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[Int J Mol Sci.](#) 2019 Sep 24;20(19). pii: E4727. doi: 10.3390/ijms20194727.

In Vitro Evaluation of Novel Hybrid Cooperative Complexes in a Wound Healing Model: A Step Toward Improved Bioreparation.

[D'Agostino A¹](#), [Maritato R²](#), [La Gatta A³](#), [Fusco A⁴](#), [Reale S⁵](#), [Stellavato A⁶](#), [Pirozzi AVA⁷](#), [De Rosa M⁸](#), [Donnarumma G⁹](#), [Schiraldi C¹⁰](#).

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Abstract

The effectiveness of hyaluronic acid (HA), also called as hyaluronan, and its formulations on tissue regeneration and epidermal disease is well-documented. High-molecular-weight hyaluronan (HHA) is an efficient space filler that maintains hydration, serves as a substrate for proteoglycan assembly, and is involved in wound healing. Recently, an innovative hybrid cooperative complex (HCC) of high- and low-molecular-weight hyaluronan was developed that is effective in wound healing and bioremodeling. The HCC proposed here consisted of a new

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formulation and contained 1.6 ± 0.1 kDa HHA and 250 ± 7 kDa LHA (low molecular weight hyaluronic acid). We investigated the performance of this HCC in a novel in vitro HaCaT (immortalized human keratinocytes)/HDF (human dermal fibroblast) co-culture model to assess its ability to repair skin tissue lesions. Compared to linear HA samples, HCC reduced the biomarkers of inflammation (Transforming Growth Factor- β (TGF- β), Tumor Necrosis Factor receptor- α (TNF- α), interleukin-6 (IL-6), and interleukin-8 (IL-8)), and accelerated the healing process. These data were confirmed by the modulation of metalloproteases (MMPs) and elastin, and were compatible with a prospectively reduced risk of scar formation. We also examined the expression of defensin-2, an antimicrobial peptide, in the presence of hyaluronan, showing a higher expression in the HCC-treated samples and suggesting a potential increase in antibacterial and immunomodulatory functions. Based on these in vitro data, the presence of HCC in creams or dressings would be expected to enhance the resolution of inflammation and accelerate the skin wound healing process.

KEYWORDS:

biorepair; hyaluronic acid; inflammation; wound healing

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31554177

DOI:

[10.3390/ijms20194727](https://doi.org/10.3390/ijms20194727)

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Select item 31496779 ☐ 2. **Include**

[Clin Cosmet Investig Dermatol](#). 2019 Aug 13;12:563-572. doi: 10.2147/CCID.S209256. eCollection 2019.

Facial skin revitalization with CPM[®]-HA20G: an effective and safe early intervention treatment.

[Hertz-Kleptow D¹](#), [Hanschmann A²](#), [Hofmann M²](#), [Reuther T¹](#), [Kerscher M¹](#).

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University of Hamburg, Division of Biochemistry and Molecular Biology, Cosmetic Science, D-20146 Hamburg, Germany.

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Global Clinical Development, Merz Pharmaceuticals GmbH, Frankfurt, Germany.

Abstract

BACKGROUND:

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Select item 31185059 ☐ 3. **.Include**

[PLoS One](#). 2019 Jun 11;14(6):e0218287. doi: 10.1371/journal.pone.0218287. eCollection 2019.

Hyaluronan-based hydrogels as dermal fillers: The biophysical properties that translate into a "volumetric" effect.

[La Gatta A¹](#), [Salzillo R¹](#), [Catalano C¹](#), [D'Agostino A¹](#), [Pirozzi AVA¹](#), [De Rosa M²](#), [Schiraldi C¹](#).

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Abstract

Biophysical and biochemical data on hyaluronan (HA)-based dermal fillers strongly support their optimal use and design to meet specific requisites. Here, four commercially available (in Europe) HA "volumetric" fillers, among the most used in the clinical practice, have been characterized in vitro. Analyses revealed the highest amounts of water-soluble HA reported so far and provided hydrodynamic data for these soluble polymeric fractions. Volumetric gels exhibit a wide range of rigidity with most of them showing G' values around 200-300Pa. They greatly differ in cohesivity. 1mL of gel hydrates up to 2.4-3.2mL. The products completely solubilize due to Bovine Testicular Hyaluronidase (BTH)'s action, thus predicting in vivo complete resorption. For the first time, filler degradation due to reactive oxygen species (ROS) was studied by rheological measurements and a rank in stability was established. Studies using Human Dermal Fibroblasts (HDF) indicated a positive biological response to the HA networks. Further, gel capacity to prompt collagen I, elastin and aquaporin3 synthesis was demonstrated, thus suggesting a positive effect on skin elasticity and hydration, besides the physical volumetric action. The findings are the first wide assessment of features for the volumetric class of HA-fillers and include first data on their resistance to degradation by ROS and biological effects on HDF. The study represents a valuable contribution to the understanding of HA-fillers, useful to optimize their use and manufacture.

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Hyaluronic acid (HA) fillers are popular for the treatment of signs of facial skin aging.

OBJECTIVE:

The objective of this study was to confirm the performance and safety of a new cohesive polydensified matrix HA filler ([CPM®-HA20G, Belotero Revive®, lidocaine-free], Merz Pharmaceuticals GmbH, Frankfurt, Germany) for the treatment of early signs of facial skin aging by use of biophysical measurements as well as subject and investigator satisfaction.

METHODS:

Twenty-five healthy female subjects with signs of facial skin aging were enrolled in this open-label, rater-blinded, observational post-market clinical follow-up study, and received 20 micropuncture treatments of 50 µL CPM®-HA20G each into the lower cheek area at three injection visits 4 weeks apart. Objective biophysical assessments were conducted to demonstrate effects on viscoelastic properties of the skin, surface roughness, tone and radiance, and hydration, at baseline and at all follow-up visits up to 36 weeks.

RESULTS:

CPM®-HA20G significantly increased gross elasticity of the skin (at weeks 9 and 12), skin firmness (up to week 24), skin tone and radiance and skin hydration (all up to 36 weeks). Significant reduction of skin fatigue (up to 9 weeks), skin roughness (up to 28 weeks), and redness (up to 36 weeks) was also observed. Subjects and blinded investigator were highly satisfied with the treatment outcomes. The treating investigator reported a high level of satisfaction with the ease of injection and the clinical performance of the device. Moreover, data demonstrated a good safety profile of the device.

CONCLUSION:

CPM®-HA20G is considered to be an effective and safe HA injectable for skin revitalization in patients suffering from signs of skin aging and loss of skin elasticity. It seems to be a perfect early intervention approach in patients that do not need volumizing treatment and a combination approach in older patients with more pronounced aging.

KEYWORDS:

cohesive polydensified matrix; filler; hyaluronic acid; skin revitalization

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[PMC6559669](#)

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[Plast Reconstr Surg.](#) 2019 Jun;143(6):1277e-1289e. doi: 10.1097/PRS.0000000000005607.

Effective Rejuvenation with Hyaluronic Acid Fillers: Current Advanced Concepts.

[McKee D¹](#), [Remington K](#), [Swift A](#), [Lambros V](#), [Comstock J](#), [Lalonde D](#).

[Author information](#)

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Vancouver, British Columbia; Calgary, Alberta; Montreal, Quebec; and Saint John, New Brunswick, Canada; Newport Beach, Calif.; and Tucson, Ariz. From the University of British Columbia; Remington Laser; McGill University; private practice; Skin Spectrum; and Dalhousie University.

Abstract

LEARNING OBJECTIVES:

After studying this article, the participant should be able to: 1. Process several patient-specific factors before reaching an optimal treatment strategy with appreciation for facial balance. 2. Define the advantages and disadvantages of various hyaluronic acid preparations and delivery techniques, to achieve a specific goal. 3. Perform advanced facial rejuvenation techniques adapted to each facial zone, combining safety considerations. 4. Prevent and treat complications caused by inadvertent intraarterial injections of hyaluronic acid.

SUMMARY:

The growing sophistication and diversity of modern hyaluronic acid fillers combined with an increased understanding of various delivery techniques has allowed injectable filler rejuvenation to become a customizable instrument offering a variety of different ways to improve the face: volume restoration, contouring, balancing, and feature positioning/shaping-beyond simply fading skin creases. As more advanced applications for hyaluronic acid facial rejuvenation are incorporated into practice, an increased understanding of injection anatomy is important to optimize patient safety.

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Hyaluronic acid-cross-linked filler stimulates collagen type 1 and elastic fiber synthesis in skin through the TGF- β /Smad signaling pathway in a nude mouse model.

[Fan Y¹](#), [Choi TH²](#), [Chung JH³](#), [Jeon YK⁴](#), [Kim S⁵](#).

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Abstract

Compared to pure hyaluronic acid filler, cross-linked hyaluronic acid (HAc) exhibits superior biocompatibility and longevity as a dermal filler. We previously developed composite HAc-hydroxyapatite (HAp) fillers. Herein, we systematically compared the protein-level increase and gene expression between HAc-micro-HAp and HAc-nano-HAp in mice and determined the mechanisms underlying the biological responses to HAc and HAp. Five-week-old female BALB/c-nude mice were classified into five groups: normal skin, Radiesse, Restylane, HAc-nano-HAp, and HAc-micro-HAp. Fillers (200 μ l) were injected to evenly fill the back of mice. Skin biopsies were performed to investigate collagen and elastic fiber synthesis after filler injections. Western

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blot analysis, real-time polymerase chain reaction analysis, and immunohistochemistry were performed to investigate protein and gene expression changes. Organ (liver, lung, spleen, and kidney) toxicity of HAc-nano-HAp was determined by hematoxylin and eosin staining after 12 weeks. Protein and gene expression analyses indicated that, compared with pure fillers, HAc-nano-HAp and HAc-micro-HAp hydrogels preferentially promoted collagen and elastic fiber formation through the TGF- β pathway. The composite fillers also exhibited no evidence of organ toxicity. HAc-HAp filler might play an important role in collagen and elastic fiber regeneration. HAc filler stimulates collagen type 1 and elastic fiber synthesis through the TGF- β /Smad pathway. The role of HAc-HAp composite fillers in photoaging in animal models and their effects on skin, including elasticity and tensile strength, should be investigated.

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KEYWORDS:

Collagen type 1; Dermal filler; Elastic fiber; HAc-micro-HAp; HAc-nano-HAp; TGF- β /Smad pathway

PMID:

31036501

DOI:

[10.1016/j.bjps.2019.03.032](https://doi.org/10.1016/j.bjps.2019.03.032)

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[Plast Reconstr Surg.](#) 2019 Apr;143(4):707e-720e. doi: 10.1097/PRS.0000000000005429.

Rheologic and Physicochemical Properties Used to Differentiate Injectable Hyaluronic Acid Filler Products.

[Fagien S](#)¹, [Bertucci V](#), [von Grote E](#), [Mashburn JH](#).

Author information

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Boca Raton, Fla.; Toronto and Woodbridge, Ontario, Canada; and Fort Worth, Texas From private practice; the Division of Dermatology, University of Toronto and private practice; and Galderma Laboratories, L.P.

Abstract

BACKGROUND:

Injectable hyaluronic acid fillers are routinely used for correction of soft-tissue volume loss and facial rejuvenation. Product differentiation has primarily been based on the rheologic parameter known as elastic modulus (G'), although other physicochemical properties are being explored to characterize potential product performance. As clinical data regarding product

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[AAPS PharmSciTech](#), 2019 Mar 25;20(4):152. doi: 10.1208/s12249-019-1355-6.

Optimization and Evaluation of Beclomethasone Dipropionate Micelles Incorporated into Biocompatible Hydrogel Using a Sub-Chronic Dermatitis Animal Model.

[Assem M¹](#), [Khowessah OM²](#), [Ghorab D²](#).

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Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Cairo University, Kasr El Aini Street, Cairo, 11562, Egypt.

Abstract

The current study is concerned with the development and characterization of mixed micelles intended for the dermal delivery of beclomethasone dipropionate, which is a topical corticosteroid used in the management of atopic dermatitis. Mixed micelles were prepared using thin-film hydration technique, employing different concentrations of pluronic L121 with either poloxamer P84 or pluronic F127 with different surfactant mixture-to-drug ratios. The prepared formulae were characterized concerning entrapment efficiency, particle size, and zeta potential. Two formulae were chosen for ex vivo skin deposition studies: one formulated using pluronic L121/poloxamer P84 mixture while the other using pluronic L121/pluronic F127 mixture. The optimum formula with the highest dermal deposition was subjected to morphological examination and was formulated as hydroxypropyl methylcellulose hydrogel. The hydrogel was evaluated regarding viscosity and was subjected to ex vivo deposition study in comparison with the commercially available cream Beclozone®. In vivo histopathological study was conducted for both the hydrogel and Beclozone® in order to evaluate their healing efficiency. In vivo histopathological study results showed that the prepared hydrogel successfully treated sub-chronic dermatitis in an animal model within a shorter period of time compared to Beclozone®, resulting in better patient compliance and fewer side effects.

KEYWORDS:

beclomethasone dipropionate; dermal; hydrogel; in vivo histopathology; mixed micelles

PMID:

30911861

DOI:

[10.1208/s12249-019-1355-6](#)

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performance are lacking, the practical experience of injectors provides a valuable bridge in the knowledge gap between product rheologic data and product use.

METHODS:

Rheologic and physicochemical measurements (swelling factor and cohesion) were collected for 18 products. To observe the impact of G' and hyaluronic acid concentration on swelling factor and cohesion, proportional relationships were evaluated. Contributing authors were queried regarding their G'-based selection of products when considering skin quality, degree of correction, injection depth, and anatomical location.

RESULTS:

Relationships were observable between G' and swelling factor and G' and cohesion only when limited to products manufactured by the same crosslinking technology and the same concentration. No relationship between isolated hyaluronic acid concentration and swelling factor or cohesion was apparent. Although rheological parameters and the assumptions of ex vivo data translating to in vivo performance are oftentimes not completely aligned, in the clinical experience of the authors, in general, higher G' products are better suited for thicker skin and deeper injection planes, whereas lower G' products are better for more superficial planes, although exceptions to these trends are also made based on technical experience.

CONCLUSIONS:

While rheologic and physicochemical characteristics can vary widely between products and the methods and measurements of these parameters are often difficult to correlate, G' represents a useful and consistent parameter for product differentiation. Understanding how to select products based on G' is valuable knowledge for customizing injection plans and contributes to an optimal aesthetic outcome.

PMID:

30921116

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[10.1097/PRS.00000000000005429](https://doi.org/10.1097/PRS.00000000000005429)

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Select item 30681787 ☐ 8. **.Include**

[J Drugs Dermatol](#). 2019 Jan 1;18(1):9-16.

Oral Collagen Supplementation: A Systematic Review of Dermatological Applications

[Choi FD](#), [Sung CT](#), [Juhasz ML](#), [Mesinkovsk NA](#).

Abstract

IMPORTANCE:

The use of nutraceuticals such as collagen for skincare has been rising, but regulations are lacking on quality, absorption, and efficacy. To address this knowledge gap, clinical studies regarding the potential effects of collagen-based dietary supplements on skin are being completed.

OBJECTIVE:

To review the literature and assess available randomized-controlled trials using collagen supplementation for treatment efficacy regarding skin quality, anti-aging benefits, and potential application in medical dermatology.

EVIDENCE REVIEW:

A literature search was conducted with PubMed using search criteria (collagen) AND (supplement OR food OR nutrition). No lower limit on the year of publication was set. Inclusion criteria were: randomized, placebo-controlled trials using collagen supplementation in human subjects related to dermatology and written in English.

FINDINGS:

Eleven studies with a total of 805 patients were included for review. Eight studies used collagen hydrolysate, 2.5g/d to 10g/d, for 8 to 24 weeks, for the treatment of pressure ulcers, xerosis, skin aging, and cellulite. Two studies used collagen tripeptide, 3g/d for 4 to 12 weeks, with notable improvement in skin elasticity and hydration. Lastly, one study using collagen dipeptide suggested anti-aging efficacy is proportionate to collagen dipeptide content.

CONCLUSIONS AND RELEVANCE:

Preliminary results are promising for the short and long-term use of oral collagen supplements for wound healing and skin aging. Oral collagen supplements also increase skin elasticity, hydration, and dermal collagen density. Collagen supplementation is generally safe with no reported adverse events. Further studies are needed to elucidate medical use in skin barrier diseases such as atopic dermatitis and to determine optimal dosing regimens. *J Drugs Dermatol*. 2019;18(1):9-16.

PMID:

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Select item 30558672 ☐ 9. Not relevant

[Trials](#). 2018 Dec 17;19(1):689. doi: 10.1186/s13063-018-3035-3.

A randomized controlled trial testing a hyaluronic acid spacer injection for skin toxicity reduction of brachytherapy accelerated partial breast irradiation (APBI): a study protocol.

[Struik GM](#)^{1,2}, [Godart J](#)³, [Verduijn GM](#)³, [Kolkman-Deurloo IK](#)³, [de Vries KC](#)³, [de Boer R](#)³, [Koppert LB](#)⁴, [Birnie E](#)^{5,6}, [Ghandi A](#)⁷, [Klem TM](#)⁸, [Pignol JP](#)^{3,9}.

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Department of Radiation Oncology, Dalhousie University, 5820 University Avenue, Halifax, NS, B3H1V7, Canada.

Abstract

BACKGROUND:

Accelerated partial breast irradiation (APBI) is a treatment option for selected early stage breast cancer patients. Some APBI techniques lead to skin toxicity with the skin dose as main risk factor. We hypothesize that a spacer injected between the skin and target volume reduces the skin dose and subsequent toxicity in permanent breast seed implant (PBSI) patients.

METHODS:

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In this parallel-group, single-center, randomized controlled trial, the effect of a subcutaneous spacer injection on skin toxicity among patients treated with PBSI is tested. Eligibility for participation is derived from international guidelines for suitable patients for partial breast radiotherapy, e.g. women aged ≥ 50 years with a histologically proven non-lobular breast carcinoma and/or ductal carcinoma in situ (DCIS), tumor size ≤ 3 cm, node-negative, and PBSI technically feasible. Among exclusion criteria are neoadjuvant chemotherapy, lymphovascular invasion, and allergy for hyaluronic acid. For the patients allocated to receive spacer, after the PBSI procedure, 4-10 cc of biodegradable hyaluronic acid (Barrigel[®], Palette Life Sciences, Santa Barbara, CA, USA or Restylane SubQ[®], Galderma Benelux, Breda, the Netherlands) is injected directly under the skin using ultrasound guidance to create an extra 0.5-1 cm space between the treatment volume and the skin. The primary outcome is the rate of telangiectasia at two years, blindly assessed using Bentzen's 4-point scale. Secondary outcomes include: local recurrence; disease-free and overall survival rates; adverse events (pain, redness, skin/subcutaneous induration, radiation dermatitis, pigmentation, surgical site infection); skin dose; cosmetic and functional results; and health-related quality of life. A Fisher's exact test will be used to test differences between groups on the primary outcome. Previous studies found 22.4% telangiectasia at two years. We expect the use of a spacer could reduce the occurrence of telangiectasia to 7.7%. A sample size of 230 patients will allow for a 10% lost to follow-up rate.

