IFSCC 2025 full paper (IFSCC2025-1114)

"Lipidomics and KEGG Enrichment Analysis Revealed Key Differences Between Dry Sensitive Skin and Oily Sensitive Skin"

Jianhua Zhang [1,2,*], Shichao Liu [1,2], Wenjiao Guo [1,2] and Yun Huang [1]

[1] N.O.D topia (GuangZhou) Biotechnology Co., Ltd. Guangdong Guangzhou, 510000, China; [2] Simpcare (GuangZhou) Biotechnology Co., Ltd. Guangdong Guangzhou, 510000, China.

1. Introduction

Skin types such as dry, oily, and sensitive skin exhibit distinct physiological characteristics and responses to external factors [1]. Dry skin is typically characterized by insufficient moisture and low sebum levels, resulting in symptoms such as dryness, redness, itching, and peeling. Oily skin, on the other hand, is characterized by excessive sebum production, which can lead to clogged pores, acne, and inflammation. Sensitive skin, often seen in both dry and oily skin types, is more reactive to environmental stressors, such as pollutants and skincare products [2]. Both dry and oily sensitive skin are prone to challenges such as compromised barrier function, altered immune responses, and increased neurosensitivity [3]. However, the physiological and biochemical mechanisms underlying these conditions remain insufficiently understood. Research comparing dry sensitive skin to oily sensitive skin, especially in terms of lipid profiles and their effects on skin function, is limited, necessitating further exploration to provide a comprehensive understanding of the unique attributes of each subtype and their associated skin issues.

The application of lipidomics in dermatological research has gained substantial interest in recent years. Lipidomic profiling offers a detailed analysis of the lipid composition in the skin, facilitating the identification of biomarkers for various skin conditions [4]. Lipidomic techniques, such as ultrahigh-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UHPLC-QTOF-MS), enable precise characterization of lipid species involved in skin metabolism and their alterations in disease states [5,6]. Lipidomic analysis has proven valuable not only in elucidating the molecular mechanisms behind skin disorders such as eczema, acne, and psoriasis, but also in advancing the development of targeted cosmetic and therapeutic interventions [7]. Despite its potential, the application of lipidomics in understanding the complex interactions between skin type, sensitivity, and lipid composition remains underexplored.

This study aims to investigate the lipid differences between dry and oily sensitive skin by employing lipidomic and clinical analysis. By analyzing the lipid profiles and exploring the associated pathways, this research seeks to provide deeper insights into the distinctive features of these skin types and their relevance to skin health. In addition, the study will investigate various physiological indicators, such as pore count, skin redness, and current perception threshold (CPT), to further elucidate the differences between dry and oily sensitive skin. The findings of this study will contribute to the understanding of skin sensitivity mechanisms and inform the development of personalized skincare solutions.

2. Materials and Methods

2.1. Study design and population

The clinical study was conducted in Beijing, China, from August to September 2024. A total of 130 female volunteers aged 20-30 years were recruited and classified into three groups: dry sensitive skin (n = 35), oily sensitive skin (n = 35), and healthy skin (non-sensitive, n = 60). Participants were selected based on self-assessment, the Baumann questionnaire (to determine skin type and sensitivity), and a lactic acid sting test (positive for sensitive skin groups). Inclusion criteria included good health, no history of allergies or facial dermatoses, and residency in Beijing for at least one year. Exclusion criteria comprised pregnancy, recent use of topical/oral medications affecting skin physiology, or significant facial injuries.

2.2. Assessments

Under standardized conditions (20–22°C, 40–60% humidity), physiological parameters were evaluated after a 45-minute acclimatization period. Facial images were acquired using VISIA-CR for pore analysis and redness assessment (a* value, erythema index), while skin hydration, sebum secretion, and barrier function (TEWL) were measured on the cheeks and forehead using a Corneometer, Sebumeter, and Tewameter, respectively. Neurosensitivity was quantified *via* current perception threshold (CPT) testing at the nasolabial fold, and subjective symptoms such as stinging and tightness were recorded through self-reports.

