

PEP UP™ COLLAGEN RENEWAL FACE & NECK TREATMENT MULTICENTER STUDY

SUMMARY

An 8-week, multicenter study involving 158 patients, assessed improvements in skin quality and patient satisfaction after using Colorescience Pep Up™ Collagen Renewal Face & Neck Treatment. This was the largest skincare study conducted by Colorescience® to date.

Key Findings

After 8 weeks of treatment:

- Significant improvement in overall skin health ($p < 0.001$) and skin hydration ($p < 0.001$) was reported by investigators, while 91% of patients saw an improvement in their overall skin health after using Pep up™ and 85% of patients saw an improvement in skin hydration.
- 84-94% of patients demonstrated improvements in each area of concern associated with visible skin aging based on investigator scoring.
- 94% of patients reported that their skin felt more rejuvenated as early as week 4 and at week 8.

BACKGROUND

Proteins are the structural building blocks for bone, muscle, cartilage and skin. Proteins differ from one another by their length and the sequence of their constituent amino acids. The most abundant protein in the body is collagen, a major component of connective tissues and skin. In fact, collagen comprises 80% of our dermis.¹ Another important protein is elastin, a highly elastic protein in the dermis which enables it to resume its shape after stretching or contracting.² Together, collagen and elastin are largely responsible for maintaining the healthy, youthful appearance of skin.

Unfortunately, we are continually exposed to environmental aggressors that contribute to skin damage throughout our lifetimes, such as ultraviolet radiation, pollution, high energy visible and blue light. This damage includes the loss of collagen and elastin, resulting in wrinkles and skin laxity. Additionally, the body produces about 1% less skin collagen each year beginning at age 20.³ In contrast with proteins, peptides are short chains of amino acids. Peptides are integral in the process of making new collagen and elastin. Topical peptides, which may be more easily absorbed than longer-chain proteins, can be categorized into two general groups as up- and down-regulating peptides.⁴

An effective strategy to improve the appearance of wrinkles and other signs of aging is to help the body replace lost collagen and elastin by applying peptides as a topical product directly on the skin.⁵ When applied in this way, they signal the skin to repair itself. Their small size enables peptides to penetrate the skin more effectively than larger proteins. While it is useful to help stimulate the production of new collagen and elastin, it is also essential to halt ongoing loss due to environmental factors by using products that contain antioxidants and provide broad-spectrum mineral sun protection benefits. Equally important is deep hydration for maintaining healthy, youthful skin.

Pep Up™ Collagen Renewal Face & Neck Treatment is a topical product developed by Colorescience®. It is designed to promote collagen and elastin synthesis and improve skin hydration while providing protection against damaging environmental factors. Pep Up™ Collagen Renewal Face & Neck Treatment has been formulated to include a blend of 10 up- and down-regulating peptides, which make up 22% of the total formulation, antioxidants and deep hydration ingredients (see **Table 1** for a detailed description):

- Decaplex-10™, a proprietary blend of 10 different peptides, provides a comprehensive approach to rebuilding collagen and elastin in the skin.
- Lipochroman® is a powerful antioxidant that prevents skin aging due exposure to pollution, UV light and other environmental aggressors.
- Physavie® is an antioxidant which soothes and calms the skin while helping to protect against the effects of infrared radiation.
- Hyaluronic acid is a naturally occurring plant humectant.
- Phytomoist® is a combination of plant-based hyaluronic acid and betaine, derived from beets, which helps restore moisture in the skin and defend against the signs of aging.

Additional specialty ingredients and their functions are described in **Table 2**.

The objective of this 8-week, multicenter study was to assess improvements in skin quality and patient satisfaction after using Pep Up™ Collagen Renewal Face & Neck Treatment.

