Photoprotection and Treating Sun Damage: Spectrum of Treatment

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Relevant Disclosures

Investigator/speaker and/or consultant:

AbbVie, Almirall, Amgen, Apogee, Arcutis, Biofrontera, Boehringer-Ingelheim, Bristol Myers Squibb, Cara Therapeutics, Castle Biosciences, Dermsquared, Eli Lilly and Company, Galderma, Incyte, Janssen, Novartis, Pfizer Inc., Regeneron, Sanofi, SiSaf, Sun Pharma, Takeda, RBC Consultants, Verrica and UCB.

Key Topics

- Growth factors
- Retinoids
- Peptides
- Antioxidants
- Sunscreens
- Exosomes
- Postbiotics

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Growth Factors

- Growth factors applied topically can reduce signs of photoaging by promoting fibroblast and keratinocyte proliferation and inducing extracellular matrix formation 1-3

1.Pamela R. D. (2018). Topical Growth Factors for the Treatment of Facial Photoaging: A Clinical Experience of Eight Cases. *The Journal of clinical and aesthetic dermatology*, *11*(12), 28–29.
2. Shin, S. H., Koh, Y. G., Lee, W. G., Seok, J., & Park, K. Y. (2023). The use of epidermal growth factor in dermatological practice. *International wound journal*, *20*(6), 2414–2423. https://doi.org/10.1111/iwj.14075 3. Andrade, M. J., Van Lonkhuyzen, D. R., Upton, Z., & Satyamoorthy, K. (2020). Unravelling the insulin-like growth factor I-mediated photoprotection of the skin. *Cytokine & growth factor reviews*, *52*, 45–55. https://doi.org/10.1016/j.cytogfr.2019.11.004

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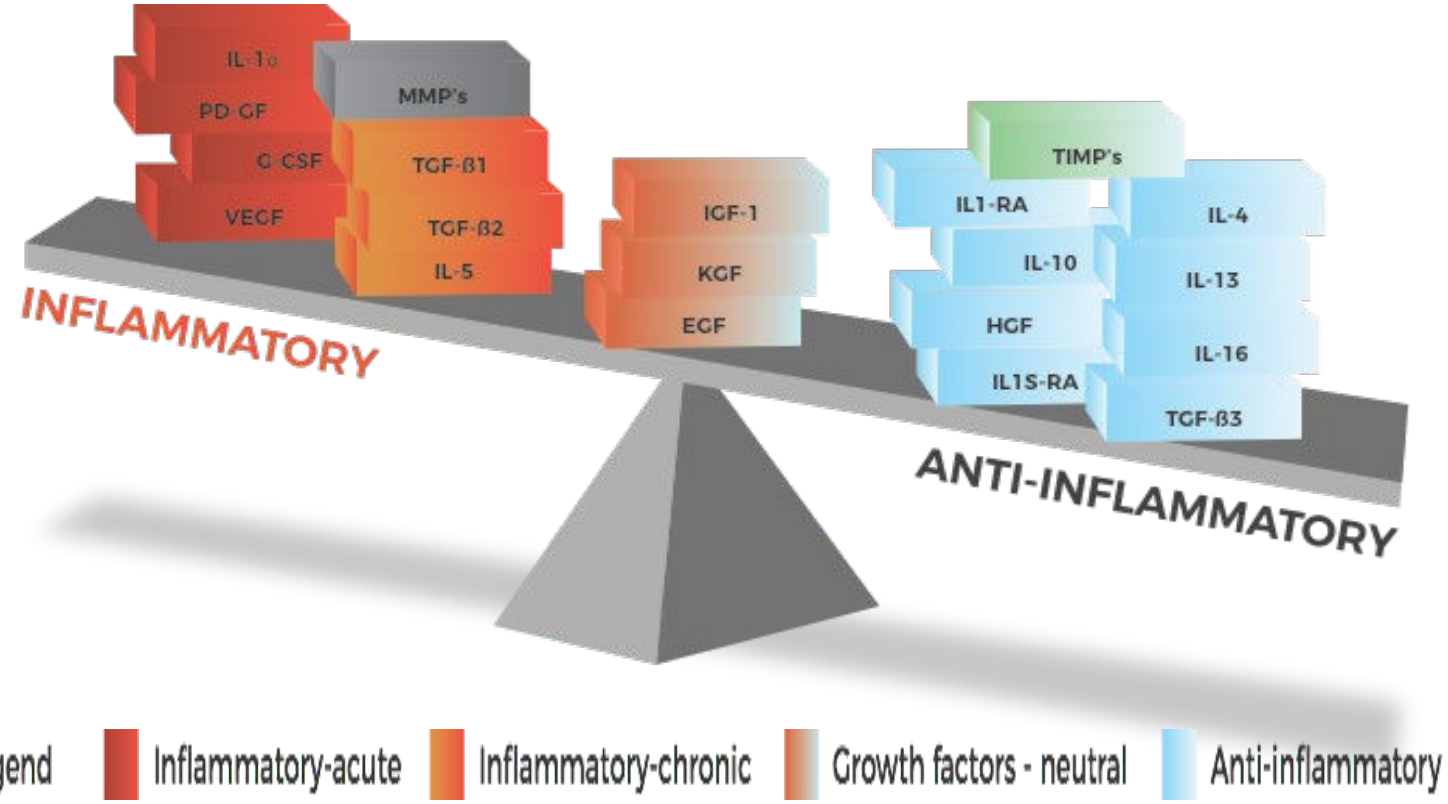
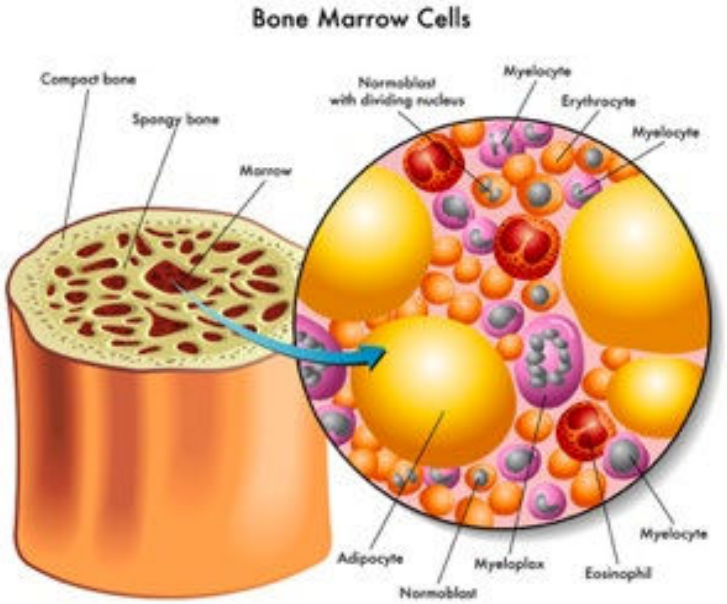
Growth Factors

- Bone Marrow Mesenchymal Stem Cell Growth Factors





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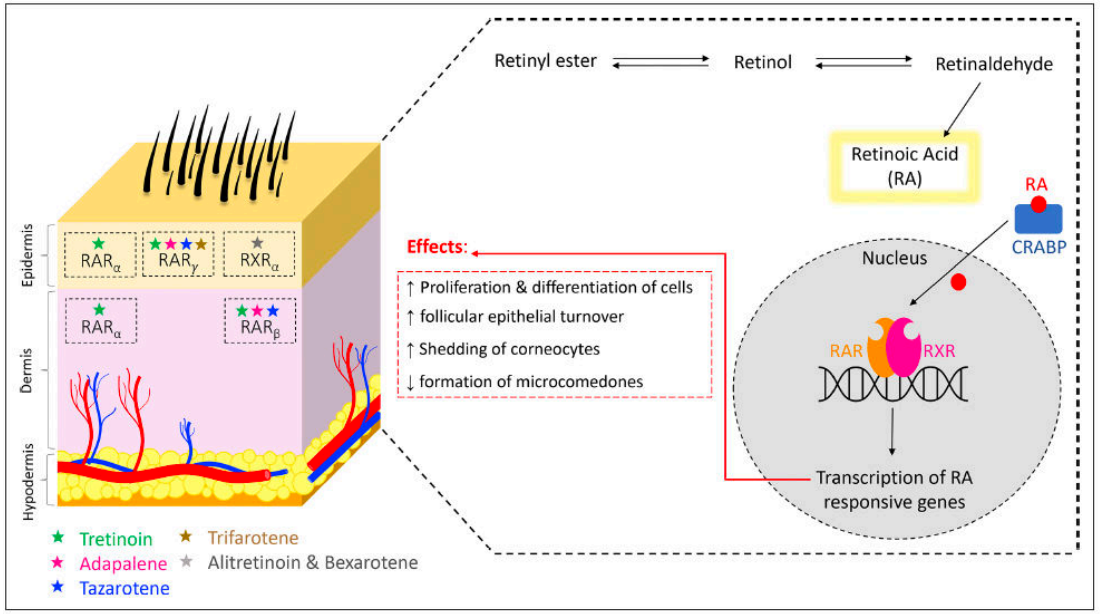
Retinoids

- Retinol: natural form of vitamin A
- Retinoic acid: formed from oxidation of retinaldehyde
- Adapalene: selective for RAR Beta and RAR
- Tretinoin: only retinoid indicated for photoaging and wrinkles
  - Binds RAR, RAR Beta, and RAR Alpha



Motamedi, M., Chehade, A., Sanghera, R., & Grewal, P. (2022). A Clinician's Guide to Topical Retinoids. *Journal of cutaneous medicine and surgery*, *26*(1), 71–78. https://doi.org/10.1177/12034754211035091

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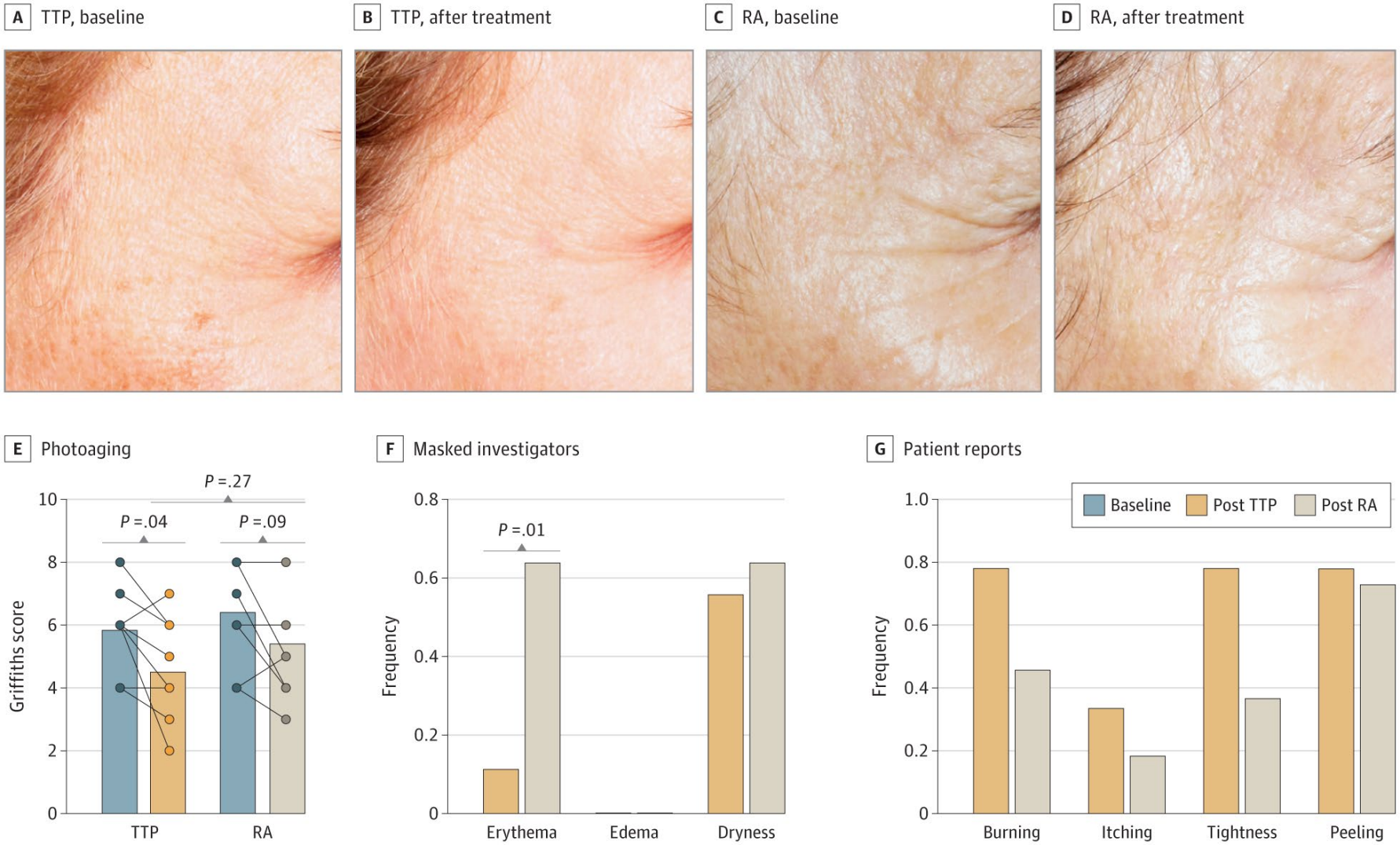
Retinoids



