Enhancing Niacinamide Delivery into Human Skin with Hydrosome H_2O^{TM}

Abstract:

This study evaluated the influence of Hydrosome H_2O (deionized water containing a proprietary blend of ultrafine bubbles at a specific size and concentration) on the delivery of niacinamide, a widely used cosmetic active ingredient, into human skin samples using confocal Raman microscopy. Two formulations were tested: one containing 3% niacinamide in deionized water (DI) and another with 3% niacinamide in Hydrosome H_2O. The results demonstrated that Hydrosome H_2O transported the niacinamide formulation through the stratum corneum and into the viable epidermis while the DI water formulation remained on the surface of the skin. Furthermore, the Hydrosome formulation displayed significantly higher hydration levels within the stratum corneum, and viable epidermis compared to the DI water formulation. The combination of niacinamide with Hydrosome H_2O increases hydration levels and active delivery into the skin, which can amplify product effects.

Introduction:

Ultrafine bubbles (UFBs) are small gas-filled spheres with diameters less than one micron but generally between 100-300 nm, significantly smaller than conventional bubbles[1]. These bubbles possess unique properties that set them apart from their larger counterparts[1]. Notably, their high surface-to-volume ratio endows them with enhanced surface activity, enabling efficient mass transfer and improved solubility of gases[2–4]. Additionally, UFBs exhibit exceptional stability, owing to their increased internal pressure and reduced buoyancy, which prolongs their lifespan in liquids[5–7]. Moreover, their small size improves transport, making them ideal carriers for delivering active ingredients and nutrients in various applications, including cosmetics, pharmaceuticals, and agriculture[8–10].

Hydrosome Labs has developed a proprietary technology that creates UFBs in deionized water with a targeted bubble size and concentration, thus creating Hydrosome H_2O. The unique size and concentration of UFBs produced using this technology gives them enhanced biological activity and shelf life of over 1 year in water and over 2 years in topical formulations. This prolonged stability sets Hydrosome H_2O apart from other UFB solutions, which typically tout UFB stability from a few months to less than 1 year[11–13]. Additionally, advanced liquid cell transmission electron microscopy (LC-TEM) has revealed significant populations of UFBs in Hydrosome H_2O with sizes less than 50 nm. These small sizes also have not previously been reported in peer reviewed scientific literature and are a key factor in the efficacy and long shelf-life of Hydrosome H_2O. The distinctive characteristics of the UFBs generated through Hydrosome Labs' technology distinguish them into a new category known as: "*Hydrosomes*^{TM}."

Niacinamide, also known as nicotinamide, is a form of vitamin B3 widely used in cosmetic formulations for its various benefits, including improving skin barrier function, reducing hyperpigmentation, and exhibiting anti-aging properties[14]. However, the effective delivery of niacinamide into deeper layers of the skin can be challenging due to the barrier posed by the stratum corneum. This study aimed to investigate the potential of Hydrosome H_2O to enhance the delivery of niacinamide into human skin samples compared to a formulation with conventional deionized (DI) water.

Materials & Methods:

Two formulations were tested in this study. Formulation 1 contained DI water, and Formulation 2 contained Hydrosome H_2O. Both had the same level of niacinamide (3% w/w) and were identical except for the type of water used in the formulation. The other ingredients in descending order were, water (DI or Hydrosome H_2O), MCT oil, Polyaquol 2W, glycerin, Symdiol 68, Hydrolite 5 Green. Human skin samples were from the same batch and purchased from a licensed supplier.

Ex-vivo studies were conducted using confocal Raman spectroscopy to visualize the permeation of niacinamide into the stratum corneum and viable epidermis. The skin samples (1 cm in diameter) were treated with 40 mg of each formulation, massaged with a glass rod for 60 seconds, placed in a Franz diffusion cell, and incubated for 2 hours at 32°C.

