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Technical Note

Innovation in Skin Regeneration: Novel Approaches with β-1,3/1,6-Glucan-Based Treatments

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Abstract

Skin regeneration is a multidisciplinary topic that involves plastic surgery, aesthetics, and dermatology. In the last few years, several molecules have been used to prevent or delay the skin aging process. Recently, promising investigations on novel β-1,3/1,6-glucan-based treatments, associated with sodium hyaluronate, have demonstrated the induction of a naïve biological stimulus in soft tissues. Serum Revitalizing Face (Lot 00118a0051 of 11/19/2018 approved by the Italian Ministry of Health as a Medical Device-Class I) was administered mainly on the face and forearms of the enrolled patients. The Serum Revitalizing Face was administered at T0 (first week), T1 (second week), and T2 (third week). Patients were asked to apply 1.5 mL of the serum on their skin until the product was completely absorbed. All patients were also examined by clinical assessments at different time points. The results showed that a daily application of the β-1,3/1,6-glucan induced a statistically significant increase in the elasticity of the skin.

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Keywords
β-1,3/1,6-Glucan; sodium hyaluronate; tissue regeneration

1. Introduction

Skin regeneration is a multidisciplinary approach that includes experts from plastic surgery, aesthetics, and dermatology. In some recent studies, several molecules have been reported, which can considerably slow down the aging of the skin. Further, some researchers reported desirable outcomes with novel β-1,3/1,6-glucan-based treatments, associated with sodium hyaluronate, in the induction of a naïve biological stimulus in soft tissues [1].

The use of sodium hyaluronate polymers has been successfully and widely reported in the treatment of skin disorders. For example, Castangia et al. reported the use of the liquorice extract with liposomes and hyalurosomes to protect the skin against oxidative stress injuries [2]; on the other hand, Manca et al. investigated the use of curcumin-loaded sodium hyaluronate in skin inflammation and wound repair [3]. Both these examples demonstrate that the extracellular matrix compounds exert an important influence on skin health and safety.

β-1,3/1,6-Glucan can be isolated from the cell membrane of *Saccharomyces cerevisiae* and other sources such as fungi and cereals. The structure of β-glucan is based on D-glucose polysaccharides containing the β-1,3-backbone and branch points at positions of β-1,6. Such a structure can create 3D networks that entrap cells and local growth factors. The molecular structure of β-glucans belongs to a group of molecules related to the pathogen-associated molecular patterns (PAMPs). Interestingly, the β-glucan mimics the structure of specific pathogen-associated molecules but does not show any infective behavior. An immunological reaction typically occurs when the PAMPs are bound to specific host receptors, called the pattern recognition receptors (PRRs), such as the toll-like receptor (TLR)-2/6, dectin-1, or CR-3 on the surface of the Langerhans cells [1]. The most important PRRs are the Dectin-1 receptors: they are highly expressed in many immunological cells, such as the neutrophils, eosinophils, macrophages, monocytes, several T-lymphocytes, and some cutaneous cells (e.g., keratinocytes and fibroblasts). The activated form of β-glucan can stimulate the production of many cytokines [3].

The clinical usefulness of β-glucan was assessed separately with clinical trials. Several authors reported the effects of different vitamins and β-glucans on skin hydration and elasticity. Morganti et al. complexed β-glucan with chitin nanocrystals and administered them topically as well as orally. They reported reduced wrinkling, better skin appearance, and overall general wellness. When MEBs were complexed with CN, the results were statistically more positive ($p<0.05$) for all the biophysical and clinical parameters considered [4].

Generally, the effectiveness of different molecules from the extracellular matrix, such as collagen, has been highlighted. Collagen-peptides are effective in the improvement of hydration, elasticity, and wrinkling in human skin. Do-Un et al. reported that collagen-peptides could be safely used in skin regeneration and repair [5].