Chien AL, Kim DJ, Cheng N, et al. Biomarkers of Tretinoin Precursors and Tretinoin Efficacy in Patients With Moderate to Severe Facial Photodamage: A Randomized Clinical Trial. *JAMA Dermatol.* 2022;158(8):879–886. doi:10.1001/jamadermatol.2022.1891

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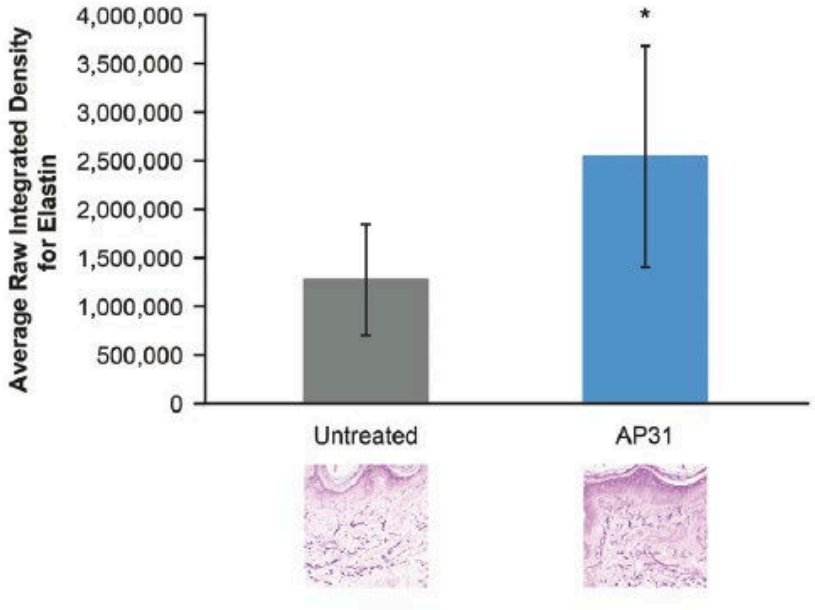
Peptides

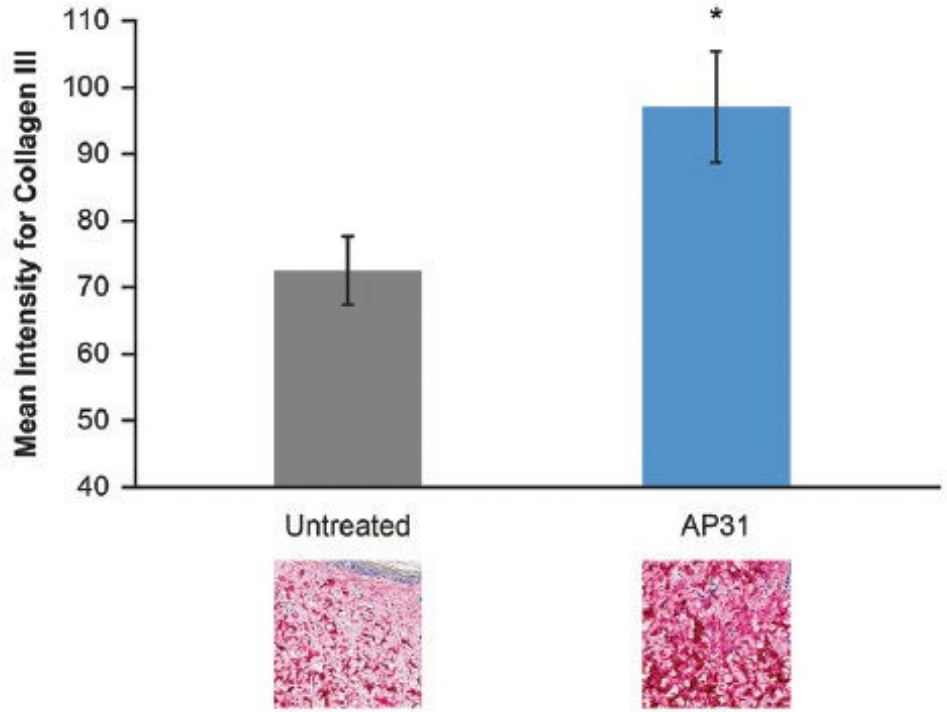
- In 1973, Pickart first proposed a synthetic carrier peptide, GHK (glycyl-histidyl-lysine), coupled with copper[1,2]
- Since then, many peptides have been developed to target and module extracellular matrix components [1,3]
- Acetyl dipeptide-31 amide (AP31) is a novel multifunctional micropeptide evaluated for anti-inflammatory and anti-aging benefits

1Edison B, Parsa R, Dufort, M, et al. Acetyl Dipeptide-31 Amide: A novel Cosmetic Anti-Inflammatory Peptide That Demonstrates Anti-Aging, Firming, and Lifting Benefits. *Journal of Drugs in Dermatology: JDD*,24(1), 23-33. https://doi.org/10.36849/JDD.8786
2 Pickart L, Thaler MM. Tripeptide in human serum which prolongs survival of normal liver cells and stimulates growth in the neoplastic liver. *Nat New Biol*. 1973;243(124):85-87
3 Rodan K, Fields K, Falla T. Bioactive peptides. IN: Farris PK, Ed. Cosmeceuticals and Cosmetic Practice. West Sussex, UK: John Wiley & Sons Ltd.;2014:142-152

Peptides

- **Acetyl Dipeptide-31 Amide (AP31)** significantly increases:
  - Procollagen
  - Elastin





*** P < 0.05**

Edison B, Parsa R, Dufort, M, et al. Acetyl Dipeptide-31 Amide: A novel Cosmetic Anti-Inflammatory Peptide That Demonstrates Anti-Aging, Firming, and Lifting Benefits. *Journal of Drugs in Dermatology: JDD*,24(1), 23-33. https://doi.org/10.36849/JDD.8786

AP31

FIGURE 5. Clinical improvement from baseline in aging parameters of the lower face following use of AP31 0.4% cream twice daily for 16 weeks.

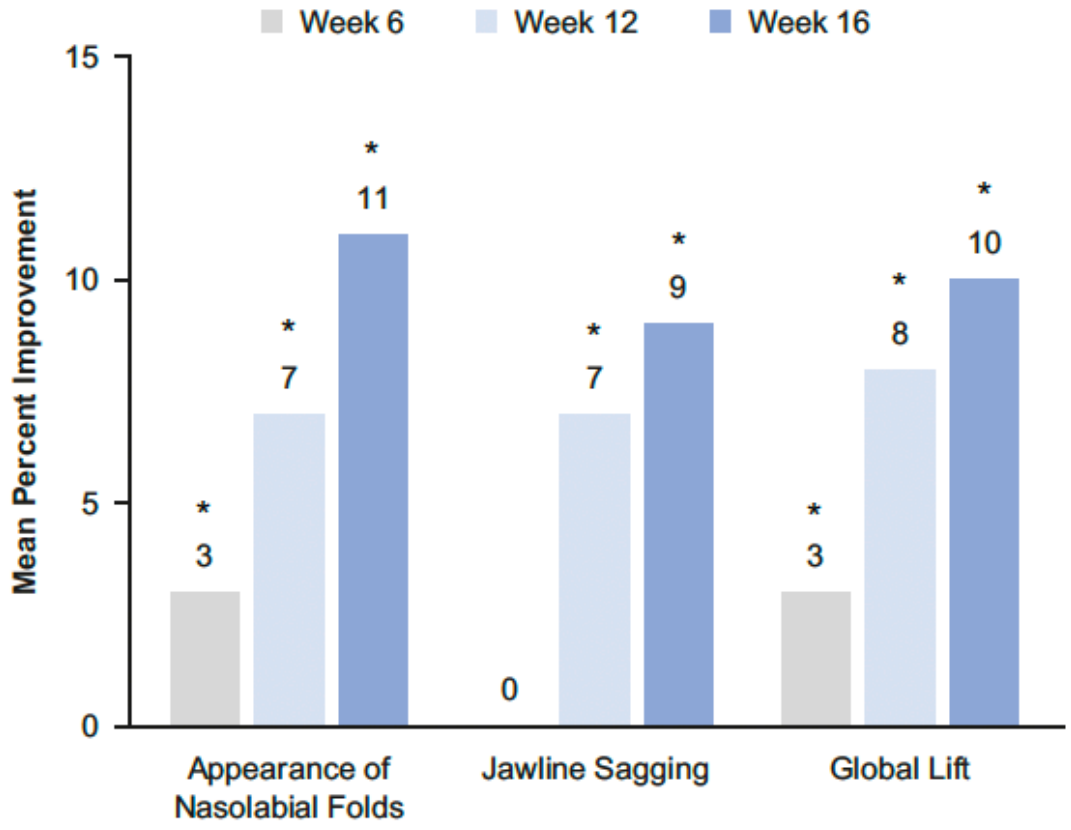


FIGURE 6. Improved jawline contour and lift of the lower face following use of AP31 0.4% cream twice daily for 16 weeks, compared with baseline.

AP31, acetyl dipeptide-31 amide.

FIGURE 7. Diminished lines and lift on the forehead following use of AP31 0.4% cream twice daily for 16 weeks, compared with baseline.

