

Enhanced Follicular Delivery of Salicylic Acid *In Vivo* by a Novel Microgel Technology

I-Ting Wu, M.S.^a • Theresa Chen, Ph.D.^a • Yang Liu, Ph.D.^b • Jeff Wu, Ph.D.^b • Nhan Cao, B.S.^a • Nikiforos Kollias, Ph.D.^b • Yohini Appa, Ph.D.^a

^aNeutrogena Corporation, Los Angeles, CA • ^bJohnson & Johnson Consumer & Personal Products Worldwide, Skillman, NJ

INTRODUCTION

Excessive sebum production and hyperkeratotic infundibulum contribute to the formation of keratinous plugs that obstruct the follicles and result in the formation of microcomedones, which are the precursors of acne. It is thus essential to break through the sebum barrier to effectively target delivery of actives such as salicylic acid, a well-known keratolytic agent, into the follicles where acne begins. A novel synergistic Microgel complex has previously been shown to promote sebum solubilization *in vitro* and enhance deposition of salicylic acid into the pilosebaceous unit.¹⁻² Utilizing follicular biopsies and a newly developed two-dimensional fluorescence imaging method, we have shown that the microgel complex promotes salicylic acid penetration into the follicles in all three distinct formulation bases, which indicates not only its efficacy, but its compatibility with various formulation bases.

STUDY DESIGN

To evaluate the effect of the microgel complex (MGC) in boosting salicylic acid (SA) delivery, we conducted a split-face study using three different formulation bases, with and without MGC. The test products, with and without MGC, were applied once on different sides of the nose. Pore plug samples were then collected by follicular biopsy method.³ SA deposition in the pores was examined using HPLC and fluorescence imaging.

STUDY MATERIALS

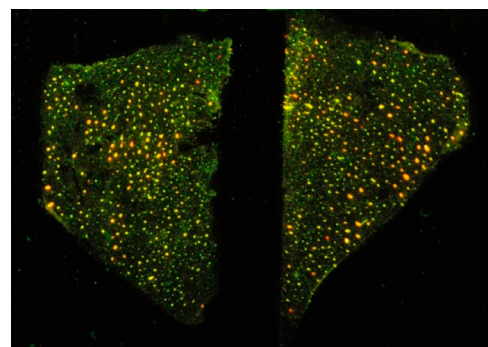
- 2-in-1 cleanser mask (CM) with and without MGC, both with 1% SA.
- A scrub with and without MGC, both with 2% SA.
- A leave-on spot treatment gel (STG) with and without MGC, both with 2% SA.

STUDY METHODS

Follicular Biopsy

Modifications were made to the follicular biopsy method by including a larger sampling area of the nose, between rhinion, the tip defining point, and alar sidewall, to improve the quality and quantity of extracted pore plugs. (Fig. 1).

Fig. 1 – Blue Fluorescence Image of a Pair of Follicular Biopsy Slides From the Nose

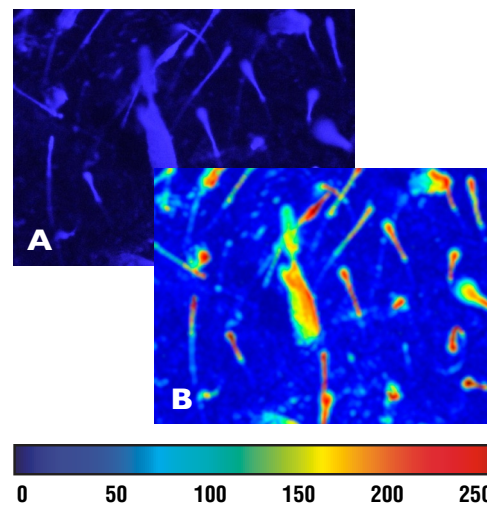


The follicular horns fluoresce as greenish-white areas, and with the presence of *P. acnes* porphyrins, the horns fluoresce as orange red areas.⁴⁻⁶

Digital Imaging

A commercially available microscope with a customized tunable light source ranging from UV to near IR radiation was used to obtain magnified pore plugs (Fig. 2). The visible images were acquired using a filtered light from a Xenon lamp (290nm excitation and emission bandpass filter centered at 406nm) to capture the fluorescence of SA.

Fig. 2 – Fluorescence Imaging of Salicylic Acid in the Pore Plugs



(A) Magnified fluorescence image of pore plugs. (B) Reconstructed image to visualize concentration of SA. The red color represents the highest concentration and the blue color represents no salicylic acid.

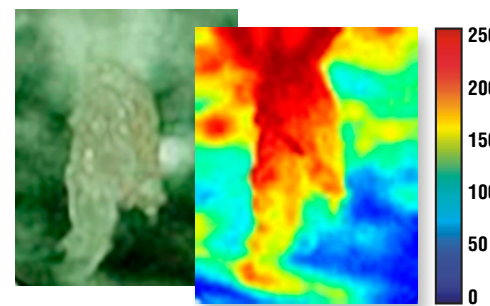
HPLC Analysis

Pore plugs were carefully harvested from the follicular biopsy slides. Methanol mobile phase was added to the collected pore plugs. The extract was filtered and injected into a phase column. The amount of salicylic acid was then determined from the peak absorbance at 305nm.

