

A NOVEL 3-DIMENSIONAL IMAGING METHOD TO EVALUATE THE COMEDOLYTIC EFFECT OF AN ANTI-ACNE DERMOCOSMETIC PRODUCT

C. MIAS¹, T. NOCERA¹, E. GONTIER², C. LAUZE¹, J. LE DIGABEL¹, A. BACQUEY¹, G. JOSSE¹, A. HOUCINE¹, A. STENNEVIN³, G. DOAT³, S. BESSOU-TOUYA¹, P. REYGAGNE⁴, JH. SAURAT⁵, H. DUPLAN¹

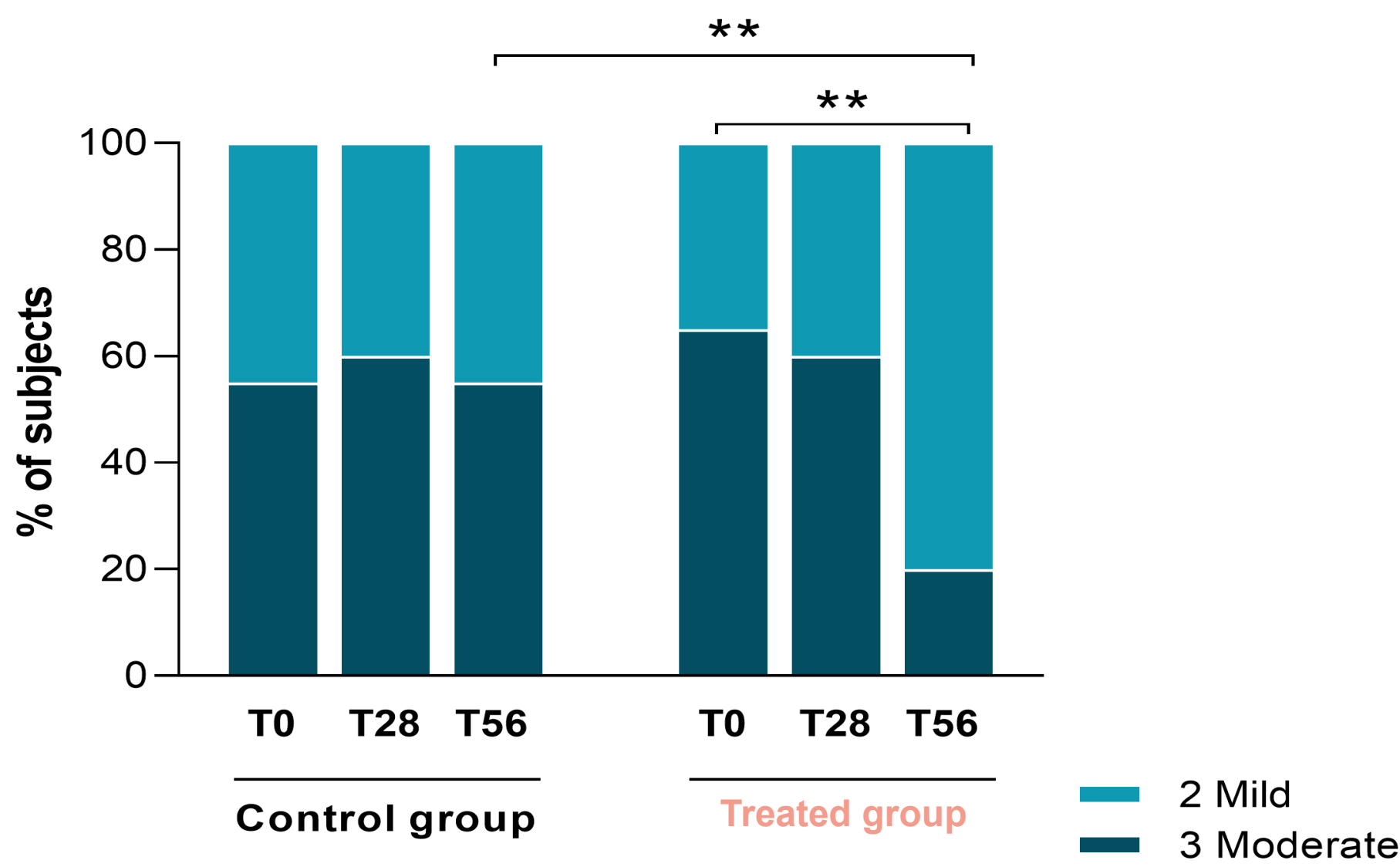
¹R&D, Pierre Fabre Dermo-Cosmétique et Personal Care, Toulouse, France ; ²Bordeaux Imaging Center, France ; ³Laboratoires dermatologiques Avène, Lavalur, France ; ⁴Centre de santé Sabouraud, Hôpital Saint-Louis, France ; ⁵University of Geneva, Switzerland