Edison B, Parsa R, Dufort, M, et al. Acetyl Dipeptide-31 Amide: A novel Cosmetic Anti-Inflammatory Peptide That Demonstrates Anti-Aging, Firming, and Lifting Benefits. *Journal of Drugs in Dermatology: JDD*,24(1), 23-33. https://doi.org/10.36849/JDD.8786

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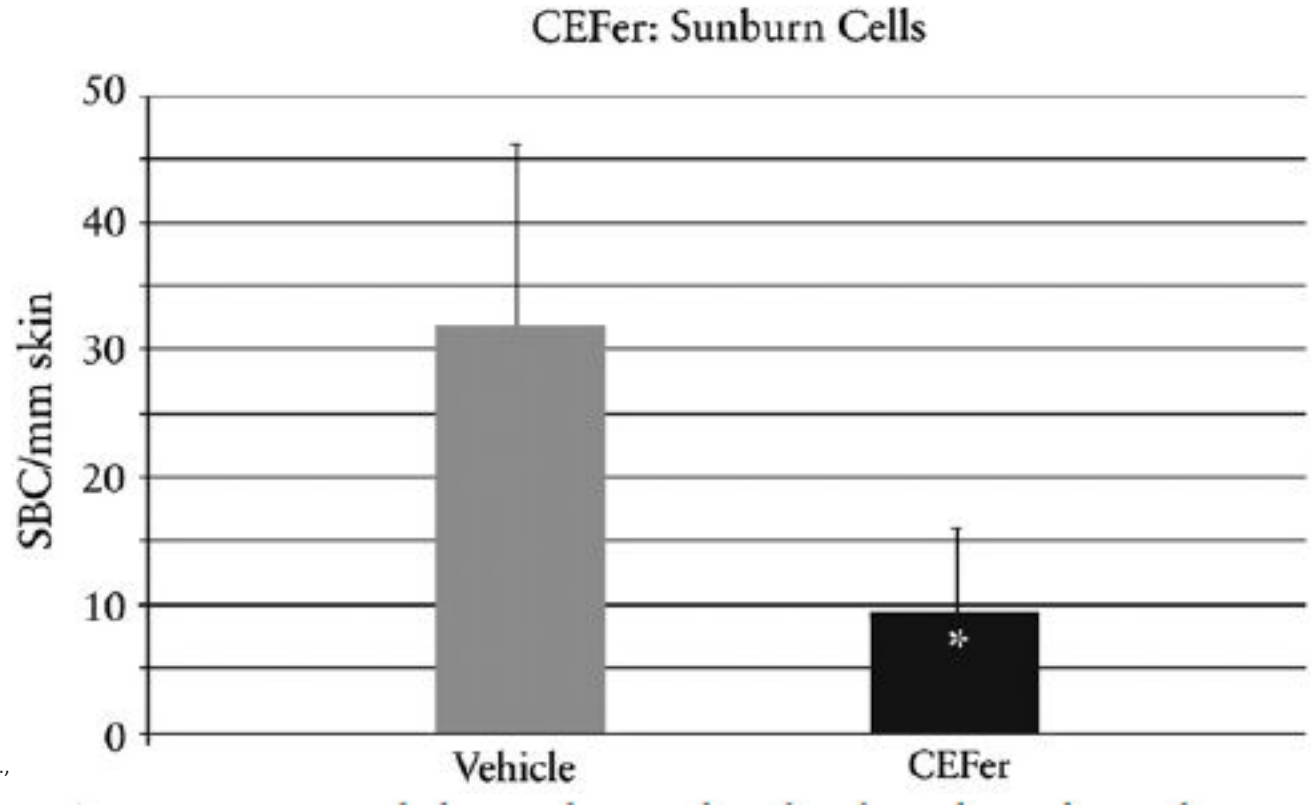
Antioxidants

- **Vitamin C, Vitamin E, and Ferulic Acid**
  - In formulations as 15% L-ascorbic acid, 1% alpha-tocopherol, and 0.5% ferulic acid (CEFer)
  - Ferulic acid is a
    vitamin C + E im
    photoprotectior



1.Lin, F. H., Lin, J. Y., Gupta, R. D., Tournas, J. A., Burch, J. A., Selim, M. A., Monteiro-Riviere, N. A., Grichnik, J. M., Zielinski, J., & Pinnell, S. R. (2005). Ferulic acid stabilizes a solution of vitamins C and E and doubles its photoprotection of skin. *The Journal of investigative dermatology*, *125*(4), 826–832. https://doi.org/10.1111/j.0022-202X.2005.23768.x

Murray, J. C., Burch, J. A., Streilein, R. D., Iannacchione, M. A., Hall, R. P., & Pinnell, S. R. (2008). A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet irradiation. *Journal of the American Academy of Dermatology*, *59*(3), 418–425. https://doi.org/10.1016/j.jaad.2008.05.004

Antioxidants

- **Tranexamic acid**
  - Antifibrinolytic agent and synthetic derivative of lysine
  - Main purpose: reduce bleeding by inhibiting conversion of plasminogen to plasmin [1,2]
  - Also has anti-inflammatory properties and ability to suppress melanogenesis [1,3]
  - Not very effective topically. Better if applied with microneedle/nonablative fractional laser
  - Likely best if taken orally if applicable

1.Gaćina, K., & Krstanović Ćosić, A. (2023). THE USE OF TRANEXAMIC ACID IN DERMATOLOGY. *Acta clinica Croatica*, *62*(2), 368–372. https://doi.org/10.20471/acc.2023.62.02.16
2. Cai J, Ribkoff J, Olson S, et al. The many roles of tranexamic acid: An overview of the clinical indications for TXA in medical and surgical patients. *Eur J Haematol*. 2020; 104: 79–87. https://doi.org/10.1111/ejh.13348
3. Prudovsky I, Kacer D, Zucco VV, Palmeri M, Falank C, Kramer R, et al. Tranexamic acid: Beyond antifibrinolysis. *Transfusion*. 2022; 62(S1): S301–S312. https://doi.org/10.1111/trf.16976

Antioxidants

- **Tranexamic acid**

L: 3 sessions of microneedling and vitamin C

R: 3 sessions of microneedling and tranexamic acid

Pazyar, N., Raeispour, M., Yaghoobi, R., & Seyedtabib, M. (2023). Evaluation of the effectiveness of microneedling with tranexamic acid in comparison with microneedling with vitamin C in the treatment of melasma: A prospective and single-blind clinical trial. *Health science reports*, *6*(10), e1636. https://doi.org/10.1002/hsr2.1636

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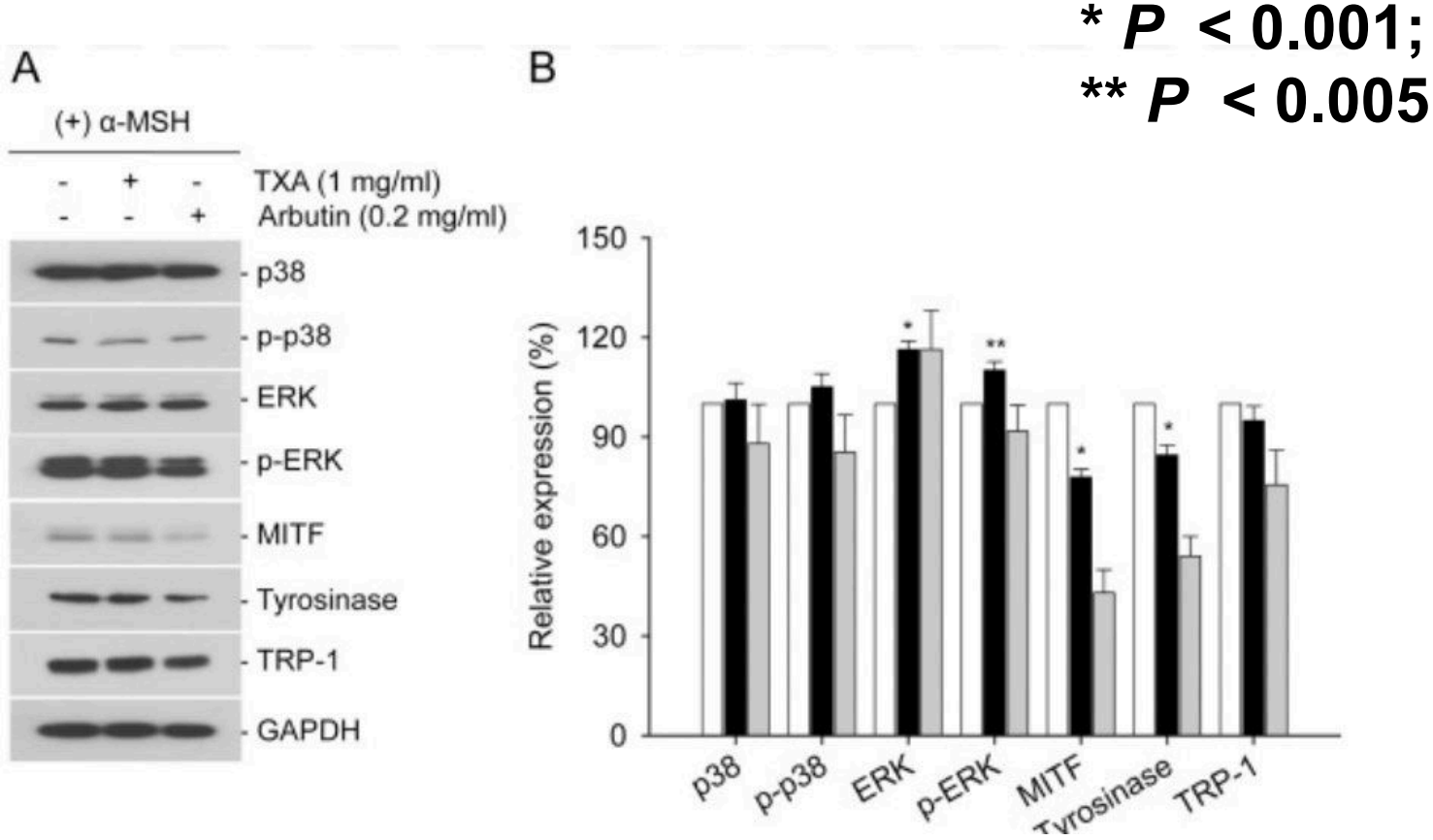
Antioxidants

