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EXPERIENCE OF USING NON-INVASIVE METHODS IN THE CORRECT AGE-RELATED SKIN CHANGES

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Summary: The aging of human skin may be caused by the passage of time (internal aging - chronoaging) and the cumulative effect of external factors (external aging) such as ultraviolet radiation, which contribute to formation of wrinkles and loss of tissue elasticity. Since both aging processes are associated with phenotypic changes of skin cells the main functional signs of aging occur as a result of structural and compositional disruption of extracellular matrix proteins, loss of interstitial fluid and lipid oxidation. The article shows an example of non-invasive correction of age-related skin changes by using a nutraceutical vitamin-collagen complex.

Keywords: collagen, elastin, hyaluronic acid, fibroblast, photoaging, chronoaging, vitamin-collagen complex, anti-aging agent.

At a young age, our skin looks fresh, supple and smooth due to the high content of collagen, elastin and hyaluronic acid. However, over the years, the content of these substances is reduced, and it leads to age-related changes, such as: the skin becomes dry, reduced elasticity and flexibility, deterioration of complexion and wrinkles may occur.

Currently, there are two types of skin aging, photoaging (external type associated with UV radiation) and chronoaging (internal type, which is a genetically conditioned process). Each of these types has its own peculiarities. During the age involution the atrophy of subulate, granular and brilliant layer of the epidermis at normal thickness of the stratum corneum and reduction of the ratio of ceramides are observed. This stratum corneum becomes lax and lesser holds a liquid. There is observed a sebum hypoproduction by sebaceous glands. At the same time these glands increase their sizes. The smooth of basement membrane is observed. The flexibility and elasticity of derma are reduced due to decrease of components of intercellular matrix. In addition to reduced fibrillar proteins, there is a significant reduction of water in the aging skin. This is due to the fact that concentration of hyaluronic acid in the intercellular matrix is decreased.

Depending on the morphological changes of skin, there are conditionally three main periods in human life, such as:

1. Age evolution period (from birth to 20-25 years).
2. Period of some stabilization of age-related changes (from 25-30 to 40-45 years). During this period, only fibrous structure of the skin is changed. Its elasticity is also reduced.
3. Age involution period (after 40-45 years). Atrophic changes of skin structures become faster and faster.

In photoaging - the stratum corneum becomes callous, thicker and dry. There is observed vascular pattern disorder - telangiectasia; pigmentation, elastosis and other skin changes are appeared.

In spite of this difference in manifestations these types of aging, in essence, have common mechanisms of damage of collagen fibers. If in the chronoaging period the collagen production is reduced by 75% along with the growth of collagen degradation processes, then a single exposure of ultraviolet radiation on the skin up to medium erythema (redness), leads to a temporary decrease of collagen synthesis by 80%. Return to normal standards is approximately in 48-72 hours. If such activity of ultraviolet happens repeatedly, suppression of collagen stays permanently low and changes become irreversible.

The situation, where the signs of photoaging gradually imposed on physiological processes of chronoaging, is a very negative scenario of strengthen and acceleration of aging rate.

For any type of skin aging, the age-related changes are directly associated with dermal fibroblasts, which become flat and rigid (by 60% from 27 to 81 years), in addition, these dermal fibroblasts are cells that have a limited life expectancy (60% of fibroblasts obtained from young donor are able to create a colony in 256 fibroblasts, and in the elderly is only 2%). Increased rigidity affects the rate of migration (transfer) of fibroblasts into the focus of inflammation or injury, and there is also complication of fibroblasts contact with existing collagen of intercellular matrix. It ultimately leads to reduction of its synthetic activity and the viscoelastic properties of organized collagen especially in the zone of papillar dermis. The reduction of antioxidant activity of proteins, involved in antioxidant defense of cells, contributes to reduction of life expectancy greatly. Increased concentration of free radicals causes quick stop of cell division and provokes their premature aging.

Consequently, both quantitative and qualitative compositions of intercellular matrix of the skin are changed with age. It is believed that homeostasis collagen matrix disorder is a distinguishing feature of aging skin which presents both in photoaging and in chronoaging. Every person after 40 loses about 1% of collagen fibers per year, and on

average the production of collagen is reduced by 3 times up to 80 years (compared to 18-26 years).