DISCUSSION:

In this study, the effect of a subcutaneous spacer injection on the skin dose, late skin toxicity, and cosmetic outcome is tested in patients treated with PBSI in the setting of breast-conserving therapy. Our results will be relevant for most forms of breast brachytherapy as well as robotic radiosurgery, as skin spacers could protect the skin with these other techniques.

TRIAL REGISTRATION:

Netherlands Trial Register, NTR6549 . Registered on 27 June 2017.

KEYWORDS:

Brachytherapy; Breast neoplasms; Hyaluronic acid; Partial breast irradiation; Permanent breast seeds implant; Skin toxicity reduction; Spacer; Telangiectasia

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30558672

PMCID:

[PMC6298013](#)

DOI:

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Select item 30293400 ☐ 10. Not relevant-off indication

[Minerva Ginecol.](#), 2018 Oct;70(5):629-634. doi: 10.23736/S0026-4784.18.04254-5.

Postpartum stretchmarks: repairing activity of an oral Centella asiatica supplementation (Centellicum®).

[Hu S](#)^{1,2}, [Belcaro G](#)^{3,2}, [Hosoi M](#)^{1,2}, [Feraqalli B](#)^{1,2}, [Luzzi R](#)^{1,2}, [Dugall M](#)^{1,2}.

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Abstract

BACKGROUND:

This registry study evaluates the effects of oral Centellicum®, a new preparation of Centella asiatica (CA) on cutaneous stretchmarks (SMs) on the lower abdominal wall in comparison with the topical treatment with a specific antistretch cream. This cream is used for pregnancy SMs. The aim of the management was to give back to the structurally damaged skin areas (apparent as SMs) a normal elasticity and resistance and improving the local microcirculation.

METHODS:

We selected 78 healthy women with SMs at least 6 months postpartum available to follow the registry plan. The subjects were evaluated in three treatment groups: Clarins, stretch mark minimizer, the hydrating control cream and Centellicum® 3X225 mg/day for 6 weeks.

RESULTS:

The three registry groups of otherwise healthy subjects were comparable at inclusion and 6 weeks: 25 women used the SMs cream 1 (mean age 34.4;3.2); 28 control women (age 35.2;2) used the hydrating control cream. The third group (25 women; mean age 35.3;1.5) used the hydrating control cream and oral Centellicum® as a supplementary management. Standard management was used in all groups. As for the safety issue, no allergy, no side effects and no tolerability problems were observed. The compliance was very good and there were no drop outs. No other drug or treatment was used during the registry period. Skin thickness (ultrasound,

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measuring at the edge of at the largest visible stretchmark) increased significantly more at 6 weeks with Centellicum® in comparison with both controls ($P<0.05$). Skin thickness at the center of the SM (skin was less dense at this level) was also increased more with the supplement in comparison with the other managements ($P<0.05$). The grey scale median improved more (increased) with Centellicum at 6 weeks ($P<0.05$). The skin included more collagen components and become whiter or denser at ultrasound. Skin perfusion measured by laser Doppler showed a higher improvement with Centellicum® ($P<0.05$). Skin temperature, considered a function of nutritional and thermoregulatory dermal perfusion, improved more with the supplement ($P<0.05$). Elasticity (measured by elastosonography) was improved more with the supplement ($P<0.05$). The subjective evaluation with an analogue score resulted better (the SMs were less visible and the score decreased) with Centellicum® ($P<0.05$). The number of visible SMs was decreased more with Centellicum® ($P<0.05$).

CONCLUSIONS:

Oral supplementation with Centellicum® appears to improve SMs in a relatively short period of time. Larger studies are needed to evaluate the protective and repairing potentials of CA.

PMID:

30293400

DOI:

[10.23736/S0026-4784.18.04254-5](https://doi.org/10.23736/S0026-4784.18.04254-5)

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Select item 30287361 ☐ 11. **.Include**

[Int J Biol Macromol.](#) 2018 Dec;120(Pt B):1682-1695. doi: 10.1016/j.ijbiomac.2018.09.188. Epub 2018 Oct 1.

Hyaluronic acid, a promising skin rejuvenating biomedicine: A review of recent updates and pre-clinical and clinical investigations on cosmetic and nutricosmetic effects.

[Bukhari SNA](#)¹, [Roswandi NL](#)², [Waqas M](#)³, [Habib H](#)³, [Hussain F](#)⁴, [Khan S](#)⁵, [Sohail M](#)⁶, [Ramli NA](#)², [Thu HE](#)⁷, [Hussain Z](#)⁸.

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Electronic address: zahid3224@puncakalam.uitm.edu.my.

Abstract

Hyaluronic acid (HA) plays multifaceted role in regulating the various biological processes such as skin repairment, diagnosis of cancer, wound healing, tissue regeneration, anti-inflammatory, and immunomodulation. Owing to its remarkable biomedical and tissue regeneration potential, HA has been numerously employed as one of the imperative components of the cosmetic and nutricosmetic products. The present review aims to summarize and critically appraise recent developments and clinical investigations on cosmetic and nutricosmetic efficacy of HA for skin rejuvenation. A thorough analysis of the literature revealed that HA based formulations (i.e., gels, creams, intra-dermal filler injections, dermal fillers, facial fillers, autologous fat gels, lotion, serum, and implants, etc.) exhibit remarkable anti-wrinkle, anti-nasolabial fold, anti-aging, space-filling, and face rejuvenating properties. This has been achieved via soft tissue augmentation, improved skin hydration, collagen and elastin stimulation, and face volume restoration. HA, alone or in combination with lidocaine and other co-agents, showed promising efficacy in skin tightness and elasticity, face rejuvenation, improving aesthetic scores, reducing the wrinkle scars, longevity, and tear trough rejuvenation. Our critical analysis evidenced that application/administration of HA exhibits outstanding nutricosmetic efficacy and thus is warranted to be used as a prime component of cosmetic products.

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KEYWORDS:

Anti-aging, nasolabial folds, dermal filler; Anti-wrinkle; Face rejuvenation; Hyaluronic acid; Nutricosmetic

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Select item 30237745 ☐ 12. **Not relevant- in-vitro study**

[Med Devices \(Auckl\)](#). 2018 Sep 7;11:313-320. doi: 10.2147/MDER.S167078. eCollection 2018.

In vitro study of RRS® Silisorg CE Class III medical device composed of silanol: effect on human skin fibroblasts and its clinical use.

[Deglesne PA¹](#), [Arroyo R¹](#), [Fidalgo López J¹](#), [Sepúlveda L¹](#), [Ranneva E¹](#), [Deprez P¹](#).

Author information

1

Research and Development, Skin Tech Pharma Group, Castelló d'Empúries, Spain, phd@estetik.com.

Abstract

INTRODUCTION:

Silanol (organic silicon) has been used for decades in the treatment of skin photoaging as it stabilizes and maintains skin structures through hydrogen bonding electrostatic interaction with extracellular matrix (ECM) proteins or glycosaminoglycans. Organic silicon-based products are often presented as silanol derivatives which are currently associated to other structural molecules such as orthohydroxybenzoate, carboxymethyl theophylline alginate, ascorbate, acetyltyrosine, sodium lactate or mannuronate. Consequently, organic silicon formulations may differ substantially between the medical devices available on the market, which may result in additional effect on the skin. Therefore, there is a real need for a better characterization of the products in terms of their action on human skin and in vitro skin model.

MATERIALS AND METHODS:

In this in vitro study, the effect of RRS® Silisorg was analyzed. RRS® Silisorg is a dermal implant (CE Class III medical device) containing monomethylsilanol mannuronate associated to an antioxidant resveratrol. Skin fibroblast viability and capacity to induce the production of key ECM genes were evaluated in the presence of different concentrations of RRS® Silisorg. The key ECM genes selected were collagen type I, elastin and hyaluronan synthase type 2 (HAS2), which is the cellular enzyme responsible for high-molecular weight hyaluronic acid (HA) production. Viability was evaluated through 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay and expression was quantified by quantitative polymerase chain reaction.

RESULTS:

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RRS® Silisorg increased fibroblast gene expression of HAS2 in the first 24 hours, 25 times in the presence of 1 mg/mL of solution, followed by a collagen type I gene expression (4.7 times) and elastin expression (2.5 times) increase after 48 hours.

CONCLUSION:

These results demonstrate that the silanol-based medical device RRS® Silisorg sustains HA, collagen and elastin production in human skin fibroblasts in vitro.

KEYWORDS:

collagen; dermal implant; hyaluronic acid; mesotherapy; organic silicon; photoaging

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Select item 30227196 ☐ 13. Not relevant

[J Am Acad Dermatol](#). 2019 Apr;80(4):e73-e74. doi: 10.1016/j.jaad.2018.09.003. Epub 2018 Sep 15.

Treatment of purpura with Nd:YAG laser in skin types IV-VI.

Saade DS¹, Vashi NA².

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Department of Dermatology, American University of Beirut, Beirut, Lebanon.

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Department of Dermatology, Boston University School of Medicine, Boston, Massachusetts. Electronic address: nvashi@bu.edu.

KEYWORDS:

Nd:YAG; ecchymosis; purpura; resolution; skin type IV-VI

PMID:

30227196

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Select item 30192908 ☐ 14. **Not relevant**

[Aesthet Surg J](#), 2019 Sep 13;39(10):1096-1106. doi: 10.1093/asj/sjy227.

Detailed Sonographic Anatomy of Dorsal Hand Augmentation With Hyaluronic Acid and Calcium Hydroxyapatite Fillers.

[Kim JS¹](#).

[Author information](#)

1

Plastic surgeon in private practice in Seoul, Korea.

Abstract

BACKGROUND:

Volume restoration using filler in the dorsum of the hand is a simple and effective procedure to improve wrinkles and hide veins and tendons. Currently, calcium-hydroxyapatite (CaHA) filler is the only FDA-accepted material to use in the hand dorsum. However, it is not easy to inject due to swelling and redness. In addition, hand anatomy through sonography is wrongly described in Plastic and Reconstructive Surgery® Journal. Through incorrect marking in sonographic hand anatomy, physicians will conduct erroneous procedures and surgeries.

OBJECTIVES:

CaHA filler and hyaluronic acid (HA) filler were both injected into the hand to compare intra-individually the effect of each filler. Through this study, the author introduced detailed and refined sonographic anatomy. Overall, the author identified the correct injection method and depth.

METHODS:

In this prospective, intra-individual, comparative study, patients were injected 1 cc of CaHA filler to the left hand and 3 cc (36 mg) of microphasic hyaluronic acid to the right. Outcomes were assessed by Merz hand grading scale, skin bio-parameters, dermoscopic finding, and Global Aesthetic Improvement Scale (GAIS) with follow-up at 3, 6, 9, and 12 months.

RESULTS:

The average GAIS score improved in both hands and generally maintained over the course of the study. There was significantly more bruising and swelling in the CaHA-injected hands compared with the HA-injected hands. The skin roughness and appearance improved in both sets of hands on dermascope. The average Trans-Epidermal-Water-Loss decreased and the average Stratum

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Corneum Hydration increased in HA-injected hands. The biopsy study showed that the HA particles lasted for 9 months.

CONCLUSIONS:

The author reestablished sonographic anatomy. Veins and tendons became less apparent after injections.

LEVEL OF EVIDENCE: 2:

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30192908

DOI:

[10.1093/asi/sjv227](https://doi.org/10.1093/asi/sjv227)

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Select item 30178790 ☐ 15. **Not relevant. Non-clinical**

[Food Funct.](#) 2018 Sep 19;9(9):4936-4947. doi: 10.1039/c8fo00843d.

Clove attenuates UVB-induced photodamage and repairs skin barrier function in hairless mice.

[Hwang E¹](#), [Lin P.](#), [Ngo HTT.](#), [Yi TH.](#)

Author information

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College of Life Science, Kyung Hee University, 1732, Deogyong-daero, Giheung-gu, Yongin-si, Gyeonggi-do 17104, Republic of Korea. drhoo@khu.ac.kr.

Abstract

Syzygium aromaticum L., commonly named clove, is widely used in the food industry due to its antioxidant and antibacterial capabilities. However, little information is available regarding its role in resisting skin photoaging. This study investigated 50% ethanol extract of *Syzygium aromaticum* L. (SA) and eugenol (EO) for anti-aging effects in UVB-irradiated normal human dermal fibroblasts (NHDFs) and hairless mice. In vitro, SA and EO suppressed matrix metalloproteinase-1, 3 (MMP-1 and MMP-3) secretion as well as the activator protein 1 (AP-1) phosphorylation. SA and EO also activated nuclear erythroid 2-related factor/antioxidant-response element (Nrf2/ARE) signaling which improves the antioxidant activity and inhibited nuclear factor-κB (NF-κB) and interleukin-6 (IL-6) expression, pro-inflammatory factors. Furthermore, SA and EO suppressed the nuclear factor of activated T cells c1 (NFATc1) which is a known activator of MMPs,

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cooperator transforming growth factor beta (TGF- β) and NF- κ B in Ca²⁺/calcineurin-regulated transcription. In vivo, SA significantly improved the levels of procollagen type I and elastin through TGF/Smad signaling. The histopathological studies found that SA reduced wrinkles. SA also increased filament aggregating protein (filaggrin), which repairs the skin barrier function and improved the skin's hydration. Altogether, SA effectively ameliorated UVB-induced photoaging. It is expected to become a promising natural product.

PMID:

30178790

DOI:

[10.1039/c8fo00843d](https://doi.org/10.1039/c8fo00843d)

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Select item 30039861 ☐ 16. **Not relevant**

[Int J Dermatol](#). 2019 Feb;58(2):131-143. doi: 10.1111/ijd.14153. Epub 2018 Jul 24.

Characteristics and management of Asian skin.

[Chan IL¹](#), [Cohen S¹](#), [da Cunha MG¹](#), [Maluf LC¹](#).

Author information

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Faculdade de Medicina do ABC, Santo André, São Paulo, Brazil.

Abstract

Color differences in skin are due to the amount and distribution of epidermal melanin. The number of melanocytes is almost the same in all skin types, but higher phototypes exhibit more melanocytes, which produce more melanin and melanosomes that are individually distributed throughout the keratinocyte layers. This characteristic ensures a natural, significant photoprotection in darker skins. Asians are a population with various skin phototypes, ranging from type III to IV Fitzpatrick's classification in Chinese and Japanese to type IV and V in Indian and Pakistani people. Asian skin tends to present postinflammatory hyperpigmentation, melasma, lentigines and freckles, nevus of Ota, and Hori nevus. The main skin diseases reported in Asians are acne, atopic dermatitis, and viral infections. Wrinkles and skin thickness, early signs of aging in Caucasians, are less evident in Asian skin. However, pigmentary changes occur earlier. Additionally, this ethnic population is increasing worldwide. The aim of this study is to show the importance of studying the characteristics of Asian skin for the better management of skin diseases in this population, which are being increasingly observed in doctor's offices.

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Based on a broad review of the medical literature, we report the characteristics of Asian skin, as well as some dyschromias and common skin disorders in this ethnic group. The objective of the article is to study the characteristics of Asian skin and differences in relation to other ethnic groups to achieve improved clinical and cosmetic management of diseases and other skin disorders. This article will discuss the concept of beauty in different ethnic groups, treatments with lasers and other light sources, and cosmiatric treatments in Asian skin. An extensive review of the literature was performed using the databases Scielo and Bireme, from Medline and Lilacs sources, over the last 50 years. The keywords used were as follows: Asian skin, ethnic skin, melanin. Due to the peculiarities of each ethnic group, this article demonstrates the importance of studying the characteristics of Asian skin to elucidate improved cosmiatric approaches for these patients.

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PMID:

30039861

DOI:

[10.1111/ijd.14153](https://doi.org/10.1111/ijd.14153)

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Select item 29897516 ☐ 17. **Not relevant**

[Aesthet Surg J](#). 2018 Apr 6;38(suppl_1):S8-S12. doi: 10.1093/asj/sjy011.

Physiochemical Characteristics of Calcium Hydroxylapatite (CaHA).

[Lorenc ZP](#)¹, [Bass LM](#)², [Fitzgerald R](#)³, [Goldberg DJ](#)⁴, [Graivier MH](#)⁵.

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Department of Dermatology, Icahn School of Medicine at Mt. Sinai, New York, NY.

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private practice in Roswell, GA.

Abstract

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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The clinical performance of fillers in soft tissue augmentation depends upon their physiochemical properties, anatomical areas injected, interaction with the recipient, and the skill and experience of the physician. Scientific measures of filler properties facilitate appropriate selection of treatments for optimal treatment outcomes, and inform adjustments to treatments that improve patient safety and aesthetic outcomes. The rheological properties of calcium hydroxylapatite (CaHA), elastic modulus (G') and viscosity, coupled with its capacity to offer both immediate results and continued stimulation of collagen type I deposition, support its distinction as an ideal treatment for the volume loss characteristic of aging. Furthermore, the comparatively higher G' of CaHA offers a physiochemical basis for the clinical performance observed by the authors, especially in regions such as the temple and chin, where the force exerted by CaHA against bone permits expansion of overlying tissue, permitting it to behave as a liquid implant.

PMID:

29897516

DOI:

[10.1093/asi/siv011](https://doi.org/10.1093/asi/siv011)

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Select item 29873844 ☐ 18. **Not relevant-technique paper**

[Skin Res Technol](#). 2019 Jan;25(1):54-59. doi: 10.1111/srt.12595. Epub 2018 Jun 6.

An objective method to assess the improvements of skin texture roughness after botulinum toxin type a treatment of crow's feet.

[Cavallini M](#)¹, [Papagni M](#)¹, [Gazzola R](#)².

Author information

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Department of Dermatosurgery and Aesthetic Medicine, CDI Hospital, Milan, Italy.

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Plastic Surgery Department, Policlinico di Monza, Monza, Italy.

Abstract

BACKGROUND:

Photo-numeric scales could lack precision and objectivity on evaluating the improvements on wrinkles after a treatment with botulinum toxin type A. The authors suggest a new digital evaluation method to analyze its effectiveness.

