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A Cutting-Edge Transcriptomic Dive into the Beauty Benefits of Rosehip Extract

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1. Introduction

In the pursuit of beauty and health, skincare has evolved to include nutricosmetics and botanical extracts, which offer both nutritional and cosmetic benefits. Among these, the traditionally renowned rosehip (*Rosa canina* L.) has gained attention for its natural properties and potential health benefits [1]. One of the most traditional uses of rosehip extracts is for arthritis and joint health related to its high anti-inflammatory and antioxidant potential and the synergistic effect with collagen [2]. The increasing interest in "beauty-from-within" applications emphasizes the significance of rosehip extracts, which are believed to support skin health and enhance overall beauty by promoting collagen synthesis and providing protection against environmental stressors [3, 4]. Among various formulations, a specific aqueous extract derived exclusively from the dried shells of the fruit has shown consistent clinical efficacy and consumer satisfaction. The success of this extract is attributed to a unique combination of raw material selection and a carefully optimized extraction process. Rosehip and its aqueous extract are rich in bioactive compounds. These antioxidants scavenge reactive oxygen species and they could reduce skin damage, increase moisture content and boost regeneration. This study explored the impact of natural compounds in a standardized Rosehip extract on gene expression in human keratinocytes, focusing on skin aging, hydration, and barrier function.This research, the exploration of rosehip and its water extracts for beauty-from-within applications, reveals a fascinating intersection of traditional knowledge and modern science, making it a notable topic in the field of natural skincare and health solutions.

2. Materials and Methods

2.0 Extract characterization

Among the various wild rose species, Rosa canina was identified as the most suitable due to its high polyphenol content, strong antioxidant capacity, and biological stability (low hybridization rate). The rosehip shells were obtained through a mechanical separation process following the crushing and drying of the whole fruit. This method ensures the removal of seeds and fruit pulp. The standardized Rosehip peel extract was produced under

an extraction process designed to maximize the yield of polyphenols without the use of lipophilic solvents (solvent: water). Extended extraction times allow for optimal swelling of the plant cell matrix, facilitating the release of polyphenols. The commercial yield of extractives is approximately 25%, with a native drug-extract ratio (DER) of 4:1. The final composition of the extract preparation was rosehip native extract and Collagen Hydrolysate type I as excipient. The chemical characterization of the extract was done related to Pharmacopea Europaea; the total polyphenols were calculated as gallic acid monohydrate (GAE) with reference to the dried extract.

2.1 Cell Culture and Treatment

Human keratinocyte (HaCaT) cells were maintained in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% FBS and 1% Penicillin/Streptomycin, at 37°C in a 5% CO2 atmosphere. For experimental treatments, HaCaT cells were treated with the rosehip extract (1 mg/mL) or the vehicle control (DMEM) for 4.5 hours. The treatments include 3 biological replicates.

2.2 RNA Extraction and RNA-seq Library Preparation

Following treatment, RNA extraction was performed using GenUP Total RNA Kit (Biotechrabbit GmbH, Germany) according to the manufacturer's instructions. RNA quality and quantity were assessed using Nanodrop spectrophotometer (Agilent technologies, USA). RNA-seq library preparation was performed using Universal Plus mRNA-Seq kit (Tecan Genomics, USA) following the manufacturer’s instructions (library type: fr-secondstrand) and sequenced on paired-end 150 bp mode on NovaSeq 6000 (Illumina, USA).

2.3 Differential Expression Analysis

Differential expression analysis of RNA-seq data was obtained by DESeq2 using DEXSeq. Genes with an adjusted P-value (False Discovery Rate, FDR) <0.05 and a |log 2 FoldChange|>1 were considered statistically significant for reporting, ensuring robust control of false positives across multiple comparisons.

2.4 Functional Enrichment Analysis

To elucidate the biological mechanisms underlying the effect of rosehip extract on HaCaT cells, a functional enrichment analysis utilizing Reactome pathway database was performed on the differentially expressed genes. Specifically, genes with a nominal p-value <0.01 were used as input, the PADOG (Pathway Analysis with Down-weighting of Overlapping Genes) method was used to identify significantly regulated pathways. The analysis encompassed 1952 pathways and integrated fold changes from 12,128 genes. Pathways showing an adjusted P-value (FDR) ≤0.05 were considered significantly regulated.

