The Investigation of a Novel Peptide Hormone Responsible for Modulating Skin Tone

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Objective: To determine whether antagonists for the MC1 receptor can reduce areas of hyper-pigmentation and even skin tone.

Introduction: Traditional skin lighteners have not focused on reducing hyper-pigmentation at the initial stage of melanogenesis, the binding of hormones to the Melanocortin 1 Receptor (MC1R) on the melanocyte. The Agouti Signal Protein (ASP) has been recognized as a regulatory protein capable of reducing the expression of the MC1R involved in melanin production. In this study, small pentapeptide and hexapeptide fractions of ASP, antagonists for the MC1 receptor, were added to a generic emulsion to determine whether they reduce hyper-pigmentation and even skin tone on human volunteers. Color measurements taken over the course of several weeks confirm a visible reduction in skin pigmentation by an average ΔE of 9.01 and average change in L values of 16.58%. The results indicate that areas of hyper-pigmentation, particularly solar lentigines, are especially sensitive to manipulation by MCIR antagonists.

Experimental: 2% of an ASP analog solution was added to a generic, oil-in-water emulsion. Fifteen volunteers applied the cream twice daily for twenty-eight days to areas of their arms marked by hyper-pigmentation. Three color measurements of the brown maculas were taken weekly for the duration of the experiment. The results generated are the differences of the averaged L and delta E values for each person.

Results: Abbreviated data from the first five volunteers is shown in Table 1. Three measurements from each location were recorded. The delta E values are calculated from the first, second and third set of colorimetry readings taken initially and the first, second and third set taken on final day[1]. These results confirm a visible reduction is skin pigmentation by an average delta-E of 9.0 and an average change in L values of 16.6%.

Table 1: Color measurements taken initially and on Day 28.

Subject 1	Day 0	Average	Day 28	Average	% Change	delta-E
L	33 37 34	34.7	43 42 43	42.7	23.1%	11.6
a	23 22 23	22.7	20 18 19	19	16.2%	6.5
b	28 29 27	28	23 28 25	25.3	-16.2%	10.1
					Average delta-E	9.4
Subject 2	Day 0	Average	Day 28	Average	% Change	delta-E
L	50 52 51	51	49 49 51	49.7	-2.6%	8.3
a	16 15 15	15.3	14 17 15	15.3	00%	7.0
b	25 26 25	25.3	33 32 28	31	22.4%	3.0
					Average delta-E	6.1
Subject 3	Day 0	Average	Day 28	Average	% Change	delta-E
L	42 44 40	42	52 55 55	54	28.6%	11.8
a	21 21 22	21.3	19 17 17	17.7	-17.2%	13.6
b	34 34 35	34.3	28 28 28	28	-18.4	17.3
					Average delta-E	14.3

Subject 4	Day 0	Average	Day 28	Average	% Change	delta-E
L	25 31 28	28	34 30 32	32	14.3%	11.2
a	23 21 21	21.7	17 23 21	20.3	-6.2%	3.7
b	26 24 25	25	29 27 28	28	12.0%	5.0
					Average delta-E	6.7

Subject 5	Day 0	Average	Day 28	Average	% Change	delta-E
L	42 44 42	42.7	51 50 52	51	19.5%	9.5
A	13 13 13	13	16 14 16	15.3	17.9%	6.1
b	37 35 35	35.7	37 35 36	36	0.9%	10.5
					Average delta-E	8.7

Discussion and Conclusion: The purpose of this study is to investigate an ASP analog's ability to even skin tone. This data shows that areas of hyper-pigmentation are sensitive to manipulation via the MC1R. Antagonists for the MC1R reduce the amount of melanin produced by the hyperactive melanocytes. Moreover, age spots, represented by the data from Subject 3, appear to be particularly affected. Such age spots, or solar lentigines, are known for elevated levels of endothelin (ET-1) and related receptors on associated melanocytes[2]. ET-1 up-regulates both MC1 receptors and their ability to bind the agonist alpha Melanocyte Stimulating Hormone (alpha-MSH)[3]. Despite ET-1's central role, these disorders are especially susceptible to MC1R antagonists.

As outlined above, there are a variety of mechanisms involved in hyper pigmentary disorders. Regardless of the mechanism, it has been shown that ASP analogs are useful tools for modulating skin tone.

References:

[1] Noboru Ohta and Alan Robertson, Colorimetry: Fundamentals and Applications, 25-98, 2006
[2] M. Yaar and B.A. Gilchrest, Clinical and Experimental Dermatology **26**, 583-591, 2001
[3] Andrzej Slominski, Desmond J. Tobin, Shigeki Shibahara and Jacobo Wortsman, Physiological Reviews, **84**, 1155-1228, 2004