- **Tranexamic acid**

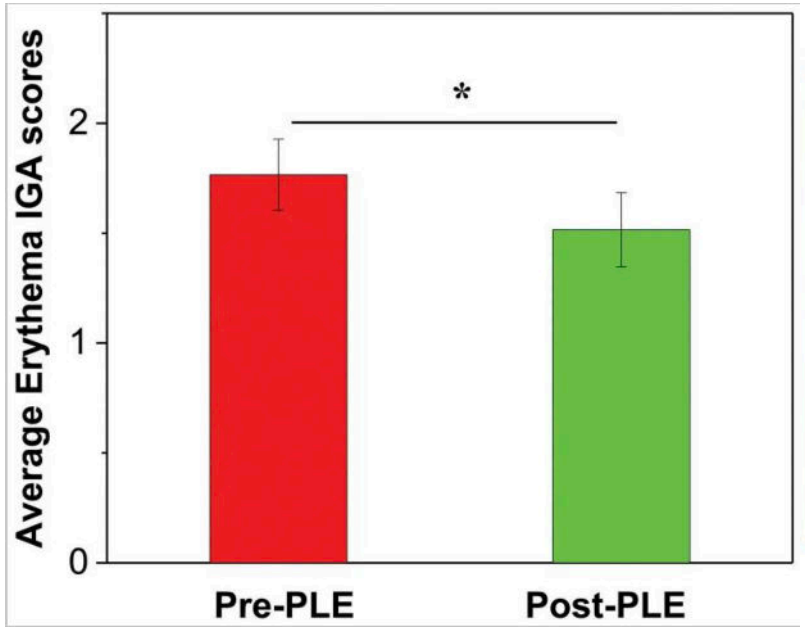


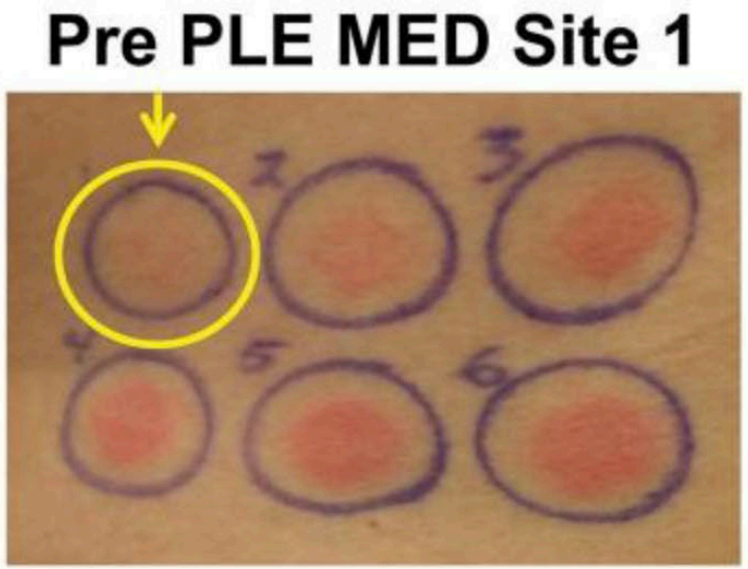
* $P < 0.001$;
** $P < 0.005$

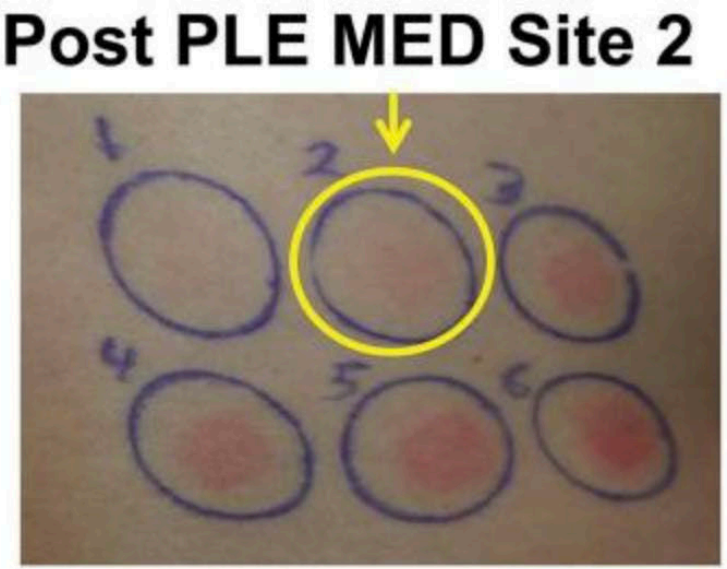
Cho, Y. H., Park, J. E., Lim, D. S., & Lee, J. S. (2017). Tranexamic acid inhibits melanogenesis by activating the autophagy system in cultured melanoma cells. *Journal of Dermatological Science*, *88*(1), 96–102. https://doi.org/10.1016/j.jdermsci.2017.05.019

Antioxidants

- **Polypodium leucotomos (PLE)**







Kohli, I., Shafi, R., Isedeh, P., Griffith, J. L., Al-Jamal, M. S., Silpa-Archa, N., Jackson, B., Athar, M., Kollias, N., Elmets, C. A., Lim, H. W., & Hamzavi, I. H. (2017). The impact of oral Polypodium leucotomos extract on ultraviolet B response: A human clinical study. *Journal of the American Academy of Dermatology*, *77*(1), 33–41.e1. https://doi.org/10.1016/j.jaad.2017.01.044

1.Segars, K., McCarver, V., & Miller, R. A. (2021). Dermatologic Applications of *Polypodium leucotomos*: A Literature Review. *The Journal of clinical and aesthetic dermatology*, *14*(2), 50–60.
2Palomino O. M. (2015). Current knowledge in Polypodium leucotomos effect on skin protection. *Archives of dermatological research*, *307*(3), 199–209. https://doi.org/10.1007/s00403-014-1535-x

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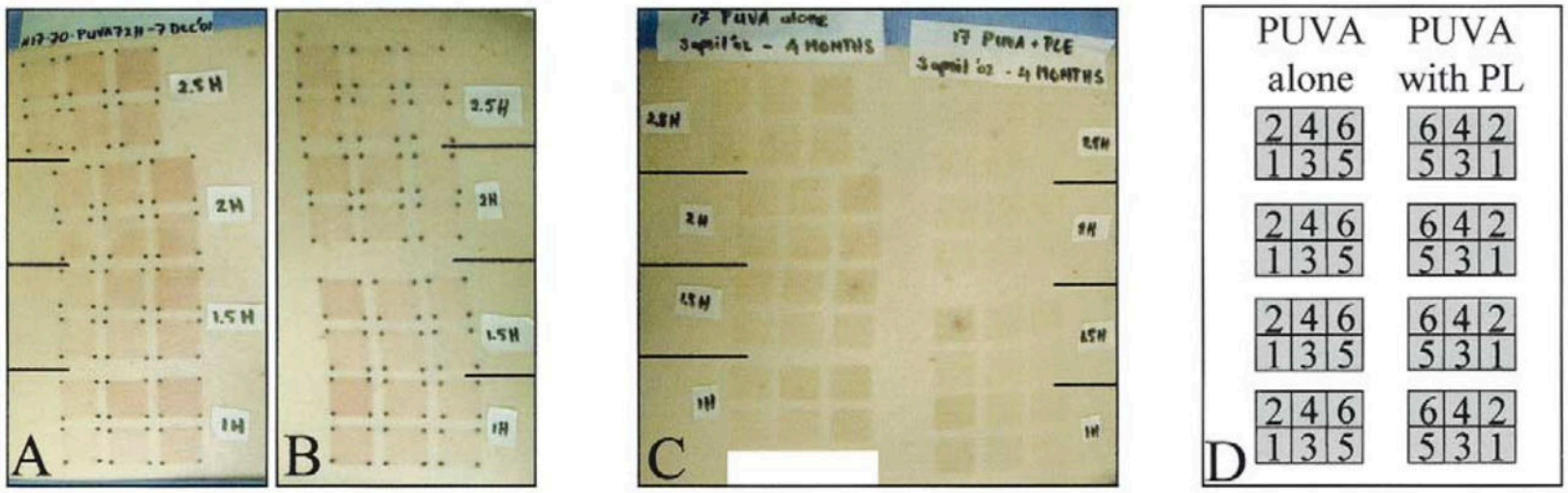
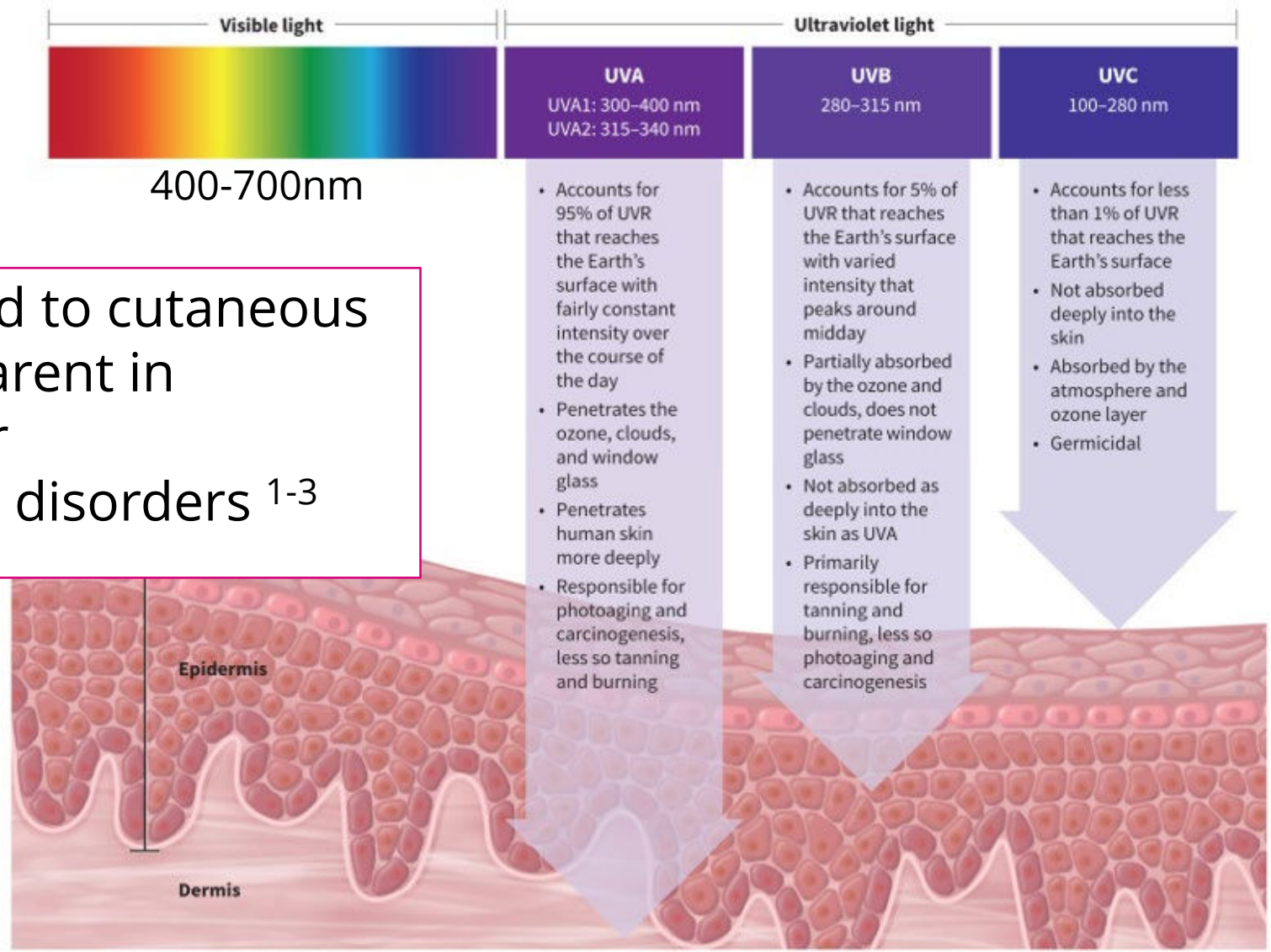
Antioxidants

- **Polypodium leucotomos (PL)**
  - PL is an effective chemophotoprotector against PUVA-induced skin phototoxicity and leads to substantial benefits of skin protection
  - Phototoxicity was always lower in PL-treated skin after 48 to 72 hours and pigmentation was also reduced 4 months later



Middelkamp-Hup, M. A., Pathak, M. A., Parrado, C., Garcia-Caballero, T., Rius-Díaz, F., Fitzpatrick, T. B., & González, S. (2004). Orally administered Polypodium leucotomos extract decreases psoralen-UVA-induced phototoxicity, pigmentation, and damage of human skin. *Journal of the American Academy of Dermatology*, *50*(1), 41–49. https://doi.org/10.1016/s0190-9622(03)02732-4

Sunscreen



Visible light can lead to cutaneous photodamage apparent in melasma and other hyperpigmentation disorders [1-3]

1.Lyons, A. B., Trullas, C., Kohli, I., Hamzavi, I. H., & Lim, H. W. (2021). Photoprotection beyond ultraviolet radiation: A review of tinted sunscreens. *Journal of the American Academy of Dermatology*, *84*(5), 1393–1397. https://doi.org/10.1016/j.jaad.2020.04.079 2. Boukari F, Jourdan E, Fontas E, Montaudie´ H, Castela E, Lacour JP, et al. Prevention of mel- asma relapses with sunscreen combining pro- tection against UV and short wavelengths of visible light: a prospective randomized comparative trial. J Am Acad Dermatol 2015;72:189e190.e1. 3. Kohli I, Chaowattanapanit S, Mohammad TF, Nicholson CL, Fatima S, Jacobsen G, et al. Synergistic effects of long-wavelength ultra- violet A1 and visible light on pigmentation and erythema. Br J Dermatol 2018;178: 1173e80.