TABLE 1. DECAPLEX-10™ PEPTIDE INGREDIENTS AND FUNCTIONS

Down-Regulating Peptides	Peptide Type	Function
Dipeptide diaminobutyroyl benzylamide diacetate	Neurotransmitter-inhibitor	Reduces the appearance of dynamic wrinkles of expression. ¹¹
Hexapeptide 2	Enzyme-inhibitor	Visibly brighten skin by decreasing the appearance of dark spots on the skin. ⁸
Up-Regulating Peptides	Peptide Type	Function
Copper Tripeptide 1	Signaling and Carrier	Makes the skin feel more supple and look visibly smoother by stimulating collagen and elastin production. ⁴
Palmitoyl Tripeptide 1 Palmitoyl Tetrapeptide 7	Signaling	Provides synergy of two matrikines, ^a Pal-GHK and Pal-GQPR, that support production of collagen and hyaluronic acid to reduce fine lines and wrinkles.
Acetyl Tetrapeptide 9	Signaling	Visibly improves skin thickness and firmness for an overall firming effect. ^{12,13}
Sh-Oligopeptide	Mimicking	A 53 amino acid peptide with a chemical structure similar to epidermal growth factor which visibly renews the skin and increases skin firmness and tone. ¹⁴
Simultaneous Up- and Down-Regulating	Peptide Type	Function
Palmitoyl Tripeptide 5	Mimicking	Unique peptide offering a synergistic benefit to assist the body in its production of collagen. ¹⁵
Tripeptide-10 Citrulline	Signaling and Carrier	Combination of peptides and proteins that helps support the production of collagen. ^{13,16}
Tripeptide-1 (also contains <i>Pseudoalteromonas</i> ferment extract and hydrolyzed wheat and soy protein)	Expression and Glycation	

^aMatrikines are bioactive fragments released from extracellular matrix proteins which regulate several physiological processes.¹⁷

TABLE 2. SPECIALTY INGREDIENTS AND FUNCTIONS

Ingredient	Type	Function
Lipochroman® (dimethylmethoxy chromanol)	Antioxidant	Prevents skin aging due to pollution and other environmental aggressors such as sunlight. ¹⁸
Physavie® (<i>Physalis angulata</i> extract)	Antioxidant	A plant extract that soothes skin while helping to protect against the effects of infrared radiation. ¹⁹
Hyaluronic acid (sodium hyaluronate)	Moisturizer	A plant-based humectant that restores moisture in the skin and defends against the signs of aging. ²⁰
Phytomoist (<i>Tremella fuciformis</i> sporocarp extract) and Betaine (trimethylglycine)	Moisturizer	Botanicals that address hydration and overall skin suppleness and maintains water balance with 4-fold greater hydrating ability than hyaluronic acid. ²¹

METHODS

Healthy adult patients seeking facial skin rejuvenation were enrolled. Patients were instructed to apply Colorescience Pep Up™ Collagen Renewal Face & Neck Treatment as part of their daily skincare routine. Study participants were assigned to Group A if they were currently using an over-the-counter daily skincare treatment regimen or Group B if they were currently using an advanced skincare regimen. Patients were evaluated at baseline and after 4 and 8 weeks of twice-daily treatment use. Changes in skin quality and overall patient satisfaction were assessed using 5-point scales.

Change in Skin Quality	Patient Satisfaction
1. Worsened	1. Strongly Disagree
2. Not Improved	2. Disagree
3. Minimal Improvement	3. Neither Disagree nor Agree
4. Meaningful Improvement	4. Agree
5. Significant Improvement	5. Strongly Agree

Investigators were provided with Adverse Event Report Forms and instructed to use them to report any treatment-related adverse events. Statistical comparisons were pairwise mean comparisons using student’s t-test.

RESULTS

There were 158 patients enrolled at 29 centers with a mean age of 45.7 years (range, 22-73 years) who were assigned to Group A (n=81) or Group B (n=77). Nearly all patients were female (n=157). The 4- and 8-week evaluations were completed by 152 and 147 patients, respectively.

Efficacy

Investigators reported significant improvements in skin hydration at 4 weeks (23%) and 8 weeks (32%) and overall skin health at 4 weeks (16%) and 8 weeks (22%) (for each, $p < 0.001$), as summarized in **Table 3**.

TABLE 3. KEY FINDINGS

Global Improvements*	Baseline	Week 4	Week 8
Overall Skin Health	3.2	3.7 ($p < 0.001$)	3.9 ($p < 0.001$)
Hydration Level	3.1	3.8 ($p < 0.001$)	4.1 ($p < 0.001$)

* Based on a scale of 1 to 5.

Specific skin improvements reported by patients and investigators at weeks 4 and 8 are summarized in **Table 4**. Based on investigator scoring, at 8 weeks, at least 84% of patients demonstrated an improvement in each of the primary skin concerns associated with visible aging as represented in **Table 4** and **Figure 1**. Similar improvement in skin concerns was also noted by patient assessment (**Table 4**).

Skin improvements by patients and investigators reported by age are shown in **Table 5**. Substantial improvements in texture and overall skin health were noted by both patients and investigators across all age groups. Overall skin health by age group based on patient assessment is shown in **Figure 2**. Unretouched images are shown of patients in Group A (**Figure 3**) and Group B (**Figure 4**).