INTRODUCTION

Acne is an inflammatory skin disease affecting the pilosebaceous units, characterized by lesions like comedones, papules, and cysts due to sebum excess, hyperseborrhea, hyperkeratinization, microbiome dysbiosis, and local immunoinflammation. Microcomedones, the earliest form of comedones, can develop and evolve into visible lesions. Acne involves keratinocyte hyperproliferation in ecosystem dysregulations, leading to comedone formation and inflammation. Anti-acne dermocosmetics are valuable for managing mild-to-moderate acne and reducing antibiotic use. Visualizing the activity of the formulation on microcomedones makes it easier to evaluate new anti-acne products. A Silybum marianum fruit extract (SMFE)-based product effectively reduced acne lesions and positively impacted the microcomedone ecosystem. This study evaluates the comedolytic effect of SMFE-based product on microcomedones structure using advanced 3D imaging with serial block-face scanning electron microscopy (SBF-SEM) and a conservative extraction method were used to analyze structural changes.

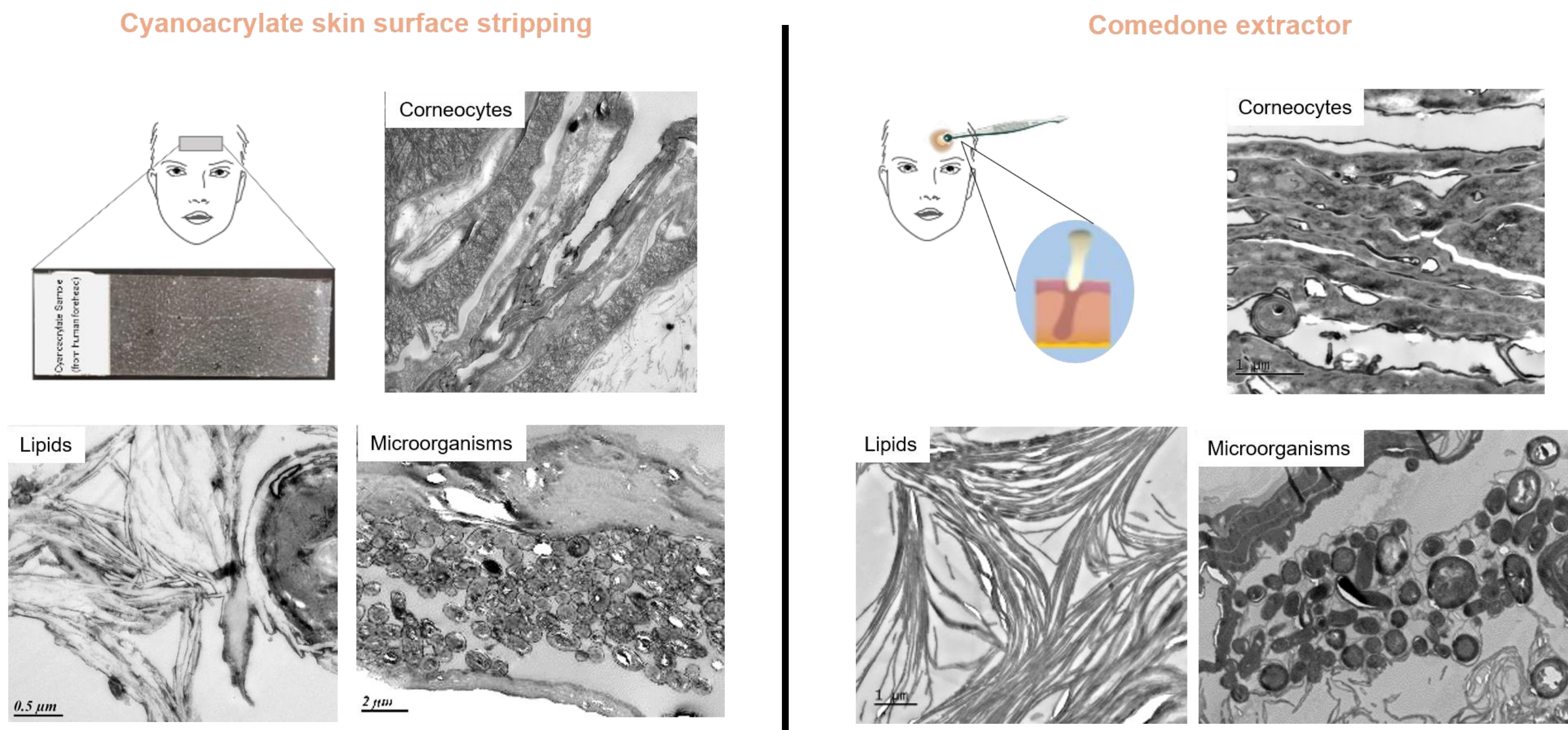
RESULTS

1/ ACNE CLINICAL EVALUATION



In Treated group, GEA was significantly improved between T0 vs T56 with a decrease of acne severity from moderate to mild (-69,2% of moderate acne and +128,6% of mild acne at T56 vs T0). These data demonstrated the clinical efficacy of SMFE-based product after two months of twice-daily application (**, $p<0,01$).