Dermatological applications of β-glucan are most interesting in the clinical landscape. β-Glucans have rapidly gained a therapeutic significance in dermatology and aesthetic medicine; in fact, β-glucans can work not only as antioxidants and anti-inflammatory agents, but they can also be

involved in several regenerative procedures [6-8]. This report aims to discuss the effects of β-1,3/1,6-glucan at low concentrations because it seems to induce bio-stimulation of the skin and becomes highly useful in aesthetic medicine and regenerative dermatology.

2. Materials and Methods

This report is based on a clinical trial carried out on 60 female volunteers, ranging from 18 to 77 years old. All patients were treated with a topical application of β-1,3/1,6-glucan on their skin for four weeks.

Written and well-explained informed consent was obtained from all the participants before starting the study. Moreover, each participant was informed about the correct use of the product, its safety, the International Nomenclature of Cosmetic Ingredients (INCI) list, and other related details. Participants were also asked to report their clinical observations.

Serum Revitalizing Face (Lot 00118a0051 of 11/19/2018 approved by the Italian Ministry of Health as a Medical Device-Class I) was administered mainly on the face and forearms of the enrolled patients. The contralateral side of the face and forearms were considered as the control side for each volunteer.

2.1 Design of the Study

Serum Revitalizing Face was used mainly on the face and forearms of volunteer women enrolled to improve their skin elasticity. Patients received a topical application of 0.5 mL of β-1,3/1,6-glucan on their face, neck, breast, and forearms.

The Serum Revitalizing Face was administered at T0 (first week), T1 (second week), and T2 (third week) time points. The patients applied 1.5 mL of the serum on their skin until its complete absorption. All patients were also examined by clinical assessments at different time points.

About 10% of the patients were treated only on one side of their face, according to a previously reported protocol. The remaining patients resumed the administration of 1.5 mL of serum at three time points: T0 (baseline), T1 (15 days), and T2 (21 days) on patients' skin.

At the end of the protocol, a biopsy of the treated hemiface of each patient was performed to compare the histological findings after β-1,3/1,6-glucan therapy. Each patient was observed by a clinician every week to assess the effects of β-1,3/1,6-glucan on the skin. Pre- and post-treatment elasticity tests were performed on 30% of patients in the study group. All the patients were maintained on the same protocol for four weeks.

2.2 Instrumental Analysis

The elastic properties of the skin were evaluated by employing the "suction/elongation method." A specific probe (Cutometer dual MPA 580 – Courage + Khazaka electronic GmbH, Germany) was used for the experimental investigations. The Cutometer test can detect the deformation of a small area of the skin after a compression called "extensibility." The Cutometer can be used both in the stress/time and in the stress/strain set up. From the stress/time curve, it is easy to obtain the elastic variables of the investigated samples.

The equation [Ua/Uf = elasticity] (R2) describes the recovery of the skin after a full deformation cycle.

The equation [Ur/Uf = recovery] (R7) describes the recovery of the skin after a full suction cycle.

The experimental results were reported in percentages.

2.3 Statistical Analysis

The average experimental values obtained with the Cutometer in comparison with the basal values were calculated as follows:

-T0 (baseline);

-T1 (after 15 days).

Finally, the variations of the average instrumental values, which describe the elasticity and the hydration, were determined according to the following formula:

% variation = [(v1 – v2) / v2] x 100

v1 is the value obtained at a specific time.

v2 is the basal value obtained at a specific time.

Student's t-test was used to assess the statistical significance of the obtained values.

3. Results

In this clinical trial, the authors observed no adverse reaction and no variation in the protocol.

3.1 Tissue Properties

In Tables 1 and 2, we report the two main parameters analyzed on the skin: R2 and R7, respectively.

Table 1 R2 – "elasticity" has been evaluated as a variation of deformation cycle, with respect to the extendibility of the skin.