2.3. Lipidomic Analysis

Facial sebum was collected non-invasively using adhesive patches from the forehead and bilateral cheeks. Lipid profiles were obtained via UHPLC-QTOF-MS, and raw data were processed with Progenesis QI for feature alignment and identification. Lipids were annotated by matching against an in-house database (>4,000 lipids) with mass error <25 ppm. Differential lipids (fold change >1.5, $P < 0.05$) were identified using multivariate statistics (PLS-DA, *t*-test). KEGG enrichment analysis was performed to elucidate pathway-level differences, with significance set at $P < 0.05$ after FDR correction.

2.4. Statistical analysis

The data, presented as mean values with standard deviations (mean ± SD), were analyzed statistically using IBM SPSS Statistics version 26. Both the Student's *t* test and one-way analysis of variance (ANOVA) were employed to assess differences between groups. The significance thresholds were designated as follows: * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$. Figures were created using GraphPad Prism version 8.0.

3. Results

3.1. Differences in skin physiological indicators between oily sensitive skin and dry sensitive skin

A total of 130 subjects were enrolled, of whom 35 had dry sensitive skin, 35 had oily sensitive skin, and 60 had healthy skin. As shown in Figure 1, transepidermal water loss (TEWL) was significantly higher in sensitive skin than in healthy skin ($P < 0.001$), with oily sensitive skin showing higher TEWL than dry sensitive skin ($P = 0.014$). This indicated an impaired barrier function in sensitive skin, especially oily sensitive skin. In addition, dry sensitive skin had higher redness (a* value) than oily sensitive skin ($P = 0.001$), suggesting enhanced vascular reactivity in dry sensitive skin (Figure 1C). Besides, current perception threshold (CPT) values were significantly lower in sensitive skin compared to healthy skin ($P < 0.05$), but no differences were found between dry and oily sensitive skin (Figure 1D). This suggested an enhanced neurosensitivity in both oily sensitive skin and dry sensitive skin.