OBJECTIVES:

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This study aims to investigate retrospectively the effect of intramuscular injection of botulinum toxin type A on skin texture in the lateral peri-orbital region with a new objective method.

METHODS:

Skin texture roughness (STR) in the lateral peri-orbital region is evaluated with a multi-directional light beam by light emitting diodes of different wavelengths (Antera 3D®), before and after injections of 12 units of botulinum toxin type A. The wrinkles and lines deeper than 0.5 mm are filtered to measure accurately skin texture.

RESULTS:

We observed an improvement of STR in all cases treated with botulinum toxin type A. A significant decrease of STR was recorded as follows: 17.08% ($P < .0001$) at 4 weeks and 12.14% at 4 months ($P = .001$).

CONCLUSION:

Botulinum toxin type A treatment of crow's feet was able to improve STR. The Antera® device and software are a valuable, objective, easy and reproducible method to assess the effects of the toxin.

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KEYWORDS:

Antera 3D®; botulinum toxin; crow's feet; roughness; texture

PMID:

29873844

DOI:

[10.1111/srt.12595](https://doi.org/10.1111/srt.12595)

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Select item 29701621 ☐ 19. Not relevant-off indication

[Dermatol Surg](#). 2018 May;44(5):670-678. doi: 10.1097/DSS.0000000000001529.

Safety and Effectiveness of the Hyaluronic Acid Dermal Filler VYC-17.5L for Nasolabial Folds: Results of a Randomized, Controlled Study.

[Monheit G](#)¹, [Beer K](#)², [Hardas B](#)³, [Grimes PE](#)⁴, [Weichman BM](#)⁵, [Lin V](#)³, [Murphy DK](#)³.

[Author information](#)

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- 1 Total Skin and Beauty Dermatology Center, Birmingham, Alabama.
- 2 Beer Surgical, Aesthetic and General Dermatology, West Palm Beach, Florida.
- 3 Allergan plc, Irvine, California.
- 4 Pigmentation Institute of Southern California, Los Angeles, California.
- 5 BMW Associates, Monroe Township, New Jersey B. Hardas is currently affiliated with Almirall, Barcelona, Spain V. Lin is currently affiliated with Health Economics and Outcomes Research, CAR T, Kite Pharma, Santa Monica, California.

Abstract

BACKGROUND:

Juvéderm Vollure XC (VYC-17.5L) belongs to a family of nonanimal hyaluronic acid (HA) gels based on the Vycross technology platform.

OBJECTIVE:

To evaluate the safety and effectiveness of VYC-17.5L for correction of moderate to severe nasolabial folds (NLFs) compared with a control HA dermal filler.

METHODS:

In this double-blind study, 123 adults with 2 moderate or severe NLFs as measured on the 5-point photonumeric NLF severity scale (NLFSS) were randomized to VYC-17.5L in 1 NLF and control in the contralateral NLF. The coprimary effectiveness end points at Month 6 were difference in improvement in mean NLFSS score for VYC-17.5L versus control and NLFSS responder rate (≥ 1 -point improvement) for VYC-17.5L.

RESULTS:

The coprimary effectiveness end points were met. NLFSS scores improved by 1.4 with VYC-17.5L and by 1.3 with control; NLFSS responder rate with VYC-17.5L was 93.2%. More than three-quarters of subjects (82%) treated with VYC-17.5L were very satisfied at Month 6. Investigators reported that VYC-17.5L was smoother and more natural looking and easier to inject and mold than control. VYC-17.5L resulted in significantly fewer severe injection site responses than control.

CONCLUSION:

VYC-17.5L was safe and effective for correcting moderate to severe NLFs, with results lasting through 6 months in 93% of subjects.

PMID:

29701621

PMCID:

[PMC6221389](#)

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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DOI:

[10.1097/DSS.0000000000001529](https://doi.org/10.1097/DSS.0000000000001529)

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Department of Dermatology, Seoul Paik Hospital, Inje University, Seoul, Korea.

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Department of Dermatology, Myongji Hospital, Goyang, Korea.

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Department of Dermatology, Chung-Ang Hospital, Chung-Ang University, Seoul, Korea.

Abstract**BACKGROUND:**

Infraorbital region is one of the most important regions that show the signs of aging. In recent years, hyaluronic acid (HA) fillers have been used to correct this region for esthetic treatments. Although HA fillers with various physical properties are used, limited research has been performed to compare their efficacy.

OBJECTIVE:

We aimed to compare three HA fillers to determine which is the most appropriate filler for the correction of the infraorbital region and evaluate the correction of such by performing a clinical test using CLEVIEL Fine.

METHODS:

We performed in vitro and in vivo tests using one new HA filler and two other commercial HA fillers. We compared the rheological properties, resistance to degradation, and in vivo duration test results of the three fillers. Nine patients participated in the clinical test using CLEVIEL Fine for 24 weeks.

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RESULTS:

CLEVIEL Fine showed good rheological and physical characteristics for the infraorbital region. It had a low elasticity and cohesiveness, low incidence of postinjection swelling, high $\tan\delta$, narrow particle distribution, and small particle size. Further, it showed better resistance to the enzymes and radicals in the in vitro test than the other two HA fillers and a similar duration in the mouse test. In the clinical test, all patients showed good elasticity and hydration in the infraorbital region for 24 weeks.

CONCLUSIONS:

CLEVIEL Fine was proven to be safe and effective based on the in vitro, in vivo, and clinical study results.

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KEYWORDS:

clinical study; dermal filler; hyaluronic acid; infraorbital region

PMID:

29687569

DOI:

[10.1111/jocd.12560](https://doi.org/10.1111/jocd.12560)

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Select item 29631280 ☐ 21. **.Include**

[Facial Plast Surg.](#) 2018 Apr;34(2):119-127. doi: 10.1055/s-0038-1637004. Epub 2018 Apr 9.

Rejuvenation of the Upper Face and Brow: Neuromodulators and Fillers.

[Lighthall JG¹](#).

Author information

1

Division of Otolaryngology-Head & Neck Surgery, Penn State Hershey Medical Center, Hershey, Pennsylvania.

Abstract

Facial aging involves a combination of volume loss and descent, loss of skin elasticity, dynamic lines due to facial mimetic muscle action, and development of static rhytids. Although surgery remains an option for treatment, minimally invasive aesthetic procedures continue to gain popularity with the use of neuromodulators and soft tissue fillers being the most sought-after

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procedures. Although these may be used in isolation to treat specific concerns, they are often combined to address multiple facets of aging. Multiple different neuromodulators and fillers are commercially available. Although relatively effective and safe, a thorough understanding of their indications, compositions, and potential adverse effects is paramount. This article will review the available aesthetic products for minimally invasive periorbital rejuvenation with botulinum toxin and injectable fillers. Although it will not focus on other therapies aimed at facial rejuvenation, such as resurfacing techniques or surgical interventions, it is important to note that an individualized treatment plan may combine multiple therapies to optimize patient outcomes and satisfaction.

Thieme Medical Publishers 333 Seventh Avenue, New York, NY 10001, USA.

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29631280

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[10.1055/s-0038-1637004](https://doi.org/10.1055/s-0038-1637004)

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Select item 29601621 ☐ 22. **.Include**

[J Drugs Dermatol](#). 2018 Apr 1;17(4):442-450.

Prospective, Randomized, Investigator-Blinded, Split-Face Evaluation of a Topical Crosslinked Hyaluronic Acid Serum for Post-Procedural Improvement of Skin Quality and Biomechanical Attributes.

[Sundaram H](#), [Cegielska A](#), [Wojciechowska A](#), [Delobel P](#).

Abstract

BACKGROUND:

This split-face, controlled study investigated the ability of a topical crosslinked hyaluronic acid formulation (RHA serum) to enhance clinical results from fillers, microneedling, or chemical peeling of aging skin. Previous comparative skin explant studies demonstrated greater efficacy of RHA serum than topical non-crosslinked high or low molecular weight hyaluronic acid in decreasing trans-epidermal water loss, increasing epidermal hydration, and improving corneocyte microstructure.

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METHODS:

24 female subjects aged 35 to 55 were enrolled. 8 received intradermal hyaluronic acid filler injection, 8 received microneedling, and 8 received superficial mandelic acid chemical peeling. Subjects initiated twice-daily, standardized application of RHA serum to one side of the face 2 days after the procedure. Topographical imaging, bioinstrumental, and blinded clinical evaluations were performed at days 0, 14, and 28.

RESULTS:

Areas treated with RHA serum showed statistically significant improvements in skin surface topography and hydration compared to untreated areas. Blinded investigator scoring showed greater improvement of RHA serum-treated skin in moisture, tone/complexion, radiance, texture, uniformity, and global appearance. Subjects' questionnaire responses correlated with these findings. Subjects expressed greater satisfaction with appearance of the treated hemiface. No adverse events were observed during the study.

CONCLUSIONS:

When initiated post-procedurally, topical RHA serum was well-tolerated and enhanced biomechanical properties, quality, and clinical appearance of the skin. Based on these data, RHA serum may be of value in improving patient outcomes and satisfaction following minimally invasive aesthetic procedures. The availability of the same hyaluronic acid technology also as a cohesive, tissue-integrating injectable filler enables synergistic, multi-level treatment plans to be devised. <p>J Drugs Dermatol. 2018;17(4):442-450.</p>.

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Select item 29601620 ☐ 23. **.Include**

[J Drugs Dermatol.](#) 2018 Apr 1;17(4):426-441.

Multi-Center, Double-Blind, Vehicle-Controlled Clinical Trial of an Alpha and Beta Defensin-Containing Anti-Aging Skin Care Regimen With Clinical, Histopathologic, Immunohistochemical, Photographic, and Ultrasound Evaluation.

[Taub A.](#) [Bucay V.](#) [Keller G.](#) [Williams J.](#) [Mehregan D.](#)

Abstract

BACKGROUND/OBJECTIVES:

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Anti-aging strategies utilizing stem cells are in the forefront. Alpha and beta defensins are natural immune peptides that have been shown to activate an LGR6-positive stem cell locus in the hair follicle, identified as the source of most new epidermal cells during acute wound healing. We investigated the ability of biomimetic alpha and beta defensin molecules, supplemented with supportive cosmetic ingredients, formulated into three skin care products, at improving the structure and function of aging skin.

METHODS:

A participant- and investigator -blinded, placebo-controlled, multi-center trial was performed in outpatient settings. Forty-four healthy female subjects, aged 41-71 years, skin types I-V, completed the study with 2/3 receiving full formula and 1/3 receiving the placebo formula. A skin care regimen of 3 products (serum, cream, and mask) containing alpha-defensin 5 and beta-defensin 3, and other cosmetic ingredients, was applied to the face, post-auricular, and neck skin two times per day for 12 weeks in those receiving full formula, whereas the placebo group received the identically packaged regimen without the active ingredients. Methods of evaluation included histopathology and immunohistochemistry (7 subjects), clinical evaluation of pores, superficial and deep wrinkles based on Griffiths scale, and high-resolution photography (all subjects). In addition, a subset of 15 patients were evaluated with the QuantifiCare system (3-dimensional imaging and skin care scores for evenness, pores, oiliness) and Cortex measurements (high-resolution skin ultrasound, TEWL, elasticity, color, and hydration). Data points for evaluation included baseline, 6 weeks, and 12 weeks. All patients used the same sunscreen and cleanser, which was provided to them.

RESULTS:

The full formula regimen caused a significantly (P equals 0.027) increased thickness of the epidermis as seen in histology, not seen in the placebo group, with no signs of inflammation. No excessive cell proliferation was detected in either group as measured by Ki67-immunohistochemistry. Reduction in visible pores, superficial wrinkles, oiliness, pigmentation, and improvement of skin evenness, were statistically significant. A trend for improvement was also observed in skin elasticity, TEWL, and hydration; these did not achieve statistical significance. Ultrasound and histopathology demonstrated increases in dermal thickness in individual patients, without statistical significance. Comprehensive improvement in all 5 parameters, including visible pores, hyperpigmentation, superficial and deep wrinkles, and epidermal thickness, was statistically significant when the subset of participants assigned for histology in full formula group was compared with the placebo group participants.

CONCLUSIONS:

A 3-product skin care regimen containing alpha and beta defensins globally improves the visual appearance and structure of aging skin without irritation, dryness, or inflammation. Specifically, this regimen increases epidermal thickness, reduces appearance of pores, reduces wrinkles, and

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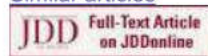
reduces melanin. This skin care regimen stimulates rejuvenation without evidence of increase of a marker of carcinogenic stimulation. This data is consistent with the hypothesis that a defensin-containing skin care regimen activates the body's own dormant stem cells to generate healthy new epidermal cells. <p>J Drugs Dermatol. 2018;17(4):426-441.</p> THIS ARTICLE HAD BEEN MADE AVAILABLE FREE OF CHARGE. PLEASE SCROLL DOWN TO ACCESS THE FULL TEXT OF THIS ARTICLE WITHOUT LOGGING IN. NO PURCHASE NECESSARY. PLEASE CONTACT THE PUBLISHER WITH ANY QUESTIONS.

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Select item 29574973 ☐ 24. **.Include**

[Int J Cosmet Sci.](#) 2018 Apr;40(2):199-206. doi: 10.1111/ics.12453.

Adenosine-loaded dissolving microneedle patches to improve skin wrinkles, dermal density, elasticity and hydration.

[Kang G](#)^{1,2}, [Tu TNT](#)³, [Kim S](#)¹, [Yang H](#)^{1,2}, [Jang M](#)^{1,2}, [Jo D](#)⁴, [Ryu J](#)⁴, [Baek J](#)⁴, [Jung H](#)^{1,2}.

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Dermapro Skin Research Center, 30 Bangbaejoongang-ro, Seocho-gu, Seoul, 06684, Korea.

Abstract

OBJECTIVE:

Although dissolving microneedle patches have been widely studied in the cosmetics field, no comparisons have been drawn with the topical applications available for routine use. In this study, two wrinkle-improving products, adenosine-loaded dissolving microneedle patches and an adenosine cream, were evaluated for efficacy, with respect to skin wrinkling, dermal density, elasticity, and hydration, and safety in a clinical test on the crow's feet area.

METHODS:

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Clinical efficacy and safety tests were performed for 10 weeks on 22 female subjects with wrinkles around their eyes. The adenosine-loaded dissolving microneedle patch was applied once every 3 days, in the evening, for 8 weeks to the designated crow's feet area. The adenosine cream was applied two times per day, in the morning and evening, for 8 weeks to the other crow's feet area. Skin wrinkling, dermal density, elasticity, and hydration were measured by using PRIMOS® premium, Dermascan® C, Cutometer® MPA580, and Corneometer® CM 825, respectively. In addition, subjective skin irritation was evaluated by self-observation, and objective skin irritation was assessed through expert interviews.

RESULTS:

The adenosine-loaded dissolving microneedle patches had a similar or better efficacy than the adenosine cream. Both groups showed statistically significant efficacy for almost all parameters ($P < 0.05$). The dissolving microneedle patches had a long-lasting effect on the average wrinkle depth ($P < 0.05$), only showed efficacy in dermal density ($P < 0.05$), had an early improving effect on elasticity ($P < 0.05$), and demonstrated better hydration efficacy ($P < 0.001$). No adverse effects were observed in either group during the test period.

CONCLUSIONS:

In the clinical efficacy test of four skin-improvement parameters, adenosine-loaded dissolving microneedle patches showed the same or better effect than the adenosine cream, although the weekly adenosine dose was 140 times lower. The dissolving microneedle patches caused no adverse reactions. These adenosine-loaded dissolving microneedle patches are expected to be safe, effective, and novel cosmetics for skin improvement.

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KEYWORDS:

delivery/vectorisation/penetration; dissolving microneedle; safety testing; skin physiology/structure; wrinkle improvement

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[10.1111/ics.12453](https://doi.org/10.1111/ics.12453)

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Select item 29523608 ☐ 25. **Not relevant**

[BMJ Case Rep.](#) 2018 Mar 9;2018. pii: bcr-2017-222916. doi: 10.1136/bcr-2017-222916.

Considering exercise-associated hyponatraemia as a continuum.

[Lewis D¹](#), [Blow A²](#), [Tye J²](#), [Hew-Butler T³](#).

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Abstract

Exercise-associated hyponatraemia (EAH) always involves a component of overhydration relative to available exchangeable sodium stores. In the majority of cases, this is purely due to excessive consumption of fluids during exercise. In a lesser number of cases, it is apparent that excessive sodium loss through sweat may play a role by decreasing the amount of acutely available exchangeable sodium. Two cases demonstrating the latter, one in an individual with cystic fibrosis (CF) and another in an endurance athlete without CF, demonstrate how elevated dermal sweat losses may contribute to a *relative* dilutional EAH along a pathophysiological continuum.

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KEYWORDS:

cystic fibrosis; fluid electrolyte and acid-base disturbances; general practice / family mMedicine; sports and exercise medicine

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Select item 29381544 ☐ 26. **.Include**

[Dermatol Surg.](#) 2018 Jun;44(6):841-845. doi: 10.1097/DSS.0000000000001460.

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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A Single Center, Prospective, Randomized, Sham-Controlled, Double-Blinded, Split-Face Trial Using Microinjections of Transparent Hyaluronic Acid Gel for Cheek Rejuvenation.

Jones IT¹, Vanaman Wilson MJ², Bolton J³, Zaleski-Larsen L⁴, Wu DC⁵, Goldman MP⁵.

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West Dermatology, San Diego, California.

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Goldman, Butterwick, Groff, Fabi & Wu, Cosmetic Laser Dermatology, a West Dermatology Company, San Diego, California.

Abstract

BACKGROUND:

"Skin boosting" with injections of hyaluronic acid has been demonstrated to improve aged skin.

OBJECTIVE:

The aim of this study was to determine the efficacy and safety of small-particle hyaluronic acid with lidocaine (SP-HAL) microaliquots for the correction of fine lines of the cheeks.

MATERIALS AND METHODS:

Twenty subjects with mild to moderate static mid to lower cheek rhytides were enrolled. The right or left cheek was randomized to receive 1 mL of SP-HAL using a microdroplet technique, with the contralateral cheek treated with sham injection of sterile normal saline. The degree of cheek wrinkling and elastosis based on the Fitzpatrick-Goldman Wrinkle and Elastosis Scale was assessed at baseline and 7, 14, 30, 90, and 180 days after treatment. Subjects rated their satisfaction at days 90 and 180.