Overall, subjects were satisfied with product attributes including ease of application (99%), scent (94%), moisturization (96%) and product texture (98%). The majority of patients reported improvements in skin hydration after 4 weeks (78%) and 8 weeks (85%) and an improvement in overall skin health after 4 weeks (84%) and after 8 weeks (91%).

Most Patients also reported an improvement in skin rejuvenation (94%) at both 4 weeks and 8 weeks. For patients on Protocol (A) 93% reported an improvement in overall skin health at 8 weeks. Whereas, for patients on Protocol (B) 88% reported an improvement in overall skin health at 8 weeks.

After using Pep up™ most patients (78%) would recommend using the product to their friends. These results are summarized in **Table 6**.

Safety

Two treatment-related adverse events were reported in Group B patients consisting of redness, burning and itching. One event led to study discontinuation; however, both resolved spontaneously after discontinuing the use of Pep Up™. A few patients developed acne-like breakouts, consistent with the introduction of a new skincare regimen, but which were not reported as treatment-related adverse events and did not lead to study withdrawal.

DISCUSSION

The results presented here are in agreement with the results of other clinical studies that demonstrated application of peptide-containing topical products increases skin quality including skin brightness, hydration, and decreases wrinkles.⁶⁻⁹ The beneficial effects on skin laxity are believed to be due to neocollagenesis and also protection against collagen degradation.¹⁰

FIGURE 1. INVESTIGATOR ASSESSMENTS. PATIENTS WITH VISIBLE IMPROVEMENTS AT WEEK 4 AND 8

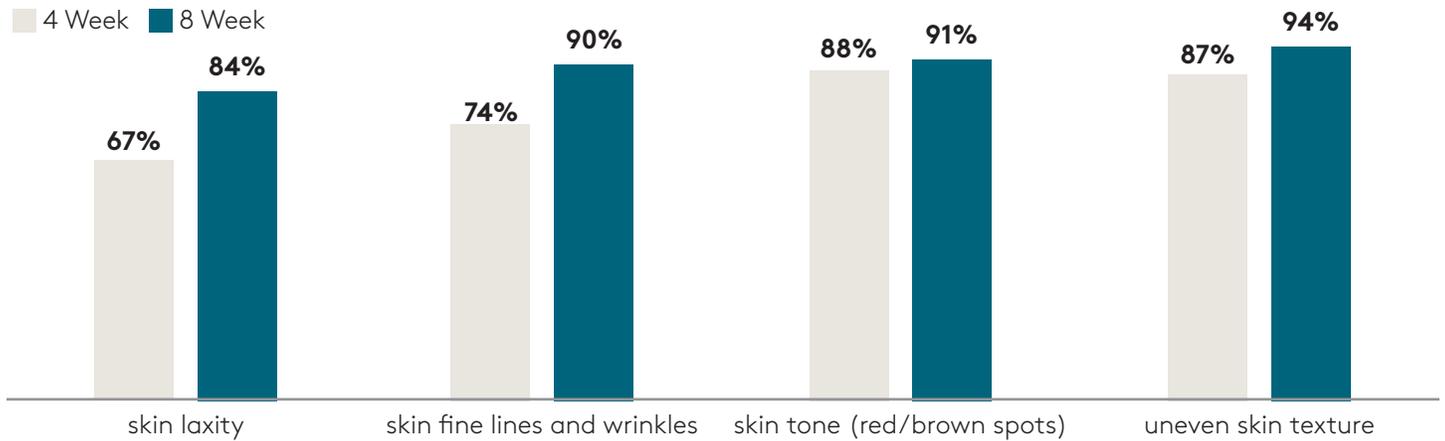
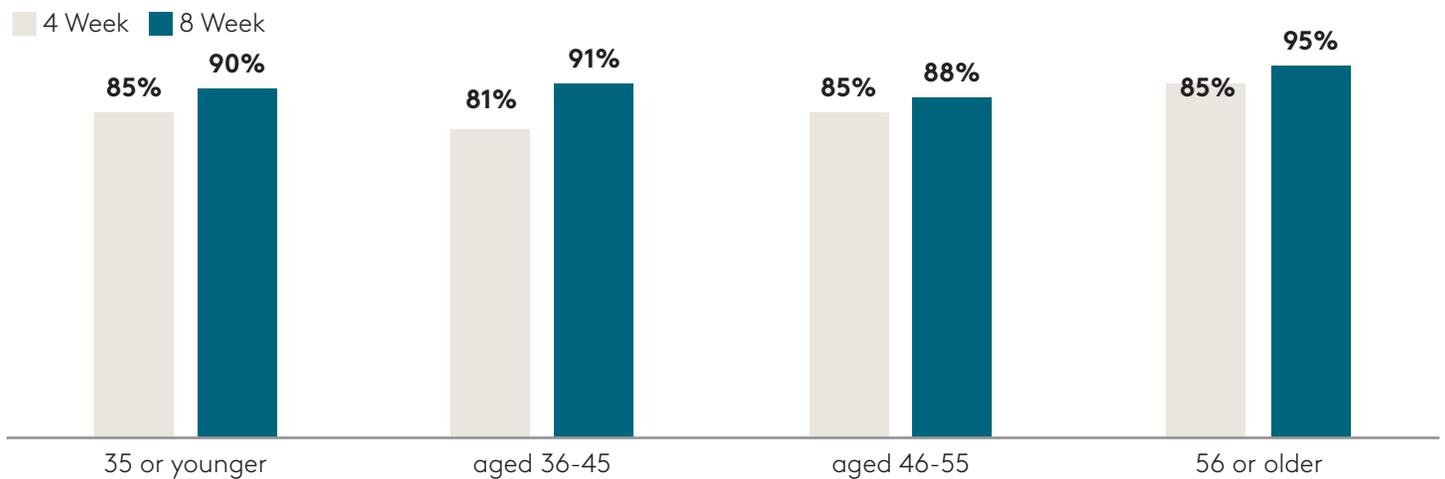