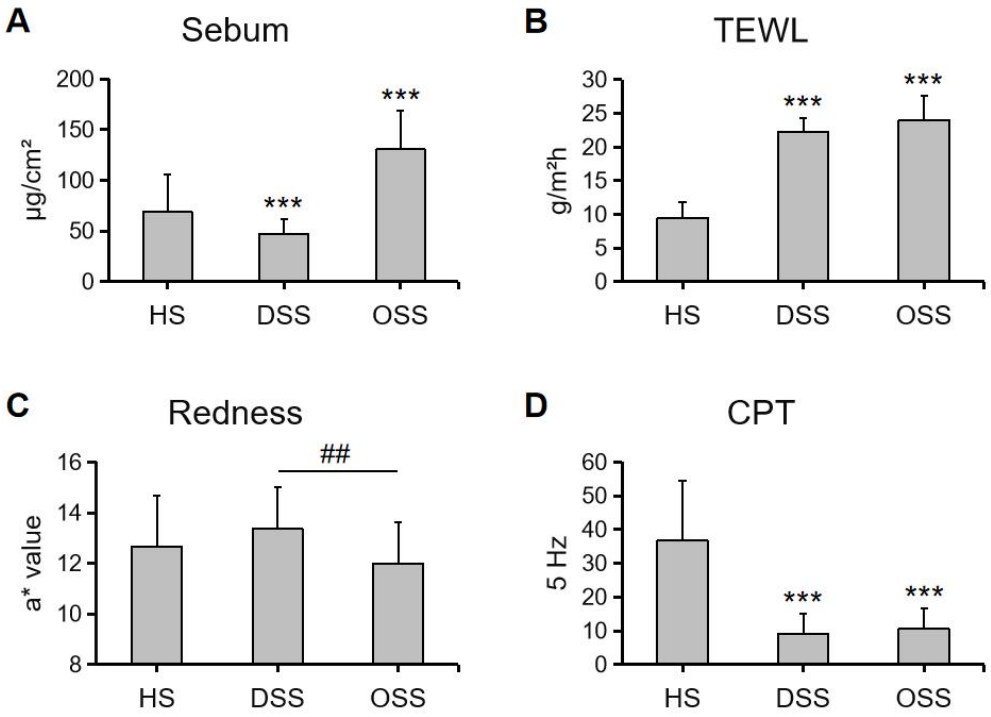

Figure 1. Differences in skin physiological indicators between oily sensitive skin and dry sensitive skin. The facial sebum content (A), transepidermal water loss (B), redness (C), and current perception threshold (D) were evaluated and compared among healthy skin (HS), dry sensitive skin (DSS), and oily sensitive skin (OSS). Student's *t* test, *** $P < 0.001$ *vs.* HS group, ## $P < 0.01$ *vs.* DSS group.

3.2. Differences in skin surface lipidomic profiles between oily sensitive skin and dry sensitive skin

Lipidomic analysis identified 220 differentially expressed lipids between oily sensitive skin and dry sensitive skin (Figure 2). Additionally, a total of 20 biomarkers specific to sensitive skin were screened out (Figure 2). Besides, oily sensitive skin had significantly higher oxidized lipid content than dry sensitive skin ($P = 0.045$, Figure 3A), potentially leading to the skin inflammation and yellowishness in oily sensitive skin. Interestingly, the ceramide quantitative

levels were slightly higher in sensitive skin than in healthy skin, possibly as a compensatory response to impaired skin barrier in sensitive skin (Figure 3B). However, oily sensitive skin showed a lower ceramide proportion than dry sensitive skin (P = 0.006, Figure 3C), consistent with the worse barrier function in oily sensitive skin.

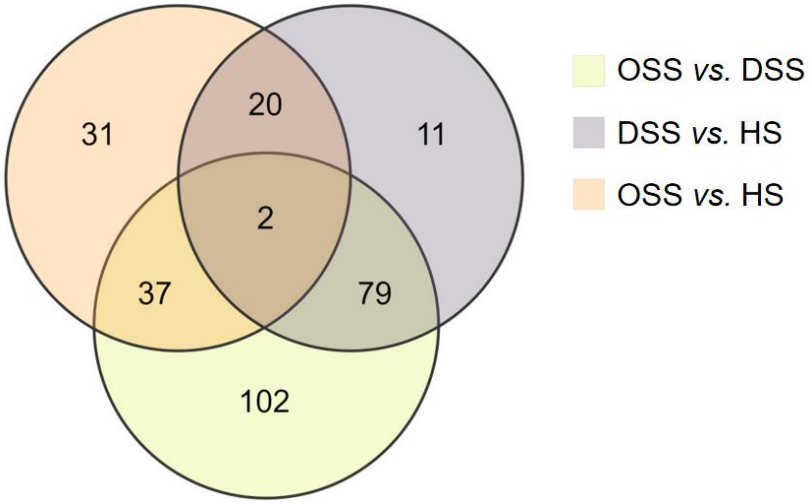

Figure 2. The differentially expressed lipids among healthy skin, oily sensitive skin, and dry sensitive skin.

