Novel Technique of Aesthetic Skin Rejuvenation with Cellular Extracted Compounds Enriched with Tissue-Specific Peptides and Hyaluronic Acid

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Abstract

The structural composition of the skin is dynamic, exhibiting various signs of aging such as the decrease in collagen and elastin content leading to increase in tactile and visual roughness, dryness, wrinkles, fine lines and stiffness as age advances. This study was done to elicit the efficacy and potency of mesotherapy using a cocktail of triple strength nano-sized peptides from the skin, placenta, mesenchyme fortified with collagen and Hyaluronic Acid (HA) in the revitalisation of the skin of the dorsum of the hand. Ten male subjects suffering from mild signs of aging of the skin were treated with the formulation of MF+ SPMC + HA over the dorsum of both hands. The treatment course spanned over eight weeks with once a week application. Baseline assessment was done before the treatment and at the end of the first and second month and 90 days post-therapy, respectively, using photography, ultrasound comparison and biophysical parameters of the skin. The results proved the application of SPMC + HA rendered long-term hydration and improved the viscoelasticity of the treated area. The study concluded that mesotherapy application of MF+ SPMC extracts/peptides in combination with hyaluronic acid could be considered as a safe and effective method for rejuvenation of the skin of the dorsum of hands.

Keywords: Aesthetic medicine; Cell therapy; Cellular extracts; Mesotherapy; Skin rejuvenation; Stem cells

Introduction

Beauty may lie within the skin’s depth, but there is more to the skin than it appears on the surface. The physiological function of human skin is numerous, and some diseases of the skin might not just be deep [1]. Being the largest organ in the body, the skin is an essential flag of systemic illnesses [2]. The skin is engineered with the complex anatomical composition, which caters numerous vital functions [2].

The pathologies of skin are vast, and aging is one of the most common and inevitable conditions which displays both pathological and cosmetic symptoms (visible and tactile) such as dryness and roughness. These could be explained collagen and elastin content of the skin, leading to impaired structural integrity and eventually the formation of deep and superficial creases and fine lines [3]. Microscopic analysis of aging skin would reveal common pathological changes which includes significant exhaustion of the epidermal HA, flattening of the epidermal-dermal junction, reduced cell turnover rate, decreased melanocytes and their unusual activities [4]. These along with intracellular matrix and collagen dysfunction lead to physically visible conditions including dehydration, loss of skin turgor, skin atrophy, pigmentations, lentigo and keratosis. Skin peptides and HA have been implicated in age-related skin conditions [5-9], well-hydrated and youthful skin retains its turgor, elasticity and suppleness. The water content of the skin is a pivotal factor to regulate and maintain optimal physiological function [10]. The ultimate pathophysiology in aging has been explained by cellular and DNA damage by free radicals as well as mitochondrial dysfunction [11].

Hyaluronic acid

Hyaluronic Acid (HA) is most abundantly found in skin, about 50% of the total body content. Reed RK et al., [12] followed by the vitreous of the eye [13], umbilical cord [14] and the synovial fluid [15]. The HA or hyaluronate is a unique non-sulphated glycosaminoglycan, a relatively large molecule weighing up to 7 million Dalton [16] found commonly in connective, epithelial and neural tissues [14,17]. The repeating polymeric disaccharides of D-glucuronic acid and N-acetyl-D-glucosamine linked by a glucuronic β (1→3) bond makes HA a unique molecule that forms numerous different types of stable polymers with an array of physiological properties, depending upon the configurations, shapes, size, salt concentration, pH and associated cations [18]. In human body, HA is produced by the mesenchymal cells, primarily the peripheral connective tissues. The key feature of this molecule is its ability to release the high number of water molecules even at low concentration and high viscosity state [19]. As skin moisturization is vital in achieving skin beauty, commercial skin care products should include active compounds such as hyaluronic acid, which can bind water to attain water retention [20].

The era of cellular extracts

The consumption of placenta for cosmetic and therapeutic purposes is dated. Laboratory trials of placental extracts date back to the 30s by Filatov VP, who demonstrated the halt of disease progression and
The past two decades are marked by invention and vast applica- 
tions and components [31-34]. These include placental tissue, amniot-
ics, placental tissue ultra filtrate for long-term topical applications, which was prepared by the extraction of 
ective tissue, fetal skin placenta and adrenal gland. Two 

trials were designed to determine the list of indications. The following indications were listed for the fetal cutaneous explant: 
burns, scalds, irradiation burns on the skin injuries, explosion injuries, 
keratosis, hyperkeratosis, anhidrosis syndromes, ulcus cruris, senile at-
rophy of the skin, trophic disturbances in circulatory trouble, Lyell 
syndrome, cosmetic lesions, keloids, scleroderma [24,25].