R2 – ua/uf - Elasticity				
N°	**T0 Not treated**	**T0 NT contralateral**	**T1 – T15 Treated (T)**	**T1 – T15 NT**
1	0.783	0.784	0.814	0.783
2	0.824	0.827	0.897	0.846
3	0.790	0.784	0.846	0.789
4	0.757	0.762	0.760	0.758
5	0.683	0.686	0.726	0.683
6	0.757	0.758	0.766	0.758
7	0.834	0.833	0.828	0.823
8	0.760	0.762	0.807	0.760
9	0.679	0.678	0.764	0.675
10	0.744	0.742	0.769	0.739
11	0.778	0.778	0.800	0.780
12	0.755	0.753	0.768	0.759
13	0.648	0.644	0.731	0.648
14	0.782	0.786	0.840	0.788
15	0.741	0.736	0.766	0.743

16	0.774	0.776	0.778	0.774
17	0.632	0.635	0.681	0.636
18	0.631	0.634	0.695	0.632
19	0.723	0.725	0.729	0.722
20	0.703	0.706	0.727	0.704
Mean	**0.739**	**0.739**	**0.775**	**0.740**
Standard Deviation	**0.059**	**0.059**	**0.054**	**0.061**
Variation %	**-0.1%**		**+4.6%**	

Table 2 R7 - "relative elastic recovery" after the suspension of the suction with respect to the maximum extendibility of the skin.

N°	**T0** **Not treated (NT)**	**T0** **NT contralateral**	**T1 – T15** **Treated (T)**	**T1 – T15** **NT contralateral**
1	0.592	0.591	0.631	0.592
2	0.641	0.644	0.686	0.641
3	0.618	0.619	0.675	0.619
4	0.589	0.589	0.592	0.590
5	0.530	0.533	0.570	0.530
6	0.614	0.616	0.626	0.615
7	0.705	0.704	0.700	0.706
8	0.639	0.642	0.660	0.635
9	0.533	0.532	0.607	0.532
10	0.612	0.610	0.628	0.612
11	0.625	0.625	0.651	0.623
12	0.608	0.605	0.621	0.607
13	0.456	0.457	0.512	0.459
14	0.646	0.650	0.701	0.652
15	0.564	0.561	0.593	0.563
16	0.575	0.570	0.581	0.575
17	0.479	0.477	0.519	0.476
18	0.481	0.479	0.523	0.478
19	0.541	0.543	0.555	0.544
20	0.557	0.553	0.571	0.554
Mean	**0.580**	**0.580**	**0.610**	**0.580**
Standard Deviation	**0.063**	**0.064**	**0.058**	**0.064**
Variation %	**+0.0%**		**+5.2%**	

4. Discussion

Scientific literature has investigated the role of local immunity and the role of tissue inflammation in the health of human skin [9].

The use of β-1,3/1,6-glucan in cosmetic treatments protects the skin from damages caused by sun exposure because of its ability to activate local macrophages and the Langerhans cells [10-12]. Furthermore, the local application of β-glucan improves wound healing and protects the skin

against infections. In our earlier work, we have described the main effects of the topical application of β-1,3/1,6-glucan on the skin [13].

The current protocol was carried out *in vivo* by using the Serum Revitalizing Face: a specific treatment devoid of any possible side effect and any form of oxidative stress. This also protects the skin from physical and environmental agents that may induce oxidative stress [14].

Our results showed that the use of β-1,3/1,6-glucan improved both elasticity and hydration of the skin and the subcutaneous area. A significant increase was observed in the values of the R2 and R7 parameters. Similar clinical and aesthetic achievements could also be obtained with concentrates of platelets, such as the PRP (platelet-rich plasma): PRP can fill wrinkles and improve skin texture and hydration. It is obtained from blood and is typically made up of two main components: red blood cells and plasma. Plasma contains white blood cells and platelets, which are rich in growth factors. In aesthetics and dermatology, PRP is infused or injected into the skin to induce collagen and elastin production. The result of such a biological regenerative process is to ensure healthy skin cells.