Sander, M., Sander, M., Burbidge, T., & Beecker, J. (2020). The efficacy and safety of sunscreen use for the prevention of skin cancer. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*, *192*(50), E1802–E1808. https://doi.org/10.1503/cmaj.201085

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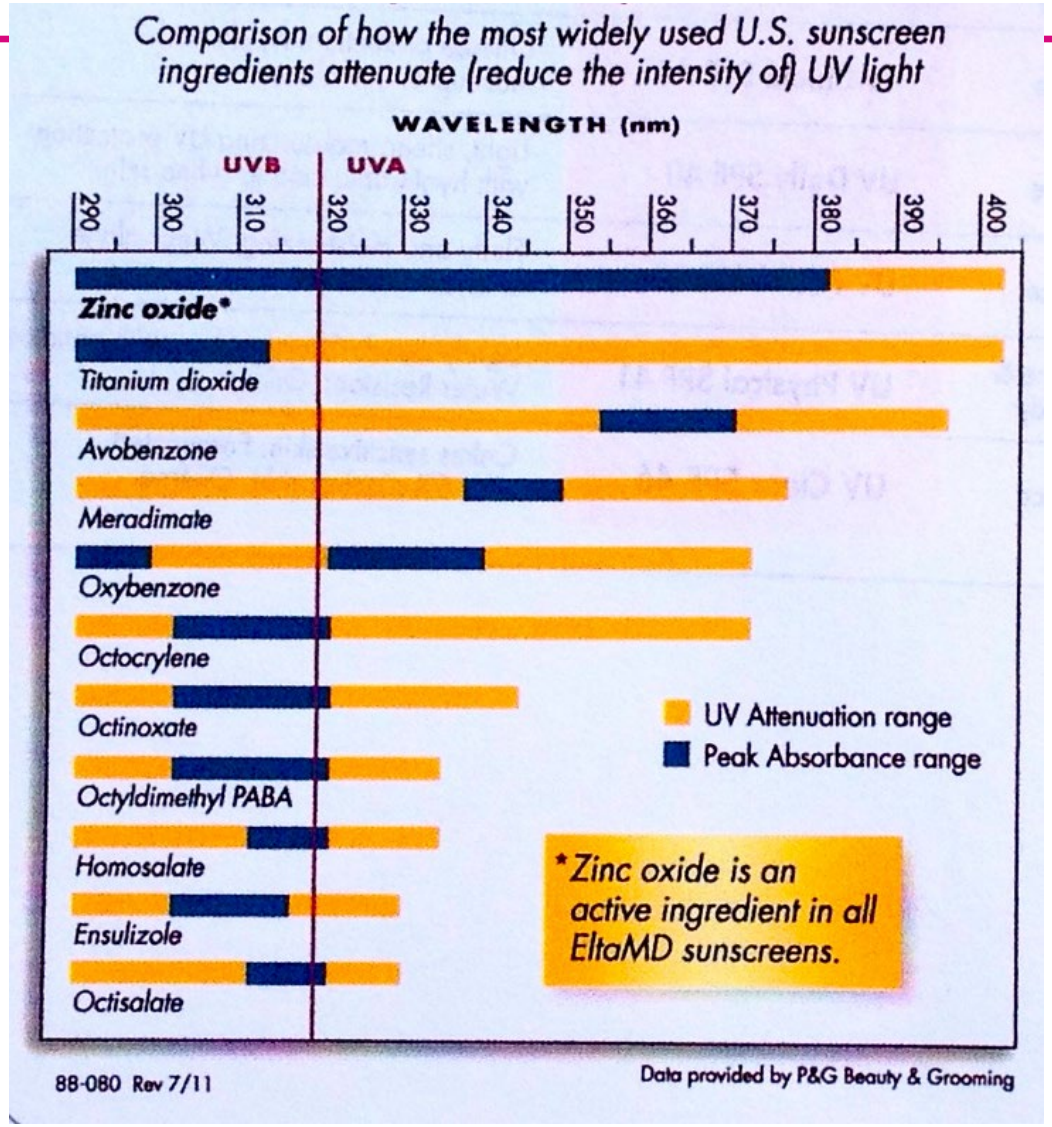
Common Ingredients



Sun Protection. Bryn Mawr Dermatology. (2024, February 8). https://www.brynmawrdermatology.com/services/medical-services/skin-cancer-prevention/

- Iron oxide, used in tinted sunscreens, can protect against visible light, including blue light[1,2]
- Mineral sunscreens contain zinc oxide or titanium dioxide, which scatter visible light in addition to UVA and UVB[2]

1. Geisler, A. N., Austin, E., Nguyen, J., Hamzavi, I., Jagdeo, J., & Lim, H. W. (2021). Visible light. Part II: Photoprotection against visible and ultraviolet light. *Journal of the American Academy of Dermatology*, *84*(5), 1233–1244. https://doi.org/10.1016/j.jaad.2020.11.074 2. Moradi Tuchayi, S., Wang, Z., Yan, J., Garibyan, L., Bai, X., & Gilchrest, B. A. (2023). Sunscreens: Misconceptions and Misinformation. *Journal of Investigative Dermatology, 143*(8), 1406-1411. doi:https://doi.org/10.1016/j.jid.2023.03.1677

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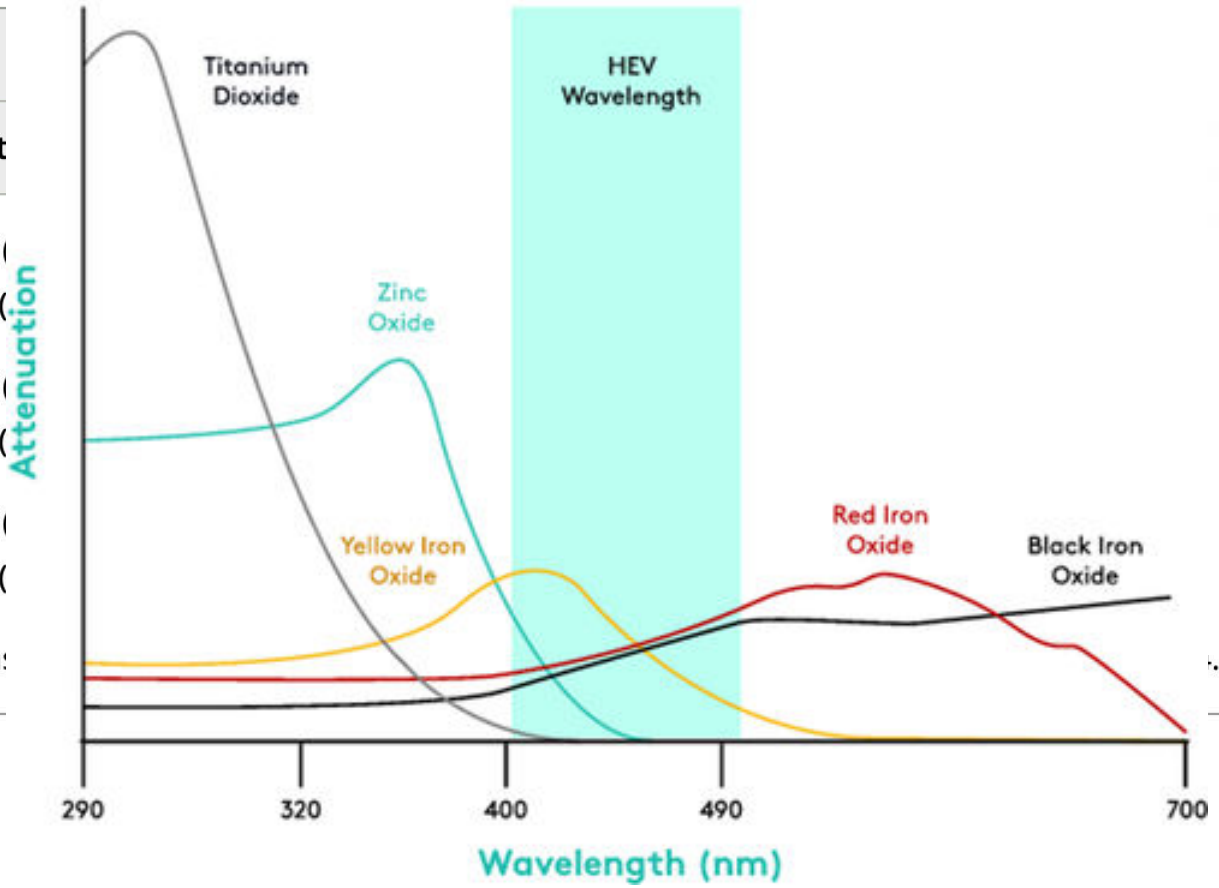
Tinted sunscreen

HEV: high-energy visible light (400-700nm)

Table 1.

Product	
SPF 35 (yellow (	
SPF 50 (yellow (	
SPF 50 (yellow (	
No suns	



Bernstein EF, Sarkas HW, Boland P. Iron oxides in novel skin care formulations attenuate blue light for enhanced protection against skin damage. *J Cosmet Dermatol*. 2021; 20: 532–537. https://doi.org/10.1111/jocd.13803

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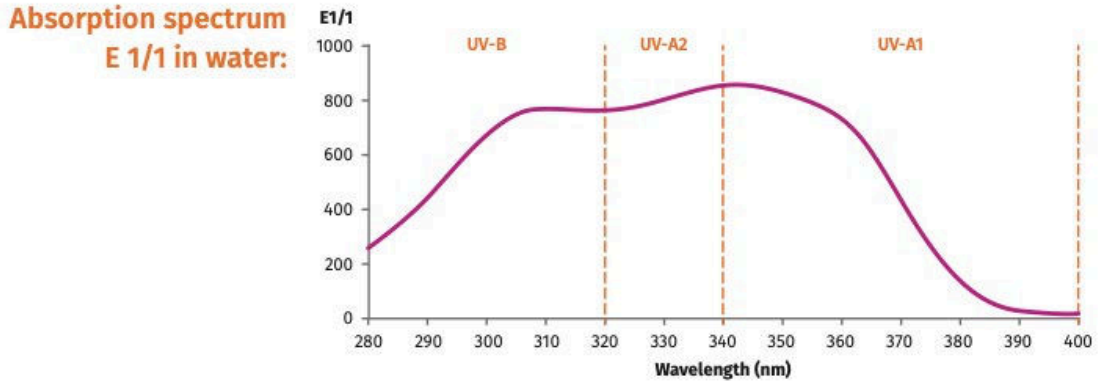
On the Horizon

- **Bemotrizinol**
  - FDA has until early 2026 to decide on approval on this ingredient
  - Chemical compound that absorbs UVA and UVB rays
  - Used in many sunscreens in Europe, Japan, and South Korea
  - Highly effective at low concentrations
  - Highly soluble in cosmetic oils
  - High photostability



From DSM – PARSOL shield

1.D'Ruiz, C. D., Plautz, J. R., Schuetz, R., Sanabria, C., Hammonds, J., Erato, C., . . . Mesaros, S. (2023). Preliminary clinical pharmacokinetic evaluation of bemotrizinol - A new sunscreen active ingredient being considered for inclusion under FDA's over-the-counter (OTC) sunscreen monograph. *Regulatory Toxicology and Pharmacology, 139*, 105344. doi:https://doi.org/10.1016/j.yrtph.2023.105344

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Exosomes

Vital for cell-to-cell communication

- Nanoparticles that package for export paracrine biosignals and nucleic acid modulators of phenotypic expression.
- Diffuse through tissue, seek target cells, alter local immune functions, and deliver their cargo through receptor-mediated endocytosis.
- Can effect changes to skin through epigenetic modulation.