Four decades of research and development of cell extracts wit- 
essed a break through in the area. The therapeutic properties of cell 

extracts were further expanded in the world of aesthetics and an-

ti-ageing and was seen to be widely used in India, Japan, Korea, 
Thailand and United States of America [26-30]. Subsequent years 
saw a different group of researchers and clinicians documenting posi-
tive therapeutic outcome using various kinds of placental prepara-
tions and components [31-34]. These include placental tissue, amniotic 

ic and chorionic membranes, amniotic fluid, umbilical cord, placental 
extracts and hyphilizates and cord blood serum, as well as number of 
differentiated cells and stem cells administered through different 
routes such as oral, subcutaneous and intramuscular [35-41].

The biological properties of placental peptides have been studied 
according to its active component. Instead of using the tissue, 
researchers have lysed placenta of full-term to obtain the bioactive 
components, an array of proteins, minerals, amino acids, and steroid 

drugs [31]. Besides cosmetic reasons, these extracts have been success-
fully used in the treatment of wounds, non-healing ulcers, and 
burns. Researchers documented an accelerated rate of reepithelialisation 
and reduced inflammation and pain syndrome [36,42].

The past two decades are marked by invention and vast applica-
tion of aesthetic formulations of organ-specific extracts from skin, 
placenta, and mesenchyme enriched with collagen via cold-enzymatic 
processing with further nano-filtration of biologically active ingredi-
ents since 2003. Nano-peptides show high bioavailability, biocom-
patibility and injectability due to the linear size of the peptides below 
ten nm and molecular weight below ten kda. The above mentioned 
advantages not only increase the biomedical applications of the na-
no-sized product but provide a unique rejuvenating and revitalising 
effect of this compelling tissue therapy, which can be applied either 
via mesotherapy or topically.

Albeit being a novel treatment modality the idea of using a nat-
urally-occurring peptides and cellular extracted compounds rich in 
growth factors and various biologically active compounds with anti-
-inflammatory, stimulatory and rejuvenation properties is not new and 
has been successfully used in aesthetic and therapeutic dermatolog-
ical and even wound-care practice. Application of cell extracts from 
skin, placenta, mesenchyme with collagen and elastin in aesthetic der-
matology and skin revitalization: evaluation of outcomes in cohort 
study [43-45].

The new dawn

Aesthetic dermatology has been of significant interest in recent 
years and it expands beyond the facial skin rejuvenation. The entire 
human body garnered much attention in this regard, with an increas-
ing concern on the hands, especially the skin of the dorsum. A casual 
handshake can reveal the state of one’s skin. Rough, wrinkly and dry 
skin of the dorsum remains a major concern despite the emergence of 
store-available hand care products. As such, the revolutionary discov-

er of cellular extracts is promising to address the above mentioned 
issues.

The application of peptides and HA has been proven to success-
fully reverse the aging manifestation of the skin [46-48]. This combi-
nation works synergistically in halting aging process as well as to 
stimulate regeneration of the tissue. Various types of skin peptides 
embedded in a meshwork of hyaluronic network provide an optimal 

micro-environment for bioactive molecules [49-51]. An important 
key feature of the peptides in this cocktail is the ability to stimulate re-
generation of fibroblasts and keratinocytes as well as collagen, elastin 
and extracellular matrix synthesis [52,53]. Besides being an excellent 
hydrating agent, the HA used in this preparation renders the structural 
integrity of dermal collagen [54]. HA has also been successfully used 
as a vector for targeted drug delivery, ensuring a more extended bio-
availability [55].

Objective

The objective of this study was to identify the efficacy, potency 
and safety of mesotherapy nano-sized peptides from the skin, placen-
ta and mesenchyme fortified with collagen and HA “SPMC + HA” in 
treating aging signs of the surface of the dorsum of the hand.

Materials and Methods

This case study was performed at the clinical research facilities 
of the European Wellness centres. A total of 10 male patients with no 
significant concurrent illness were invited in the study. All 10 under-
go eight treatment sessions using the cellular extracts concoction 
known as “SPMC + HA” (MF+ brand, Germany) and took part in the 
follow-up session. All patients were Asian; the mean age standard 
deviation was 48 ± 3.1 years old.

The used formulation “SPMC + HA” by MF+ brand (Germany) 
contains cells extracts from the skin, placenta, and mesenchyme with 
addition of pro-collagen peptides blended with HA. These compounds 
are dispersed in physiological saline solution (pH 7.0). Treatment ses-
ions were performed across eight weeks at weekly interval.