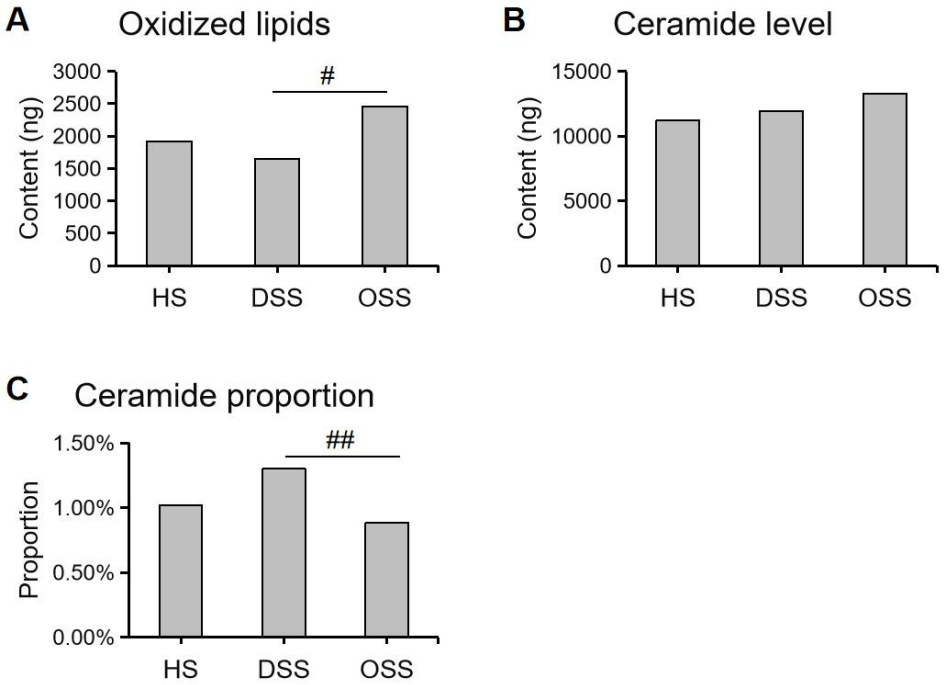

Figure 3. Differences in oxidized lipids and ceramides between oily sensitive skin and dry sensitive skin. The oxidized lipids content (A), ceramides content (B), and the proportion of ceramides (C) were evaluated and compared among healthy skin (HS), dry sensitive skin (DSS), and oily sensitive skin (OSS). Student's t test, # $P < 0.05$, ## $P < 0.01$.

3.3. KEGG enrichment analysis revealed the different biological pathways between oily sensitive skin and dry sensitive skin

To further investigate the different signaling pathways between oily sensitive skin and dry sensitive skin, the Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways of the differentially expressed lipids were enriched. The top 3 pathways were “Glycerolipid metabolism”, “Lipid and atherosclerosis”, and “Fat digestion and absorption”, indicating that lipid metabolism was the main difference between oily sensitive skin and dry sensitive skin (Figure 4). It’s noticed that immune-related pathways, including “Systemic lupus erythematosus”, “Neutrophil extracellular trap formation”, and “Th17 cell differentiation”, were observed among the top 20 pathways, suggesting the difference in skin inflammation between oily sensitive skin and dry sensitive skin.