RESULTS:

Fourteen patients completed the study. There were no statistically significant improvements in wrinkling or elastosis of the SP-HAL-treated cheek or control cheek at any time point. In addition, there were no significant differences in wrinkling, elastosis, or patient satisfaction between the treatment cheek and control cheek.

CONCLUSION:

One treatment of intradermal microdroplet injections of SP-HAL to the mid to lower cheek failed to show superiority over normal saline in improving clinical signs of skin wrinkling and elastosis.

Comment in

- [Commentary on A Single Center, Prospective, Randomized, Sham-Controlled, Double-Blinded, Split-Face Trial Using Microinjections of Transparent Hyaluronic Acid Gel for Cheek Rejuvenation.](#) [Dermatol Surg. 2018]

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Select item 29244069 ☐ 27. **Not relevant**

[Aesthet Surg J](#), 2018 Apr 6;38(5):540-556. doi: 10.1093/asj/sjx179.

Impact of Comprehensive, Minimally Invasive, Multimodal Aesthetic Treatment on Satisfaction With Facial Appearance: The HARMONY Study.

[Weinkle SH](#)¹, [Werschler WP](#)², [Teller CF](#)³, [Sykes JM](#)⁴, [Shamban A](#)⁵, [Rivkin A](#)⁶, [Narurkar VA](#)⁷, [Kaminer MS](#)⁸, [Davan S](#)⁹, [Cohen JL](#)^{10,11}, [Gallagher CJ](#)¹².

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Senior Medical Director of Facial Aesthetics at Allergan plc, Irvine, CA.

Abstract

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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BACKGROUND:

Individuals seeking aesthetic treatment have concerns regarding multiple facial areas.

OBJECTIVES:

Assess the aesthetic impact and satisfaction achieved with a multimodal approach to aesthetic treatment using a combination of minimally invasive treatments.

METHODS:

Prospective, multicenter, rater-blinded, 4-month HARMONY study evaluated patient satisfaction and aesthetic impact of a combination of fillers (VYC-20L, HYC-24L, and HYC-24L+), onabotulinumtoxinA, and bimatoprost. Males and females aged 35 to 65 years received on-label, staged treatment with fillers, as needed per investigator assessment, on day 1, with touch ups allowed on day 14. Bimatoprost was self-administered once daily for 17 weeks.

OnabotulinumtoxinA was injected into glabellar lines, crow's feet lines, or both at month 3.

Primary effectiveness measure was mean change from baseline on the FACE-Q 10-item Satisfaction with Facial Appearance Overall Scale.

RESULTS:

Of 100 patients treated, 93 underwent at least the 4-month posttreatment assessment and were assessed for efficacy. The FACE-Q Satisfaction with Facial Appearance Overall Scale total score increased from baseline (41.2) to month 4 (72.9; $P < 0.00001$; effect size, 2.7). Improvement following multimodal treatment was observed on FACE-Q individual items. Self-perceived age decreased from 0.2 years older than actual age at baseline to 4.6 years younger at month 4. Nearly all patients (99%) rated themselves as improved or much improved on the Global Aesthetic Improvement Scale. Investigator assessments also demonstrated improvement. Mild to moderate adverse events occurred in 42 patients.

CONCLUSIONS:

Minimally invasive, multimodal treatment resulted in improvements in FACE-Q scores and perceived age, indicating a high degree of patient satisfaction and a younger facial appearance.

LEVEL OF EVIDENCE 4:

PMID:

29244069

DOI:

[10.1093/asi/sjx179](https://doi.org/10.1093/asi/sjx179)

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KEYWORDS:

Filler; blue-gray dyschromia; complication; cosmetic injection; hyaluronic acid gel; malar edema; periorbital hollow; tear trough

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[10.1111/jocd.12452](https://doi.org/10.1111/jocd.12452)

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MeSH terms, Substances

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Select item 28913927 ☐ 29. **Not relevant- off indication**

[J Cosmet Dermatol](#). 2018 Aug;17(4):584-589. doi: 10.1111/jocd.12380. Epub 2017 Sep 14.

The efficacy and safety of a monophasic hyaluronic acid filler in the correction of nasolabial folds: A randomized, multicenter, single blinded, split-face study.

[Kwon HJ](#)¹, [Ko EJ](#)², [Choi SY](#)³, [Choi EJ](#)¹, [Jang YJ](#)¹, [Kim BJ](#)¹, [Lee YW](#)^{4,5}.

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Research Institute of Medical Science, Konkuk University, Seoul, Korea.

Abstract

BACKGROUND:

The different rheological properties of hyaluronic acid (HA) filler reflect their specific manufacturing processes and resultant physicochemical characteristics. However, there are few researches about the relationship between product differences and clinical outcome when HA fillers are used for nasolabial folds (NLFs).

AIMS:

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Select item 29130598 ☐ 28. **Not relevant-off indication**

[J Cosmet Dermatol](#). 2018 Aug;17(4):611-616. doi: 10.1111/jocd.12452. Epub 2017 Nov 11.

Filling the periorbital hollows with hyaluronic acid gel: Long-term review of outcomes and complications.

[Mustak H^{1,2}](#), [Fiaschetti D²](#), [Goldberg RA²](#).

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Stein Eye Institute, Division of Orbital and Oculoplastic Surgery, University of California, Los Angeles, CA, USA.

Abstract

INTRODUCTION:

Hyaluronic acid gel has been used for rejuvenation of the periorbital tissues since 2004. The in-office, nonsurgical procedural nature has resulted in the growing popularity of the use of fillers. The periorbital region poses unique challenges to the cosmetic surgeon. Malar edema, blue-gray dyschromia, and contour irregularities are well reported short-term complications. We present a long-term follow-up review of complications associated with periocular injection of hyaluronic acid gel fillers.

METHODS:

Retrospective review of 147 patients with at least a 5-year follow-up period since the first injection. Five senior masked reviewers were asked to grade photographs of patients in comparison with preinjection photographs. Grading was based on a reference photographic key looking specifically at the presence and severity of malar edema, blue-gray dyschromia, and contour irregularity.

RESULTS:

Malar edema (11%), blue-gray dyschromia (31.3%), and contour irregularities (30.5%) continue to be problems in longer term follow-up of patients. The vast majority (90%) of these complications were mild and required no intervention. There is no statistically significant difference in the mean volumes injected by severity grading of each measured complication.

CONCLUSION:

Hyaluronic acid gel fillers of the periorbital region are well tolerated in our long-term follow-up experience. The vast majority of cases of malar edema, blue-gray dyschromia, and contour irregularities are mild and do not require intervention. Conservative treatment and tailored treatment approaches, in terms of volume and frequency of injections, may decrease the tendency of these adverse effects to occur.

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This study sought to compare the rheological properties, efficacy and safety of a monophasic HA filler, and a well-studied biphasic HA filler, in the treatment of NLFs.

PATIENTS/METHODS:

A total of 72 Korean subjects with moderate to severe NLFs were randomized to receive injections with monophasic HA or biphasic HA on the left or right side of the face. Efficacy was evaluated by the change in the Wrinkle Severity Rating Scale (WSRS) at 2, 10, 18, 26, and 52 weeks. Safety was assessed on the basis of all abnormal reactions during the clinical test period. To compare the rheological characteristics of two cross-linked HA fillers, viscoelastic analysis was performed.

RESULTS:

At week 26, the mean WSRS was 2.26 ± 0.56 for the monophasic HA side and 2.24 ± 0.54 for the biphasic HA side. Both treatments were well tolerated. The adverse reactions were mild and transient. Monophasic HA filler had lower elasticity and higher viscosity than biphasic HA filler.

CONCLUSION:

Despite a number of different rheological properties, monophasic HA is noninferior to biphasic HA in the treatment of moderate to severe NLFs for 52 weeks. Therefore, monophasic HA provides an alternative option for NLFs correction.

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KEYWORDS:

hyaluronic acid (HA) filler; nasolabial fold; rheology

PMID:

28913927

DOI:

[10.1111/iocd.12380](https://doi.org/10.1111/iocd.12380)

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Select item 28892233 ☐ 30. **Include**

[Dermatol Ther.](#) 2017 Nov;30(6). doi: 10.1111/dth.12546. Epub 2017 Sep 11.

Hyaluronic acid microneedle patch for the improvement of crow's feet wrinkles.

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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[Choi SY¹](#), [Kwon HJ²](#), [Ahn GR²](#), [Ko EJ³](#), [Yoo KH⁴](#), [Kim BJ²](#), [Lee C⁵](#), [Kim D⁵](#).

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Abstract

Hyaluronic acid (HA) has an immediate volumizing effect, due to its strong water-binding potential, and stimulates fibroblasts, causing collagen synthesis, with short- and long-term effects on wrinkle improvement. We investigated the efficacy and safety of HA microneedle patches for crow's feet wrinkles. Using a randomized split-face design, we compared microneedle patches with a topical application containing the same active ingredients. We enrolled 34 Korean female subjects with mild to moderate crow's feet wrinkles. The wrinkle on each side of the subject's face was randomly assigned to a HA microneedle patch or HA essence application twice a week for 8 weeks. Efficacy was evaluated at weeks 2, 4, and 8. Skin wrinkles were measured as average roughness using replica and PRIMOS. Skin elasticity was assessed using a cutometer. Two independent blinded dermatologists evaluated the changes after treatment using the global visual wrinkle assessment score. Subjects assessed wrinkles using the subject global assessment score. Skin wrinkles were significantly reduced and skin elasticity significantly increased in both groups, although improvement was greater in the patch group at week 8 after treatment. In the primary and cumulative skin irritation tests, the HA microneedle patch did not induce any skin irritation. The HA microneedle patch is more effective than the HA essence for wrinkle improvement and is a safe and convenient without skin irritation.

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KEYWORDS:

crow's feet wrinkles; hyaluronic acid; microneedle patch

PMID:

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Select item 28786543 ☐ 31. Not relevant-off indication

[J Cosmet Dermatol](#). 2018 Aug;17(4):596-599. doi: 10.1111/jocd.12385. Epub 2017 Aug 8.

Effect analysis of intradermal hyaluronic acid injection to treat enlarged facial pores.

[Qian W¹](#), [Zhang YK¹](#), [Hou Y¹](#), [Lyu W¹](#), [Cao Q¹](#), [Li YQ¹](#), [Fan JF¹](#).

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Department of Plastic and Reconstructive Surgery, Beijing Chao-Yang Hospital, Capital Medical University, Beijing Chao-Yang Hospital, Beijing, China.

Abstract

OBJECTIVE:

To investigate the clinical application and efficacy of intradermal injection of low molecular weight hyaluronic acid (LMW-HA) for treating enlarged facial pores.

METHODS:

From January 2015 to May 2016, 42 subjects who sought aesthetic treatment underwent intradermal injection of LMW-HA to improve enlarged facial pores. For each treatment, 2.5 mL (25 mg) of LMW-HA was injected into the skin of the full face. The treatment was repeated 2-5 times with an interval of 1 to 1.5 months between consecutive treatments. The postoperative follow-up period was 1 to 6 months. Statistical analysis was used to compare the degree of enlargement of facial pores before and after injection. The clinical efficacy and adverse effects were recorded.

RESULTS:

The enlarged facial pores before and after treatment were categorized and subjected to the Wilcoxon matched-pairs signed-rank test. The difference was statistically significant ($P < .01$). The improvement rate was $40.03 \pm 18.41\%$. No infection, nodules, or pigmentation was reported at the injection sites in the subjects who sought aesthetic treatment. The overall satisfaction rate was 92.8%.

CONCLUSION:

Intradermal injection of LMW-HA can significantly improve skin texture, reduce pore size, and enhance skin radiance. The injection technique was simple, safe, and effective and could easily be extended to clinical practice.

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KEYWORDS:

enlarged pore; hyaluronic acid; intradermal injection

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PMID:

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[J Cosmet Laser Ther.](#) 2018 Feb;20(1):28-33. doi: 10.1080/14764172.2017.1358459. Epub 2017 Sep 6.

A review of hydrolifting: A new modality for skin rejuvenation.

[Youn CS](#)¹, [Hong JY](#)², [Park KY](#)², [Kim BJ](#)², [Nam Kim M](#)².

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a Yemiwon Dermatologic Clinic , Seoul , Republic of Korea.

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Abstract

BACKGROUND:

Hydrolifting is a newly developed modality of skin rejuvenation, which enhances overall facial volume augmentation and recovers skin thickness through multi-pass HA injection. Although it is commonly performed, only a few articles have reported on the rejuvenating effects of hydrolifting. Moreover, clear protocols and possible mechanisms of the procedure have not been elucidated.

OBJECTIVE:

To define a novel technique for injecting HA and to clarify how to choose an appropriate HA filler based on the procedural purpose.

METHODS:

This article is based on a review of the medical literature and the authors' clinical experience in investigating and treating skin wrinkles with the hydrolifting method.

RESULTS:

In hydrolifting, HA filler serves as a hydration source, dermal volumizer, and stimulator of dermal collagen and antioxidants. Hydrolifting is frequently indicated in minor wrinkles, minor volume depletion and rough skin texture.

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levels are significantly reduced throughout the dermis of venous leg ulcer biopsies and DFU, with a reduction in both fibril thickness and abundance. Both wound types showed a significant reduction in elastin in the upper dermis, but in DFU, the loss was throughout the dermis. Loss of extracellular matrix correlated with high levels of CD68- and CD18-positive leukocytes. 2-photon imaging of the extracellular matrix in the intact tissue surrounding a chronic wound with a hand-held device may provide a useful clinical indicator on the healing progression or deterioration of these wounds.

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KEYWORDS:

Chronic wounds; Extracellular matrix; Second harmonic imaging

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28730726

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[10.1111/iji.12789](https://doi.org/10.1111/iji.12789)

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[Orphanet J Rare Dis](#). 2017 Jun 28;12(1):120. doi: 10.1186/s13023-017-0670-9.

Neural stem cells for disease modeling of Wolman disease and evaluation of therapeutics.

[Aquisanda F](#)^{1,2}, [Yeh CD](#)¹, [Chen CZ](#)¹, [Li R](#)¹, [Beers J](#)³, [Zou J](#)³, [Thorne N](#)^{4,5}, [Zheng W](#)⁶.

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CONCLUSION:

The hydrolifting method is a newly introduced antiaging treatment modality. It effectively covers the blind spots of conventional HA injection, such as infraorbital, perioral and hand dorsal wrinkles. However, further investigations are needed to reach a consensus on the basic concepts of treatment, choice of appropriate fillers and optimal technique in hydrolifting.

KEYWORDS:

Filler; hydrolifting; mechanism; technique

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Select item 28730726 ☐ 33. **Not relevant**

[Int Wound J.](#) 2017 Dec;14(6):1225-1236. doi: 10.1111/iwj.12789. Epub 2017 Jul 20.

Changes in the extracellular matrix surrounding human chronic wounds revealed by 2-photon imaging.

[Sutcliffe JES](#)¹, [Thrasivoulou C](#)¹, [Serena TE](#)², [Madden L](#)³, [Richards T](#)⁴, [Phillips ARJ](#)⁵, [Becker DL](#)^{3,6}.

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School of Biological Sciences, Auckland University, Auckland, New Zealand.

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Abstract

Chronic wounds are a growing problem worldwide with no effective therapeutic treatments available. Our objective was to understand the composition of the dermal tissue surrounding venous leg ulcers and diabetic foot ulcers (DFU). We used novel 2-photon imaging techniques alongside classical histology to examine biopsies from the edges of two common types of chronic wound, venous leg ulcers and DFU. Compared to normal intact skin, we found that collagen

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National Center for Advancing Translational Sciences, National Institutes of Health,
Bethesda, MD, USA. wzhenh@mail.nih.gov.

Abstract

BACKGROUND:

Wolman disease (WD) is a rare lysosomal storage disorder that is caused by mutations in the LIPA gene encoding lysosomal acid lipase (LAL). Deficiency in LAL function causes accumulation of cholesteryl esters and triglycerides in lysosomes. Fatality usually occurs within the first year of life. While an enzyme replacement therapy has recently become available, there is currently no small-molecule drug treatment for WD.

RESULTS:

We have generated induced pluripotent stem cells (iPSCs) from two WD patient dermal fibroblast lines and subsequently differentiated them into neural stem cells (NSCs). The WD NSCs exhibited the hallmark disease phenotypes of neutral lipid accumulation, severely deficient LAL activity, and increased LysoTracker dye staining. Enzyme replacement treatment dramatically reduced the WD phenotype in these cells. In addition, δ -tocopherol (DT) and hydroxypropyl-beta-cyclodextrin (HPBCD) significantly reduced lysosomal size in WD NSCs, and an enhanced effect was observed in DT/HPBCD combination therapy.

CONCLUSION:

The results demonstrate that these WD NSCs are valid cell-based disease models with characteristic disease phenotypes that can be used to evaluate drug efficacy and screen compounds. DT and HPBCD both reduce LysoTracker dye staining in WD cells. The cells may be used to further dissect the pathology of WD, evaluate compound efficacy, and serve as a platform for high-throughput drug screening to identify new compounds for therapeutic development.

KEYWORDS:

Cell-based disease model; Induced pluripotent stem cells; Lysosomal storage disease; Neural stem cells; Wolman disease

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Select item 28595250 ☐ 35. **Include**

[Dermatol Surg.](#) 2017 Dec;43(12):1448-1457. doi: 10.1097/DSS.0000000000001193.

Prospective, Split-Face, Randomized, Long-Term Blinded Objective Comparison of the Performance and Tolerability of Two New Hyaluronic Acid Fillers.

[Trevidic P¹](#), [Andre P²](#), [Benadiba L²](#), [Deutsch JJ²](#), [Galatoire O³](#), [Garcia P¹](#), [Grand-Vincent A²](#), [Boisnic S⁴](#), [Kerihuel JC⁵](#), [Salomon C⁶](#).

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- 2 Private Practice, Paris, France.
- 3 Fondation Rothschild, Paris, France.
- 4 GREDECO, Paris, France.
- 5 Société VERTICAL, Paris, France.
- 6 Laboratoires FILORGA, Paris, France.

Erratum in

- [Prospective, Split-Face, Randomized, Long-Term Blinded Objective Comparison of the Performance and Tolerability of Two New Hyaluronic Acid Fillers: ERRATUM.](#) [Dermatol Surg. 2018]

Abstract

BACKGROUND:

There are requirements for long-term, objective comparisons of hyaluronic acid (HA) dermal fillers.

OBJECTIVE:

To compare efficacy and tolerability of ART FILLER Universal (AFU) and ART FILLER Fine lines (AFFL) with the existing HA fillers for the treatment of nasolabial folds and crow's feet.

