Wrinkle Relief GHK-Cu Proprietary Blend Roll-on

Background

Wrinkle Relief GHK-Cu proprietary blend is a convenient external use roll-on supplement formulary designed to be gently applied directly to facial folds to promote wrinkle relief and enhance youthful appearance. According to Veiga et al. (2023), the skin plays a significant role in overall personal aesthetics and image, serving as the frontline indicator of visible aging. [13] The skin serves as both a covering and protective organ and aging is observed by the breakdown of its structure and decreased ability to regenerate and in functionality. [13] External or extrinsic aging can be an outcome of outside environmental factors to the body, primarily alcohol consumption, diet, pollution, smoking, repetitive muscle movements, and sunlight exposure. [14] Although there are intrinsic aging influences present that promote natural cell aging which is an endogenous and physiological process marked by genetic factors and hormonal imbalances, this product is designed to target extrinsic or exogenous aging factors. [13] In other words, this product is designed to be a potent disruptor of the pathogenesis involved in premature or extrinsic skin aging at the molecular level, reversing skin imperfections and wrinkles caused by ultraviolet light and environmental toxins. [15, 16] Some of the mechanisms involved in exogenous aging, and, by extension, the appearance of wrinkles are presence of reactive oxygen species (ROS) caused by ultraviolet light and environmental toxins which lead to DNA, protein, and lipid oxidation, downregulation of collagen and elastin (proteins that provide skin elasticity, smoothness, and forms connective tissue), shortens telomeres, this complex process leading to wrinkling and sagging skin. [15]

The main wrinkle relief agent in this product is **GHK-Cu**. Copper peptide GHK-Cu is a naturally occurring copper compound of the tripeptide glycyl-L-histidyl-L-lysine. The peptide has shown strong affinity for copper and is naturally detected in saliva and urine. The tripeptide was initially isolated in human plasma, and it was noticed that it was naturally released from tissues following an injury. [1] The peptide's ability to bind copper ions and precise activation for targeted gene expression involved in natural healing and regenerative properties make it popular for multiple anti-aging therapies. GHK-Cu is associated with accelerated wound healing, through its mechanism of action to promote angiogenesis (e.g., the formation of new blood vessels), nerve outgrowth, and stimulates antioxidant enzyme levels. [1, 10, 11] The peptide has already been used frequently in hair and skin products connected to potent protective and regenerative actions. [2]

The human peptide GHK (glycyl-l-histidyl-l-lysine) is also associated with increasing collagen, elastin, and glycosaminoglycan synthesis, coupled with enhancing the function of dermal fibroblasts. [1] In its multiple health positive biological actions, the significant role GHK-Cu plays in augmented skin and tissue repair coupled with enhanced cell protective properties are gaining the most attention for therapeutic applications. In other words, this peptide has multiple healing and protective properties with some that remain to be discovered. [1] It is likely that positive GHK-Cu actions originate from its affinity to bind copper ions and the role it plays in copper metabolism. [1, 4] The current supplement blend is available in a convenient external use roll-on application.

To amplify wrinkle relief actions, this roll-on supplement is fortified with a robust homeopathic anti-aging, protective, and skincare ingredient matrix. This homeopathic proprietary blend includes **Aloe Barbadensis** leaf extract (heal, moisturize, protect the skin from free radicals, and soothe), **Butcher's Broom** (European shrub used in herbal medicine to promote blood flow and treat varicose veins), **Horse Chestnut** (a tree that holds a substance that can help prevent excess fluid buildup, water retention and swelling in the tissues), **Cucumber** (powerful moisturizer, reduces dark circles, dark spots, inflammation, and puffiness), and **Acetyl Hexapeptide-3**. Acetyl Hexapeptide-3 has shown actions to downregulate the release of neurotransmitters, followed by anti-wrinkle properties and moisturizing effects. [17] Blanes-Mira et al. (2002) explains a study on the topical synthetic peptide that produced 30% improvement in wrinkles in the eye area when applied twice daily (n = 10 women, 30-day duration), suggesting an improvement in skin firmness and tone. [18] Other headliner ingredients include the gut-brain axis peptide **Body Protective (Protein) Compound (BPC)-157**, a fifteen amino acid sequence peptide discovered initially within human gastric juice and formulated synthetically. Its mechanism of action is to promote angiogenesis (e.g., vascular development) through regulating Vaso Endothelial Growth Factor (VEGF), and, thus, supporting capillary growth and increased blood and nutrient transport. In relation to accelerated healing and recovery, researchers point to the BPC-157 and nitric oxide (NO) relationship. Nitric oxide can have potent actions to increase blood flow, reduce blood pressure, and has even been implicated in normalizing mental health and restoring vascular capacity. [19, 20, 21] The interplay of BPC-157 and NO to ameliorate free radical induced injuries and other health conditions accelerated by oxidative stress appears to be significant, the skin a major organ that can be damaged by unchecked free radical expansion. [22] Finally, other recognized skin moisture retention and texture improvement agents round out the proprietary blend such as CBD oil, potassium sorbate, hyaluronic acid, and citric acid.