[Infuse Medical. (2020, May, 20). Exosome 3D Medical Animation – Infuse. Youtube. https://www.youtube.com/watch?v=F2kLBh-rvLY]

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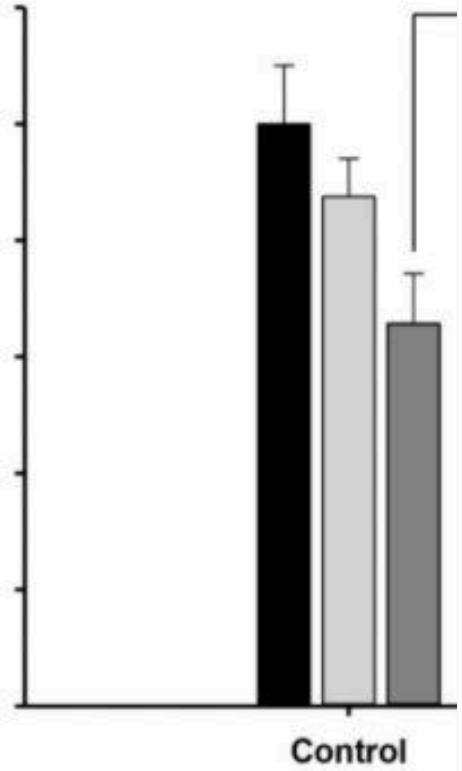
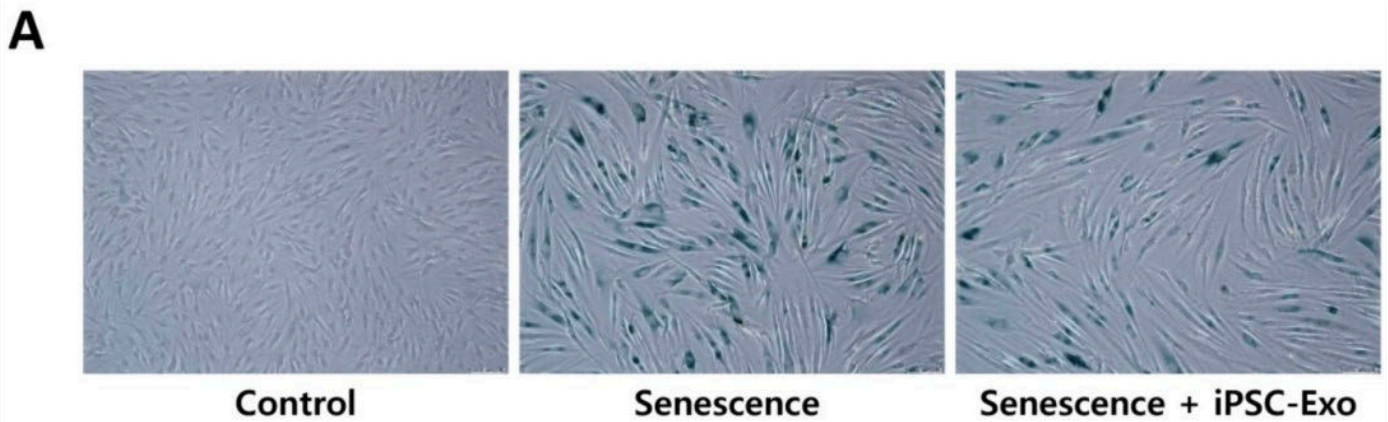
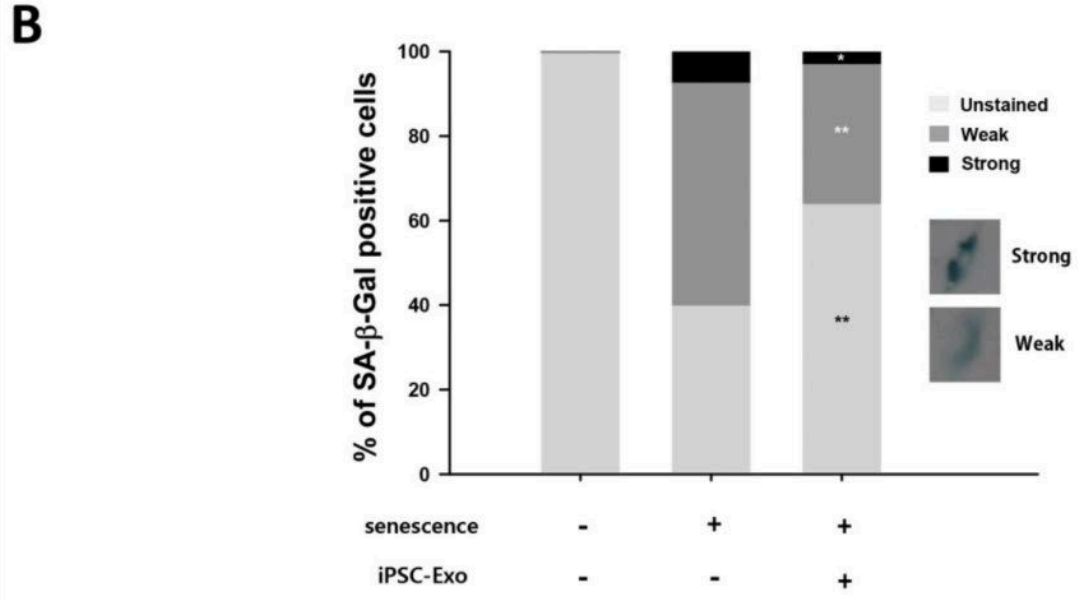
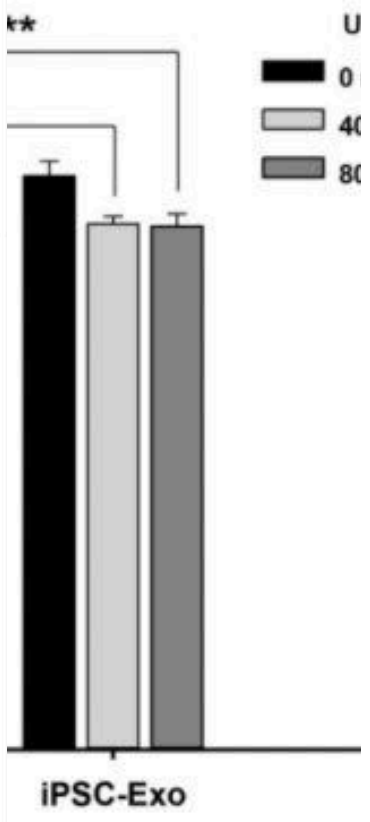
Exosomes









Oh, M., Lee, J., Kim, Y. J., Rhee, W. J., & Park, J. H. (2018). Exosomes Derived from Human Induced Pl
Aging of Skin Fibroblasts. *International Journal of Molecular Sciences*, *19*(6), 1715. https://doi.org/10.339
Y., Kim, C.-H., Kim, K. S., Hyun, S. H., Woo, H. G., . . . Kim, J.-R. (2019). Embryonic Stem Cell–Derived
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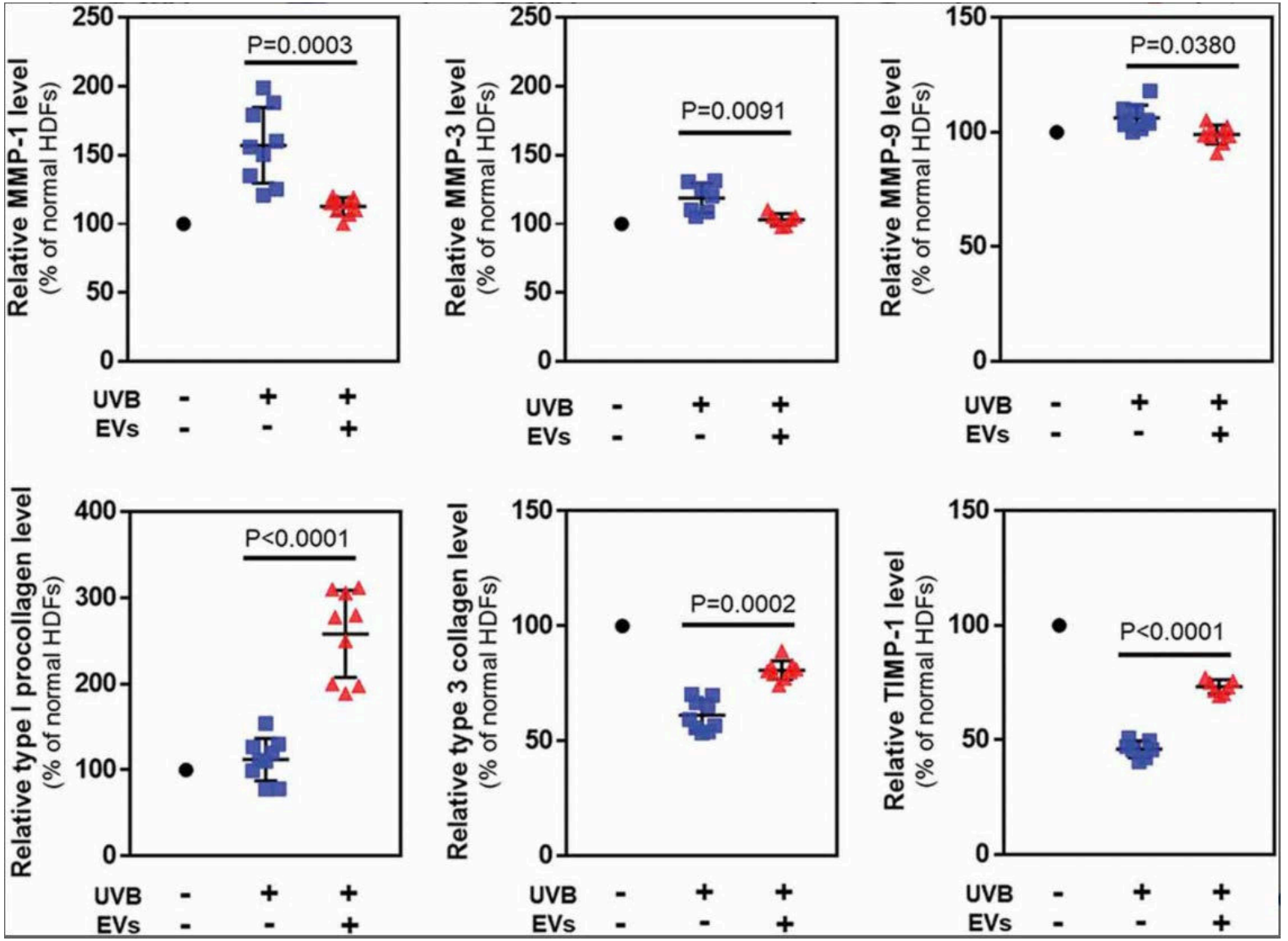
1367. doi:10.1093/gerona/gly208