3. Results

3.1 Chemical characterization

The primary bioactive compounds in the extract are polyphenols, which are known for their anti-inflammatory and antioxidant properties. These include: Gallic acids, Ellagic acids, Caffeoylquinic acids, Flavonoids and Tiliroside. The extraction method achieves a polyphenol transfer rate of up to 90%, significantly higher than the 30% typically obtained from simple tea infusions, which means a toat polyphenol content with a minimum of 1.5 % referenced to the dried extract.

3.2 Transcriptomic Landscape of Rosehip Treatment

The transcriptomic analysis revealed significant alterations in gene expression profiles in human keratinocytes (HaCaT cells) following rosehip treatment, providing molecular insights into its beneficial dermatological effects. Both individual gene expression changes and their collective impact on biological pathways contribute to a comprehensive understanding of rosehip's mechanism of action on skin, focusing on aspects of aging, hydration, and barrier function. To assess the overall similarity and clustering of our samples, a heatmap of Euclidean distances based on variance stabilized transformed (VST) counts was generated (Figure 1), demonstrating distinct clustering of the rosehip-treated samples and confirming the substantial transcriptomic impact of the rosehip extract

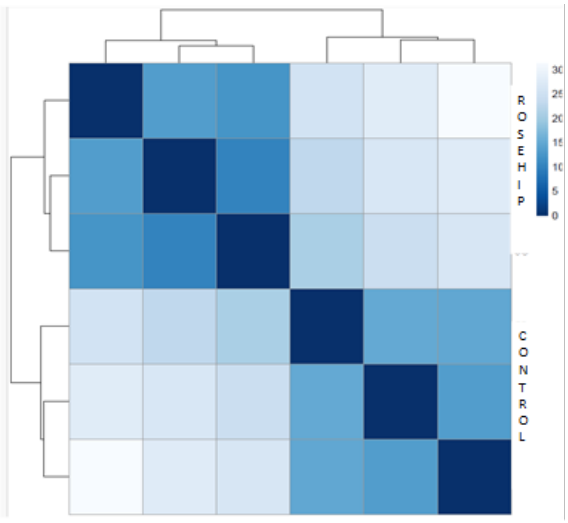


Figure 1. VST Sample Distance Heatmap representing the Euclidean distances between samples based on variance stabilized transformed (VST) RNA-seq counts. The darker blue colors indicate higher similarity (shorter distance), while lighter colors indicate greater dissimilarity. The clear clustering of rosehip-treated samples (ROSEHIP) away from control samples (CONTROL) demonstrates a significant and consistent transcriptional response to the treatment.

3.3 Differential Gene Expression Analysis

Differential expression analysis, employing DESeq2, identified 5305 genes with significant regulation ($p<0.05$). The overall landscape of gene expression changes is summarized in a volcano plot (Figure 2), which visually represents the log2FC against the negative log10 of the p-value for all genes. This plot highlights genes that are both statistically significant and have a substantial fold change.

