Clinical Outcomes of Stem Cell Metabolites Formula Derived from Placenta for Skin Regeneration

by Dr Purwati

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ABSTRACT

Background: Previous research focused on in vitro and animal study of stem cell metabolites formula derived from the placenta for skin regeneration.
Objective: This further study is a clinical trial to evaluate the effectiveness of stem cell metabolites formula in skin regeneration.
Methods: Priorly, subjects' facial conditions were examined and recorded using Janus skin analyzer to observe marks and blemishes present on their skin. Stem cell metabolites were applied on the face twice a day, day and night, with single-use doses of three pumps. We evaluated before and after stem cell metabolites application using Janus over the period six months, with three times repeated evaluation every two months. The Janus evaluation results are Spot, Pore, Roughness, Wrinkle, UV Acne, UV Spot, and UV Moisture.
Results: The percentage of spot, pore, roughness, wrinkle, UV acne, and UV spots were noticeably reduced. Meanwhile, the percentage of UV moisture increased in almost all subjects who were evaluated for six months. From a qualitative aspect, 90% of subjects are satisfied with the results of the application of stem cell metabolites. The subjects felt that facial wrinkles had reduced, the face was smoother and supple, and reduction in dark pigmentation.
Conclusion: It can be concluded that stem cell metabolites are useful in face skin regeneration.

INTRODUCTION

Aging in humans is a gradual and continuous process of natural change, a slowly receding process in the ability of the tissue to replace and maintain its normal functions.[1,2] In adults, individuals experience many changes, both physical and mental, especially reduction in efficiency of various bodily functions and abilities. The decrease is related to various gradual systemic changes in the body such as decreased memory, muscle weakness, hearing, vision, feelings and changing physical appearance and other biological functions.[3,4] Skin aging is a normal process in which the process of renewing skin cells production goes down, in line with the decreasing of the natural protective layer of the skin and the internal support structure. The deterioration of the skin renewal process, together with the lifestyle and environmental factors, such as drink alcohol and eat junk food, smoking, lack of sleep, and pollution, can cause signs of aging to appear earlier.[5] Basically, premature aging often occurs in someone who has a dry skin type because sebum which is an oily secretion to protect the skin from pollution and moisturizes the skin is low among those with dry skin type. There are several anti-aging therapies that are widely used to take care of aging, include cosmetological treatments such as protective cosmetics from UVA and UVB; Topical agents such as tretinoin to stimulate the synthesis of type I collagen and vitamin C for antioxidants; Systemic agents which include vitamins C and E, glutathione, polyphenols, melatonin and selenium; and Procedural Therapy which offers services such as physician-performed or device-driven procedures such as laser therapy.[6,7]

Stem cell therapy was initially carried out to treat degenerative diseases. The role of stem cell metabolites in skin aging is to repair injured tissue or replace other cells in programmed cell death. Stem cell metabolites have many kinds of growth factors such as cytokines interleukin 4 (IL-4), interleukin 10 (IL-10), Epidermal Growth Factor (EGF), Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), and Tumor Necrosis Factor-beta (TGF-β). These cytokines can go through the skin layer to encourage the growth of the new cells and enhance nutrition, stimulate skin metabolism to inhibit premature aging, and also accelerate the cell skin to produce new proteins, collagen, and eastin fibers, while also assist in reducing dark pigments and induces basal cells to proliferate resulting in the growth of epidermal keratinocytes.[8–11] In this way, stem cells keep the skin healthy and prevent premature aging. These stem cells act like our own microscopic dermatology doctor forces.[12,13]

In this research, stem cell metabolite formula is derived from the human placenta containing more mesenchymal precursor cells and hematopoietic stem cell populations than adult blood or bone marrow. Prior to conduct the study, stem cell metabolites must be validated their purity, plasticity, and contamination. Cells must be free of infectious diseases such as Bovine Spongiform Encephalopathy (BSE), Gonorrhoea, Hepatitis, Herpes, HIV/AIDS, and cancer cells. Moreover, the level of cell

viability and cell phenotype must also be in accordance with the desired target.[14]

Previous research focused on in vitro and animal study of stem cell metabolites formula derived from the placenta for skin regeneration. We have done in vitro study include cytotoxicity test, cytokine detection, and apoptosis assay. From the study results, stem cell metabolites are not toxic with a percentage of cell viability exceeds 50%, did not cause any systemic immune response to the tissues by decreasing of cytokine release levels, and did not induce apoptosis by increasing percentage of expression of Hsp70 (anti-apoptotic gene) and decreasing percentage of expression of p53 and caspase-3 (pro-apoptotic gene) in the treatment samples compared to controls.[15]

This further study is a clinical trial to evaluate the effectiveness of stem cell metabolites formula in skin regeneration.

