A Molecular Investigation of the Anti-Aging Effects of Cosmeceutical Peptides

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Abstract

A trend in modern skin care industry is the wide adoption of cosmeceutical peptides to interfere or reverse the aging process of the skin. Specifically, the following peptides are in question, trifluoroacetyl tripeptide-2, palmitoyl pentapeptide-4 and palmitoyl tripeptide-38. These peptides signal the TGF-B pathway which is a critical pathway in extracellular matrix maintenance. Another pathway that palmitoyl tripeptide-38 signals is the wnt pathway which is responsible for wound healing (Shagen 2017) (Shi 2015). To potentially track this visible antiaging process, the scientific image processing software ImageJ (developed by NIH) was used; specifically, a plugin called SurfCharJ, which was used to evaluate skin textural details such as roughness and wrinkles (Chinga 2007). Benchmark photos were obtained and processed though the program which resulted in increasing roughness values as the represented age in the benchmark photos increased. Having successfully analyzed the benchmark photos, we are confident that our method can be readily applied to studies concerning topical anti-aging agents such as the peptides listed above.

Introduction - Skin

The skin consists of the epidermis (superficial) and the dermis (deep). The dermis plays vital roles in maintaining skin texture. The fibroblasts in this layer produce a large amount of collagen and elastin fibers in the extracellular matrix (ECM). The collagen provides the framework and slight pressure on the skin that gives it a smoother texture, while the elastin holds the epidermis to the collagen-rich dermis and supports its flexibility and shape retention (Baumann 2021). The dermis is vascular and provides nutrients to the epidermal keratinocytes osmotically through the dermal-epidermal junction ("Anatomy" 2022).

Signaling

Peptides travel deep into the skin by traveling down the sweat glands, hair follicles, or direct penetration (Aguirre-Cruz 2020). Palmitoyl pentapeptide-4 and palmitoyl tripeptide-38, are highly polar which causes them to travel down the hair follicles or sweat glands contrary to trifluoroacetyl tripeptide-3 which penetrates directly (Yotsumoto 2018).

TGF-β – All the three aforementioned peptides activate this pathway through the TGF-β receptor complex. The activation of its target genes helps to increase the structural integrity of the skin and provides a younger appearance (Shi 2015).

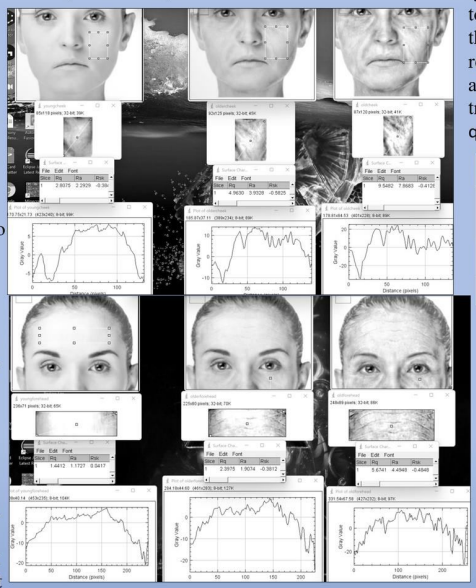
WNT - This pathway activates wound healing processes through the c-MYC gene by inducing a faster healing rate and thus reducing scar tissue appearances (Varga 2012). The palmitoyl pentapeptide-4 triggers this pathway (Shagen 2017).

Methodology – Automated Skin-Texture Evaluation

Photo documentation and automated image processing have been commonly accepted as a noninvasive approach to monitor changes in skin texture (Logger 2020). Here, we present a unique workflow to evaluate facial wrinkles using the scientific image processing software ImageJ (developed by NIH). Specifically, we used a plugin called SurfCharJ, which specializes in evaluating image details such as surface roughness and gradient analysis (Chinga 2007). To demonstrate the methodology of this program in evaluating the results of an anti-aging peptide application experiment where visual data would be collected from participants' skin, three sample photographs were obtained that depicted various degrees of aging. The surface chart below serves as a visual representation of the change in depth of the skin where each peak or valley represented a wrinkle or change in texture. Afterward, a roughness value was calculated as the arithmetic mean deviation (Ra value) with the SurfCharJ plugin. The Ra value numerically measures skin roughness and is impacted by changes in skin texture, including the length and depth of wrinkles (GSCA 2011).

Results

With our benchmark photographs of the cheek, the young, older, and oldest photos had Ra values of 2.29, 3.93, and 7.87 respectively. The increase in Ra values is expected due to the increased variation in skin texture as the individual's skin ages. With the forehead, the young, older, and oldest photos had Ra values of 1.17, 1.91, and 4.49 respectively. Again, the older an individual's skin, the higher the Ra value, and the greater variation in skin texture. Having successfully analyzed the benchmark photos, we are confident that our method can be readily applied to studies concerning topical anti-aging agents, including the peptides we investigated, and the Ra value is a reliable, sensitive, and an objective parameter to evaluating skin texture.

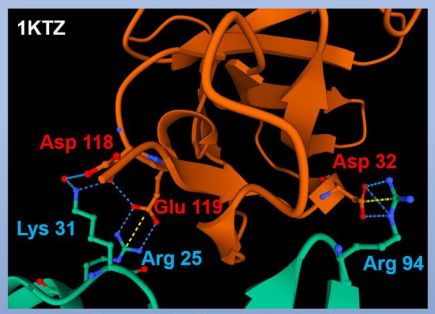


Discussion and Conclusion

To assess the potential of these peptides to activate the TGF-β receptors, we identified a structure consisting of a TGF-β type I receptor in complex with a transforming growth factor (PDB id 1KTZ). We used the iCn3D molecular viewer (from MMDB) and Mol* to analyze the ligand-receptor interactions and discovered a striking bidentate ionic hydrogen bonding pattern, involving two positive residues (Lys 31 and Arg 25) from the hormone, that mediates the highly specific interaction between the hormone and the receptor. The counterparts on the receptors for these cationic residues are two adjacent anionic residues: Asp118 and Glu119. These two residues serve as a targeting site for bioactive peptides (Hart 2002) (David 2021).

Palmitoyl Pentapeptide-4 and Palmitoyl Tripeptide-38 both contain adjacent lysine residues separated by one or two amino acids, reminiscent of the TGF arginine and lysine residues. Since the lysine side chains are close together, it is very likely that these lysine residues anchor the peptide to Asp118 and Glu119, the binding site, of the receptor and produce a signal. The positively charged amino acids mimic the regular interaction between the transforming growth factor and the receptor. The question remains whether such binding is agonistic.

Peptide	Sequence
Trifluoroacetyl Tripeptide-2	TFA-Val-Try-Val-OH
Palmitoyl Pentapeptide-4	Pal-Lys-Thr-Thr-Lys-Ser
Palmitoyl Tripeptide-38	Pal-Lys-Met(O2)-Lys



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