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Novel melanogenesis-modulating peptides for dermocosmetic applications

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Background

Melanogenesis is the process by which melanin is synthesized in melanocytes and transferred to keratinocytes, contributing to skin color and UV protection. Altered melanogenesis can lead to **hyper-** or **hypopigmentation disorders**, often associated with psychological distress. Current pigmentation-modulating agents frequently show poor bioavailability or cytotoxicity, highlighting the need for safer alternatives. **Peptides** represent **promising dermocosmetic ingredients** due to their tunable stability, specificity, and safety. **AIMP1** (Aminoacyl-tRNA synthetase complex-interacting multifunctional protein 1) is a multifunctional protein with distinct biological domains.[1] A peptide corresponding to residues **6–46** of AIMP1 (AdP) was reported to **reduce melanin content and tyrosinase activity in melanocytes**.[2] However, AdP may also promote fibroblast proliferation, an undesirable effect in cosmetic applications.

Aim of the project

This PhD project aims to **identify minimal AIMP1-derived peptide sequences that modulate melanogenesis while avoiding fibroblast-proliferative activity,** enabling the development of safe and effective dermocosmetic peptides.

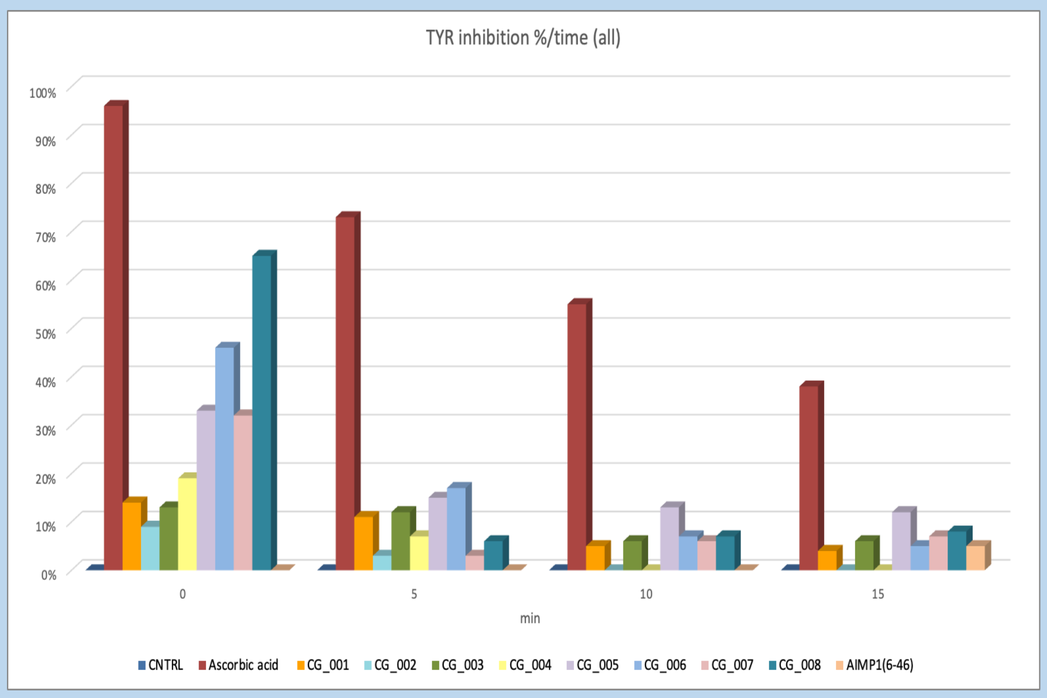
Peptides Design and Synthesis

Eight overlapping peptides spanning the AIMP1(6–46) region were designed to map melanogenesis-regulating domains. Peptides were synthesized by **solid-phase peptide synthesis** (SPPS), purified by RP-HPLC or flash chromatography, and characterized by RP-HPLC and mass spectrometry, achieving purities >95%.

Tyrosinase Inhibition Assay

Peptides were initially screened using a mushroom tyrosinase assay with L-DOPA as substrate.[3] Enzyme activity was monitored spectrophotometrically at 475 nm. **Ascorbic acid** was used as a **positive control**.

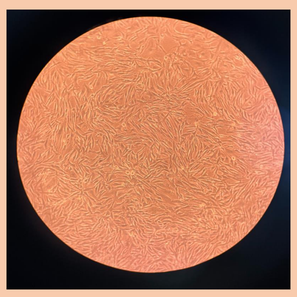
Key finding: **None of the peptides**, including AIMP1(6–46), **showed significant tyrosinase inhibition**, suggesting that melanogenesis modulation may occur through indirect or non-enzymatic mechanisms.



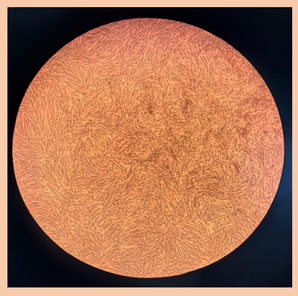
Melanin Content Assay

B16F10 mouse melanoma cells were used to evaluate melanogenesis-related effects. Cells were treated with peptides or **α-MSH** as a **positive control**. Melanin content was quantified spectrophotometrically at 405 nm.

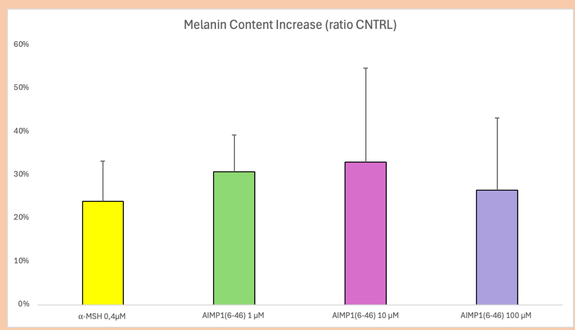
Key Findings: Parent **AIMP1(6–46)** peptide significantly **stimulated melanin content** at 10 μM. Interestingly, **screening of the eight overlapping peptides revealed divergent biological activities**. Certain fragments induced a strong, decrease in melanin production, whereas others stimulated synthesis.

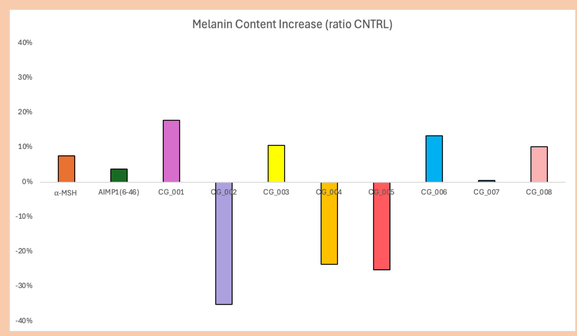


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Conclusions

Our results showed that **AIMP1-derived peptides do not directly inhibit mushroom tyrosinase**, suggesting that their effects on melanogenesis may involve **cell-mediated mechanisms** rather than direct enzyme inhibition. Interestingly, the screening of the **overlapping peptides revealed opposite effects on melanin production**, with different fragments showing either stimulatory or inhibitory activities. These findings highlight the potential of AIMP1-derived sequences as **melanogenesis modulators** and provide a basis for further investigation of the mechanisms underlying their distinct biological effects.

References

[1]J. M. Han et al., *Biochem. Biophys. Res. Commun.* **2006**, *342(1)*, 113–118.
[2] J. Kim et al., *J Cosmet Dermatol.* **2019**; *18(1)*, 251-257.
[3] Y.Y. Liu et al., *Fish Physiol Biochem.* **2017**; *43(2)*, 517-525.

Acknowledgements

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