Research

Pickart and Margolina (2018) state that the human peptide GHK (glycyl-l-histidyl-l-lysine) is capable of many biological actions such as increases collagen, elastin, and glycosaminoglycan synthesis, stimulates blood vessel and nerve outgrowth, and supports the function of dermal fibroblasts. [1] Recent comprehensive transcriptional responses data used to examine genome-wide effects of GHK find the molecule increases gene expression in 59% of the genes, while suppressing it in 41%, in other words it up- and down-regulates a sizable quantity of human genes. [1, 5, 6] By employing connectivity map tools and new understandings of genome-wide actions of peptides and molecules, researchers can better understand mechanism of action and effects on gene expression, e.g., applying specialized molecules and peptides to recalibrate the human genome to health. [7]

Externally, GHK-Cu plays a role in restoration of youthful skin appearance by regulating protein breakdown in skin (reducing buildup of damaged proteins) and bolstering strength in the dermal matrix. [8, 9] As a conduit for overall health, GHK-Cu is associated with powerful antioxidant and anti-inflammatory actions. The molecule can deactivate damaging free radical by-products of lipid

peroxidation, additionally decreasing iron release from ferritin (a stimulus of lipid peroxidation and source of free radical release). [1, 12]

Conclusion

Wrinkle Relief roll-on supplement blend product is designed to be a potent disruptor of the pathogenesis involved in premature skin aging, working at the molecular level to reverse skin imperfections and wrinkles caused by ultraviolet light and environmental toxins. [15, 16] Some of the mechanisms associated with exogenous aging and the appearance of wrinkles are accumulation of reactive oxygen species (ROS) caused by ultraviolet light and environmental toxins leading to DNA, protein, and lipid oxidation, degradation of collagen and elastin (proteins that provide skin elasticity, smoothness, and forms connective tissue), shortening of telomeres, a multipart process leading to wrinkling and sagging skin. [15]

GHK has actions to improve tissue repair coupled with potent cell protective abilities and anti-inflammatory properties. [1] Additionally, GHK is thought to provide comprehensive anti-aging and age-related disease support by reducing nuclear factor kappa-light-chain-enhancer (NFκB) molecules and pro-activation potential of the proteasome system which promotes DNA repair and cell cleansing. [1] Mitchell, Vargas, & Hoffmann (2016) state that the nuclear factor kappa B (NFκB) transcription factors family is a primary regulator of immune development & responses, also cancer and inflammation, suggesting GHK's age-related disease protection is associated with actions to moderate NFκB signaling. [3] GHK-Cu may be the headliner topical synthetic peptide leading this formulary but is only the beginning of a robust proprietary blend matrix designed to promote anti-aging skin actions and restoration of youthful appearance.

References

[1] Pickart L, Margolina A. Regenerative and Protective Actions of the GHK-Cu Peptide in the Light of the New Gene Data. Int J Mol Sci. 2018 Jul 7;19(7):1987. doi: 10.3390/ijms19071987. PMID: 29986520; PMCID: PMC6073405.

[2] Pickart L. The human tri-peptide GHK and tissue remodeling. J Biomater Sci Polym Ed. 2008;19(8):969-88. doi: 10.1163/156856208784909435. PMID: 18644225.