In fact, the name "collagen" is used to refer to 18 proteins, 11 of which contain the dermis. It provides tissues a specific mechanical strength. In addition the collagen influences on the growth, migration, differentiation, secretion and activity of various synthetic cell, also it provides the correct location of all tissue elements and maintains the tissue structure. Thank to collagen fibers the skin has that elasticity which is inherent in young body. Collagen fibrils are constantly renewed and the processes of their synthesis and decay, which is carried out by fibroblasts, are strictly coordinated.

But as we get older, this balance is disturbed and the synthesis of new fibers is slowed. There is observed a defragmentation of collagen, which becomes more rigid with randomly oriented fibrils. There is also the accumulation of debris with creation of crosslinks between collagen, which leads to a damage of its cellular structure. It leads to disturbance of direct contact between collagen fibrils and fibroblast, eliminating its ability to be in a stretched, spindle-shaped state that is a physiologically necessary condition for its normal growth and functioning.

Collagen fibers are strong and flexible but not elastic. Together with elastin, another protein of connective tissue, they form the basis (frame) of the dermis of the skin. Elastin is presented in a small amount compared to collagen, and its main function is to provide important feature for the skin - reverse deformation (ability to return to its former shape after stretching). In the dermis elastin is also synthesized by fibroblasts, and as a result of fibroblasts cellular aging, the synthesis of elastin is decreased. It leads to skin aging changes. The glycation process, which is the main mechanism of dermis aging – joining the remaining sugar molecules (glucose or fructose) to collagen and protein intracellular matrix (Maillard reaction), leads to accumulation of final products of glycation on collagen and elastin fibers, as a result of which the collagen lattice of dermis loses elasticity and elastic fibers become more resistant for remodeling.

As a result of age-related changes of the skin, there is thinning of the dermis and disturbance of "glycocalyx-fibrillar fibers" ratio, caused by a decrease of the concentration of one of the important components of glycocalyx - glycosaminoglycan with a wide range of biological activity - hyaluronic acid.

Anti-aging effect of hyaluronic acid of the dermis is associated with the ability to retain an intersticial fluid in the intercellular space, as well as involvement in ion exchange, transportation and distribution of intercellular liquid. During the process of aging hyaluronic acid undergoes quantitative and qualitative changes. The hyaluronic acid bioavailability is proportionally reduced to the reduction of endogenous hyaluronic acid synthesis and its binding fraction. As we get older, this mucopolysaccharide is more tightly bound with the tissues. In infants, 7% of hyaluronic acid is associated with tissue, while this amount is increased by 23% in old skin. Hyaluronic acid is also deposited in deep layers of the skin, and its amount is significantly reduced in epidermis

as we get old. These changes cause dry skin followed by the formation of fine and eventually deep wrinkles (Fig.1.).