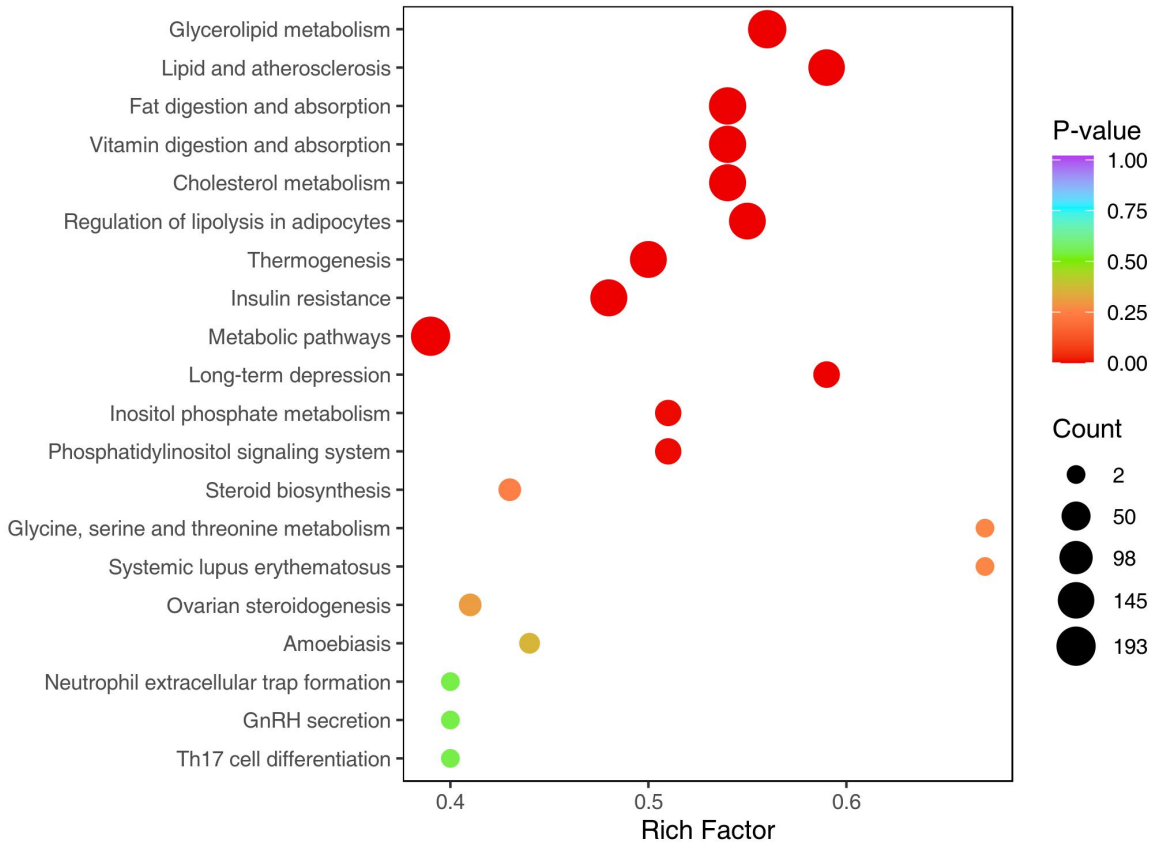

Figure 4. *KEGG enrichment analysis revealed the different biological pathways between oily sensitive skin and dry sensitive skin*.

4. Discussion

In recent years, skin sensitivity, especially in dry and oily skin types, has garnered significant attention due to its complex interplay of physiological and biochemical factors. While both dry and oily sensitive skin share a heightened reactivity to environmental factors, their distinct lipid profiles and their implications for skin function remain insufficiently explored. Previous studies have primarily focused on general skin sensitivity or individual skin types, but comparative analyses of lipidomic characteristics between dry and oily sensitive skin are limited. This research aims to fill this gap by examining the lipidomic differences between these two subtypes, alongside a detailed investigation of associated clinical parameters such as transepidermal water loss (TEWL), redness, and neurosensitivity.

The results of this study underscore significant differences between dry and oily sensitive skin in terms of both physiological indicators and lipid composition. Notably, TEWL was found to be significantly higher in sensitive skin compared to healthy skin, with oily sensitive skin exhibiting more severe barrier impairment. Furthermore, dry sensitive skin showed enhanced vascular reactivity, as evidenced by higher redness values, while both subtypes exhibited heightened neurosensitivity, as indicated by reduced current perception threshold (CPT) values. The lipidomic analysis revealed 220 differentially expressed lipids between oily sensitive skin and dry sensitive skin. A noteworthy finding was the higher oxidized lipid content in oily sensitive skin, which may contribute to inflammation and the yellowish appearance commonly associated with this skin type. Additionally, the lower ceramide proportion in oily sensitive skin, as compared to dry sensitive skin, was consistent with its poorer barrier function.

Furthermore, the KEGG enrichment analysis highlighted key differences in lipid metabolism and immune-related pathways between the two skin types. Lipid metabolism, particularly in glycerolipid metabolism and fat digestion and absorption, was identified as a central distinction, suggesting that these pathways may play a critical role in the pathophysiology of oily and dry sensitive skin. The observation of immune-related pathways, such as neutrophil extracellular trap formation and Th17 cell differentiation, provides further insight into the potential inflammatory mechanisms differentiating the two skin types.