2/ COMPARISON OF EXTRACTION



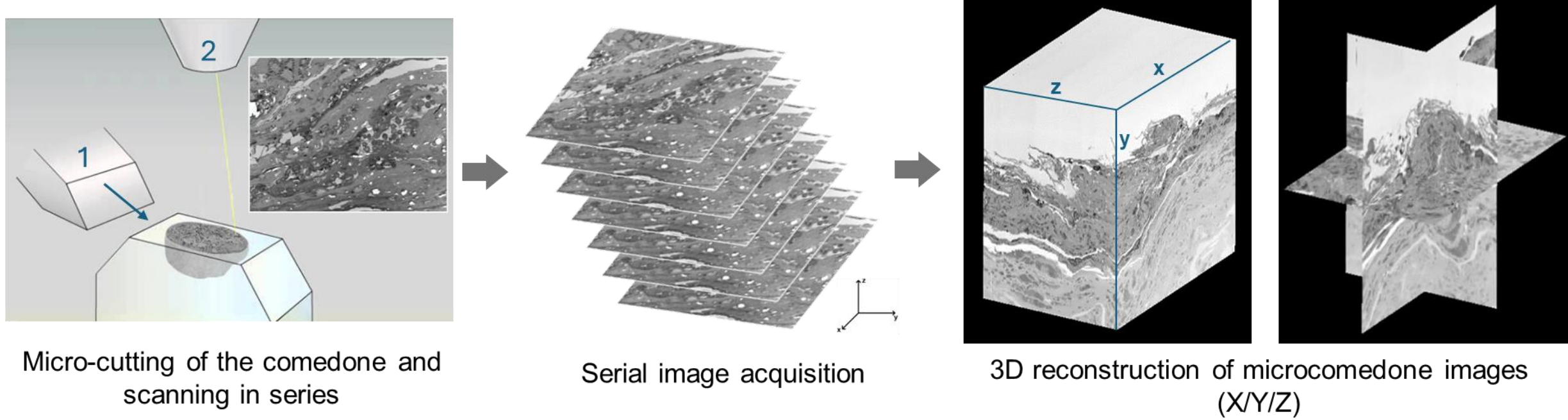
2D-TEM images of microcomedones extracted from the forehead using either cyanoacrylate skin surface stripping or a comedone extractor revealed the typical components of microcomedone structure, including corneocytes, lipids, and microorganisms. Corneocytes were arranged in cohesive and dense layers. Lipids appeared as filaments or tubes between corneocyte layers. Microorganisms were visible as rounded or oval structures. Comparing both methods showed that the ultrastructure of microcomedone was preserved with the comedone extractor. Therefore, this method was validated for further 2D and 3D-imaging, and ultrastructure analysis.

CONCLUSIONS

These 2D and 3D ultrastructural data confirmed that the anti-acne product demonstrated an alteration of the structural integrity of the microcomedone, particularly in the outermost layers of corneocytes. This study confirms the comedolytic efficacy of the SMFE-based product (Treated group) in acne patient, altering microcomedone structure and reducing hyperkeratosis. This is the first experimental study on the 3D structure of microcomedones, to be conducted as part of a clinical study, paving the way for further investigations into the comedolytic activity of topical agents for acne treatment.