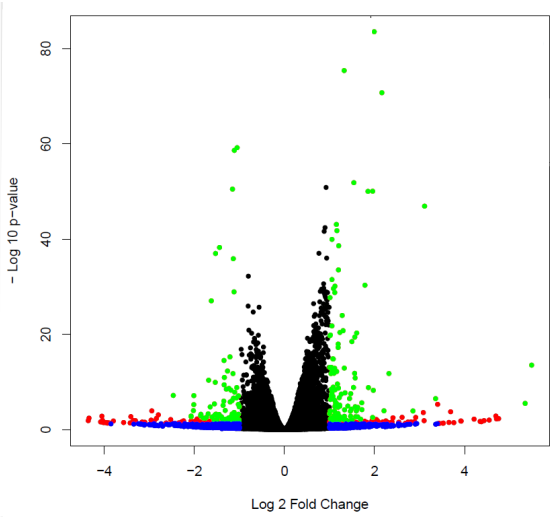
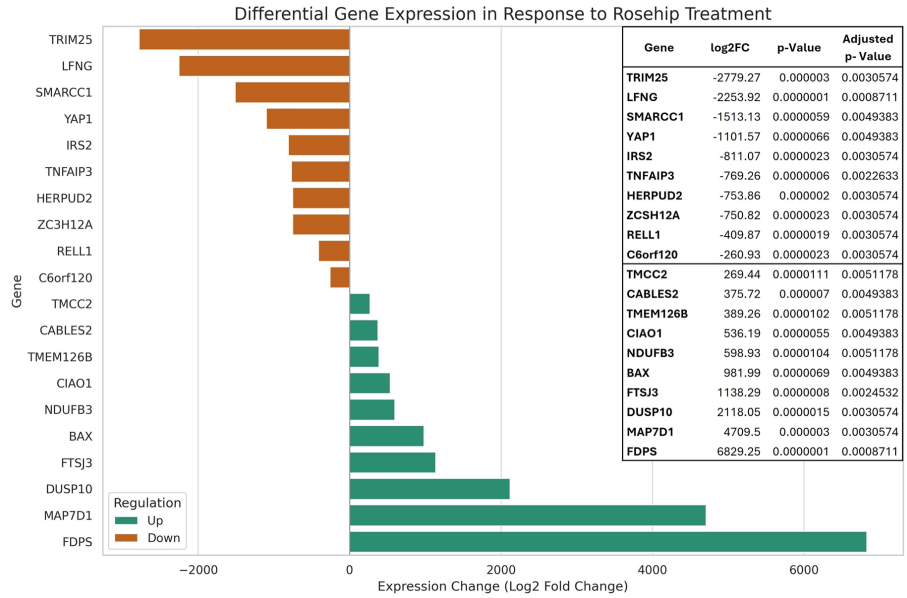


Figure 2. Volcano Plot of Differentially Expressed Genes. A volcano plot illustrating the magnitude and statistical significance of gene expression changes between rosehip-treated and control HaCaT cells. The x-axis represents the log2FC, and the y-axis represents the –log10(p-value). Green dots indicate genes that are significantly differentially expressed, meeting the criteria of abs|log2FC| > 1 and an adjusted p-value < 0.05. Red dots represent genes with abs|log2FC| > 1 and a p-value < 0.05. Blue dots represent genes with abs|log2FC| > 1 but are not statistically significant (a p-value ≥ 0.05). Black dots represent genes with |log2FC|≤ 1, indicating no substantial change in expression.

Among these, a robust set of genes showed a marked up- and down-regulation in response to rosehip treatment. The top 10 most significantly up-regulated and down-regulated genes, along with their log2FC, P-values, and adjusted P-values (eg. Values are presented as: log2FC), are represented as Figure 3.



Gene	log2FC	p-Value	Adjusted p- Value
TRIM25	-2779.27	0.000003	0.0030574
LFNG	-2253.92	0.0000001	0.0008711
SMARCC1	-1513.13	0.0000059	0.0049383
YAP1	-1101.57	0.0000066	0.0049383
IRS2	-811.07	0.0000023	0.0030574
TNFAIP3	-769.26	0.0000006	0.0022633
HERPUD2	-753.86	0.000002	0.0030574
ZCSH12A	-750.82	0.0000023	0.0030574
RELL1	-409.87	0.0000019	0.0030574
C6orf120	-260.93	0.0000023	0.0030574
TMCC2	269.44	0.0000111	0.0051178
CABLES2	375.72	0.000007	0.0049383
TMEM126B	389.26	0.0000102	0.0051178
CIAO1	536.19	0.0000055	0.0049383
NDUFB3	598.93	0.0000104	0.0051178
BAX	981.99	0.0000069	0.0049383
FTSJ3	1138.29	0.0000008	0.0024532
DUSP10	2118.05	0.0000015	0.0030574
MAP7D1	4709.5	0.000003	0.0030574
FDPS	6829.25	0.0000001	0.0008711

Figure 3. Diagram representing the 10 most regulated genes in response to the treatment with rosehip extract. In orange colours bars are the 10 most down reglated genes while in green the top 10 most up regulated.

A heatmap illustrating the expression patterns of the top 60 differentially expressed genes further confirms the distinct transcriptional responses between rosehip-treated and control cells (Figure 4). This visualization clearly shows clusters of genes that are consistently up-regulated (red) or down-regulated (blue) in the rosehip group.