MATERIALS AND METHODS:

Prospective, randomized, rater- and patient-blind, split-face comparison of AFU with JUVEDERM Ultra 3 (JUV) and AFFL with FIRST LINES PureSense (FLPS). The severity of nasolabial folds and crow's feet was assessed by independent blinded evaluators using the Lemperle scale at baseline, day (D) 30/D45, D90, and D180. Tolerability, Global Aesthetic Improvement Scale (GAIS), wrinkle volumes, and skin thickness and density were also measured at D30/D45, D90, and D180.

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RESULTS:

At D30 and D180 respectively, 61 and 57 patients were assessed. Scores for nasolabial folds and crow's feet showed statistically significant improvements at D30, D90, and D180. AFU and AFFL were noninferior to JUV and FLPS, respectively. Most patients showed GAIS improvements, maintained until at least D180 and significant increases of collagen synthesis in crow's feet and nasolabial folds. Treatments were well tolerated.

CONCLUSION:

AFU and AFFL are noninferior to comparators. The methodology used represents a novel approach to augment existing clinical assessment of HA fillers.

PMID:

28595250

DOI:

[10.1097/DSS.0000000000001193](https://doi.org/10.1097/DSS.0000000000001193)

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Select item 28453913 ☐ 36. **Not relevant**

[Exp Dermatol](#). 2018 May;27(5):453-459. doi: 10.1111/exd.13376. Epub 2017 Jul 10.

Bioprinting of biomimetic skin containing melanocytes.

[Min D¹](#), [Lee W²](#), [Bae JH¹](#), [Lee TR¹](#), [Croce P²](#), [Yoo SS²](#).

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Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA.

Abstract

This study reports a three-dimensional (3D) bioprinting technique that is capable of producing a full-thickness skin model containing pigmentation. Multiple layers of fibroblast (FB)-containing collagen hydrogel precursor were printed and crosslinked through neutralization using sodium bicarbonate, constituting the dermal layer. Melanocytes (MCs) and keratinocytes (KCs) were sequentially printed on top of the dermal layer to induce skin pigmentation upon subsequent air-liquid interface culture. Histological analysis was performed not only to confirm the formation of distinct skin layers, but also to identify the presence of pigmentation. The bioprinted skin structure

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showed the dermal and epidermal layers as well as the terminal differentiation of the KC that formed the stratum corneum. Moreover, the MC-containing epidermal layer showed freckle-like pigmentations at the dermal-epidermal junction, without the use of external ultraviolet light or chemical stimuli. The presented method offers the capability of producing engineered ephelides in biomimetic skin, thus rendering 3D bioprinting techniques as productive on-demand options for the creation of skin models available for therapeutic or research use.

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KEYWORDS:

3D bioprinting; skin pigmentation; tissue engineering; type I collagen

PMID:

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[10.1111/exd.13376](https://doi.org/10.1111/exd.13376)

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Select item 28121477 ☐ 37. **Not relevant**

[Orbit](#). 2017 Feb;36(1):22-26. doi: 10.1080/01676830.2017.1279641. Epub 2017 Jan 25.

Tear trough rejuvenation: A safety evaluation of the treatment by a semi-cross-linked hyaluronic acid filler.

[Berquiga M¹](#), [Galatoire O¹](#).

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a Department of Oculoplastic Surgery , Fondation Rothschild , Paris , France.

Abstract

The aim of this study is to describe the experience of 33 physicians, dermatologists and surgeons, with the use of a semi-cross-linked hyaluronic acid (HA) gel as a tear trough deformity filler within one month following injection, and to assess patient satisfaction with the procedure. This study is a case series conducted between February 2012 and December 2012 with the use of semi-cross-linked HA to correct tear trough deformity. The filler was administered in the preperiosteal tissues. The study involved case note review and a patient satisfaction survey. A total of 302 eyes of 151 patients were treated by 33 physicians, with a mean follow-up of 3 weeks. Patients were mainly female (86%), and middle-aged (mean age 48 years old). The gel was placed preperiosteally, deep to the orbicularis, anterior to the inferior orbital rim, with a mean

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volume of 0.48 ml per eye to achieve correction. The injection procedure was performed without local anesthetic for 79% of the patients. No serious adverse event was recorded. Side effects reported by investigators immediately after injection included bruising (11%), swelling (12%), and redness (inflammation 12%). Very few transitional blue discolorations (2.6%) were observed. No patient required dissolution with hyaluronidase. According to our satisfaction survey, all patients had cosmetic improvement. Most patients (97%) described marked or moderate satisfaction with the treatment. At one month, 18% requested additional hyaluronic acid gel for a touch-up injection. This case series confirms the effective use of a semi-cross-linked HA gel in tear trough rejuvenation. It has excellent patient tolerability, minimal complications, and excellent patient satisfaction.

KEYWORDS:

Cosmetic medicine; hollow ring; hyaluronic acid fillers; non-invasive facial rejuvenation; tear trough

PMID:

28121477

DOI:

[10.1080/01676830.2017.1279641](https://doi.org/10.1080/01676830.2017.1279641)

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[Ann Chir Plast Esthet.](#) 2017 Jun;62(3):261-267. doi: 10.1016/j.anplas.2016.12.002. Epub 2017 Jan 6.

[Hyaluronic acid rheology: Basics and clinical applications in facial rejuvenation].

[Article in French]

[Billon R](#)¹, [Hersant B](#)², [Meningaud JP](#)¹.

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Service de chirurgie maxillofaciale et de chirurgie plastique, réparatrice et esthétique, hôpital Henri-Mondor, 51, avenue du Maréchal-de-Lattre-de-Tassigny, 94010 Créteil, France. Electronic address: barbara.hersant@gmail.com.

Abstract

Hyaluronic acid (HA) is the most widely used dermal filler to treat facial volume deficits and wrinkles specially for facial rejuvenation. Depending on various areas of the face, filler is exposed

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to two different forces (shear deformation and compression/stretching forces) resulting from intrinsic and external mechanical stress. The purpose of this technical note is to explain how rheology, which is the study of the flow and deformation of matter under strains, can be used in our clinical practice of facial volumization with fillers. Indeed, comprehension of the rheological properties of HA has become essential in selection of dermal filler targeted to the area of the face. Viscosity, elasticity and cohesivity are the main three properties to be taken into consideration in this selection. Aesthetic physicians and surgeons have to familiarize with those basics in order to select the HA with the right rheological properties to achieve a natural-looking and long-lasting outcome.

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KEYWORDS:

Acide hyaluronique; Facial rejuvenation; Filler; Hyaluronic acid; Produit de comblement; Rajeunissement facial; Rheology; Rhéologie

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28069316

DOI:

[10.1016/j.anplas.2016.12.002](https://doi.org/10.1016/j.anplas.2016.12.002)

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Select item 27923810 ☐ 39. **Not relevant**

[Aesthet Surg J](#), 2017 May 1;37(5):573-581. doi: 10.1093/asj/sjw161.

Durability of Three Different Types of Hyaluronic Acid Fillers in Skin: Are There Differences Among Biphasic, Monophasic Monodensified, and Monophasic Polydensified Products?

[da Costa A](#)^{1,2}, [Bicciqo DGZ](#)³, [de Souza Weimann ET](#)³, [Mercadante LM](#)³, [Oliveira PRG](#)⁴, [Prebianchi SB](#)⁵, [Abdalla BMZ](#)⁶.

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Student of Medicine, Pontifical Catholic University of Campinas, Campinas, SP, Brazil.

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Resident of Internal Medicine, ABC Medical School, Santo Andre, SP, Brazil.

Abstract

BACKGROUND:

Hyaluronic acid fillers are used for facial rejuvenation and are classified as non-cross-linked or cross-linked (monophasic mono- or polydensified).

OBJECTIVES:

To histologically assess the intradermal durability of three types of fillers (biphasic, monophasic monodensified, and monophasic polydensified), to compare the durability of the products over 6 months, and to evaluate the structural changes after application.

METHODS:

In all, 25 volunteers received injections of three different fillers in the dermis of the right lumbar region (in one line), and equal amounts of the fillers were injected into three different sites (in the same column), yielding nine points of application in each patient. Each line was biopsied on days 2, 92, and 184; these skin samples were analyzed histologically, and the presence or absence of these fillers was verified by a dermatopathologist.

RESULTS:

The histological analysis showed that over 182 days, the amount of the injected monophasic polydensified, monophasic monodensified, and biphasic filler products decreased by 62.5%, 25%, and 12.5%, respectively.

CONCLUSIONS:

The biphasic and monophasic monodensified fillers presented greater intradermal durability than did the monophasic polydensified filler at 6 months after intradermal injection.

LEVEL OF EVIDENCE 2:

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[10.1093/asi/siw161](https://doi.org/10.1093/asi/siw161)

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Select item 24962508 ☐ 40. **.Include**

Pharm Res. 2016 Dec;33(12):2879-2890. Epub 2014 Jun 25.

Experimental and Clinical Efficacy of Two Hyaluronic Acid-based Compounds of Different Cross-Linkage and Composition in the Rejuvenation of the Skin.

Iannitti T^{1,2}, Morales-Medina JC³, Coacci A^{4,5}, Palmieri B^{4,5}.

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Department of General Surgery and Surgical Specialties, University of Modena and Reggio Emilia Medical School, Surgical Clinic, Modena, Italy.

Abstract

BACKGROUND:

In the field of aesthetic medicine there is an increasing demand for safe and effective hyaluronic acid (HA) fillers to counteract the aging process.

METHODS AND AIMS:

We designed a study to evaluate the safety and histological biocompatibility of Aliaxin® Global Performance, a cross-linked HA filler and Viscoderm® Skinkò E, a product composed of non-cross-linked HA and a complex including vitamins, antioxidants, amino acids and minerals injected into the skin of guinea pigs. Then, we translated our findings into the clinical setting, administering a combination of these compounds to patients seeking a facial rejuvenation procedure targeting moderate-to-severe wrinkles affecting the nasolabial folds.

RESULTS:

The animal study showed that the two compounds did not induce any significant inflammatory reactions and increased collagen and elastic fibers in the skin. In the clinical setting, injection of Aliaxin® Global Performance, followed by Viscoderm® Skinkò E, resulted in a higher improvement in nasolabial fold hydration, trans-epidermal water loss and wrinkle aesthetic appearance, if compared with a protocol based on Aliaxin® Global Performance alone.

CONCLUSION:

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In summary, we show evidence on the safety and mechanism underlying two new HA-based compounds of different cross-linkage and composition, proposing that they can be safely used in combination in patients seeking facial rejuvenation procedures with long-lasting efficacy.

KEYWORDS:

collagen; connective tissue; elastic fibers; elasticity; hyaluronic acid; hydration; inflammation; trans-epidermal water loss; wrinkles

PMID:

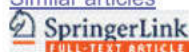
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[10.1007/s11095-014-1354-y](https://doi.org/10.1007/s11095-014-1354-y)

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Select item 27672079 ☐ 41. **Not relevant**

[Drug Deliv Transl Res](#), 2017 Feb;7(1):53-65. doi: 10.1007/s13346-016-0331-x.

Tocopheryl phosphate mixture (TPM) as a novel lipid-based transdermal drug delivery carrier: formulation and evaluation.

Gavin PD¹, El-Tamimy M², Keah HH², Boyd BJ^{3,4}.

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ARC Centre of Excellence in Convergent Bio-Nano Science and Technology, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville Campus, 381 Royal Parade, Parkville, VIC, 3052, Australia.

Abstract

Transdermal drug delivery is a useful route of administration that avoids first-pass metabolism and more invasive delivery options. However, many drugs require enhancers to enable sufficient drug absorption to reach therapeutic effect. Alpha-tocopheryl phosphate (TP) and di-alpha-tocopheryl phosphate (T2P) are two phosphorylated forms of vitamin E which form tocopheryl phosphate mixture (TPM) when combined, and have been proposed to enhance the dermal and transdermal delivery of actives of interest. Here, we report the physicochemical characteristics

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the past. We conducted a pilot study using a sample of six middle-aged male subjects. Using an automatic intradermal injector with 0.020 mL of material contained in each injection point with a total of 100 points, 2 mL of non-cross-HA filler was injected into the entire face at every treatment session. We administered injections of HA for a total of three sessions per subject at 2-week intervals and evaluated the results using a corneometer, TEWL, cutometer, measures of patient satisfaction, and the global aesthetic improvement scale (GAIS). Corneometer values increased steadily at each measurement, while the average value of TEWL increased in comparison with baseline after each application of the procedure. However, values returned to readings similar to those at 4 weeks after complete termination of the procedures. Cutometer values differed between the baseline and after procedures. All patients were assessed as "very much improved" or "much improved" according to GAIS, and all were pleased with the outcomes of treatment in terms of the enhancement of moisture, elasticity, and brightness.

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KEYWORDS:

hyaluronic acid; hydration; intradermal injector; skin rejuvenation; stamp-type microneedle

PMID:

27401775

DOI:

[10.1111/jocd.12244](https://doi.org/10.1111/jocd.12244)

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Select item 27324942 ☐ 43. **.Include**

[J Cosmet Dermatol](#). 2016 Dec;15(4):520-526. doi: 10.1111/jocd.12237. Epub 2016 Jun 21.

Physiochemical properties and application of hyaluronic acid: a systematic review.

Salwowska NM¹, Bebenek KA², Źądło DA³, Wcisło-Dziadecka DL⁴.

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and morphological properties of TPM formulations, including particle size, deformability and morphology, and its ability to facilitate the transport of carnosine, vitamin D3, CoEnzyme Q10 and caffeine into, and across, the skin. Results demonstrate that TPM self-assembles to form vesicular structures in hydroethanolic solutions ranging in mean size from 101 to 162 nm depending on the amount of TPM and ethanol present in the formulation. The ratio of TP to T2P in TPM formulations altered vesicle size and elasticity, with vesicles high in TP found to be more deformable than those rich in T2P. TPM produced a significant ($p < 0.05$) 2.4-3.4-fold increase in the absorption of carnosine, vitamin D3, CoEnzyme Q10 and caffeine into, or through, the skin. The TPM delivery platform was able to deliver a diverse range of actives with differing size and solubility profiles and therefore has significant potential to expand the number and types of drugs available for topical application and transdermal delivery.

KEYWORDS:

Drug delivery; TPM; Tocopherol; Tocopheryl phosphate mixture; Transdermal; Vitamin E

PMID:

27672079

DOI:

[10.1007/s13346-016-0331-x](https://doi.org/10.1007/s13346-016-0331-x)

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Select item 27401775 ☐ 42. **.Include**

[J Cosmet Dermatol](#). 2016 Dec;15(4):578-582. doi: 10.1111/jocd.12244. Epub 2016 Jul 11.

A potential relationship between skin hydration and stamp-type microneedle intradermal hyaluronic acid injection in middle-aged male face.

[Seok J¹](#), [Hong JY¹](#), [Choi SY^{1,2}](#), [Park KY¹](#), [Kim BJ¹](#).

Author information

1

Department of Dermatology, Chung-Ang University College of Medicine, Seoul, Korea.

2

Department of Dermatology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea.

Abstract

There is an increasing interest in skin rejuvenation using hyaluronic acid (HA) fillers beyond the improvement of deep wrinkles and volume deficiencies, which have been primary research foci in

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Department of Skin Structural Studies, Chair of Cosmetology, School of Pharmacy with
Division of Medicine in Sosnowiec, Medical University of Silesia, Sosnowiec, Poland.

Abstract

BACKGROUND:

Hyaluronic acid is a widely available, biocompatible, polysaccharide with distinguishing physiochemical properties which inspire its application throughout several fields of medicine.

OBJECTIVE:

We aim to investigate the application of hyaluronic acid and its effectiveness throughout several fields of medicine, including several therapies administered and prescribed by general health practitioners.

METHODS:

We conducted a systematic review on randomized controlled trials about the physiochemical properties of hyaluronic acid and its application through primary care. Studies included in this review were peer reviewed and met our inclusion criteria.

FINDINGS:

Factors were clustered into the following: uses throughout several fields of medicine, physiochemical properties, bioavailability, tolerance, effectiveness, and adverse effects. Therapies with hyaluronic acid provided long-lasting, pain relieving, moisturizing, lubricating, and dermal filling effect. Tissue hydration, elasticity, and durability improved.

CONCLUSIONS:

Adjunct therapy with hyaluronic acid provides longer-lasting therapeutic effect when compared to the use of glucocorticosteroids and NSAIDs in osteoarthritic chronic diseases, is well-established in ophthalmology due to its lubricating properties for the corneal endothelium, and improves tissue hydration and cellular resistance to mechanical damage in aesthetic dermatology, and has marginal adverse effects. Several trials indicated its role in tumor markers, liver diseases, and in pharmaceuticals, but further research would be necessary to draw conclusive results in those fields.

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KEYWORDS:

adjuvant therapy; bioavailability; hyaluronic acid; long-lasting effect; tolerability; wound healing

PMID:

27324942

DOI:

[10.1111/iod.12237](https://doi.org/10.1111/iod.12237)

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Select item 27272082 ☐ 44. **.Include**

[J Drugs Dermatol](#). 2016 Jun 1;15(6):738-41.

The Effect of a Combination of Recombinant EGF Cosmetic Serum and a Crosslinked Hyaluronic Acid Serum as Compared to a Fibroblast-Conditioned Media Serum on the Appearance of Aging Skin.

[Draelos ZD](#).

Abstract

Anti-aging cosmeceutical efficacy is hampered by lack of active ingredient purity and lack of dosing standardization. These are two important key factors necessary to insure consistent, reproducible, and documentable skin effects. Without this type of standardization, it is not possible for cosmeceutical science to advance. Growth factors are interesting cosmeceutical ingredients with established cosmetic skin effects that can now be standardized due to the recent ability to manufacture recombinant epidermal growth factor. The concomitant use of a recombinant epidermal growth factor with a filler grade hyaluronic acid (EGF/RHA) was studied over 12 weeks in 60 females with mild to moderate photoaging as compared to a currently marketed spent fibroblast growth media and moisturizer (TNS). Investigator, noninvasive, and subject assessments were collected at baseline and weeks 2, 4, 8, and 12. The blinded investigator noted a statistically significant preference for the EGF/RHA at week 2 in terms of smoothness ($P = 0.003$) and firmness ($P = 0.003$). This improvement continued into weeks 4 and 8 with continued superior EGF/RHA results in fine lines ($P = 0.002$), radiance ($P = 0.014$), and overall appearance ($P = 0.027$) by week 12. Transepidermal water loss was reduced for the EGF/RHA over the TNS at week 12 ($P = 0.005$). The subjects gave high ratings to both study products. This research demonstrates the utility of recombinant growth factors, when combined with hyaluronic acid hydration, in improving skin cosmetic attributes. The ability to manufacture consistent pure recombinant growth factors lays the foundation for improved scientific study of this category of cosmeceutical actives. [J Drugs Dermatol](#). 2016;15(6):738-741.