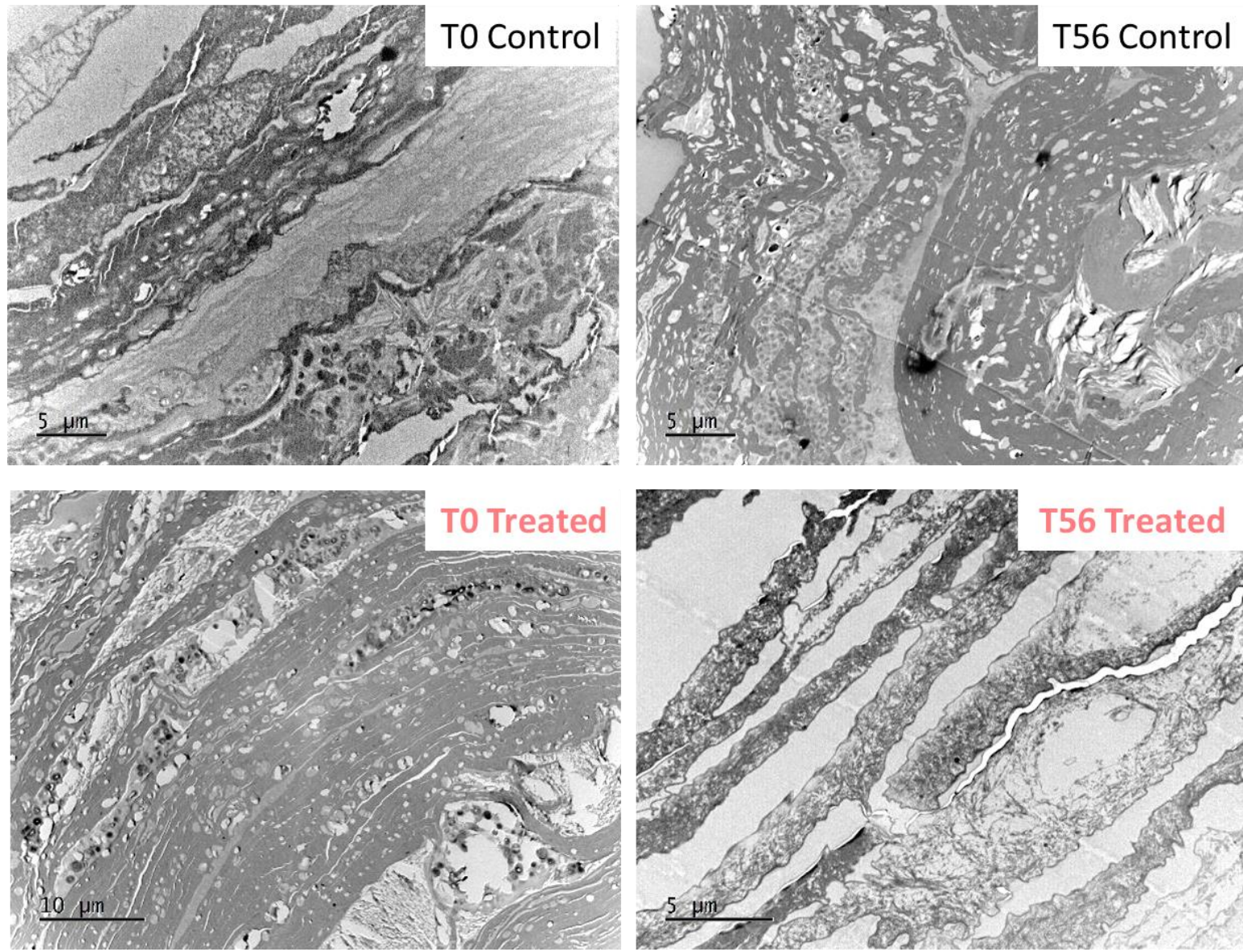
MATERIALS AND METHODS

Forty subjects with mild-to-moderate acne were randomly assigned in two comparative groups: one receiving SMFE-based product (Treated group) twice daily for 56 days, and a Control group using a hydrating skincare product. Clinical, and ultrastructural imaging analyses were performed at days 0, 28, and 56. Microcomedones were selected based on standardized photographs of the subject face (8 subjects per condition) and extracted using a comedone extractor. Microcomedones were analyzed using transmission electron microscopy (TEM) and serial block-face scanning electron microscopy (SBF-SEM, see method below).