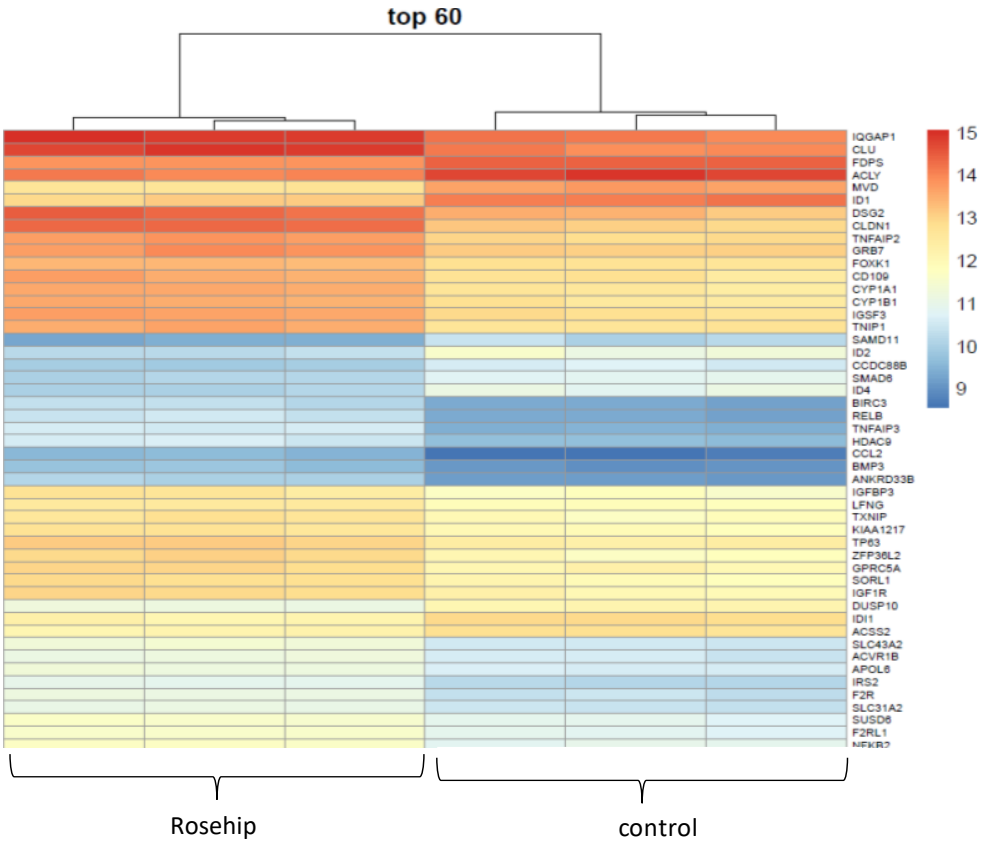


Figure 4. Heatmap of Top 60 Differentially Expressed Genes. A hierarchical clustering heatmap showing the expression levels of the top 60 most differentially expressed genes between rosehip-treated and control HaCaT cells. Rows represent individual genes, and columns represent samples (rosehip-treated on the left (n=3), control on the right(n=3)). The colour intensity reflects gene expression levels (red = high expression, blue = low expression).

To provide a high-level, hierarchical view of the biological pathways or functional categories that are significantly enriched among the differentially expressed genes, a Reactome Pathway Enrichment Analysis was performed (Figure 5). The analysis identified 63 significantly regulated pathways ($p<0.001$, FDR 0.001), with 30 pathways demonstrating increased activity, indicating a profound impact on essential cellular processes. Key affected areas were identified. Widespread upregulation was observed in broad categories such as "Signal Transduction", "Cell Cycle", and "Post-translational protein modifications". This suggests that Rosehip extract broadly influences cellular communication, cellular proliferation, and protein synthesis/modification processes within keratinocytes. Significant downregulation was notably concentrated in sub-pathways related to "Transcription" and "Reproduction"