Exosomes



Choi, J.S., Lee Cho, W., Choi, Y.J., Kim, J.D., Park, H.-A., Kim, S.Y., Park, J.H., Jo, D.-G. and Cho, Y.W. (2019), Functional recovery in photo-damaged human dermal fibroblasts by human adipose-derived stem cell extracellular vesicles. Journal of Extracellular Vesicles, 8: 1565885. https://doi.org/10.1080/20013078.2019.1565885

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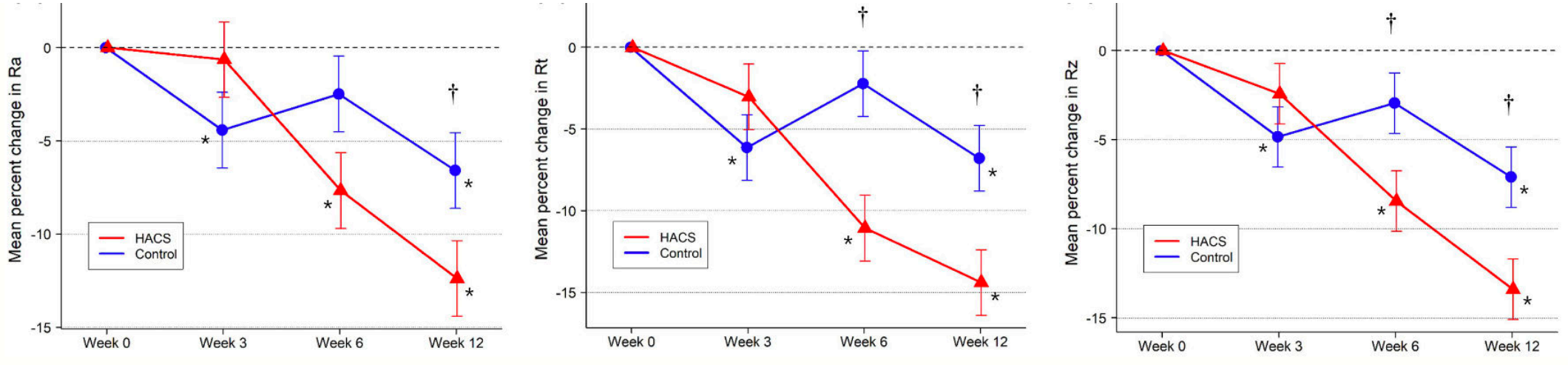
The First Human Clinical Study Using Adipose-Derived Stem Cell Exosomes for Skin Aging



IL-13, IL-6, IL-4, IL-1B, TNF-a, IFN-y[2-3]

MMPs[4]

Peroxiredoxins[1]

TGF-B[4]

Generate fibroblasts and collagen, increase remodeling and dermal thickening = reducing skin wrinkling[5]

1. Shin KO, Ha DH, Kim JO, et al.
2. Feng N, Jia Y, Huang X.
3. Xiong M, Zhang Q, Hu W, et al.
4. Heidari N, Abbasi-Kenarsari H, Namaki S, et al.
5. Liang JX, Liao X, Li SH, et al.

Park G-H, Kwon HH, Seok J, et al. Efficacy of combined treatment with human adipose tissue stem cell-derived exosome-containing solution and microneedling for facial skin aging: A 12-week prospective, randomized, split-face study. *J Cosmet Dermatol*. 2023;22:3418-3426. doi:10.1111/jocd.15872

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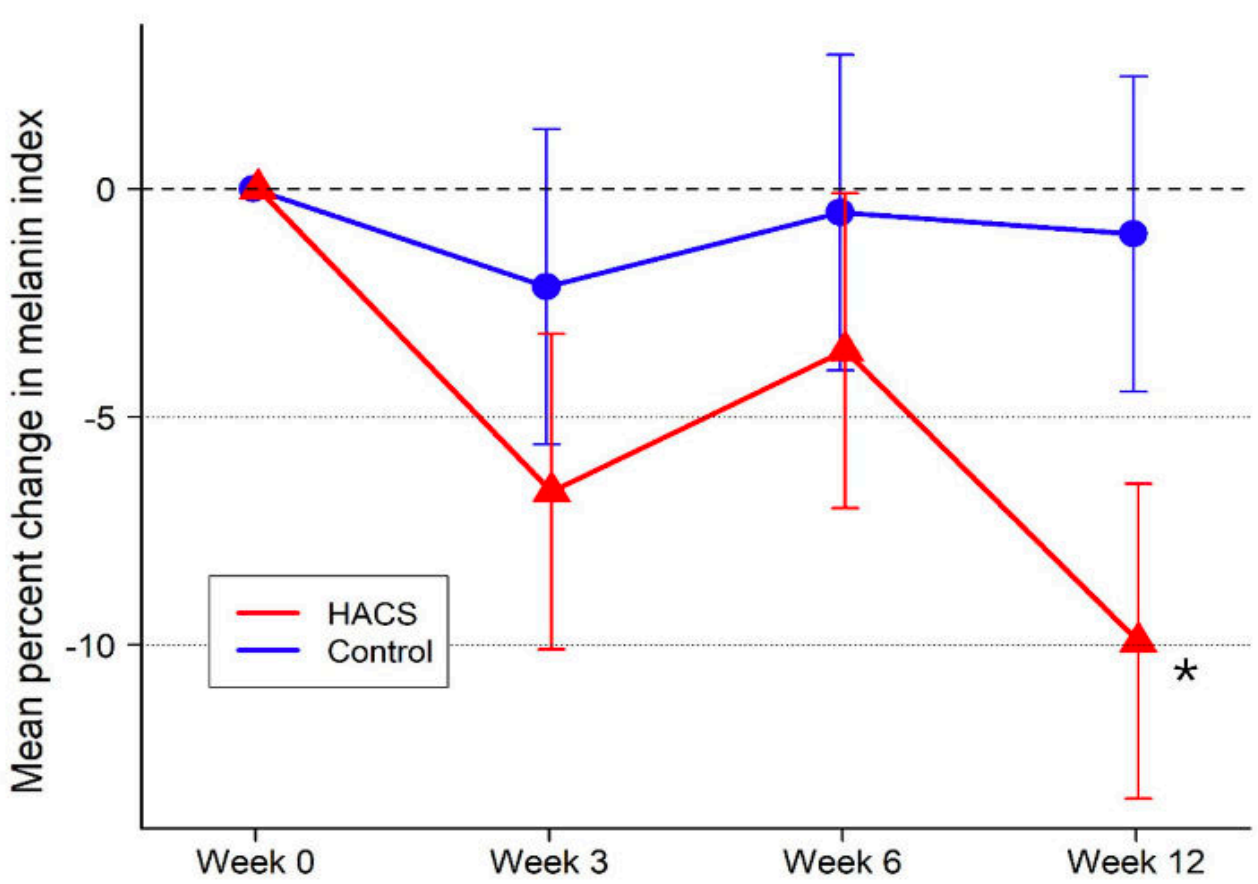
The First Human Clinical Study Using Adipose-Derived Stem Cell Exosomes for Skin Aging

- NRF2 pathway improves hyperpigmentation[1]
- Lentigines have decreased NRF2 expression[1]
- ASCEs upregulate NRF2[2]



1 Kerns ML, Miller RJ, Mazhar M, et al.
2. Shen K, Jia Y, Wang X, et al.

Park G-H, Kwon HH, Seok J, et al. Efficacy of combined treatment with human adipose tissue stem cell-derived exosome-containing solution and microneedling for facial skin aging: A 12-week prospective, randomized, split-face study. *J Cosmet Dermatol*. 2023;22:3418-3426. doi:10.1111/jocd.15872
Kuo Shen, Yanhui Jia, Xujie Wang, Jinxin Zhang, Kaituo Liu, Jing Wang, Weixia Cai, Jin Li, Shaohui Li, Ming Zhao, Yunchuan Wang, Dahai Hu, Exosomes from adipose-derived stem cells alleviate the inflammation and oxidative stress via regulating Nrf2/HO-1 axis in macrophages,Free Radical Biology and Medicine,Volume 165,2021, Pages 54-66, ISSN 0891-5849,

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Postbiotics

- What are they?
  - Substances derived after the micro-organism is no longer alive but may retain microbe-produced substances such as metabolites, proteins, or peptides [1]

1.Vinderola, G., Sanders, M. E., & Salminen, S. (2022). The Concept of Postbiotics. *Foods (Basel, Switzerland)*, *11*(8), 1077. https://doi.org/10.3390/foods11081077