In conclusion, the results obtained from our clinical report have shown that the topical application of β-1,3/1,6-glucan causes a reduction in wrinkles, results in better wound healing, and offers good repair from sun damage. Finally, β-1,3/1,6-glucan can be considered as a promising tool for use in skincare products, ensuring an overall improvement of skin health.

Author Contributions

Francesco Calvani drafted the manuscript, and performed the surgical activities; Emanuele Bartoletti, Giancarlo Folchitto, Stefania Santini, Michele Fontevecchia and Alessandra Alhadeff were involved in the clinical and observational activities, end supported the first author in the drafting of the manuscript.

Conflict of Interest

The authors have declared that no competing interests exist.

References

1. Novak M, Vetvicka V. Beta-glucans, history, and the present: Immunomodulatory aspects and mechanisms of action. J Immunotoxicol. 2008; 5: 47-57.
2. Castangia I, Caddeo C, Manca ML, Casu L, Latorre AC, Díez-Sales O, et al. Delivery of liquorice extract by liposomes and hyalurosomes to protect the skin against oxidative stress injuries. Carbohydr Polym. 2015; 134: 657-663.
3. Manca ML, Castangia I, Zaru M, Nácher A, Valenti D, Fernàndez-Busquets X, et al. Development of curcumin loaded sodium hyaluronate immobilized vesicles (hyalurosomes) and their potential on skin inflammation and wound restoring. Biomaterials. 2015; 71: 100-109.
4. Morganti P, Fabrizi G, Palombo P, Palombo M, Guarneri F, Cardillo A, et al. New chitin complexes and their anti-aging activity from inside out. J Nutr Health Aging. 2012; 16: 242-245.

5. Do-Un K, Hee-Chul C, Jia C, Yasuo S, Boo-Yong L. Oral intake of low-molecular-weight collagen peptide improves hydration, elasticity, and wrinkling in human skin: A randomized, double-blind, placebo-controlled study. Nutrients. 2018; 10: 826.
6. Sun L, Zhao Y. The biological role of dectin-1 in immune response. Int Rev Immunol. 2007; 26: 349-364.
7. Kanlayavattanakul M, Lourith N. Carboxymethylglucan in cosmetics. Thai Pharm Health Sci J. 2008; 3: 378-382.
8. Ballini A, Cantore S, Scacco S, Coletti D, Tatullo M. Mesenchymal stem cells as promoters, enhancers, and playmakers of the translational regenerative medicine 2018. Stem Cells Int. 2018; 2018: 6927401.
9. Tatullo M, Codispoti B, Pacifici A, Palmieri F, Marrelli M, Pacifici L, et al. Potential use of human periapical cyst-mesenchymal stem cells (hpcy-mscs) as a novel stem cell source for regenerative medicine applications. Front Cell Dev Biol. 2017; 5: 103.
10. Inchingolo F, Tatullo M, Abenavoli FM, Marrelli M, Inchingolo AD, Inchingolo AM, et al. Non-Hodgkin lymphoma affecting the tongue: Unusual intra-oral location. Head Neck Oncol. 2011; 3: 1.
11. Tatullo M, Marrelli M, Amantea M, Paduano F, Santacroce L, Gentile S, et al. Bioimpedance detection of oral lichen planus used as preneoplastic model. J Cancer. 2015; 6: 976-983.
12. Barry M, Pearce H, Cross L, Tatullo M, Gaharwar AK. Advances in nanotechnology for the treatment of osteoporosis. Curr Osteoporos Rep. 2016; 14: 87-94.
13. Kerativitayanan P, Tatullo M, Khariton M, Joshi P, Perniconi B, Gaharwar AK. Nanoengineered osteoinductive and elastomeric scaffolds for bone tissue engineering. ACS Biomater Sci Engin. 2017; 3: 590-600.
14. Tatullo M, Marrelli M, Scacco S, Lorusso M, Doria S, Sabatini R, et al. Relationship between oxidative stress and "burning mouth syndrome" in female patients: A scientific hypothesis. Eur Rev Med Pharmacol Sci. 2012; 16: 1218-1221.

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