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Select item 27139014 ☐ 45. **Not relevant**

[G Ital Dermatol Venereol.](#) 2016 Oct;151(5):507-14. Epub 2016 Apr 1.

Clinical and instrumental evaluation of a cross-linked hyaluronic acid filler dermal injection: effects on nasolabial folds skin biophysical parameters and augmentation from a single-dose, monocentric, open-label trial.

[Cameli N¹](#), [Mariano M](#), [Serio M](#), [Berardesca E](#).

Author information

¹

Department of Dermatology, San Gallicano Institute IRCCS, Rome, Italy - cameli@ifo.it.

Abstract

BACKGROUND:

When a hyaluronic acid dermal device to fill soft tissues is chosen, efficacy, safety and durability are key concerns. This is an open-label prospective study to instrumentally evaluate the effects of HA filler dermal injection on nasolabial folds skin biophysical parameters and augmentation.

METHODS:

A single Italian site treated female subjects aged 40-55, for nasolabial folds, with a single standardized injection. The outcome was evaluated with objective quantitative measurements after 90 (T1) and 180 days (T2) from the injection comparing to baseline (T0) by means of Corneometer (skin hydration measurement), Cutometer (skin elasticity measurement), and Visioface devices for digital and UV computerized image analysis. Secondary endpoints were safety assessment, subject investigator satisfaction with the intervention. Assessment of aesthetic results included photographic documentation.

RESULTS:

The computerized image analysis confirmed the clinical assessment showing statistically significant reduction in nasolabial folds both at T1 and T2. Visioface® indexes showed a marked and statistical significant response. An excellent profile of satisfaction of the product at T2 from investigators and patients was recorded. Skin hydration and elasticity did not show significant changes.

CONCLUSIONS:

In our study, a standardized HA filler dermal injection on nasolabial folds did not influence skin biophysical parameters such as skin hydration and elasticity. Nasolabial folds showed a persistent and significative response at T2 confirmed by instrumental evaluation. The tolerability and safety profile of the product was excellent.

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Providing multiple treatments in 1 session improves patient satisfaction by producing greater improvements in a shorter amount of time and with less overall downtime than would be necessary with multiple office visits.

PMID:

27128248

DOI:

[10.1097/DSS.0000000000000740](https://doi.org/10.1097/DSS.0000000000000740)

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Select item 27128246 ☐ 47. **Not relevant**

[Dermatol Surg.](#) 2016 May;42 Suppl 2:S177-91. doi: 10.1097/DSS.0000000000000743.

A Comprehensive Approach to Multimodal Facial Aesthetic Treatment: Injection Techniques and Treatment Characteristics From the HARMONY Study.

[Narurkar VA¹](#), [Cohen JL](#), [Dayan S](#), [Kaminer MS](#), [Rivkin A](#), [Shamban A](#), [Sykes JM](#), [Teller CF](#), [Weinkle SH](#), [Werschler WP](#), [Drinkwater A](#), [Pucci ML](#), [Gallagher CJ](#).

Author information

1

*Bay Area Laser Institute, San Francisco, California; [□]AboutSkin Dermatology and DermSurgery, Englewood, Colorado; [□]DeNova Research, Chicago, Illinois; [§]SkinCare Physicians, Chestnut Hill, Massachusetts; ^{||}Division of Dermatology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California; [¶]AVA MD, Santa Monica, California; [#]UC Davis Medical Group, Sacramento, California; ^{**}Bellaire Dermatology Associates, Bellaire, Texas; ^{□□}Private Practice, Bradenton, Florida; ^{□□}University of Washington, School of Medicine, Seattle, Washington; ^{§§}Peloton Advantage, Parsippany, New Jersey; ^{|||}Allergan plc, Irvine, California.

Erratum in

- [A Comprehensive Approach to Multimodal Facial Aesthetic Treatment: Injection Techniques and Treatment Characteristics From the HARMONY Study: ERRATUM.](#) [Dermatol Surg. 2016]

Abstract

BACKGROUND:

The HARMONY study is the first clinical trial to assess the impact of a global approach to facial rejuvenation with several minimally invasive modalities, using patient-reported outcome measures.

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Select item 27128248 ☐ 46. **.Include**

[Dermatol Surg.](#) 2016 May;42 Suppl 2:S77-82. doi: 10.1097/DSS.0000000000000740.

Rejuvenation of the Upper Face and Periocular Region: Combining Neuromodulator, Facial Filler, Laser, Light, and Energy-Based Therapies for Optimal Results.

[Langelier N¹](#), [Beleznay K](#), [Woodward J](#).

Author information

1

*Department of Ophthalmology, Duke University Medical Center, Durham, North Carolina; [□]Department of Dermatology & Skin Science, University of British Columbia, Vancouver, British Columbia, Canada; Departments of [□]Ophthalmology, and [§]Dermatology, Duke University Medical Center, Durham, North Carolina.

Abstract

BACKGROUND:

The upper face and periocular region is a complex and dynamic part of the face. Successful rejuvenation requires a combination of minimally invasive modalities to fill dents and hollows, resurface rhytides, improve pigmentation, and smooth the mimetic muscles of the face without masking facial expression.

METHODS:

Using review of the literature and clinical experience, the authors discuss our strategy for combining botulinum toxin, facial filler, ablative laser, intense pulsed light, microfocused ultrasound, and microneedle fractional radiofrequency to treat aesthetic problems of the upper face including brow ptosis, temple volume loss, A-frame deformity of the superior sulcus, and superficial and deep rhytides.

RESULTS:

With attention to safety recommendations, injectable, light, laser, and energy-based treatments can be safely combined in experienced hands to provide enhanced outcomes in the rejuvenation of the upper face.

CONCLUSION:

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OBJECTIVE:

Provide details of this treatment approach and describe investigators' experiences and recommendations based on this study.

METHODS:

This multicenter, 4-month study evaluated subject satisfaction with and psychological impact of combined treatment with VYC-20L (Juvéderm Voluma XC), HYC-24L (Juvéderm Ultra XC), HYC-24L+ (Juvéderm Ultra Plus XC), onabotulinumtoxinA (Botox), and bimatoprost 0.3% ophthalmic solution (Latisse). Treatment-naïve adults with moderate-to-severe facial lines and folds and eyelash hypotrichosis received on-label, staged treatment with fillers. Bimatoprost was self-administered once daily for 17 weeks from day 1. OnabotulinumtoxinA was administered for glabellar lines, crow's feet lines, or both at month 3.

RESULTS:

Overall, 100 subjects received bimatoprost for eyelash hypotrichosis, 96 received onabotulinumtoxinA for glabellar lines and/or crow's feet lines, and 96 received VYC-20L for midface volume deficit. From 17 to 96 subjects received HYC-24L and/or HYC-24L+ for nasolabial folds, oral commissures, marionette lines, perioral lines, or radial cheek lines. Injections of filler generally progressed from cranial to caudal, with midface injected first. Investigator-reported factors that may have contributed to the potential benefits of this approach include the critical role of the midface in facial aesthetics, use of lower volumes of filler in individual facial areas, and anesthetic effects.

CONCLUSION:

The investigators' perspectives and experience with the injection pattern, sequencing, volumes, and techniques may provide valuable guidance for a multimodal approach to facial aesthetic treatment.

PMID:

27128246

DOI:

[10.1097/DSS.0000000000000743](https://doi.org/10.1097/DSS.0000000000000743)

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Select item 27050698 ☐ 48. **Not relevant. Non clinical**

[J Drugs Dermatol](#). 2016 Apr;15(4):434-41.

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.

Sundaram H, Mackiewicz N, Burton E, Peno-Mazzarino L, Lati E, Meunier S.

Abstract

BACKGROUND:

Hyaluronic acid (HA) is a popular ingredient in topical formulations for cosmetic improvement of the skin. Most formulations contain linear, non-crosslinked HA oligomers, low molecular weight (LMW) HA, and/or high molecular weight (HMW) HA. Crosslinking of HA enhances its clinical longevity and mechanical characteristics. The objective of this study was to characterize the topical effects of a new, crosslinked resilient HA (RHA) that is also available as a cohesive, tissue-integrating injectable filler, compared with non-crosslinked HMW HA and LMW HA. Living human skin explants that preserve the 3-dimensional structure of in vivo skin were used to maximize clinical relevance.

METHODS:

Standardized doses of each HA product were applied daily for 9 days to human skin explant surfaces. Untreated explants served as controls. Water content of the stratum corneum and entire epidermis was analyzed by Raman spectroscopy. Transepidermal water loss (TEWL) was measured to assess skin barrier function. Explant morphology and microrelief were evaluated by optical and scanning electron microscopy.

RESULTS:

Crosslinked RHA achieved a significant increase in epidermal water content (7.6%) over the control. Spectral cartography confirmed a higher epidermal water content with RHA than with HMW HA or LMW HA. TEWL was reduced by 27.8% with RHA, and by 15.6% with HMW HA, but increased by 55.5% with LMW HA. Cutaneous microrelief improved with RHA. Corneocyte cohesion improved with RHA and HMW HA.

CONCLUSIONS:

This comparative, multimodal study demonstrated greater benefits of topical crosslinked RHA over linear HMW HA or LMW HA in reducing TEWL, retaining and redistributing water within the epidermis, maintaining skin integrity, and improving skin barrier structure and function. RHA was a more efficacious humectant than LMW HA, and a more efficacious occlusive moisturizer than HMW HA. These integrative epidermal repair activities are of significant value for addressing primary deficits of aging skin, improving tolerance to retinoids and other topical agents, and optimizing procedural outcomes. A combination of topical and injectable HA provides an elegant model of synergistic, multi-level skin restoration.

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26966384

PMCID:

[PMC4770068](#)

DOI:

[10.2147/CCID.S95108](#)

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Select item 26964566 ☐ 50. **..Include**

[Glycobiology](#), 2016 Jun;26(6):553-9. doi: 10.1093/glycob/cww033. Epub 2016 Mar 9.

Hyaluronan: More than just a wrinkle filler.

[Maytin EV](#)¹.

Author information

1

Department of Dermatology Department of Biomedical Engineering, Cleveland Clinic, Cleveland, OH 44195, USA maytin@ccf.org.

Abstract

Dermatology is a field that strives not only to alleviate skin disease (therapeutics) but also to improve the perception of wellness (cosmetics). Thus, in this special issue of *Glycobiology*, it seems appropriate to discuss the biology of a glycosaminoglycan, called hyaluronic acid (hyaluronan, or HA), that has become the most popular agent today for intradermal injections to improve wrinkles and other cosmetic defects. HA is a simple linear polymer in which a simple disaccharide is repeated thousands of time, thereby creating a huge hydrophilic molecule that confers a large volume of hydration and contributes to the turgor and flexibility of healthy skin. Beyond cosmetic considerations, however, HA also has important biological and physiological functions that were largely under-appreciated until recently. New research has confirmed that HA is dynamically produced by most skin cells, not only fibroblasts (the cells that make most of the skin's extracellular matrix) but also by keratinocytes in the outer protective layer (epidermis). For both fibroblasts and keratinocytes, HA plays a regulatory role in controlling cell physiology through interaction of extracellular HA with a major cell-surface receptor, CD44. This interaction mediates intracellular signaling both directly and indirectly, through CD44 interactions with the cytoskeleton and with EGF and TGF β receptors. Furthermore, degradation of HA by specific hyaluronidase enzymes produces HA fragments that can help to regulate inflammatory

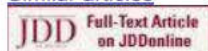
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27050698

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Select item 26966384 ☐ 49. **Not relevant- non clinical**

[Clin Cosmet Investig Dermatol](#). 2016 Feb 23;9:41-53. doi: 10.2147/CCID.S95108. eCollection 2016.

In vitro study of RRS HA injectable mesotherapy/biorevitalization product on human skin fibroblasts and its clinical utilization.

[Deglesne PA¹](#), [Arroyo R¹](#), [Ranneva E¹](#), [Deprez P¹](#).

Author information

¹

Research and Development, SKIN TECH PHARMA GROUP, Castelló d'Empúries, Spain.

Abstract

Mesotherapy/biorevitalization with hyaluronic acid (HA) is a treatment approach currently used for skin rejuvenation. Various products with a wide range of polycomponent formulations are available on the market. Most of these formulations contain noncross-linked HA in combination with a biorevitalization cocktail, formed by various amounts of vitamins, minerals, amino acids, nucleotides, coenzymes, and antioxidants. Although ingredients are very similar among the different products, in vitro and clinical effects may vary substantially. There is a real need for better characterization of these products in terms of their action on human skin or in vitro skin models. In this study, we analyzed the effect of the RRS(®) (Repairs, Refills, Stimulates) HA injectable medical device on human skin fibroblasts in vitro. Skin fibroblast viability and its capacity to induce the production of key extracellular matrix were evaluated in the presence of different concentrations of RRS HA injectable. Viability was evaluated through colorimetric MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) assay, and key extracellular matrix genes, type I collagen and elastin, were quantified by quantitative polymerase chain reaction. Results demonstrated that RRS HA injectable could promote human skin fibroblast viability (+15%) and increase fibroblast gene expression of type I collagen and elastin by 9.7-fold and 14-fold in vitro, respectively. These results demonstrate that mesotherapy/biorevitalization products can, at least in vitro, effectively modulate human skin fibroblasts.

KEYWORDS:

RRS; collagen; elastin; extracellular matrix; medical device; mesotherapy

PMID:

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processes. In this review, current knowledge about the role of HA in skin inflammation and wound healing are reviewed and possible future applications of such knowledge discussed.

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KEYWORDS:

fibrosis; glycosaminoglycan; inflammation; skin; wound healing

PMID:

26964566

PMCID:

[PMC4847620](#)

DOI:

[10.1093/qlycob/cww033](#)

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Select item 26910661 ☐ 51. **.Include**

[Plast Reconstr Surg.](#) 2016 Mar;137(3):809-16. doi: 10.1097/01.prs.0000480686.68275.60.

A Split-Face Study of the Effects of a Stabilized Hyaluronic Acid-Based Gel of Nonanimal Origin for Facial Skin Rejuvenation Using a Stamp-Type Multineedle Injector: A Randomized Clinical Trial.

[Roh NK¹](#), [Kim MJ](#), [Lee YW](#), [Choe YB](#), [Ahn KJ](#).

[Author information](#)

1

Seoul, Republic of Korea From the Department of Dermatology, Konkuk University School of Medicine, and the Research Institute of Medical Science, Konkuk University.

Abstract

BACKGROUND:

The mid-dermal injection of stabilized hyaluronic acid-based gel of nonanimal origin has been shown to be an effective method for skin rejuvenation. The previous manual technique, using a prefilled syringe, made it difficult to precisely control the injection into the mid-dermal layers and to achieve an even distribution of gel across the area. This single-center, evaluator-blinded,

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prospective, split-face, randomized controlled trial investigated the efficacy and safety of nonanimal stabilized hyaluronic acid using a stamp-type electronic multineedle injector.

METHODS:

Twenty-five patients (aged 27 to 59 years) were recruited into this study. Each participant submitted to a single treatment with a nonanimal stabilized hyaluronic acid injection to one side of the lower cheek. The skin hydration, melanin content, erythema, and elasticity of both cheeks were evaluated at each follow-up visit, at 1, 2, 4, 8, and 12 weeks after treatment.

RESULTS:

Stratum corneum hydration was significantly improved after injection. Although no significant improvement was observed at 1 week after treatment, the Corneometer readings for the treated side were significantly higher than those for the untreated the side after the 2-, 4-, 8-, and 12-week treatment visits. Skin elasticity was also significantly improved during the study. The injection had no significant effect on the melanin and erythema indices throughout the follow-up period. The treatment was well tolerated, and no serious adverse events were reported.

CONCLUSIONS:

Nonanimal stabilized hyaluronic acid treatment resulted in improved hydration and elasticity of the facial skin. The specialized stamp-type electronic multineedle injector enables the hyaluronic acid filler to rejuvenate the skin effectively and safely.

CLINICAL QUESTION/LEVEL OF EVIDENCE:

Therapeutic, II.

TRIAL REGISTRATION:

ClinicalTrials.gov [NCT02312154](https://clinicaltrials.gov/ct2/show/study/NCT02312154).

PMID:

26910661

DOI:

[10.1097/01.prs.0000480686.68275.60](https://doi.org/10.1097/01.prs.0000480686.68275.60)

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Publication types, MeSH terms, Substances, Secondary source ID

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Select item 26839493 ☐ 52. **Not relevant**
[J Korean Med Sci](#). 2016 Feb;31(2):330. doi: 10.3346/jkms.2016.31.2.330. Epub 2016 Jan 25.

Notice of Retraction: Pak CS, et al. A Phase III, Randomized, Double-Blind, Matched-Pairs, Active-Controlled Clinical Trial and Preclinical Animal Study to Compare the Durability, Efficacy and Safety between Polynucleotide Filler and Hyaluronic Acid Filler in the Correction of Crow's Feet: A New Concept of Regenerative Filler. J Korean Med Sci 2014; 29(Suppl 3): S201-S209.

[No authors listed]

Retraction of

- [A phase III, randomized, double-blind, matched-pairs, active-controlled clinical trial and preclinical animal study to compare the durability, efficacy and safety between polynucleotide filler and hyaluronic acid filler in the correction of crow's feet: a new concept of regenerative filler.](#) [J Korean Med Sci. 2014]

PMID:

26839493

PMCID:

[PMC4729519](#)

DOI:

[10.3346/jkms.2016.31.2.330](#)

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Select item 26814448 ☐ 53. **Not relevant**
[Dermatol Ther](#). 2016 Jan-Feb;29(1):37-40. doi: 10.1111/dth.12299. Epub 2015 Nov 2.

Long-chain polynucleotide filler for skin rejuvenation: efficacy and complications in five patients.

[Park KY](#)¹, [Seok J](#)¹, [Rho NK](#)², [Kim BJ](#)¹, [Kim MN](#)¹.

Author information

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The article is a detailed update regarding cosmetic injectable fillers, specifically focusing on hyaluronic acid fillers. Hyaluronic acid-injectable fillers are used extensively for soft tissue volumizing and contouring. Many different hyaluronic acid-injectable fillers are available on the market and differ in terms of hyaluronic acid concentration, particle size, cross-linking density, requisite needle size, duration, stiffness, hydration, presence of lidocaine, type of cross-linking technology, and cost. Hyaluronic acid is a natural component of many soft tissues, is identical across species minimizing immunogenicity has been linked to wound healing and skin regeneration, and is currently actively being studied for tissue engineering purposes. The biomechanical and biochemical effects of HA on the local microenvironment of the injected site are key to its success as a soft tissue filler. Knowledge of the tissue-device interface will help guide the facial practitioner and lead to optimal outcomes for patients.