METHODS

This clinical study received ethical clearance No. 101/KEH/2019 from the law and medical research ethics committees of Universitas Airlangga Hospital, Surabaya, Indonesia, following the regulatory guidelines. The study analyzed data from 13 men and 11 women in various aged between 40-70. The inclusion and exclusion criteria were used in selecting the subjects. The inclusion criteria for the subjects are men or women, aged 40 or above, having no infectious diseases, having no allergic diseases, willing to be donors, as evidenced by the signing of informed consent. Exclusion criteria are using other skincare during the study and not willing to sign an informed consent.

Prior to application, facial conditions of all subjects were examined and recorded using a Janus skin analyzer to observe marks and blemishes present on their skin. Stem cell metabolites were applied on the face twice a day, at day and night, with single-use doses of three pumps. We evaluated before and after stem cell metabolites application using Janus over the period six months, with three times repeated evaluation every two months. The results of the Janus evaluation are Spot, Pore, Roughness, Wrinkle, UV Acne, UV Spot, and UV Moisture.

SPSS Statistics were used to perform data analysis. Data are expressed in mean, standard deviation, frequency distribution and percent on descriptive analysis and frequency. Significance limit is that if $p < 0.05$ with 95% confidence interval.[16]

RESULTS

We performed statistical data analysis to evaluate the differences in the subject's skin condition, including Spot, Pore, Roughness, Wrinkle, UV Acne, UV Spot, and UV Moisture before and after treatment with metabolite stem cell formula in six weeks Evaluation conducted three times every two months. Data are presented in Table 1.

Table 1. The average of subject's skin condition before and after treatment with metabolites stem cell

Group	$\dot{x} \pm SD$ (%)						
	Spot	Pore	Roughness	Wrinkle	UV Acne	UV Spot	UV Moisture
Pre	$68{,}16^a \pm 20{,}67$	$97{,}53^a \pm 0{,}97$	$96{,}73^a \pm 1{,}59$	$73{,}30^a \pm 17{,}82$	$45{,}96^a \pm 9{,}30$	$75{,}70^a \pm 19{,}83$	$70{,}53^a \pm 7{,}17$
Post 1	$57{,}96^b \pm 25{,}81$	$95{,}56^b \pm 1{,}92$	$96{,}10^b \pm 1{,}47$	$65{,}63^b \pm 22{,}42$	$35{,}30^b \pm 9{,}89$	$70{,}46^b \pm 21{,}84$	$86{,}66^b \pm 8{,}57$
Post 2	$54{,}16^c \pm 26{,}04$	$90{,}53^c \pm 1{,}92$	$91{,}00^c \pm 1{,}59$	$61{,}16^c \pm 22{,}50$	$33{,}93^c \pm 13{,}72$	$66{,}20^c \pm 21{,}65$	$90{,}56^c \pm 7{,}13$
Post 3	$49{,}73^d \pm 24{,}69$	$85{,}86^d \pm 2{,}77$	$86{,}20^d \pm 2{,}29$	$56{,}26^d \pm 22{,}69$	$30{,}66^d \pm 13{,}13$	$62{,}23^d \pm 21{,}85$	$94{,}00^d \pm 5{,}81$

a,b,c,d indicates data between pre treatment and 3x post treatment are statistically significant difference

DISCUSSION

As we know, stem cells have an outstanding potential to develop into many types of cells in the body during early life and growth, so that way, rejuvenation occurs. Metabolite products are produced using stem cells. In the process, the cell will produce metabolite materials that are rich in growth factors. This process can be repeated several times for collecting the supernatant. This metabolite is then used as the main ingredient in topical preparations. Gradually, stem cell metabolites reduce dull skin and wrinkle, which occurs due to a decrease in collagen production by the degenerative process. Some practitioners claim that stem cell metabolites will promote more skin elasticity and reduce pigmentation so that the appearance is enhanced and more appealing.[8]