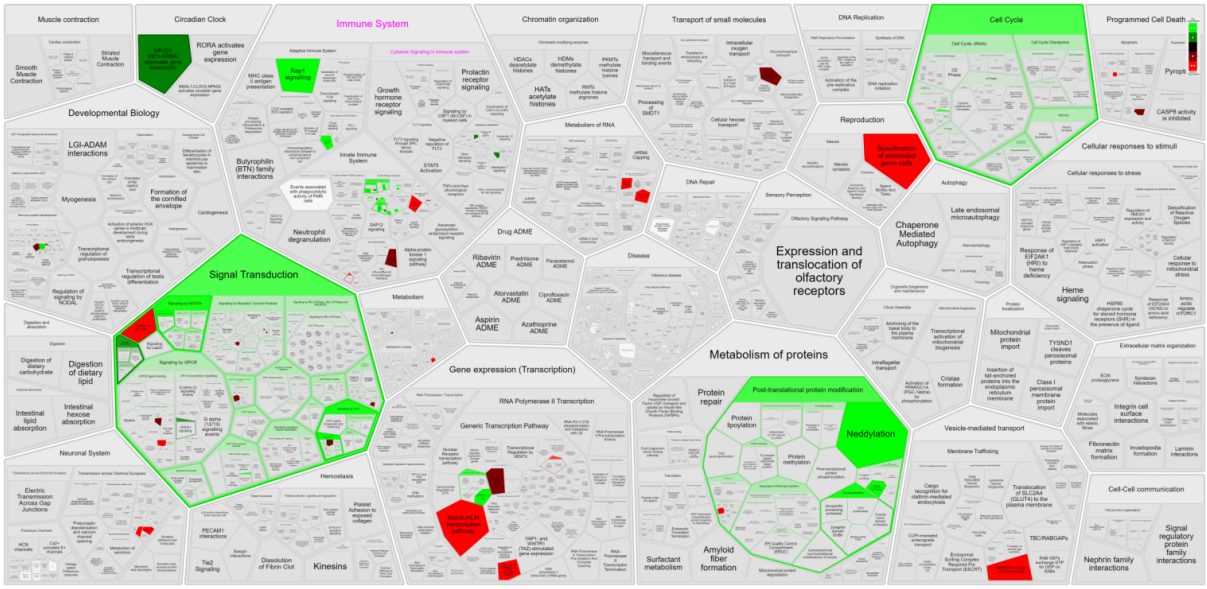


Figure 5: Enriched Biological Pathways in Response to Rosehip Treatment showing the hierarchical organization of significantly enriched pathways**.** Pathways were identified using Reactome-GSA PADOG analysis on genes with a p-value < 0.01 from DESeq2 differential expression results. Individual pathways are colored red if their constituent genes are predominantly down-regulated, green if predominantly up-regulated, and grey/white if not significantly altered

The observed differential gene expression patterns together with the pathway enrichment analysis, paint a comprehensive picture of how rosehip treatment impacts skin at a molecular level, supporting its purported beneficial dermatological effects on aging, hydration, and barrier function.

- Upregulated pathways: The pathway analysis revealed a significant activation of processes particularly relevant to cell signaling, cell cycle, and protein modifications, all critical for maintaining healthy and resilient skin.

Rosehip treatment led to strong up-regulation of Notch signaling (Av. FC ~36), essential for epidermal differentiation, repair, and barrier integrity, suggesting enhanced skin regeneration. Broad activation of Signal Transduction (Av. FC ~23) reflects increased keratinocyte responsiveness to environmental cues, improving cellular communication.

Notably, WNT signaling (Av. FC ~65) and TCF-dependent WNT signaling (Av. FC ~53), both central to stem cell maintenance and wound healing, were highly activated—supporting epidermal renewal. The PI3K/Akt pathway (Av. FC ~453), vital for cell survival and proliferation, also showed substantial upregulation, promoting keratinocyte viability.

Rap1 signaling (Av. FC ~53), which governs cell adhesion and barrier strength, suggests improved skin cohesion and defense. Interestingly, increased expression of negative regulators of MAPK signaling (Av. FC ~8.3), including DUSP10, points to a balanced anti-inflammatory response, preventing overactivation of stress pathways.

An extensive up-regulation was observed in protein modification pathways, including Deubiquitination (Av. FC: 127.921), and Post-translational protein modification (Av. FC: 42.222). These processes are crucial for maintaining cellular homeostasis, regulating protein

function and stability, and facilitating robust cellular responses to stress. Such widespread activation in protein quality control mechanisms directly impacts skin cell resilience, adaptability, and the proper functioning of structural proteins like collagen and elastin, contributing to overall skin texture and preventing age-related damage. The top up-regulated gene FDPS, involved in lipid biosynthesis, requires robust protein modification systems to ensure efficient enzyme function, supporting enhanced cellular metabolism and repair.