Overall, the findings of this study contribute valuable insights into the distinct biochemical and physiological features of dry and oily sensitive skin. By elucidating the lipidomic and pathway differences between these subtypes, this research lays the groundwork for more targeted skincare treatments and therapeutic interventions tailored to the unique needs of individuals with sensitive skin. The identification of specific biomarkers and molecular pathways paves the way for further exploration into personalized skincare solutions, offering potential benefits for the development of more effective treatments for sensitive skin conditions.

5. Conclusion

In conclusion, this study provides valuable insights into the distinct lipidomic profiles and physiological characteristics of dry and oily sensitive skin. The findings reveal significant differences in barrier function, neurosensitivity, and lipid composition between these two skin types. Oily sensitive skin exhibited more pronounced barrier impairment, as evidenced by higher transepidermal water loss (TEWL) and oxidized lipid content. In contrast, dry sensitive skin displayed enhanced vascular reactivity, reflected by higher redness levels. Lipidomic analysis identified 220 differentially expressed lipids, with 20 biomarkers specific to sensitive skin, highlighting the role of lipid metabolism in skin sensitivity. Furthermore, the study's KEGG pathway analysis revealed that glycerolipid metabolism and immune-related pathways, such as neutrophil extracellular trap formation and Th17 cell differentiation, were significantly enriched in both skin types, suggesting a distinct inflammatory response in oily sensitive skin. Overall, this research underscores the importance of lipidomic analysis in understanding the physiological and biochemical mechanisms of sensitive skin and paves the way for developing personalized skincare interventions targeting these specific skin conditions.

6. References

[1] Baumann L. Understanding and treating various skin types: the Baumann Skin Type Indicator. Dermatol Clin. 2008 Jul;26(3):359-73, vi. doi: 10.1016/j.det.2008.03.007.

[2] Misery L, Ständer S, Szepietowski JC, Reich A, Wallengren J, Evers AW, Takamori K, Brenaut E, Le Gall-Ianotto C, Fluhr J, Berardesca E, Weisshaar E. Definition of Sensitive Skin: An Expert Position Paper from the Special Interest Group on Sensitive Skin of the International Forum for the Study of Itch. Acta Derm Venereol. 2017 Jan 4;97(1):4-6. doi: 10.2340/00015555-2397.

[3] Kuang X, Lin C, Fu Y, Wang Y, Gong J, Chen Y, Liu Y, Yi F. A comprehensive classification and analysis of oily sensitive facial skin: a cross-sectional study of young Chinese women. Sci Rep. 2025 Jan 10;15(1):1633. doi: 10.1038/s41598-024-85000-z.

[4] Smirnov VV, Egorenkov EA, Myasnikova TN, Petukhov AE, Gegechkori VI, Sukhanova AM, Ramenskaya GV. Lipidomic analysis as a tool for identifying susceptibility to various skin diseases. Medchemcomm. 2019 Sep 12;10(11):1871-1874. doi: 10.1039/c9md00364a.

[5] Sochorová M, Vávrová K, Fedorova M, Ni Z, Slenter D, Kutmon M, Willighagen EL, Letsiou S, Töröcsik D, Marchetti-Deschmann M, Zoratto S, Kremslehner C, Gruber F. Research Techniques Made Simple: Lipidomic Analysis in Skin Research. J Invest Dermatol. 2022 Jan;142(1):4-11.e1. doi: 10.1016/j.jid.2021.09.017.

[6] Li S, Ganguli-Indra G, Indra AK. Lipidomic analysis of epidermal lipids: a tool to predict progression of inflammatory skin disease in humans. Expert Rev Proteomics. 2016 May;13(5):451-6. doi: 10.1080/14789450.2016.1177462.

[7] Dessì A, Pintus R, Fanos V, Bosco A. Integrative Multiomics Approach to Skin: The Sinergy between Individualised Medicine and Futuristic Precision Skin Care? Metabolites. 2024 Mar 7;14(3):157. doi: 10.3390/metabo14030157.