In this study, stem cell metabolites are taken from the human placenta which contains more mesenchymal precursor cells and hematopoietic stem cell populations when compared to adult blood or bone marrow. Stem cell metabolites have many kinds of growth factors such as cytokines interleukin 4 (IL-4), interleukin 10 (IL-10), Epidermal Growth Factor (EGF), Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), and Tumor Necrosis Factor-beta (TGF-β). These growth factors help the skin produce protein and elastic fibers and new proteins, so that skin returns to its former elasticity, reduced black pigmentation and induces basal cells to proliferate resulting in the growth of epidermal keratinocytes.[9–11]

This clinical study is conducted in 30 patients who met the inclusion and exclusion criteria, as mentioned in the methods section, to be applied with stem cell metabolites on their face. We evaluated before and after stem cell metabolites application using Janus over the period six months, with three times repeated evaluation every two months. After analysis, subjects will know their specific skin problems, determine the severity, analyze each representative of the indicator, and recommend a suitable course of treatment. There are seven skin issues: spot, pore, roughness, and wrinkle (for surface); as well as UV acne, UV spot, and UV moisture (for deep skin issues). The percentage represents the degree of skin problem. The higher the number is, the worse the skin condition will be, except for UV moisture.[16]

In surface skin issues, normal value of red, green, and blue (**RGB**) **Spot** is in 30%, indicating that the spots of

surface skin are in a normal state; if within the range of 30%-70%, indicate that it is ranging between medium to serious; if over 70%, it indicates that the skin is in a serious state, and requires freckles removal treatment urgently. For **RGB Pore**, the normal value is in 80%. This value is a little special, as everyone has pores, so the value is high. We detect the degree of clogged pores. 80%-90% indicates that it is in a medium state; over 90% indicates it is in a serious state. **RGB Roughness** is relative with Pore, so the value indication is similar to pore. 80%-90% is a medium state Over 90% is a serious state. At the same time, it is closely related to lifestyle habits and level of dehydration. Generally, **RGB Wrinkle** within 30% is fine lines. Hence, there is no need for further attention. As adults, every facial movement will contribute to having fine lines. Over 40%, the quantity of the fine lines is increased. When the blue points on detection are pictured together into a line, this is genuine wrinkling of the facial skin, a value of over 70% means it is in a serious state and requires anti-aging treatment.[16] In deep skin problems, the normal value of **UV Acne** is in 30%. 30%-70% is said to be in a medium state, but requires regular moisturizing and frequent deep cleansing treatment. A value of over 70% indicates that it is in a serious state and warrants reminding the customers do regular moisturizing, oxygen therapy, as well as deep cleansing treatment. For **UV Spot**, the normal value is in 30%. 30%-70% is in a medium state, but requires regular use of products that promote metabolism. If it is over 70%, it indicates that the problem is in a serious state and need immediate attention along with regular use of products that promote metabolism. The value of **UV Moisture** is a little special. The normal value is 80%, as everyone's face needs large amounts of moisture, so everyone faces a lack of moisture problems. 80%-90% is said to be in a medium state, over 90% is considered as a serious state, and requires moisturizing treatment urgently.[17]

From the study results, we can see that stem cell metabolites formula is effective in overcoming aging, as evidenced by the decrease of percentage in spot, pore, roughness, wrinkle, UV acne, and UV spots, while the increase happens in the percentage of UV moisture. These results were experienced by almost all subjects who were evaluated for a period of 6 months. In qualitative, almost 90% of subjects are subjectively satisfied with applied stem cell metabolites on their face. The subjects felt that facial wrinkles were reduced, the face was smoother and supple, and pigmentation was reduced.

CONCLUSION

We can conclude that stem cell metabolites are effective in overcoming aging as evidenced by the decrease of percentage in spot, pore, roughness, wrinkle, UV acne and UV spots, and the increase of percentage in UV moisture. The subjects felt that facial wrinkles were reduced, the face was smoother and supple, and pigmentation was reduced.

Declarations

Ethics approval

This clinical study received ethical clearance No. 101/KEH/2019 from the law and medical research ethics committees of Universitas Airlangga Hospital, Surabaya, Indonesia, following the regulatory guidelines of the country.

Competing interests

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