RESULTS

Deeper Salicylic Acid Pore Deposition by the Microgel Complex

(A) Spot Treatment Gel with MGC



(B) Spot Treatment Gel without MGC

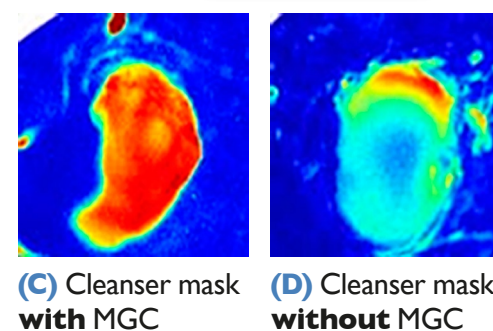
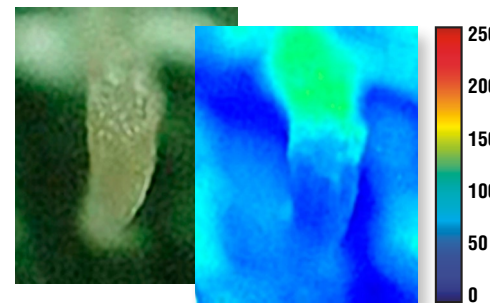


Fig. 3 – Visible and fluorescence images of pore plugs treated with STG (A) with and (B) without MGC. Cleanser mask treated pore plugs (C) with and (D) without MGC. The images are shown with the slide (or skin side) on the top and the root of the pore plug on the bottom.

HPLC Analysis of Increased Salicylic Acid Deposition

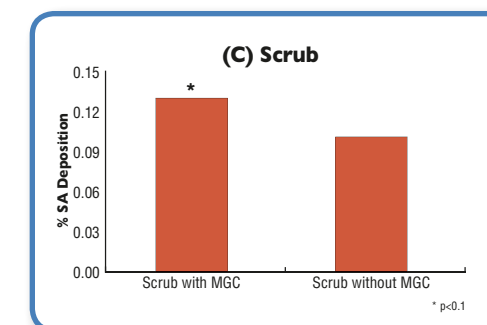
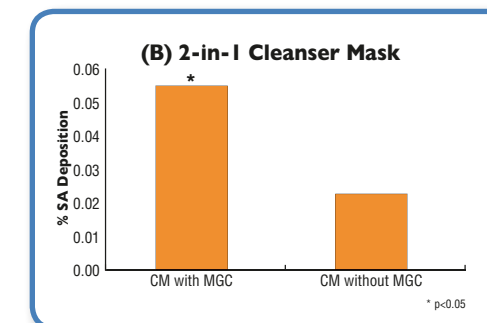
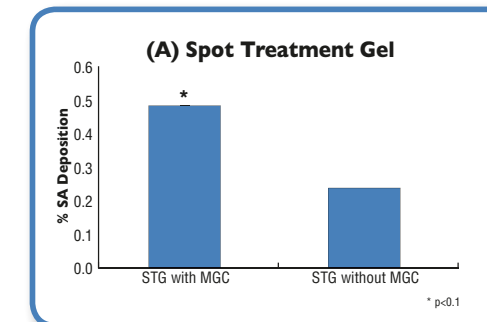


Fig. 4 – Microgel complex increased amount of salicylic acid deposition by (A) 243% in STG, (B) 203% in CM, and (C) 141% in Scrub. For all three different formulation bases, the level of salicylic acid deposition was significantly higher in the pores treated with MGC.

CONCLUSIONS

- The Microgel technology increases the amount and the depth of salicylic acid deposition in the pores.
- The Microgel technology is able to boost targeted delivery of salicylic acid into the follicles regardless of formulation variations.
- The fluorescent imaging method combined with HPLC permits qualitative and quantitative assessment of salicylic acid deposition.

REFERENCES

1. Chen T, Appa Y. *Subsurface phenomena associated with acne lesions and treatment interception*. Poster Presentation at the 65th Annual Meeting of the American Academy of Dermatology, 2007.
2. Chantalat J, Wu J, et al. *Characterization of a synergistic microgel complex that improves acne treatment efficacy*. Poster Presentation at the 64th Annual Meeting of the American Academy of Dermatology, 2006.
3. Mills OH Jr, Kligman AM. The follicular biopsy. *Dermatologica*. **167**: 57-63, 1983
4. Cornelius, III, CE. and Ludwig, GD. Red fluorescence of comedones: production of porphyrins by corynebacterium acnes. *J. Invest. Dermatol.* **49**: 368-370, 1967.
5. Sauermann G, Ebens B, Hoppe, U. Analysis of facial comedos by porphyrin fluorescence and image analysis. *J. Toxicol. Cutan Ocular Toxicol.* **8**: 369-385, 1989/90.
6. Barry M, Chantalat J, Wu J, et al. *Effect of a novel microgel complex against propionibacterium acnes*. Poster Presentation at the 64th Annual Meeting of the American Academy of Dermatology, 2006.

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