FIGURE 2. OVERALL SKIN HEALTH BY AGE GROUP BASED ON PATIENT ASSESSMENT



Overall, how would you rate the health of your skin compared to 4 weeks ago before the use of Pep Up Concentrate?

Overall, how would you rate the improvement in the health of your skin from 8 weeks ago before the use of Pep Up™ Concentrate?

Five point scale: 1-Worsened 2-Same or No change 3-Minimal Improvement 4-Meaningful Improvement 5-Significant Improvement

TABLE 4. SKIN IMPROVEMENTS

	Week 4		Week 8	
	Patient	Investigator	Patient	Investigator
Laxity	76%	67%	--	84%
Fine Lines & Wrinkles	72%	74%	84%	90%
Uneven skin tones (red or brown spots)	82%	88%	86%	91%
Uneven Texture	72%	87%	88%	94%
Loss of Volume			74%	*
Sun Damage			84%	*

*Not assessed by Investigators at Week 8

FIGURE 3: GROUP A



FIGURE 4: GROUP B



TABLE 5. SKIN IMPROVEMENTS BY AGE

Week 4	Patient*	Investigator*
Texture		
≤35 years	73%	80%
36-45 years	78%	90%
46-55 years	68%	83%
≥56 years	71%	95%
Overall Skin Health		
≤35 years	85%	--
36-45 years	81%	--
46-55 years	85%	--
≥56 years	85%	--

Week 8	Patient*	Investigator*
Texture		
≤35 years	90%	90%
36-45 years	91%	100%
46-55 years	79%	88%
≥56 years	92%	100%
Overall Skin Health		
≤35 years	90%	--
36-45 years	91%	--
46-55 years	88%	--
≥56 years	95%	--

*Each value based on 31 to 41 respondents.

Table 6. Other Patient Findings

	Week 4	Week 8
Patients reporting satisfaction with product attributes including ease of use, scent,	--	94-99%
Patients that would recommend Pep Up™ to their friends	--	78%
Patients reporting an increase in skin hydration	78%	85%
Patients reporting their skin felt more rejuvenated	94%	94%
Patients reporting improvement in overall skin health	84%	91%
Patients on Protocol (A) reporting improvement in overall skin health	87%	93%
Patients on Protocol (B) reporting improvement in overall skin health	81%	88%

CONCLUSION

Colorescience Pep Up™ Collagen Renewal Face & Neck Treatment may help promote collagen and elastin synthesis and improve hydration while providing protective support against damaging environmental factors.

After 8 weeks of treatment, 84% or more of patients demonstrated improvements in each sign of visible aging, 85% of patients reported improved hydration, and 94% of patients demonstrated improved skin rejuvenation regardless of prior skincare regimen.