The elevated activity in Toll Like Receptor cascades (TLR5, TLR9, TLR10) (Av. FC: 111.7 - 117.974) and TICAM1-dependent activation of IRF3/IRF7 (Av. FC: 103.735) points towards an enhanced innate immune response. This strengthening of the skin's first line of defense is beneficial for protecting against pathogens and environmental stressors, bolstering overall skin health and resilience.

Cell Cycle & Protein Modification: The up-regulation of Cell Cycle (Av. FC: 60.879) and Regulation of APC/C activators between G1/S and early anaphase (Av. FC: 68.48) reflects a modulated, potentially optimized, proliferative state rather than outright suppression. This controlled proliferation is crucial for skin regeneration, ensuring the efficient replacement of old or damaged cells without leading to abnormal growth, which is critical for maintaining a youthful and healthy epidermis.

- Downregulated Pathways and their Role in Mitigating Inflammatory and Pathological Processes: The down-regulated pathways primarily signify the suppression of detrimental processes, further contributing to skin health by reducing inflammation, modulating immune responses, and regulating cellular growth dynamics.

Immune/Inflammatory Modulation: Significant down-regulation specific inflammatory and innate immune responses aligns with rosehip's traditional anti-inflammatory effects, suggesting a mechanism by which it could reduce skin damage associated with chronic or excessive inflammation, a common underlying factor in many skin conditions.

The combined analysis of differentially expressed genes and enriched pathways reveals a sophisticated and orchestrated molecular response to rosehip treatment in HaCaT cells. The simultaneous activation of pathways promoting regeneration, barrier function, and innate immunity, coupled with the fine-tuned suppression of specific inflammatory, senescent, and aberrant growth pathways, collectively underscores rosehip's multifaceted dermatological benefits. This comprehensive molecular fingerprint supports its efficacy in not only addressing existing skin concerns but also in fostering a healthier, more resilient skin microenvironment.

4. Discussion

This article presents the scientific rationale behind the development of a rosehip (Rosa canina L.) extract produced using a patented extraction process with a specific chemical profile, particularly its polyphenol content. Combined analysis of differentially expressed genes and enriched pathways reveals an intricate and coordinated molecular response to rosehip treatment in HaCaT cells. The simultaneous activation of pathways that promote regeneration, barrier function and innate immunity, coupled with the precise suppression of specific inflammatory, senescent and aberrant growth pathways, collectively highlights the

multifaceted dermatological benefits of rosehip. This comprehensive molecular profile not only supports the efficacy of addressing existing skin concerns, but also fosters a healthier, more resilient skin microenvironment. The findings clearly demonstrate the capacity of rosehip to enhance skin integrity, manage inflammatory conditions and support cellular vitality. This provides a robust functional framework for understanding its significant role in promoting skin health and beauty. These findings are in accordance with traditional uses of rosehip, as well as those founded in other in vitro or human studies. Further research should be focused in translate the in-vitro data to human studies.

5. Conclusion

The gene expression analysis following rosehip treatment on HaCat cells reveals a complex interplay of pathways relevant to skin health, regeneration, and protection.

The upregulation of several genes like FDPS, DUSP10 and FTSJ3 which are related to lipid metabolism, RNA processing and anti-inflammatory responses, suggest a positive effect of rosehip extract on skin barrier reinforcement.Additionally, an increased expression of mitochondrial-related genes like NDUFB3 indicates an improved cellular energy metabolism directly linked to skin cell vitality and resilience against oxidative stress.

On the other hand, genes related to inflammatory and stress such as TRIM 25 or TNFAIP3 were downregulated, correlating with a reduction of inflammatory signaling.

To summarize, we could show on a genetic level the anti-inflammatory, anti-aging and regenerative effects of rosehip extract as a powerful potential active ingredient for holistic cosmetics, maintaining skin integrity, elasticity, and youthfulness.

The success of this rose hip peels (*Rosa canina* L.) standard extract lies in its scientifically grounded approach to raw material selection and extraction. By focusing on the polyphenol-rich shells of Rosa canina and employing a gentle, solvent-free extraction process, a highly bioactive and stable product has been developed. This extract stands out in the nutricosmetics market for its efficacy, purity, and sustainable production. This study validates the traditional uses of rosehip in personal care and beauty from within and also paves the way for its targeted application in advanced cosmetic and innovative formulations aimed at maintaining and restoring optimal skin health.

References

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