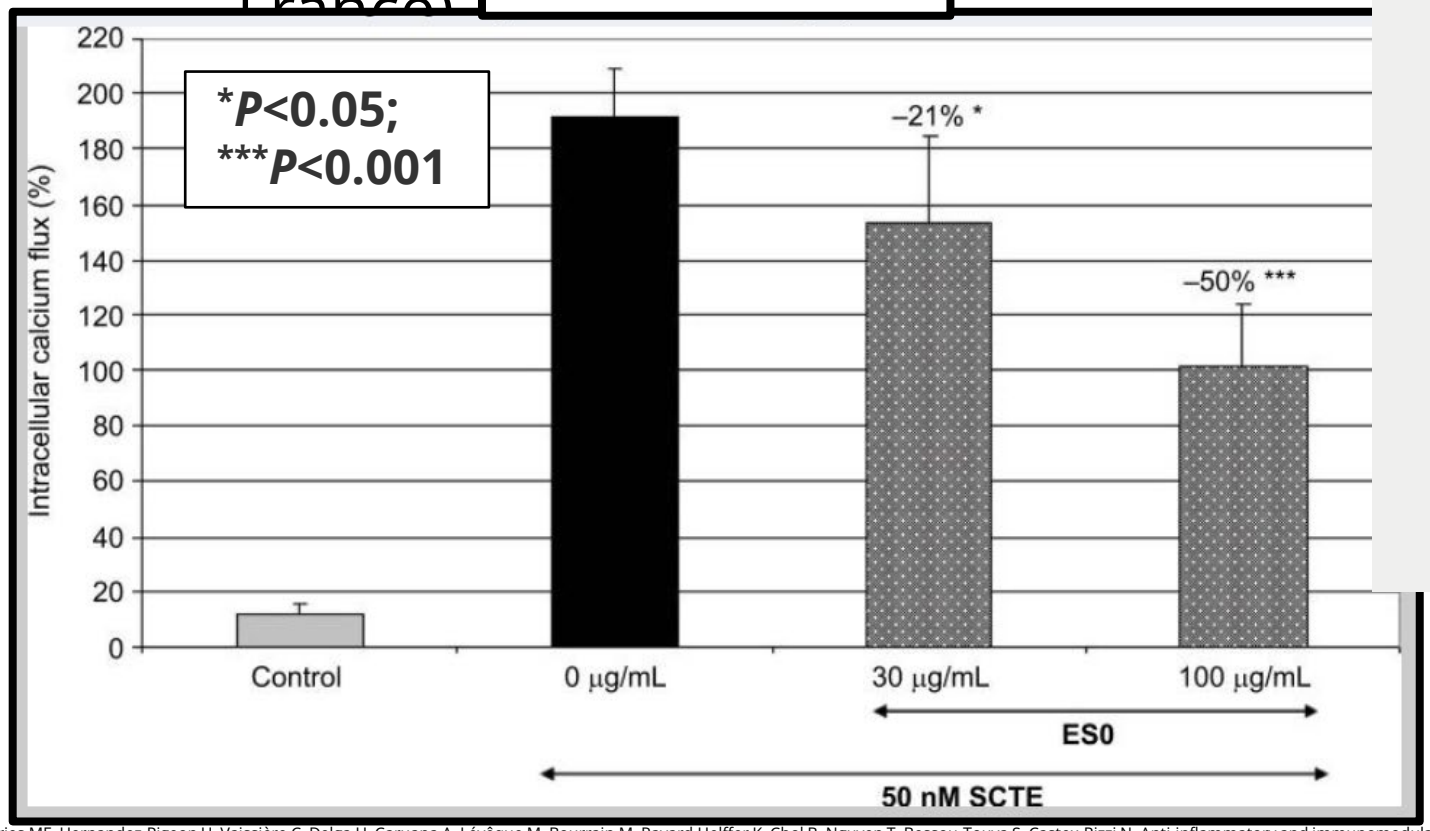
Postbiotics

- ***Aquaphilus dolomiae* derived postbiotic**

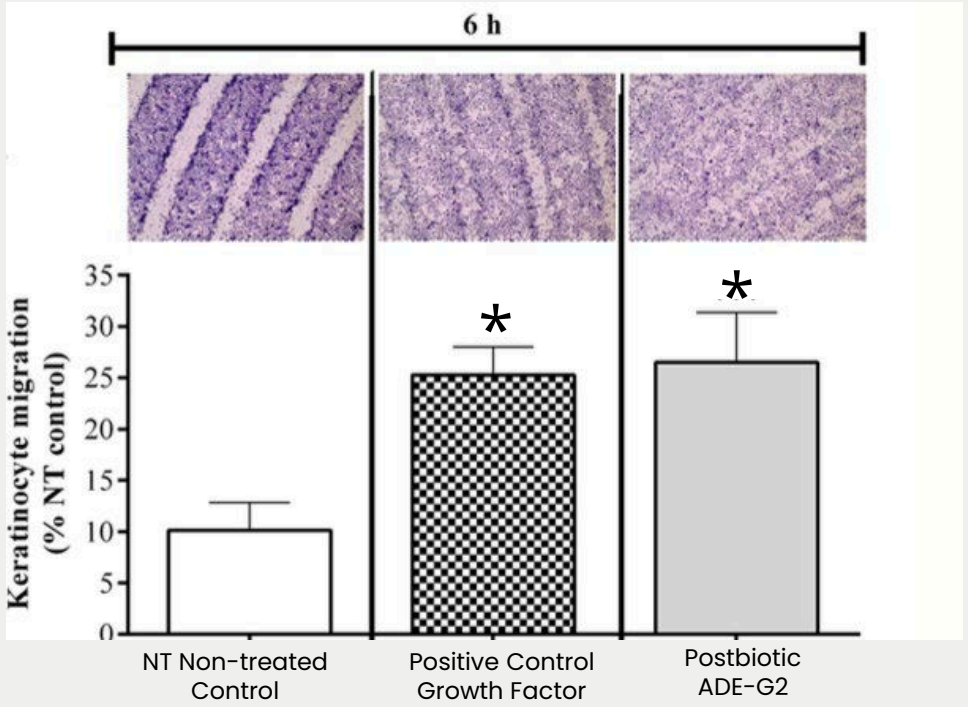
  gram- negative, non-spore-forming b

  - Can only survive in deep, pure waters
    France)

PAR-2 Inhibition



STATISTICALLY SIGNIFICANT KERATINOCYTE MIGRATION[1]



*Statistically significant at p<0.001

(1) Noizet, M., Bianchi, P., Galliano, MF., Caruana, A., Brandner, JM., Bessou-Touya, S., Duplan, H. (2020). Broad spectrum repairing properties of an extract of Aquaphilus Dolomia on in vitro and ex vivo models of injured sk Rodriguez LG, Wu X, Guan JL (2005). "Wound-healing assay". Cell Migration. Methods in Molecular Biology. Vol. 294. pp. 23–9.in. *JEADV*

Aries MF, Hernandez-Pigeon H, Vaissière C, Delga H, Caruana A, Lévêque M, Bourrain M, Ravard Helffer K, Chol B, Nguyen T, Bessou-Touya S, Castex-Rizzi N. Anti-inflammatory and immunomodulatory effects of Aquaphilus dolomiae extract on in vitro models. Clin Cosmet Investig Dermatol. 2016 Nov 10;9:421-434. doi: 10.2147/CCID.S113180. PMID: 27877060; PMCID: PMC5108493.

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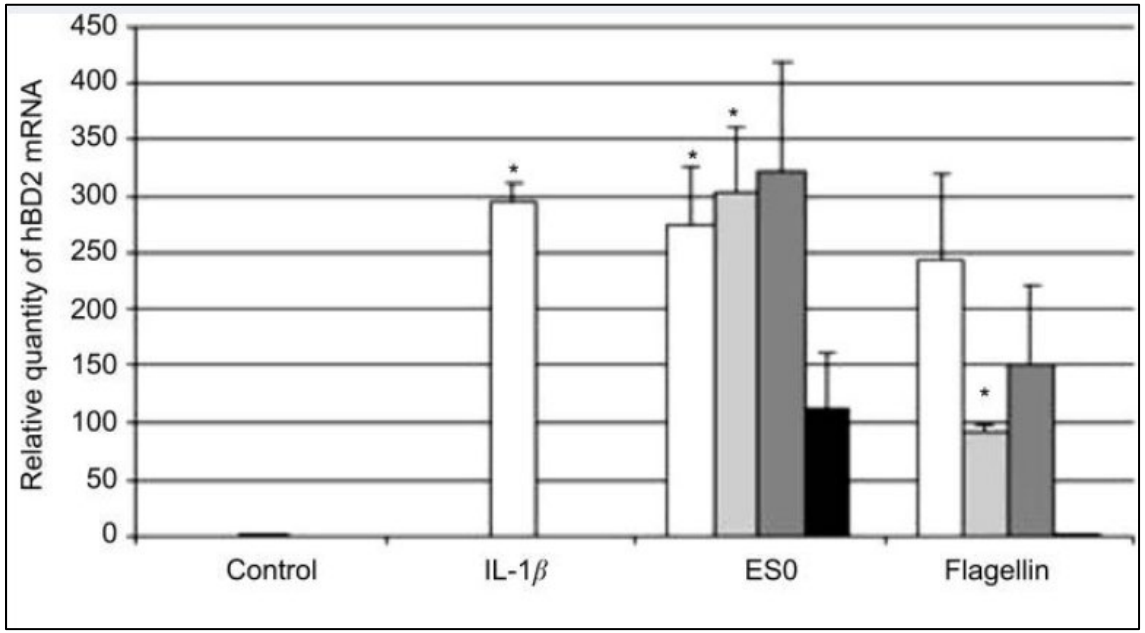
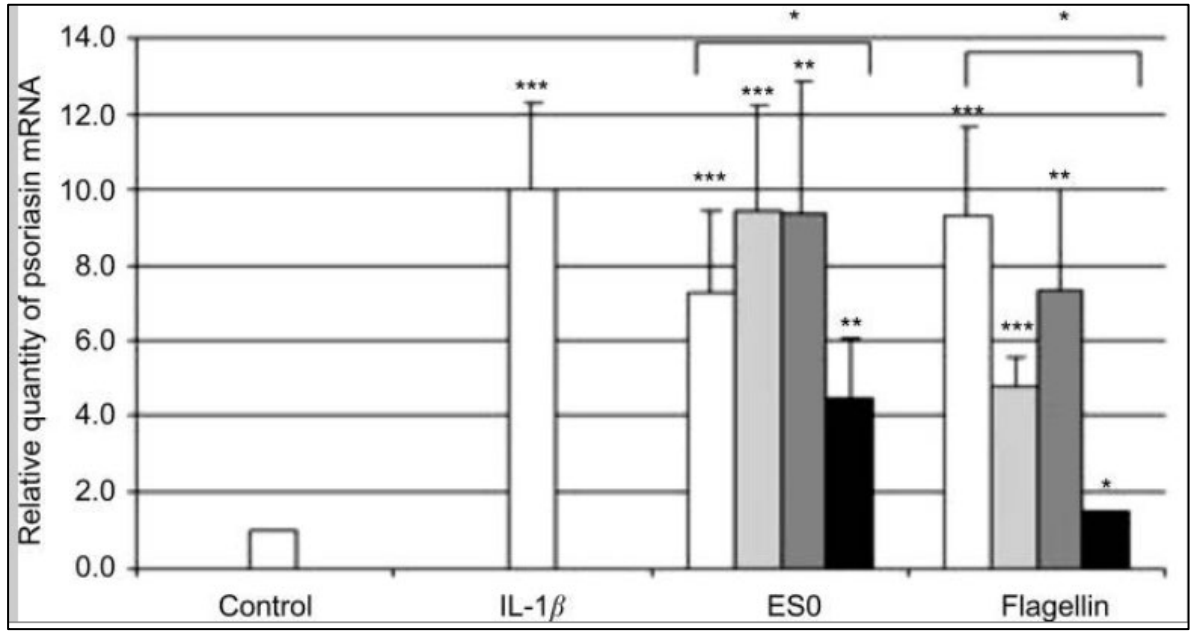
Postbiotics

Anti-inflammatory and immunomodulatory effects of *Aquaphilus dolomiae* extract on in vitro models

Induction of antimicrobial peptides expression



hBD-2 (*P*<0.05)



psoriasin (*P*<0.001)

Aries MF, Hernandez-Pigeon H, Vaissière C, Delga H, Caruana A, Lévêque M, Bourrain M, Ravard Helffer K, Chol B, Nguyen T, Bessou-Touya S, Castex-Rizzi N. Anti-inflammatory and immunomodulatory effects of Aquaphilus dolomiae extract on in vitro models. Clin Cosmet Investig Dermatol. 2016 Nov 10;9:421-434. doi: 10.2147/CCID.S113180. PMID: 27877060; PMCID: PMC5108493.

Evidence is Lacking

Table 4 Regenerative interventions and their evidence level

Intervention	Claimed effects	Level of evidence	Critique of existing evidence
Exosome therapy	Enhances skin regeneration and repair	None: No Level 1 or 2 evidence available	Relies on preliminary studies; lacks large-scale, randomized controlled trials. Data often derived from small case series or observational studies without control groups.
Polydeoxyribonucleotide (PDRN)	Promotes skin renewal and healing	None: No Level 1 or 2 evidence available	Clinical trials are few and lack rigour; methodologies and outcome measures are inconsistently reported, leading to inconclusive results.
Cellular senescence modulators	Reduces ageing effects by targeting senescent cells	None: No Level 1 or 2 evidence available	Predominantly theoretical and experimental data with minimal translation into clinical practice. Lack of direct clinical trials demonstrating efficacy and safety in humans.
Stem cell treatments	Restores tissue and improves skin quality	Level 1 or 2 evidence available	Existing studies often non-randomized, with variable protocols and outcomes. Concerns over cell sourcing, standardization, and long-term effects are poorly addressed.
Peptide therapies	Stimulates collagen production and skin elasticity	None: No Level 1 or 2 evidence available	Early research typically conducted in vitro or with small human samples; lack of comprehensive trials with robust statistical power and follow-up.
Photobiomodulation	Reduces wrinkles and enhances skin appearance	None: No Level 1 or 2 evidence available	Studies show mixed results, often with small sample sizes and short durations. Reproducibility and standardization of treatment parameters remain issues.
Bioactive peptides	Promotes healing and rejuvenates skin	None: No Level 1 or 2 evidence available	Initial studies show promise, but research often lacks depth in mechanism exploration and lacks follow-up data to confirm long-term efficacy and safety.

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Thank you!!

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