REFERENCES

- Lodish H, Berk A, Zipursky SL, et al. *Molecular Cell Biology*. 4 ed. New York: WH Freeman; 2000
- Alberts B, Johnson A, Lewis J, et al. *Molecular Biology of the Cell*. 4 ed. New York: Garland Science; 2002
- Obagi S. Why does skin wrinkle with age? What is the best way to slow or prevent this process? *Scientific American* Sept. 26, 2005. Available: <<https://www.scientificamerican.com/article/why-does-skin-wrinkle-wit/>>. Accessed: Dec. 17, 2018
- Gorouhi F, Maibach HI. Role of topical peptides in preventing or treating aged skin. *Int J Cosmet Sci* 2009;31:327-345
- Benabio J. Do peptides in skin care products work? *The Derm Blog*; June, 2008. Available: <http://thedermblog.com/2008/06/23/do-peptides-in-skin-care-products-work/>. Accessed Dec. 18, 2018
- Garre A, Narda M, Valderas-Martinez P, Piquero J, Granger C, et al. Antiaging effects of a novel facial serum containing L-ascorbic acid, proteoglycans, and proteoglycan-stimulating tripeptide: ex vivo skin explant studies and in vivo clinical studies in women. *Clin Cosmet Investig Dermatol* 2018;11:253-263
- Reivitis A, Karimi K, Griffiths C, Banayan A. A single-center, pilot study evaluating a novel TriHex peptide- and botanical-containing eye treatment compared to baseline. *J Cosmet Dermatol* 2018;17:467-470
- Widgerow AD, Jiang LI, Calame A. A single-center clinical trial to evaluate the efficacy of a tripeptide/hexapeptide antiaging regimen. *J Cosmet Dermatol* 2018;Mar 4 [Epub ahead of print]
- Robinson LR, Fitzgerald NC, Doughty DG, et al. Topical palmitoyl pentapeptide provides improvement in photoaged human facial skin. *Int J Cosmet Sci* 2005;27:155-160
- Bae JS, Kim JM, Kim JY, et al. Topical application of palmitoyl-RGD reduces human facial wrinkle formation in Korean women. *Arch Dermatol Res* 2017;309:665
- McArdle JJ, Lentz TL, Witzemann V, et al. Waglerin-1 selectively blocks the epsilon form of the muscle nicotinic acetylcholine receptor. *J Pharmacol Exp Ther* 1999;289:543-550
- Hajem N, Chapelle A, Bignon J, et al. The regulatory role of the tetrapeptide AcSDKP in skin and hair physiology and the prevention of ageing effects in these tissues--a potential cosmetic role. *Int J Cosmet Sci* 2013;35:286-298
- Raikou V, Varvaressou A, Panderi I, Papageorgiou E. The efficacy study of the combination of tripeptide-10-citrulline and acetyl hexapeptide-3. A prospective, randomized controlled study. *J Cosmet Dermatol* 2017;16:271-278
- Kim J, S K, Kwon H, Moon H, Park MC. Dual functional bioactive-peptide, AIMP1-derived peptide (AdP), for anti-aging. *J Cosmet Dermatol* 2018;Jun 19:[Epub ahead of print]
- Trookman NS, Rizer RL, Ford R, Ho E, Gotz V, et al. Immediate and long-term clinical benefits of a topical treatment for facial lines and wrinkles. *J Clin Aesthet Dermatol* 2009;2:38-43
- Pitman S. Tripeptide features as key ingredient in anti-aging launches. *CosmeticsDesign.com* July, 2008 Available: <https://www.cosmeticsdesign.com/Article/2007/04/16/Tripeptide-features-as-key-ingredient-in-anti-aging-launches>
- Sivaraman K SC. Matrikines for therapeutic and biomedical applications. *Life Sci* 2018;214:22-33
- Souza C, Campos PMBGM. Development and photoprotective effect of a sunscreen containing the antioxidants Spirulina and dimethylmethoxy chromanol on sun-induced skin damage. *Eur J Pharm Sci* 2017;104:52-64
- Pinto NB, Morais TC, Carvalho KM, et al. Topical anti-inflammatory potential of physalin E from *Physalis angulata* on experimental dermatitis in mice. *Phytomedicine* 2010;17:740-743
- Sundaram H, Mackiewicz N, Burton E, et al. Pilot comparative study of the topical action of a novel, crosslinked resilient hyaluronic acid on skin hydration and barrier function in a dynamic, three-dimensional human explant model. *J Drugs Dermatol* 2016;15:434-441
- Wang X, Zhang Z, Zhao M. Carboxymethylation of polysaccharides from *Tremella fuciformis* for antioxidant and moisture-preserving activities. *Int J Biol Macromol* 2015;72:526-530