[3] Mitchell S, Vargas J, Hoffmann A. Signaling via the NFκB system. Wiley Interdiscip Rev Syst Biol Med. 2016 May;8(3):227-41. doi: 10.1002/wsbm.1331. Epub 2016 Mar 16. PMID: 26990581; PMCID: PMC8363188.

[4] Pickart L, Freedman JH, Loker WJ, Peisach J, Perkins CM, Stenkamp RE, Weinstein B. Growth-modulating plasma tripeptide may function by facilitating copper uptake into cells. Nature. 1980 Dec 25;288(5792):715-7. doi: 10.1038/288715a0. PMID: 7453802.

[5] Lamb J. The Connectivity Map: a new tool for biomedical research. Nat Rev Cancer. 2007 Jan;7(1):54-60. doi: 10.1038/nrc2044. PMID: 17186018.

[6] Kimoto E, Tanaka H, Gyotoku J, Morishige F, Pauling L. Enhancement of antitumor activity of ascorbate against Ehrlich ascites tumor cells by the copper:glycylglycylhistidine complex. Cancer Res. 1983 Feb;43(2):824-8. PMID: 6293704.

[7] Pickart L, Vasquez-Soltero JM, Margolina A. GHK and DNA: resetting the human genome to health. Biomed Res Int. 2014;2014:151479. doi: 10.1155/2014/151479. Epub 2014 Sep 11. PMID: 25302294; PMCID: PMC4180391.

[8] Siméon A, Monier F, Emonard H, Gillery P, Birembaut P, Hornebeck W, Maquart FX. Expression and activation of matrix metalloproteinases in wounds: modulation by the tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu2+. J Invest Dermatol. 1999 Jun;112(6):957-64. doi: 10.1046/j.1523-1747.1999.00606.x. PMID: 10383745.

[9] Siméon A, Emonard H, Hornebeck W, Maquart FX. The tripeptide-copper complex glycyl-L-histidyl-L-lysine-Cu2+ stimulates matrix metalloproteinase-2 expression by fibroblast cultures. Life Sci. 2000 Sep 22;67(18):2257-65. doi: 10.1016/s0024-3205(00)00803-1. PMID: 11045606.

[10] Cangul IT, Gul NY, Topal A, Yilmaz R. Evaluation of the effects of topical tripeptide-copper complex and zinc oxide on open-wound healing in rabbits. Vet Dermatol. 2006 Dec;17(6):417-23. doi: 10.1111/j.1365-3164.2006.00551.x. PMID: 17083573.

[11] Gul NY, Topal A, Cangul IT, Yanik K. The effects of topical tripeptide copper complex and helium-neon laser on wound healing in rabbits. Vet Dermatol. 2008 Feb;19(1):7-14. doi: 10.1111/j.1365-3164.2007.00647.x. PMID: 18177285.

[12] Cebrián J, Messeguer A, Facino RM, García Antón JM. New anti-RNS and -RCS products for cosmetic treatment. Int J Cosmet Sci. 2005 Oct;27(5):271-8. doi: 10.1111/j.1467-2494.2005.00279.x. PMID: 18492208.

[13] Veiga Eliana, Laura Ferreira, Mafalda Correia, Patrícia C. Pires, Huma Hameed, André R.T. S. Araújo, Letícia Caramori Cefali, Priscila Gava Mazzola, Hamed Hamishehkar, Francisco Veiga, Ana Cláudia Paiva-Santos, Anti-aging peptides for advanced skincare: Focus on nanodelivery systems, Journal of Drug Delivery Science and Technology, Volume 89, 2023, 105087, ISSN 1773-2247, https://doi.org/10.1016/j.jddst.2023.105087. (https://www.sciencedirect.com/science/article/pii/S1773224723009395).

[14] Ahmed, I.A., Mikail, M.A., Zamakshshari, N. *et al.* Natural anti-aging skincare: role and potential. *Biogerontology* **21**, 293–310 (2020). https://doi.org/10.1007/s10522-020-09865-z.

[15] Kim M, Hyun Jeong, Park. Molecular mechanisms of skin aging and rejuvenation. In: Shiomi H, editor. *Molecular Mechanisms of the Aging Process and Rejuvenation*. London: IntechOpen; 2016:57–76.