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KEYWORDS:

Cosmetic injectables; HA fillers; Hyaluronic acid; Injectable fillers; Tissue device interface

PMID:

26505539

DOI:

[10.1016/j.fsc.2015.07.002](https://doi.org/10.1016/j.fsc.2015.07.002)

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Select item 26446059 ☐ 55. **Not relevant**

[Aesthet Surg J.](#) 2016 Feb;36(2):132-5. doi: 10.1093/asj/sjv195. Epub 2015 Oct 7.

Complications and Management of Polymethylmethacrylate (PMMA) Injections to the Midface.

[Limongi RM¹](#), [Tao J¹](#), [Borba A¹](#), [Pereira F¹](#), [Pimentel AR¹](#), [Akaishi P¹](#), [Velasco e Cruz AA¹](#).

Author information

1

Dr Limongi is an Affiliate Professor, Ophthalmology Referral Center at the Hospital das Clínicas, Federal University of Goiás, Goiânia, Goiás, Brazil. Dr Tao is an Affiliate Professor, Gavin Herbert Eye Institute, University of California, Irvine, CA, USA. Dr Borba is an Affiliate Professor, Department of Ophthalmology, University of São Paulo, São Paulo, Brazil. Drs Pereira and Akaishi are Affiliate Professors, and Dr Cruz is Chairman and Professor, Department of Ophthalmology, University of São Paulo - Ribeirão Preto, São Paulo, Brazil. Dr Pimentel is an Affiliate Professor, Department of Ophthalmology, University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil.

Abstract

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- 1 Departments of Dermatology, Chung-Ang University College of Medicine, Seoul, Korea.
- 2 Leaders Aesthetic Laser and Cosmetic Surgery Center, Seoul, Korea.

Abstract

Aging well has become the new target of preventative medicine, and aesthetic dermatology can contribute to this request. The polynucleotide (PN) containing products not only fill the space, but improve tissue regeneration, resulting in more natural tissue regeneration. Five Korean women received four times injections of long-chain PN filler in two-week intervals for skin rejuvenation. About 0.05 mL of material was injected in 40 points of one-side cheek. The pore and skin thickness were markedly improved in the patients in their 30s, whereas skin tone, melanin, wrinkles, and sagging were noticeably improved for patients in their 40s. There are no serious side effects. In conclusion, intradermal long-chain PN filler injection seems to be an effective and safe treatment for skin rejuvenation.

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KEYWORDS:

filler; polynucleotide; skin rejuvenation

PMID:

26814448

DOI:

[10.1111/dth.12299](https://doi.org/10.1111/dth.12299)

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Select item 26505539 ☐ 54. **.Include**

[Facial Plast Surg Clin North Am](#), 2015 Nov;23(4):423-32. doi: 10.1016/j.fsc.2015.07.002.

The Hyaluronic Acid Fillers: Current Understanding of the Tissue Device Interface.

[Greene JJ¹](#), [Sidle DM²](#).

Author information

- 1 Department of Otolaryngology - Head and Neck Surgery, Northwestern University, 676 N. St. Clair, Suite 1325, Chicago, IL 60611, USA.
- 2 Department of Otolaryngology - Head and Neck Surgery, Northwestern University, 676 N. St. Clair, Suite 1325, Chicago, IL 60611, USA. Electronic address: dsidle@nm.org.

Abstract

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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BACKGROUND:

Polymethylmethacrylate (PMMA) has been used as an injectable filler to treat hollows and reduce rhytids. PMMA injections have been associated with several side effects, however, the literature is scarce on periorbital complications and their treatments.

OBJECTIVES:

The purpose of this study is to report a series of complications after periorbital PMMA injections to the midface and to describe their management.

METHODS:

Retrospective chart review, including photography and histopathology when available.

RESULTS:

The authors identified 11 cases of complications of PMMA injections to the midface. Patient ages ranged from 36 to 62 years (mean, 47 years; median, 44 years). Two (18%) were males and 9 (82%) were females. Adverse effects began between 2 to 24 months after injection (mean, 7.2 months; median, 6 months). All patients had edema, erythema, and contour irregularity. Seven (64%) patients had nodules, 4 (36%) had yellow, xanthomatous skin changes, and 2 (18%) had eyelid malposition. Histopathology demonstrated a giant cell inflammation in 5 of 6 cases. Corticosteroid injection was tried in 6 cases but was associated with minimal clinical improvement. Surgical debulking of the implanted material was performed in 9 (82%) cases and was effective in improving edema, erythema, and nodularity.

CONCLUSIONS:

PMMA injection to the midface may be associated with chronic inflammation, fibrotic nodules, yellowing of the skin, and eyelid malposition. Intralesional corticosteroid injections yielded minimal or no improvement; surgical debulking achieved favorable results. LEVEL OF EVIDENCE 4: Therapeutic.

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PMID:

26446059

DOI:

[10.1093/asi/siv195](https://doi.org/10.1093/asi/siv195)

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DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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Select item 26441095

56. **.Include**

[Plast Reconstr Surg.](#) 2015 Nov;136(5 Suppl):149S-163S. doi: 10.1097/PRS.0000000000001835.

Cohesive Polydensified Matrix Hyaluronic Acid for Fine Lines.

[Sundaram H¹](#), [Fagien S.](#)

[Author information](#)

1

Rockville, Md.; and Boca Raton, Fla. From the Private Practice, Dermatology, Cosmetic & Laser Surgery; and private surgical practice.

Abstract

BACKGROUND:

Fine lines and crepey skin are dermal manifestations of multilevel, age-related volume loss. It is, therefore, logical to combine intradermal volumetry for fine lines with subcutaneous volumetry for contours. This publication provides evidence- and experience-based rationales for application of cohesive polydensified matrix hyaluronic acid filler (Belotero Balance).

METHODS:

Evidence level II data demonstrate efficacy of this product and longevity for up to a year or more with intradermal, superficial blanch injection. Its softness, flow tendencies, and homogeneous tissue integration are informed by low elasticity (G') and viscosity, high cohesivity, and high tan delta. Ultrastructural analysis confirms variable-density cross-linking, intended to confer resilience, and absence of detectable particles, minimizing Tyndall effect.

RESULTS:

Scientific properties of Belotero Balance predict its 3-dimensional tissue expansion with prominent horizontal vectoring. We define this as superficial flow volumetry. High cohesivity and resilience can maintain structural integrity in typically mobile facial areas with strong muscular forces, uneven pressure, and significant hyaluronidase activity. This facilitates a natural appearance, both in repose and animation.

CONCLUSIONS:

Based on available evidence and experience, cohesive polydensified matrix hyaluronic acid is a notably efficacious fine line filler. The ideal fine line filler would restore dermis structurally and dynamically-moving as one with it, efficaciously expanding it, withstanding mechanical stress, swelling minimally, and potentially stimulating collagenesis. The relative contributions of space-filling, water binding, and collagenesis have implications for efficacy. A focus of current research is to determine the impact of filler cohesivity and tissue integration on these ideal qualities.

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26441095

DOI:

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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Select item 26441093 ☐ 57. **.Include**

[Plast Reconstr Surg.](#) 2015 Nov;136(5 Suppl):132S-138S. doi: 10.1097/PRS.0000000000001834.

Current Concepts in the Use of Small-Particle Hyaluronic Acid.

[Bertucci V¹](#), [Lynde CB](#).

[Author information](#)

1

Toronto, Ontario, Canada From the Division of Dermatology, University of Toronto.

Abstract

BACKGROUND:

Soft-tissue augmentation with hyaluronic acid (HA) fillers has become one of the most popular cosmetic procedures performed. HA fillers represent safe and commonly used fillers. Several different HA fillers are available. The differences lie in the manufacturing process, allowing for tailored uses. A small-particle HA with lidocaine (SP-HAL; Restylane Silk; Galderma, Uppsala, Sweden) was approved by the US Food and Drug Administration in June 2014 but has been available for many years in Canada as Restylane Fine Lines and in Europe as Restylane Vital.

METHODS:

Relevant articles were reviewed relating to the composition, effectiveness, and safety of SP-HAL. We also discuss the author's extensive clinical experience in the use of this product in Canada.

RESULTS:

SP-HAL has demonstrated proven benefits for lip fullness, augmentation, and treatment of perioral rhytides. Although off-label in the United States, SP-HAL is also well suited for the treatment of superficial fine lines, including periorbital, forehead, marionette, and smile lines. In addition, it has also been used in the tear trough region. A novel application for SP-HAL includes use as a skinbooster with intradermal micropuncture. In this technique, small aliquots of product are injected so as to gradually rejuvenate the skin in areas such as the face and hands. Side effects of SP-HAL were generally transient and mild. The most common side effects were swelling, tenderness, bruising, pain, and redness.

CONCLUSION:

SP-HAL is an effective and safe HA filler with varied clinical uses.

PMID:

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26441093

DOI:

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Select item 26354254 ☐ 58. **Not relevant**

[Mater Sci Eng C Mater Biol Appl.](#) 2015 Dec 1;57:189-96. doi: 10.1016/j.msec.2015.07.059. Epub 2015 Jul 30.

Novel hydrogels based on carboxyl pullulan and collagen crosslinking with 1, 4-butanediol diglycidylether for use as a dermal filler: initial in vitro and in vivo investigations.

[Li X¹](#), [Xue W²](#), [Zhu C¹](#), [Fan D³](#), [Liu Y¹](#), [XiaoxuanMa¹](#).

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Shaanxi Key Laboratory of Degradable Biomedical Materials, Department of Chemical Engineering, Northwest University, Taibai North Road 229, Xi'an, Shaanxi 710069, China.

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Shaanxi Provincial Institute of Microbiology, Xi'an 710043, China.

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Shaanxi Key Laboratory of Degradable Biomedical Materials, Department of Chemical Engineering, Northwest University, Taibai North Road 229, Xi'an, Shaanxi 710069, China. Electronic address: fandaidi@nwu.edu.cn.

Abstract

Novel hydrogels based on carboxyl pullulan (PC) and human-like collagen (HLC) crosslinking with 1,4-butanediol diglycidyl ether (BDDE) are promising soft fillers for tissue engineering due to their highly tunable properties. Recent studies, however, have shown that incorporating hyaluronic acid and BDDE results in hydrogels with a microporous structure, a large pore size and high porosity, which reduce cell adhesion and enhance degradation in vivo. To improve biocompatibility and prevent biodegradation, the use of PC to replace hyaluronic acid in the fabrication of PC/BDDE (PCB) and PC/BDDE/HLC (PCBH) hydrogels was investigated. Preparation of gels with PC is a promising strategy due to the high reactivity, superb selectivity, and mild reaction conditions of PC. In particular, the Schiff base reaction of HLC and PC produces the novel functional group -RCONHR' in PCBH hydrogels. Twenty-four weeks after subcutaneous injection of either PCB or PCBH hydrogel in mice, the surrounding tissue inflammation, enzymatic response and cell attachment were better compared to hyaluronic acid-based hydrogels. However, the biocompatibility, cytocompatibility and non-biodegradability of PCBH were milder than those of the PCB hydrogels both in vivo and in vitro. These results show

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that the proposed use of PC and HLC for the fabrication of hydrogels is a promising strategy for generating soft filler for tissue engineering.

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KEYWORDS:

BDDE; Carboxyl pullulan; Collagen; Soft filler; Tissue engineering

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26354254

DOI:

[10.1016/j.msec.2015.07.059](https://doi.org/10.1016/j.msec.2015.07.059)

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Select item 26311237 ☐ 59. **Not relevant- technique paper**

[J Cosmet Dermatol](#). 2015 Sep;14(3):254-9. doi: 10.1111/jocd.12155. Epub 2015 Jul 16.

Temporal fossa defects: techniques for injecting hyaluronic acid filler and complications after hyaluronic acid filler injection.

[Juhász ML](#)¹, [Marmur ES](#)^{1,2}.

Author information

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Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA.

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Marmur Medical, New York, NY, USA.

Abstract

Facial changes with aging include thinning of the epidermis, loss of skin elasticity, atrophy of muscle, and subcutaneous fat and bony changes, all which result in a loss of volume. As temporal bones become more concave, and the temporalis atrophies and the temporal fat pad decreases, volume loss leads to an undesirable, gaunt appearance. By altering the temporal fossa and upper face with hyaluronic acid filler, those whose specialty is injecting filler can achieve a balanced and more youthful facial structure. Many techniques have been described to inject filler into the fossa including a "fanned" pattern of injections, highly diluted filler injection, and the method we describe using a three-injection approach. Complications of filler in the temporal fossa include bruising, tenderness, swelling, Tyndall effect, overcorrection, and chewing discomfort. Although rare, more serious complications include infection, foreign body granuloma, intravascular necrosis, and blindness due to embolization into the ophthalmic artery. Using

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reversible hyaluronic acid fillers, hyaluronidase can be used to relieve any discomfort felt by the patient. Injectors must be aware of the complications that may occur and provide treatment readily to avoid morbidities associated with filler injection into this sensitive area.

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KEYWORDS:

cosmetic procedure; filler; hyaluronic acid; temporal fossa; volume deficit

PMID:

26311237

DOI:

[10.1111/iocd.12155](https://doi.org/10.1111/iocd.12155)

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Select item 26148564 ☐ 60. **.Include**

[HNO](#). 2015 Jul;63(7):497-503. doi: 10.1007/s00106-015-0033-6.

[Transfer of autologous fat and plasma : The future of anti-aging medicine?].

[Article in German]

[Bioulac B](#)¹, [Heppt W](#), [Heppt M](#).

Author information

1

Fachabteilung für Gynäkologie, Krankenhäuser Landkreis Freudenstadt gGmbH,
Akademisches Lehrkrankenhaus der Universität Tübingen, Karl-von-Hahn-Straße 120,
72250, Freudenstadt, Deutschland, Bruno.Bioulac@klf-net.de.

Abstract

BACKGROUND:

Aging is a complex process driven by endogenous and exogenous stimuli. The distinct cellular and noncellular components of skin and adjacent connective tissue are constantly and irreversibly degraded during aging.

OBJECTIVES:

The aim was to provide an overview of the biology of skin aging and the therapeutic options for rejuvenation.

METHODS:

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A review of the current literature and a demonstration of autologous fat transfer and platelet-rich plasma (PRP) are presented from a clinical perspective.

RESULTS:

The aging process affects cellular components and the extracellular matrix (ECM); thus, the first stage is the degradation of the ECM. The loss of skin elasticity is induced by a breakdown of fibers such as collagen, elastin, or reticulin, whereas the degradation of proteoglycans results in decreased turgor and skin hydration. Synthetic filling agents primarily compensate for volume loss, but do not rejuvenate biologically. In contrast, the transfer of autologous fat and PRP is based on activating stem cell populations and growth factors, in addition to providing volume to target regions.

CONCLUSIONS:

A profound comprehension of the cellular and molecular mechanisms of aging is important in anti-aging medicine. The transfer of autologous fat and PRP offers interesting alternatives in the sense of more biological skin rejuvenation.

PMID:

26148564

DOI:

[10.1007/s00106-015-0033-6](https://doi.org/10.1007/s00106-015-0033-6)

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[Publication types, MeSH terms, Substance](#)

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Select item 26148563 ☐ 61. **Not relevant-have similar paper presented in CER**

[HNO](#). 2015 Jul;63(7):472-80. doi: 10.1007/s00106-015-0030-9.

[Fillers and associated side effects].

[Article in German]

Heppt M¹, Hartmann D, Reinholz M, Feller-Heppt G, Ruzicka T, Gauglitz GG.

Author information

1

Klinik und Poliklinik für Dermatologie und Allergologie, Klinikum der Universität München (LMU), Frauenlobstr. 9-11, 80337, München, Deutschland, Markus.Heppt@med.uni-muenchen.de.

Abstract

BACKGROUND:

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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A variety of fillers is commonly used for tissue augmentation as well as skin rejuvenation, and consist of a large heterogeneous group of biomaterials. The objective was to provide an overview and classification of the most commonly injected filler materials and filler-related complications including therapy.

METHOD:

A summary of the current literature and common associated side effects is provided from a personal clinical perspective.

RESULTS:

According to degradability, filler materials can be classified as temporary (degradable), semi-permanent, and permanent (nondegradable). Temporary fillers such as hyaluronic acid and collagen are completely degraded by the surrounding tissue within several months. Semi-permanent fillers are degradable, but may induce longer-lasting secondary effects. Permanent fillers such as silicone and mineral oil derivatives are not biodegradable and have been increasingly abandoned because of severe and irreversible side effects. The most common filler-related adverse events include pigmentation changes, edema and post-injection deformations. Visible or palpable nodules can be due to filler accumulation, formation of granuloma, or infection.

CONCLUSIONS:

Substantial knowledge of the chemical and clinical features of the injected materials is indispensable for safe and efficient application. Early recognition of filler-related adverse effects is important to avoid severe complications and to achieve optimal results.

PMID:

26148563

DOI:

[10.1007/s00106-015-0030-9](https://doi.org/10.1007/s00106-015-0030-9)

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[Publication types, MeSH terms, Substances](#)

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Select item 26015882 ☐ 62. **.Include**

[Arch Plast Surg.](#) 2015 May;42(3):282-7. doi: 10.5999/aps.2015.42.3.282. Epub 2015 May 14.

[Rejuvenating Effects of Facial Hydrofilling using Restylane Vital.](#)

[Lee BM](#)¹, [Han DG](#)¹, [Choi WS](#)².

[Author information](#)

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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1

Department of Plastic and Reconstructive Surgery, Catholic University of Daegu School of Medicine, Daegu, Korea.

2

V-Plastic Surgery Group, Daegu, Korea.

Abstract

BACKGROUND:

Morphological changes that accompany aging, such as wrinkles and skin laxity, are particularly prominent on facial skin. Recently, facial rejuvenation using the hydrofilling effect of hyaluronic acid (HA) filler has been employed for improvement of skin texture. In this study, we studied rejuvenating effects of stabilized HA (Restylane Vital) through direct intradermal injections.