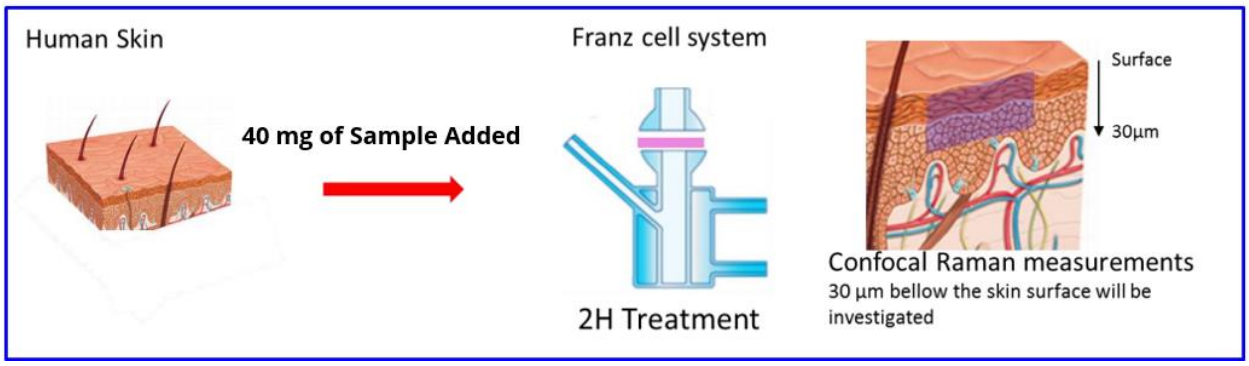

Figure 1 *Overview of the experimental design for niacinamide permeation into donated human skin using a Franz diffusion cell and confocal Raman spectroscopy for quantification. Image courtesy of TRI Princeton.*

Confocal Raman hyperspectral images were acquired at and below the skin surface to evaluate the penetration depth and distribution of niacinamide. The characteristic Raman bands at 1035 cm^{-1} and 1597 cm^{-1} were used as markers to track niacinamide penetration (**Figure 2**). Additionally, the water content within the skin was quantified using the O-H stretching vibration (3350-3550 cm^{-1}) that was normalized to the protein amide I band at 1650 cm^{-1}.

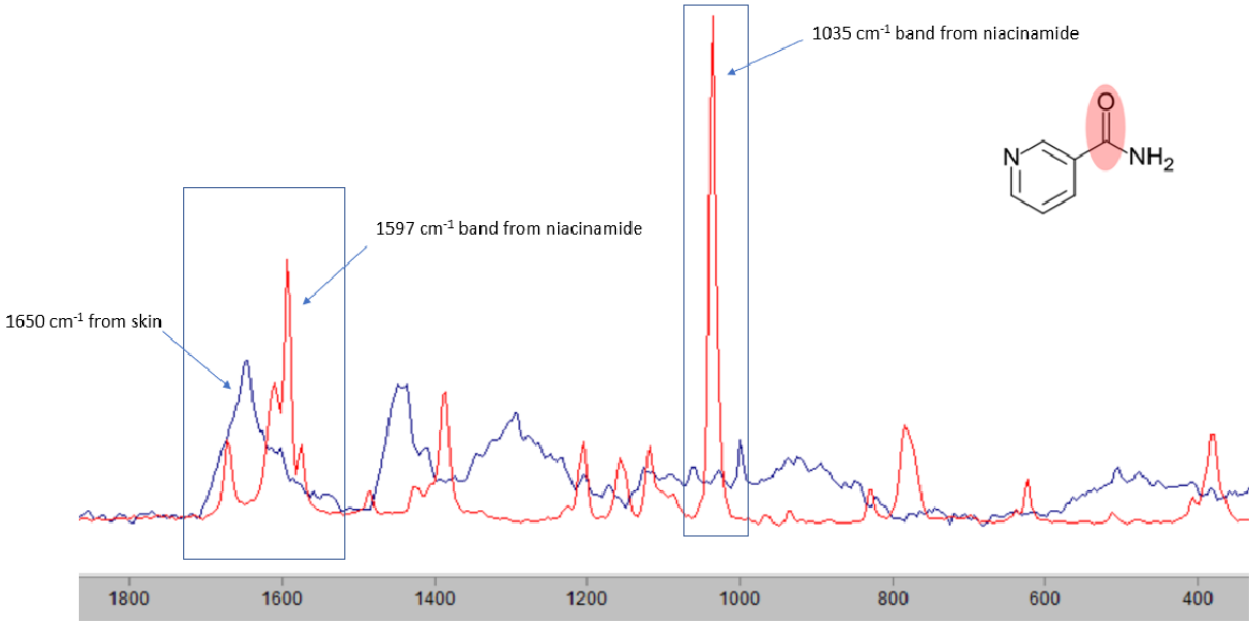

Figure 2 *Overlaid Raman finger-print region spectra of niacinamide (red) against virgin skin sample (blue). The strong band contributions at 1035 cm^{-1}, 1597 cm^{-1} from niacinamide, and the 1650 cm^{-1} amide I contribution from skin, were used to monitor the niacinamide penetration into the skin.*

Results:

The confocal Raman hyperspectral images revealed a clear distinction between the penetration behavior of niacinamide in the two formulations. Formulation 1, containing niacinamide in DI water, did not show penetration of niacinamide into the stratum corneum, with the active remaining on the surface of the skin. In contrast, Formulation 2, containing niacinamide in Hydrosome H_2O, demonstrated significant penetration of niacinamide through the stratum corneum, and extending into the viable epidermis. This finding was confirmed at two separate confirmation bands for the niacinamide molecule, 1035 cm^{-1} and 1597 cm^{-1} (**Figure 3** & **Figure 4**).