[16] Ganceviciene R, Liakou AI, Theodoridis A, Makrantonaki E, Zouboulis CC. Skin anti-aging strategies. Dermatoendocrinol. 2012 Jul 1;4(3):308-19. doi: 10.4161/derm.22804. PMID: 23467476; PMCID: PMC3583892.

[17] Schagen S.K. Topical Peptide Treatments with Effective Anti-Aging Results. Cosmetics. 2017; 4(2):16. https://doi.org/10.3390/cosmetics4020016.

[18] Blanes-Mira C, Clemente J, Jodas G, Gil A, Fernández-Ballester G, Ponsati B, Gutierrez L, Pérez-Payá E, Ferrer-Montiel A. A synthetic hexapeptide (Argireline) with antiwrinkle activity. Int J Cosmet Sci. 2002 Oct;24(5):303-10. doi: 10.1046/j.1467-2494.2002.00153.x. PMID: 18498523.

[19] Zemba M, Cilic AZ, Balenovic I, Cilic M, Radic B, Suran J, Drmic D, Kokot A, Stambolija V, Murselovic T, Holjevac JK, Uzun S, Djuzel V, Vlainic J, Seiwerth S, Sikiric P. BPC 157 antagonized the general anaesthetic potency of thiopental and reduced prolongation of anaesthesia induced by L-NAME/thiopental combination. Inflammopharmacology. 2015 Dec;23(6):329-36. doi: 10.1007/s10787-015-0249-9. Epub 2015 Nov 13. PMID: 26563892.

[20] Kokot A, Zlatar M, Stupnisek M, Drmic D, Radic R, Vcev A, Seiwerth S, Sikiric P. NO system dependence of atropine-induced mydriasis and L-NAME- and L-arginine-induced miosis: Reversal by the pentadecapeptide BPC 157 in rats and guinea pigs. Eur J Pharmacol. 2016 Jan 15;771:211-9. doi: 10.1016/j.ejphar.2015.12.016. Epub 2015 Dec 15. PMID: 26698393.

[21] Duzel A, Vlainic J, Antunovic M, Malekinusic D, Vrdoljak B, Samara M, Gojkovic S, Krezic I, Vidovic T, Bilic Z, Knezevic M, Sever M, Lojo N, Kokot A, Kolovrat M, Drmic D, Vukojevic J, Kralj T, Kasnik K, Siroglavic M, Seiwerth S, Sikiric P. Stable gastric pentadecapeptide BPC 157 in the treatment of colitis and ischemia and reperfusion in rats: New insights. World J Gastroenterol. 2017 Dec 28;23(48):8465-8488. doi: 10.3748/wjg.v23.i48.8465. PMID: 29358856; PMCID: PMC5752708.

[22] Chang, C., Tsai, W., Lin, M., Hsu, Y., & Pang, J. S. (2011). The promoting effect of pentadecapeptide BPC 157 on tendon healing involves tendon outgrowth, cell survival, and cell migration. *Journal of Applied Physiology, 110*(3), 774-780. doi:10.1152/japplphysiol.00945.2010.

Summary

Wrinkle Relief GHK-Cu proprietary blend is a convenient external use roll-on supplement formulary designed to be gently applied directly to facial folds to promote wrinkle relief and enhance youthful appearance. Externally, the main ingredient GHK-Cu plays a role in restoration of youthful skin appearance by regulating protein breakdown, e.g., collagen and elastin in skin (reducing buildup of damaged proteins) and bolstering strength in the dermal matrix, building blocks of connective tissue. To amplify wrinkle relief actions, this roll-on supplement is fortified with a robust homeopathic anti-aging, protective, and skincare ingredient matrix. This homeopathic proprietary blend includes Aloe Barbadensis leaf extract (heal, moisturize, protect the skin from free radicals, and soothe), Butcher's Broom (European shrub used in herbal medicine to promote blood flow and treat varicose veins), Horse Chestnut (a tree that holds a substance that can help prevent excess fluid buildup, water retention and swelling in the tissues), Cucumber (powerful moisturizer, reduces dark circles, dark spots, inflammation, and puffiness), and Acetyl Hexapeptide-3. Acetyl Hexapeptide-3 has shown actions to downregulate the release of neurotransmitters, followed by anti-wrinkle properties and moisturizing effects and is among a list of many more anti-wrinkle ingredients in this formulary.