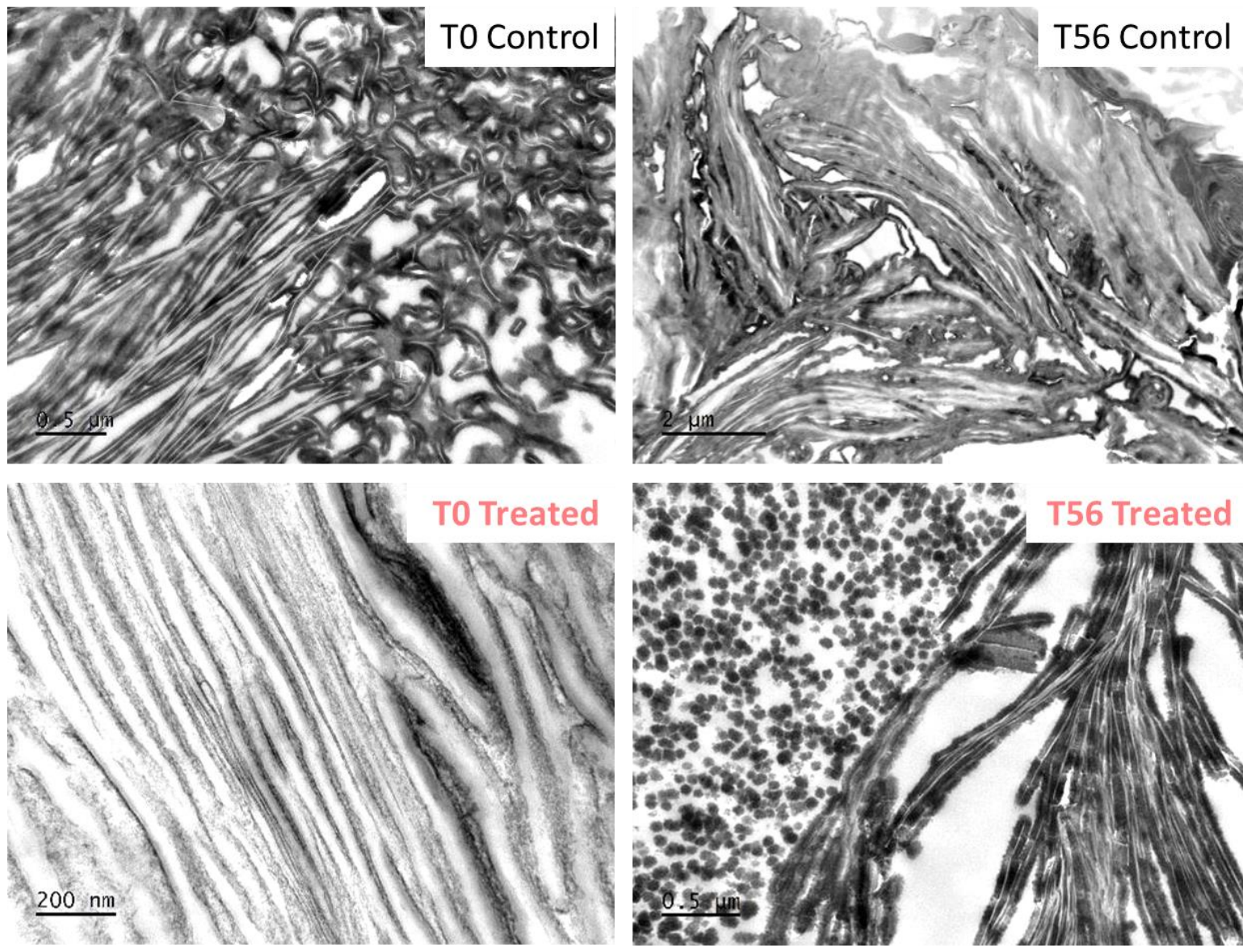


3/ COMEDONE ULTRASTRUCTURE

A. Corneocytes

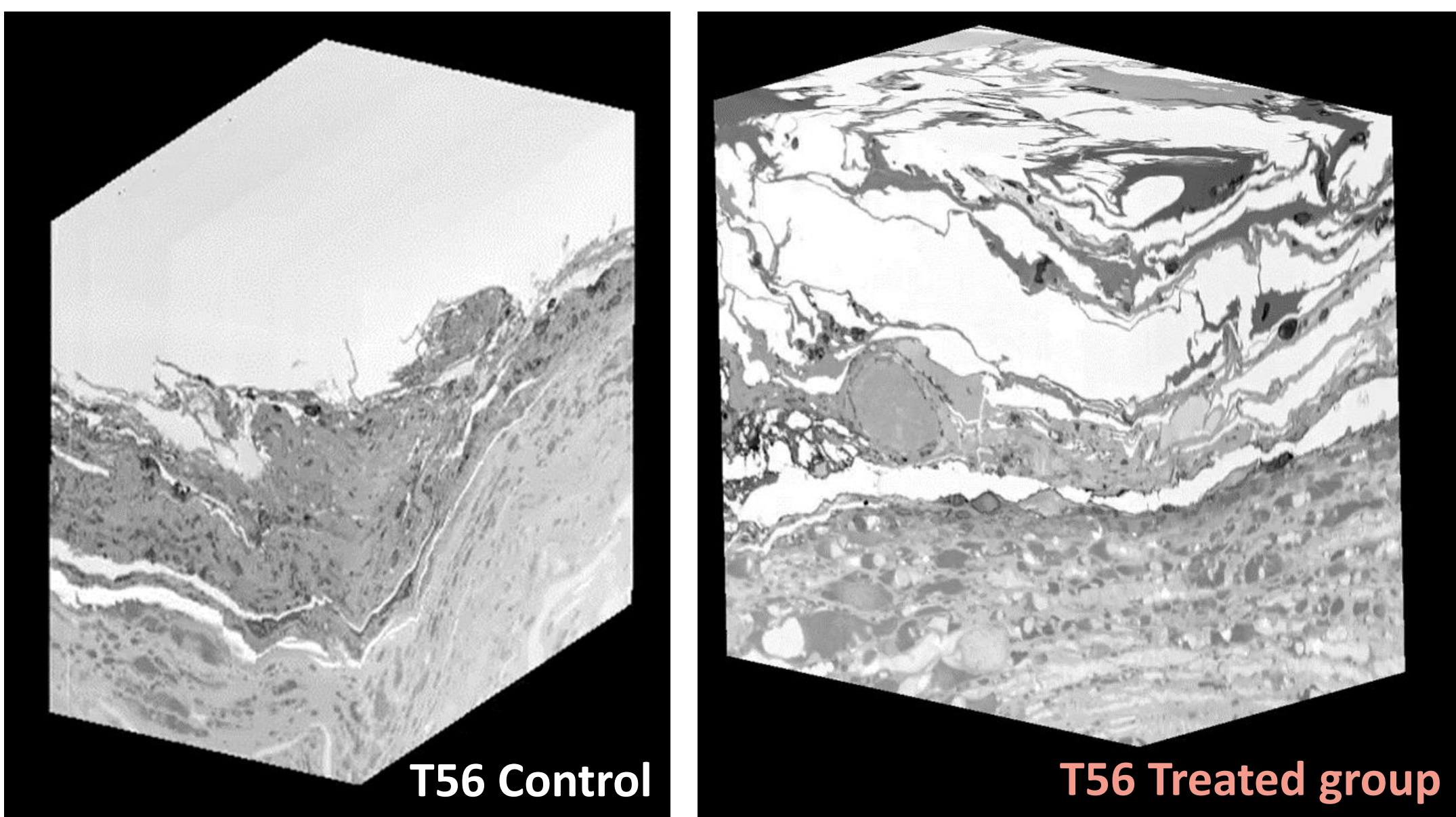


B. Lipids



Effects of the anti-acne product was observed by 2D-TEM on microcomedone ultrastructure: corneocytes, lipids and microorganisms. **In Figure A**, no changes were observed in the Control group after 56 days. In the Treated group, there was a loss of corneocyte cohesion, membrane swelling, and follicular rupture, indicating the comedolysis. **In Figure B**, at a higher magnification, lipid organization did not show apparent changes between the 2 groups.

4/ 3D VISUALIZATION OF COMEDOLYSIS



3D-TEM images of microcomedone showed a global disorganization of comedone structure after Treated product application characterized by a strong loss of corneocyte cohesion, and a swelling of corneocyte membranes compared to the Control group. This technique allowed for the analysis of all components of the microcomedone in the same sample and these observations revealed the induction of the comedolytic process under Treated product.