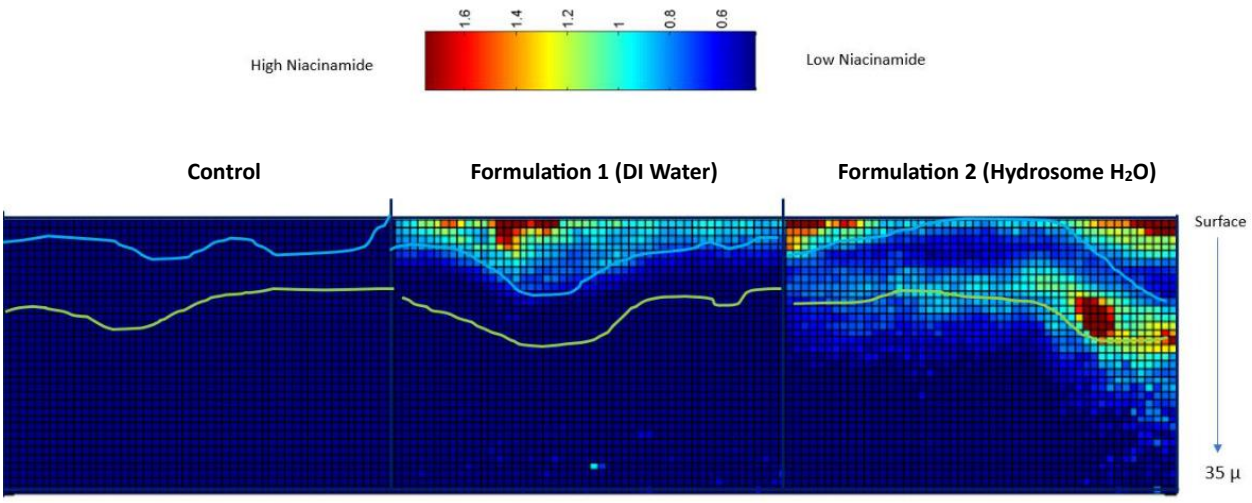

Figure 3 *Hyperspectral images of the control skin (no niacinamide), Formulation 1 (with 3% niacinamide and DI water in the formulation), and Formulation 2 (3% niacinamide and Hydrosome H_2O in the formulation The image is obtained from the integrated intensity of the* ***1035 cm^{-1} band*** *normalized to the amide I band at 1650 cm^{-1}. The blue line represents the surface of the stratum corneum, while the green line is the boundary between the stratum corneum and the viable epidermis.*

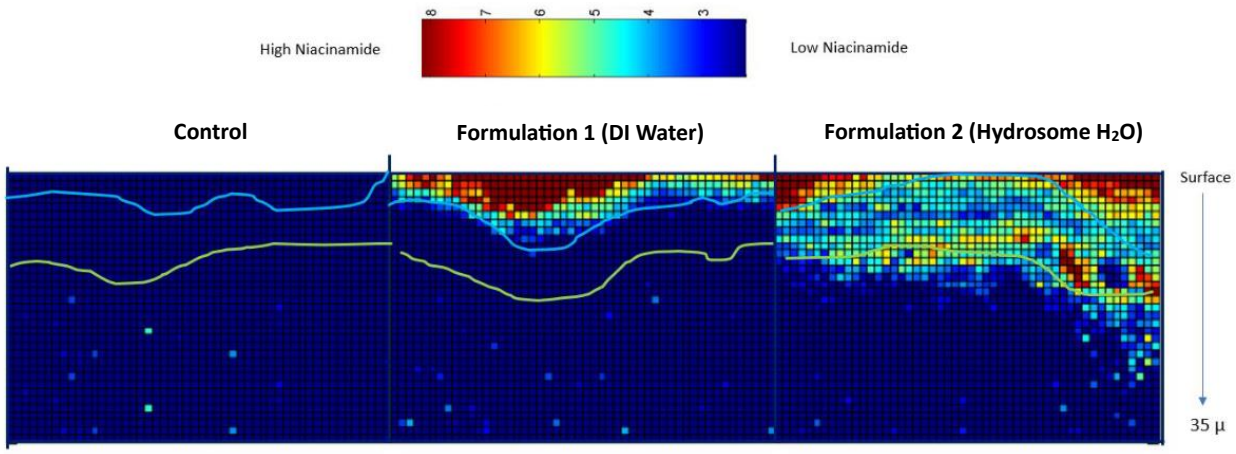

Figure 4 *Hyperspectral images of the control skin (no niacinamide), Formulation 1 (with 3% niacinamide and DI water in the formulation), and Formulation 2 (3% niacinamide and Hydrosome H_2O in the formulation). The image is obtained from the integrated intensity of the* ***1597 cm^{-1} band*** *normalized to the amide I band at 1650 cm^{-1}. The blue line represents the surface of the stratum corneum, while the green line is the boundary between the stratum corneum and the viable epidermis.*

Furthermore, quantitative analysis of the water content within the skin samples showed that Formulation 2 with Hydrosome H_2O resulted in significantly higher hydration levels on the surface, within the stratum corneum and viable epidermis in comparison to Formulation 1 with DI water (**Figure 5**).

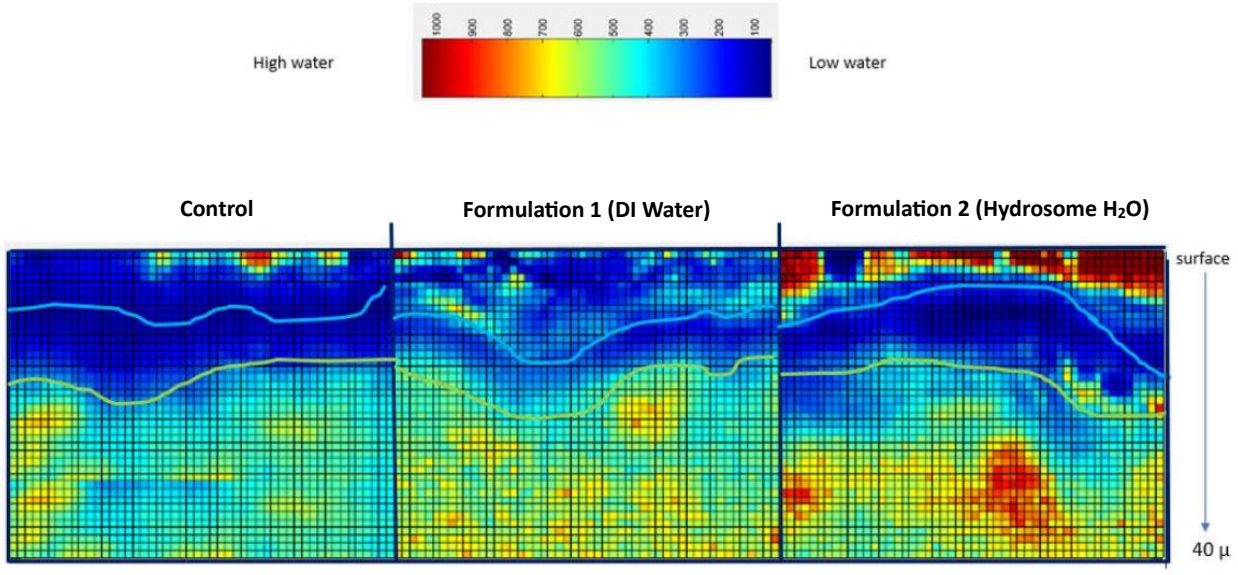

Figure 5 *Hyperspectral images of the control skin (no formulation), Formulation 1 (with 3% niacinamide and DI water in the formulation), and Formulation 2 (3% niacinamide and Hydrosome H_2O in the formulation). The image is obtained from the integrated area of a portion of the O-H stretch (3350 – 3550 cm^{-1}) that is normalized to the protein amide I band at 1650 cm^{-1}. The blue line represents the surface of the stratum corneum, while the green line is the boundary between the stratum corneum and the viable epidermis.*

The results suggest that the inclusion of Hydrosome H_2O in topical formulations improves both hydration and the delivery of niacinamide deeper into the skin, potentially enhancing its effectiveness for various cosmetic applications.

Conclusions:

This study demonstrated the beneficial effects of Hydrosome H_2O to improve the delivery of niacinamide and increase hydration levels in human skin samples. The niacinamide formulated with Hydrosome H_2O permeated through stratum corneum and reached the viable epidermis, while the formulation with DI water did not penetrate the surface of the skin. Additionally, the Hydrosome H_2O formulation provided significantly higher hydration levels within the stratum corneum compared to the DI water formulation. These findings highlight the potential of Hydrosome H_2O as a promising formulation strategy to enhance the delivery of active ingredients without the need for additional chemical additives or penetrating agents.

Hydrosome® LABS

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