All subjects were asked not to apply any local aesthetic treatments 
and to refrain from any form of commercial food supplements with 
rejuvenating and skin firming effects during the treatment. A fol-
low-up visit was scheduled 90 days after the first treatment. A topical 
aesthetic cream EMLA (Recipharm Karlskoga AB, Sweden) was
applied to the area to be treated, and all patients were administered with injection in seated positions. Tiny amounts of the tested product (approximately 0.03 – 0.04 ml) were injected intradermally after the disinfection with an aqueous solution of chlorhexidine using a 33G needle (Beaumed, Korea) with a papule technique. The spacing between two injections was approximately 0.5 - to 1.0 cm apart; around 1 ml of the product was injected into the skin of the dorsum of both hands per session over an area of about 11x9 cm.

Assessments

Assessments were performed at the baseline, after the one, two months and the 90-day clinical follow-up visit. The next biophysical parameters were evaluated: stratum corneum hydration, measured using a capacitance device (the Corneometer CM825, Courage & Khazaka, Cologne, Germany); skin thickness, investigated ultrasonographically, using the Ultrascan C22 (Courage & Khazaka, Cologne, Germany)); and skin elasticity, using a Cutometer dual MPA 580 (Courage & Khazaka, Cologne, Germany). Three elasticity parameters were assessed: skin extensibility (the maximum extent to which the skin is stretched after applying a standard force, R0), gross elasticity (a measure of the ability of the skin to return to its original position after the force is off, R2), and viscoelasticity (the ratio of extensibility caused by the skin’s viscous vs elastic components, R6).

The measurements were conducted under air-conditioned conditions (temperature 22.5±1.5°C; relative humidity 50±10%) after an acclimatisation period at least 20 minutes. Digital photographs were taken to evaluate treatment success at the 90-day follow-up treatment using a Canon IOS R camera (Japan). Every patient was photographed at the same distance from the camera using standardized light conditions. Patients also provided written consent for the photographs to be published. Adverse events observed by the investigator or reported by the patient were recorded.

Data were summarized, and analysis of variance was used to compare means. Pair-wise comparisons controlling for the family-wise error rate were done using the Tukey test (p≤.05).

Hydration

Moisturizing increased continuously during the study period. Statistically significant gradual increases from baseline in capacitance values were obtained during the trial period (p <.05 and p<.001) (Figure 1), indicating that treatment increased horny layer hydration. Degree of hydration increased more than 16% from baseline to the fourth treatment visit (p<.001) and more than 20% from baseline to the eighth treatment visit. They were maintained until at least 30 days after the last treatment visit (p<.05 vs baseline at D60 and D90). Dermal thickness ultrasound measurements showed a profound increase in skin thickness over the study period.

Skin thickness

Ultrasound measurements reflect a continuous increase in dermal thickness within the study period (Figures 2 and 3). Increases over baseline were statistically significant from 30 days after the first treatment (p<.05) and were highly significant (p<.001) at D60 and D90.

The increased echogenicity that was evidenced at the end of the treatment is related to an increased density of dermal collagen fibres resulting from treatment.

Elasticity

Generally there was a good clinical response to the tested product “SPMC + HA” characterized by dramatic improvement of the gross elasticity of the skin: after pressure was removed from the suction...
device, the skin comes back to its original position much faster after treatment (p<.05 vs baseline at D 90). Skin extensibility showed a significant reduction from D30 to D90 (p<.05). Dermal viscoelasticity was significantly decreased throughout the trial (p<.05 at all-time points vs baseline), indicating that the skin behaved more like an utterly elastic substance in response to being stretched (Figures 4-6).

Clinical photographic evaluation

Comparisons of photographs taken before and after treatment showed that the skin on the backside of both hands looked much more hydrated, radiant and smoother (Figure 7).

Adverse events

Product was well tolerated. Unexpected adverse events weren’t reported. All expected treatment-related adverse events, such as pain and discomfort at the injection site, bruising, and the hematoma were transient.

Conclusion

Overall the achieved outcomes of the “SPMC+ HA” clinical application were therapeutically and cosmetically laudable. The clinical outcome of wrinkle-free, supple, vitalised as well as rejuvenated and pigment-free skin of the hand’s dorsum is the expected result of this novel strategy. Treatment resulted in a gradual thickening of the dermis, and increased hydration of the horny layer and the enhancement in the gross elasticity of the skin was enhanced. These biophysical changes transformed into visible changes with the decrease in skin wrinkles during the clinical follow-up period.

The tested product “SPMC + HA” (MF+, Germany) provides long-lasting and promising results of mesotherapy. This combination should be made available as one of the primary therapeutic approach in treating aging changes of the skin, taking into consideration the existing guidelines. Further studies to investigate and demonstrate the longer-term effects of “SPMC + HA” for facial rejuvenation with multiple treatment cycles and investigate the efficacy of combining treatment modalities would be of interest.