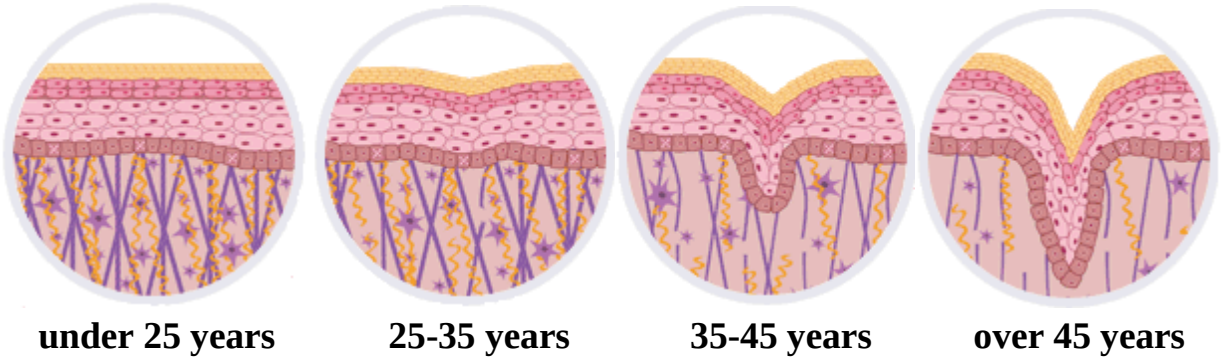


Fig.1. *Formation of wrinkles with the age*

Certainly, an adequate effect on the aging process of the skin requires a complex of measures that includes home care and treatment procedures. The complex of treatment depends on the type and condition of the skin, the patient's age and preferred type of aging. Today, much attention is given to invasive procedures (mesotherapy, biorevitalization, contour plastic surgery) that may be effective in solving aesthetic problems of age. But the invasion doesn't exhibit anti-aging activity, but the patients' desire to get rid of wrinkles demonstrates their desire to look younger. Due to this fact, the methods of non-invasive use of cosmetics and bio-stimulation remedies didn't lose the relevance in the aesthetic anti-aging medicine.

A good example of a bio-stimulation anti-age product is a complex drink "Beautisan drink" (Ananta Medicare Ltd, UK). Its composition corresponds to advanced scientific thought about aging of the skin and includes basic ingredients of effective anti-age effect: collagen peptide (fish), shark cartilage extract, hyaluronic acid, coenzyme Q10, DNA (albino protein extract), vitamin B2, vitamin B6, ceramide (rice), β-carotene, vitamin C, vitamin E and vitamin B1.

Collagen peptide is a biogenic peptide obtained from collagen hydrolyzate. Both in a society, and in a science, the dominant view is that after the consumption of any protein its complete splitting into individual amino acids is occurred in the digestive tract, then only these fractions are absorbed (Fig.2.).

Fig. 2. *Enzymatic hydrolysis of collagen molecule*

Collagen is hydrolyzed by digestive enzymes to peptides which are transported by enterocyte specific receptors, which are located above lymphoid Peyer glands and small clusters of lymphoid tissue. By pinocytosis the proteins are transported in vesicles to the cell membranes, and then by exocytosis they are transported into the lymph and blood in the form of di- or tripeptides. As they get to the specific tissues of the body (including the dermis), some peptides of collagen hydrolyzate are recognized by fibroblasts as a signal for proliferation and synthesis of collagen, elastin and hyaluronic acid. Other small peptides, which molecular weight is 500-3000 Da, in the form of free amino acids become an available building material for active metabolism processes and storage in the skin.

For today, preclinical and clinical studies have shown that collagen peptide may slow down age-related changes in the body, improve skin condition and protect the skin from UV damage.

It is proved that shark cartilage extract sufficiently improves an anti-angiogenesis, exhibits an anti-inflammatory and anti-collagenolytic activity. The basic amino acids, involved in the liquid extract, are amino acids of proteins and peptides of the cartilage. For instance: lysine, glycine, aspartic acid and glutamic acid are the majority of the amino acids in the liquid extract and they are the main components of N-telopeptide intramolecular cross-link in collagen of the skin. The use of shark cartilage extract is considered as a method to reduce inflammation or irritation, to regulate the formation of wrinkles or atrophy of the skin, to slow down a premature aging, to improve skin barrier functions, to lower the level of dark circles around the eyes, to reduce vascular pattern and to provide a soothing effect on the skin.

In oral administration, same as collagen, hyaluronic acid is quickly absorbed from the small intestine due to well-established mechanisms of catabolism. Oral administration of hyaluronic acid provides the intake of building material for the synthesis of its own acid and does not cause inhibition of its production even after prolonged use.

Considering that synthesis of hyaluronic acid is reduced with age (at 60 years, its level is 20% from the quantity at 20 years), the use of it as a major nutraceutical for restoration of youth and beauty of the skin is constantly needed. Oral intake, unlike local injections, provides the whole body with hyaluronic acid, because not only the skin requires hyaluronic acid. It is a very important component of intra-articular fluid and cartilage.