METHODS:

A total of 30 female patients underwent a series of procedures on face, including three sessions at intervals of four weeks. A total of 2 mL of Restylane Vital was injected along the whole face using an automatic injector. Improvement of skin surface roughness, elasticity, brightness, moisture, and fine wrinkles was evaluated. Patient satisfaction was evaluated, and pictures of patients were taken at each visit and 6 months after last treatment session. Scoring for each patient was performed by three doctors according in five subjects. Moisture, oil and elasticity were measured before the procedure and before the last treatment in 10 patients.

RESULTS:

The majority of patients (77%) were satisfied with the therapeutic outcomes. Approximately 66% of patients responded that the effects of this procedure persisted for longer than four months, and the majority of patients (77%) wanted to undergo this procedure again and would recommend this procedure to acquaintances. Regarding doctors' evaluation, scores for improvement of skin surface roughness, elasticity, and brightness were significantly higher than those for improvement of moisture and fine wrinkle.

CONCLUSIONS:

Intradermal injection of HA can have a rejuvenating effect on dry and tired facial skin, especially in improvement of skin surface roughness.

KEYWORDS:

Hyaluronic acid; Injection, intradermal; Rejuvenation

PMID:

26015882

PMCID:

[PMC4439586](#)

DOI:

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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[10.5999/aps.2015.42.3.282](#)

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[Lasers Surg Med.](#) 2015 Jul;47(5):388-95. doi: 10.1002/lsm.22361. Epub 2015 May 6.

Efficacy of different modes of fractional CO2 laser in the treatment of primary cutaneous amyloidosis: A randomized clinical trial.

[Esmat SM¹](#), [Fawzi MM¹](#), [Gawdat HI](#), [Ali HS¹](#), [Sayed SS²](#).

Author information

1

Department of Dermatology, Kasr Al Ainy Hospital, Cairo University, Cairo, Egypt.

2

Department of Histology, Kasr Al Ainy Hospital, Cairo University, Cairo, Egypt.

Abstract

BACKGROUND:

Primary cutaneous amyloidosis (PCA) comprises three main forms: macular, lichen, and nodular amyloidosis. The current available treatments are quite disappointing.

OBJECTIVES:

Assess and compare the clinical and histological changes induced by different modes of Fractional CO2 laser in treatment of PCA.

PATIENTS AND METHODS:

Twenty five patients with PCA (16 macular and 9 lichen amyloidosis) were treated by fractional CO2 using; superficial ablation (area A) and deep rejuvenation (area B). Each patient received 4 sessions with 4 weeks intervals. Skin biopsies were obtained from all patients at baseline and one month after the last session. Patients were assessed clinically and histologically (Congo red staining, polarized light). Patients were followed-up for 3 months after treatment.

RESULTS:

Both modes yielded significant reduction of pigmentation, thickness, itching, and amyloid deposits (P-value < 0.001). However, the percentage of reduction of pigmentation was significantly higher in area A (P-value = 0.003). Pain was significantly higher in area B. Significant reduction in dermal amyloid deposits denotes their trans-epidermal elimination induced by fractional photothermolysis.

CONCLUSION:

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Both superficial and deep modes of fractional CO2 laser showed comparable efficacy in treatment of PCA. Superficial mode being better tolerated by patients, is recommended as a valid therapeutic option.

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KEYWORDS:

Deep rejuvenation; Fractional CO2; Primary cutaneous amyloidosis; Superficial ablation

PMID:

25946210

DOI:

[10.1002/ism.22361](https://doi.org/10.1002/ism.22361)

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[Publication types, MeSH terms, Supplementary concept](#)

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Select item 25828036 ☐ 64. **Not relevant**

[Dermatol Surg.](#) 2015 Apr;41 Suppl 1:S120-6. doi: 10.1097/DSS.0000000000000334.

Basics of dermal filler rheology.

[Pierre S¹](#), [Liew S](#), [Bernardin A](#).

Author information

1

*Research and Development, Allergan Industrie, Pringy, France; [□]Shape Clinic, Darlinghurst, Australia.

Abstract

BACKGROUND:

Hyaluronic acid injectable fillers are the most widely used dermal fillers to treat facial volume deficits, providing long-term facial aesthetic enhancement outcomes for the signs of aging and/or facial contouring.

OBJECTIVES:

The purpose of this article was to explain how rheology, the study of the flow of matter, can be used to help physicians differentiate between dermal fillers targeted to certain areas of the face.

METHODS:

This article describes how rheological properties affect performance when filler is used in various parts of the face and exposed to mechanical stress (shear deformation and

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compression/stretching forces) associated with daily facial animation and other commonly occurring external forces.

RESULTS:

Improving facial volume deficits with filler is linked mainly to gel viscoelasticity and cohesivity. These 2 properties set the level of resistance to lateral and vertical deformations of the filler and influence filler tissue integration through control of gel spreading.

CONCLUSION:

Selection of dermal filler with the right rheological properties is a key factor in achieving a natural-looking long-lasting desired aesthetic outcome.

PMID:

25828036

DOI:

[10.1097/DSS.0000000000000334](https://doi.org/10.1097/DSS.0000000000000334)

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[MeSH terms. Substances](#)

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Select item 25790150 ☐ 65. **.Include**

[J Cosmet Dermatol](#). 2015 Jun;14(2):145-51. doi: 10.1111/jocd.12141. Epub 2015 Mar 19.

Ocular adverse effects after facial cosmetic procedures: a review of case reports.

[Ricci LH](#)¹, [Navajas SV](#)¹, [Cameiro PR](#)¹, [Söderberg SA](#)¹, [Ferraz CA](#)^{1,2}.

Author information

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School of Medicine, Anhembi Morumbi University, Laureate International Universities, São Paulo, SP, Brazil.

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Department Ophthalmology, School of Medicine, Anhembi Morumbi University, Laureate International Universities, São Paulo, SP, Brazil.

Abstract

To review indexed literature concerning adverse ocular effects of the most common aesthetic facial procedures (light-emitting therapy, dermal fillers injection, and botulinum toxin). Literature search using three online databases - PubMed, SciELO, and Capes - selecting case reports, series of cases and reviews, with no language restriction, published in a period of the last twenty years (1995-2015). After reviewing 48 case reports and most recent reviews, the authors found the most common ocular adverse effects of dermal fillers were related to vascular

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future there were tested such properties as in vitro adhesion and occlusion related to in vivo hydration. From the silicone rubbers double layer silicone film was prepared: a non-adhesive elastomer as a drug carrier (the matrix for active substances - enoxaparin sodium - low molecular weight heparin) and an adhesive elastomer, applied on the surface of the matrix. The novel adhesive silicone film was found to possess optimal properties in comparison to commercially available silicone dressing: adhesion in vivo, adhesion in vitro - 11.79N, occlusion F=85% and water vapor permeability in vitro - WVP=105g/m(2)/24h, hydration of stratum corneum in vivo H=61-89 (RSD=1.6-0.9%), oxygen permeation in vitro - 119-391 cm(3)/m(2)/24 (RSD=0.17%). In vitro release studies indicated sufficient LMWH release rate from silicone matrix. Developed novel adhesive silicone films were considered an effective treatment of scars and keloids and a potential drug carrier able to improve the effectiveness of therapy.

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KEYWORDS:

Adhesion; Hydration; Occlusion; Oxygen and water permeation; Skin dressing

PMID:

25639195

DOI:

[10.1016/j.iiparm.2015.01.050](https://doi.org/10.1016/j.iiparm.2015.01.050)

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Select item 25607908 ☐ 67. **Not relevant**

[J Drugs Dermatol](#), 2015 Jan;14(1):50-4.

Biological properties of a new volumizing hyaluronic acid filler: a systematic review.

[Ho D, Jagdeo J.](#)

Abstract

BACKGROUND:

Hyaluronic acid (HA) dermal fillers are effective and safe for correction of facial rhytides. A new volumizing HA filler, 20 mg/ml HA dermal filler (Juvéderm® Voluma®, Allergan Inc., Irvine, CA), is the only HA filler with a FDA indication for facial volumization due to age-related facial volume loss.

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occlusion; light-emitting therapy was associated with pigmented tissue damage leading to anterior uveitis and iris atrophy, and ptosis presented the higher relative risk associated with botulinum toxin. Even though ocular adverse effects are not very frequent, some of them can lead to permanent ocular dysfunction and visual impairment. Professionals involved in cosmetic procedures should be aware of the risks.

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KEYWORDS:

botulinum toxin; dermal fillers; facial cosmetics; intense pulsed light; ocular effects; radiofrequency

PMID:

25790150

DOI:

10.1111/jocd.12141

[Indexed for MEDLINE]

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Select item 25639195 ☐ 66. **Not relevant**

[Int J Pharm.](#) 2015 Mar 15;481(1-2):18-26. doi: 10.1016/j.ijpharm.2015.01.050. Epub 2015 Jan 29.

Double layer adhesive silicone dressing as a potential dermal drug delivery film in scar treatment.

[Mojsiewicz-Pieńkowska K¹](#), [Jamrógiewicz M²](#), [Żebrowska M³](#), [Mikolaszek B³](#), [Sznitowska M³](#).

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3

Department of Pharmaceutical Technology, Faculty of Pharmacy with Subfaculty of Laboratory Medicine, Medical University of Gdansk, 80-416 Gdańsk, Al. Gen. Hallera 107, Poland.

Abstract

The present studies focused on the evaluation of design of an adhesive silicone film intended for scar treatment. Developed silicone double layer film was examined in terms of its future relevance to therapy and applicability on the human skin considering properties which included in vitro permeability of water vapor and oxygen. In order to adapt the patches for medical use in the

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OBJECTIVE:

Evaluate the biological properties, including biochemical, biophysical and rheological, of this new 20 mg/ml HA dermal filler and discuss the importance of these properties in clinical applications.

METHODS AND MATERIALS:

A systematic search of the computerized bibliographic databases Medline, Embase, Embal, Biosis, SciSearch, Pascal, HCAPlus, IPA, and Dissertation Abstracts with key term "Voluma." Four articles on the biological properties of this new 20 mg/ ml HA dermal filler were suitable for inclusion in this review.

RESULTS:

Biological analysis of elasticity and viscosity values of this new 20 mg/ml HA dermal filler demonstrated intermediate properties in three studies and high in one study compared to other HA dermal fillers. This 20 mg/ml HA dermal filler retained the highest elasticity and viscosity values at temperature of 37°C. Histology demonstrated that this 20 mg/ml HA dermal filler has an intermediate pattern of distribution within the superficial and deep reticular dermis.

CONCLUSION:

This 20 mg/ml HA dermal filler demonstrated volumizing ability, and maintaining viscosity and free-flowing characteristics for easy injection, tissue lifting, and molding. We hope future research incorporates biological properties analysis of this HA dermal filler in clinical trials.

PMID:

25607908

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Select item 25539986 ☐ 68. **.Include**

[Aesthetic Plast Surg.](#) 2015 Feb;39(1):129-33. doi: 10.1007/s00266-014-0432-1. Epub 2014 Dec 25.

Mesotherapy with an Intradermal Hyaluronic Acid Formulation for Skin Rejuvenation: An Inpatient, Placebo-Controlled, Long-Term Trial Using High-Frequency Ultrasound.

[Tedeschi A](#), [Lacarrubba F](#), [Micali G](#).

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1

Dermatology Clinic, University of Catania, A.O.U. Policlinico-Vittorio Emanuele, Via Santa Sofia, 78, 95123, Catania, Italy.

Abstract

DOC Code C_CT_CER_005_05	Valid from 09.03.2020	Valid until 08.06.2025	Print date 09.04.2020
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Mesotherapy with hyaluronic acid (HA) is a treatment approach currently used for skin rejuvenation. High-frequency ultrasound (20-100 MHz) is a non-invasive technique that has been used to evaluate age-related dermal changes. The presence and the degree of a typical subepidermal low-echogenic band (SLEB) are photoaging related: the lower the SLEB echogenicity, the higher the photoaging. The aim of this trial was to evaluate, through ultrasound imaging, the long-term effects of microinjections of HA on SLEB echogenicity. Twenty-two women with clinical and ultrasound signs of moderate photoaging were enrolled in the study. Treatment consisted of multiple microinjections of HA salts of biotechnological origin on the dorsum of one hand, once weekly for 4 weeks and, successively, once monthly for 4 months (group A) or 9 months (group B). The dorsum of the other hand of each subject was injected with saline solution and used as a control. In all subjects, high-frequency ultrasound (22 MHz) was performed to evaluate SLEB echogenicity changes during treatment. Eighteen out of 22 patients completed the study. At the end of 4 weeks, an ultrasound increase of dermal echogenicity was observed in 13 subjects (seven of group A and six of group B), which we considered as "responders". In these patients, the Student's t-test showed a significant increase from baseline of SLEB pixel numbers of +24 % ($P < 0.01$) versus +6 % with placebo. In the same subjects, after an additional 4 months of monthly injections, the mean increase was +18 % ($P < 0.05$) versus +4 % with placebo. In patients from group B that completed 10 months of treatment, the increase from baseline of SLEB pixel numbers was +18 % ($P < 0.05$) versus 0 % with placebo. Our study suggests that mesotherapy with HA may effectively improve skin aging and photoaging, as supported by quantifiable ultrasound data showing significant changes in SLEB density over time.

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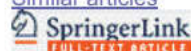
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DOI:

[10.1007/s00266-014-0432-1](https://doi.org/10.1007/s00266-014-0432-1)

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RETRACTED ARTICLE

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[J Korean Med Sci](#). 2014 Nov;29 Suppl 3:S201-9. doi: 10.3346/jkms.2014.29.S3.S201. Epub 2014 Nov 21.

A phase III, randomized, double-blind, matched-pairs, active-controlled clinical trial and preclinical animal study to compare the durability, efficacy and safety between polynucleotide filler and hyaluronic acid filler in the correction of crow's feet: a new concept of regenerative filler.

[Pak CS¹](#), [Lee J¹](#), [Lee H¹](#), [Jeong J¹](#), [Kim EH¹](#), [Jeong J¹](#), [Choi H¹](#), [Kim B¹](#), [Oh S²](#), [Kim I³](#), [Heo CY¹](#).

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Retraction in

- [Notice of Retraction: Pak CS, et al. A Phase III, Randomized, Double-Blind, Matched-Pairs, Active-Controlled Clinical Trial and Preclinical Animal Study to Compare the Durability, Efficacy and Safety between Polynucleotide Filler and Hyaluronic Acid Filler in the Correction of Crow's Feet: A New Concept of Regenerative Filler. J Korean Med Sci 2014; 29\(Suppl 3\): S201-S209. \[J Korean Med Sci. 2016\]](#)

Abstract

The Rejuran® is a new filler product made from purified polynucleotides. Here we present data from an animal study and a clinical trial to examine the durability, efficacy and safety of the Rejuran® on crow's feet. For the animal study, 25 mice were divided into three groups: Group 1 received phosphate buffered saline (PBS); Group 2 were treated with Yvoire®; and Group 3 were treated with Rejuran®. The durability and efficacy of each treatment were assessed by microscopy and staining. In the clinical trial, 72 patients were randomized to receive Rejuran® treatment for crow's feet on one side and Yvoire-Hydro® on the contralateral side, at a ratio of 1:1. Repeated treatments were performed every two weeks for a total of three times, over a total of 12 weeks' observation. All injections and observations of efficacy and safety were performed by the same two investigators. In the animal study, the Rejuran® group showed similar durability and inflammatory response to the Yvoire® group. Upon efficacy assessment, the Rejuran® group showed the greatest elasticity and collagen composition, and a significant difference in skin surface roughness and wrinkle depth. In the clinical trial, the primary and secondary objective efficacy outcome measure showed no statistical significance between the two groups, and in safety outcomes there were no unexpected adverse effects. Our data suggest that the Rejuran®, as a new regenerative filler, can be useful to reduce wrinkles, by showing evidence for its efficacy and safety.

KEYWORDS:

Polydeoxyribonucleotides; Polynucleotides; Rejuvenation; Wound Healing

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[PMC4248006](#)

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[10.3346/jkms.2014.29.S3.S201](#)

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Select item 25399623 ☐ 70. **Not relevant, indication: nasolabial folds (NLF)**[J Cosmet Dermatol](#). 2014 Dec;13(4):307-14. doi: 10.1111/jocd.12116.

A new dermal filler made of cross-linked and auto-cross-linked hyaluronic acid in the correction of facial aging defects.

[Sparavigna A¹](#), [Fino P](#), [Tenconi B](#), [Giordan N](#), [Amorosi V](#), [Scuderi N](#).[Author information](#)

1

Derming, Clinical Research and Bioengineering Institute, Monza, MB, Italy.

Abstract

BACKGROUND:

A novel Hyaluronic Acid (HA) derivative dermal filler has been developed with characteristics especially suited for nasolabial folds (NLF) and facial defects due to volume loss.

AIMS:

An open-label prospective study was carried out to evaluate this HA filler's performance in correcting facial defects due to volume loss.

METHODS:

A single Italian site treated subjects aged 30-65 for facial defects due to volume loss with a new dermal filler injectable gel; subjects returned to the clinic at 7 and 14 days, and 1, 3, 6, 9, and 12 months for follow-up. The primary effectiveness endpoint was improvement in wrinkle severity (measured using the Wrinkle Severity Rating Scale) (WSRS) and facial volume (measured using the Facial Volume Loss Scale) (FVLS) at 6 and 12 months from baseline. Secondary endpoints were safety evaluation, performance duration, product handling, subjects' and investigator's

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treatment evaluation. Assessment of aesthetic results included the skin hydration, image analysis of nasolabial folds (3D), and photographic documentation.

RESULTS:

The reduction in nasolabial wrinkles was statistically significant at 6 months after the first implant. The aesthetic improvement of 1 grade on WSRS was evident in 95% of subjects up to 3 months, in 84% of subjects up to 6 months and in 27% up to 12 months. A clinically (> 1 point improvement) and statistically significant improvement in the FVLS was observed at each study visit; in 100% of treated cases, up to 3 months and in 61% up to 9 months. Good results were obtained during the study in skin hydration. There were no severe adverse events related to treatment.

CONCLUSION:

This injectable gel is well tolerated and has been demonstrated to provide a smooth and natural improvement in facial defects due to volume loss in nasolabial folds and the malar region that lasts for up to 1 year.

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KEYWORDS:

dermal filler; facial defects; hyaluronic acid; patient satisfaction; volume loss

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Select item 25226002 ☐ 71. Not relevant, indication, correction of infraorbital hollow

[J Drugs Dermatol](#). 2014 Sep;13(9):1030-6.

Safety and efficacy of a cohesive polydensified matrix hyaluronic acid for the correction of infraorbital hollow: an observational study with results at 40 weeks.

[Hevia O](#), [Cohen BH](#), [Howell DJ](#).

Abstract

BACKGROUND: