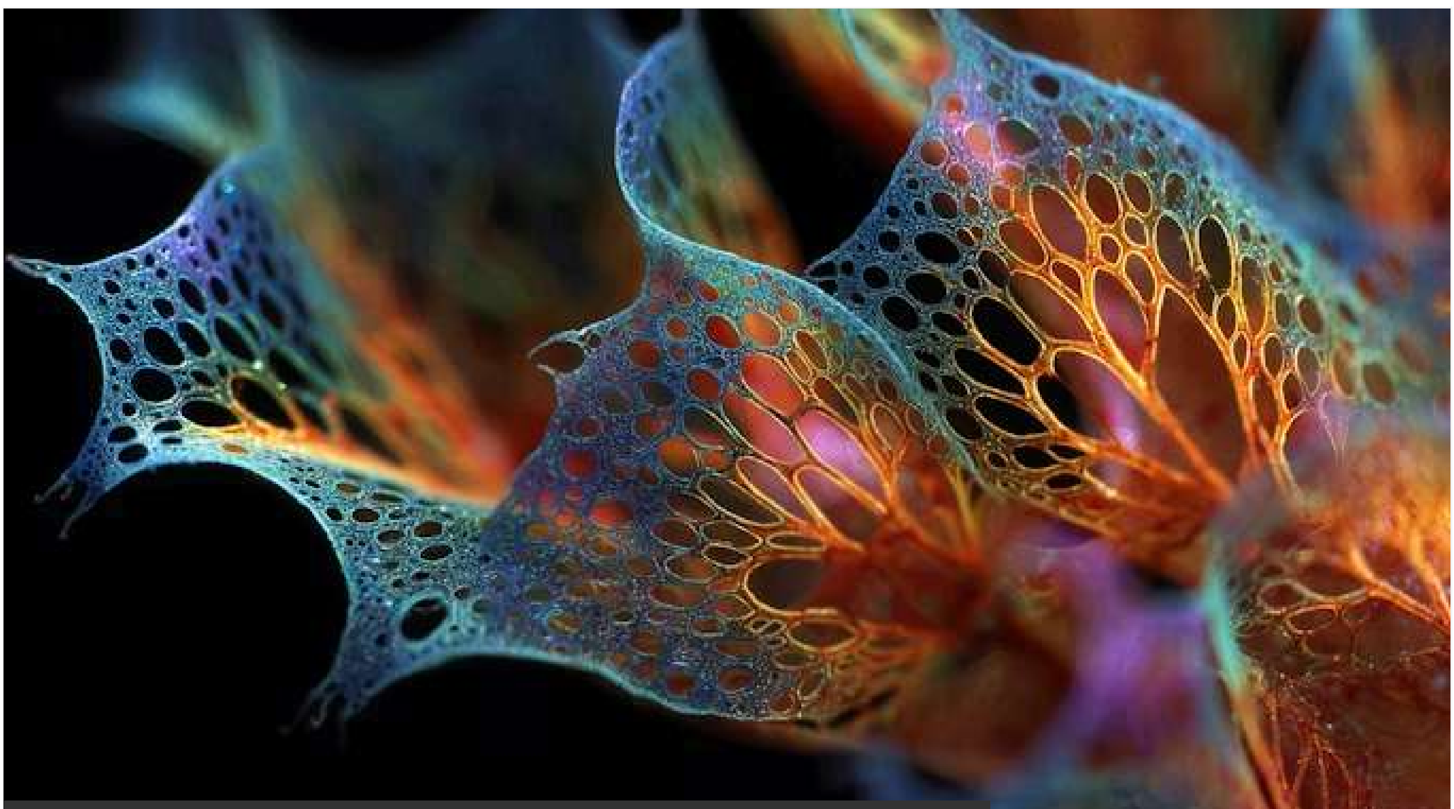

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