Coenzyme Q10 is a fat soluble coenzyme that has antioxidant properties. It may be synthesized in the body. Adequate intake of coenzyme Q10 in the body is necessary to obtain energy from carbohydrates and fats. This energy is needed for life support and antioxidant protection of cells, tissues and organs from the damaging effects of free radicals involved in the aging process and the development of various diseases.

DNA (albino protein extract) is a substance, obtained from salmon caviar, which presents in all cells (except red blood cells). DNA is very important for cell regeneration

to counteract the effect of premature aging. Therefore, it is presented as a component in many food supplements which maintain a youthful appearance of the skin.

Vitamin B1 (thiamine) is actively involved in many metabolic processes and it influences on the performance of almost all cells of the body. Especially thiamin is necessary for normal brain activity, because thiamin normalizes cerebral blood flow and improves learning ability. Thiamine has also antioxidant properties. This vitamin reduces the negative effects of alcohol and tobacco, protects the body from infectious agents and slows the aging process.

Vitamin B2 (riboflavin) is a popular vitamin that is widely used in food supplements worldwide and usually has many expressed features such as increased levels of energy, maintenance of the immune system, protection of healthy hair, skin, mucous membranes and nails. In addition it slows the aging process.

Vitamin B6 (pyridoxine) is a water-soluble vitamin that is involved in the synthesis of amino acids and proteins. It plays an important role in fat and carbohydrate metabolism, reduces the levels of cholesterol and lipids in the blood and promotes proper synthesis of nucleic acids that prevent aging. Vitamin B6 is necessary for normal functioning of the central and peripheral nervous system. Since the body can not accumulate vitamin B6 and the remaining amount is excreted in urine, a constant intake of such vitamins is necessary.

Ceramide is an essential lipid component of the cell membrane, which directly influences both on permeability of the skin in both directions, and on the "cementing" of corneocytes. Also, they are signaling molecules of cell differentiation, proliferation and apoptosis.

ß-carotene is a pro-vitamin of vitamin A, which is necessary in a normal diet. Beta-carotene is considered effective to reduce the age of molecular degeneration.

Vitamin E is an essential component of cell membranes. It has an antioxidant effect that protects body tissue from damage caused by free radicals.

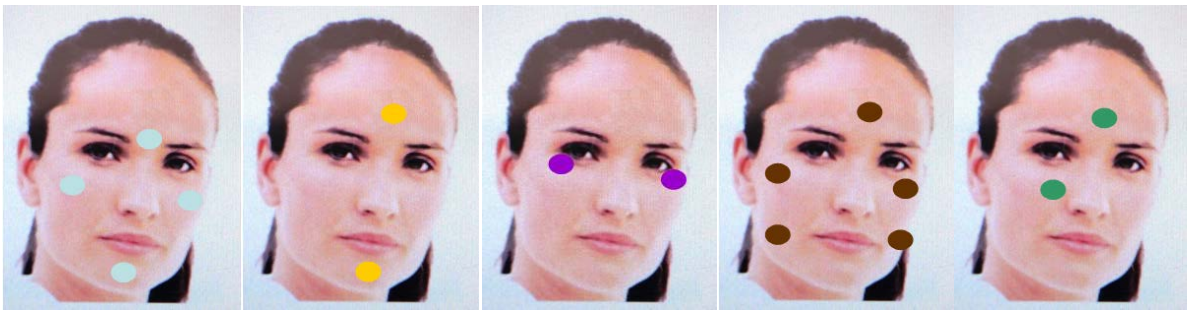
Vitamin C is an ascorbic acid which plays an important role in neocollagenesis at the level of gene expression. It regulates both the synthesis of collagen, and metalloproteinase-1 tissue inhibitor, thereby reducing the induced degradation of collagen. In addition, vitamin C inhibits the formation of melanin, by reducing the production of ortho-quinones such as dopa-quinones.

Materials and methods

Considering the appropriate composition of drinking complex "Beautisan drink" for the prevention of skin aging and reduction of the manifestations of the negative effect of exogenous environmental factors, we have carried out a clinical monitoring of patients (n = 30) aged 30 to 50 years. Male (n = 5) and female (n = 25) patients took 1 bottle (50 ml) of "Beautisan drink" every day within 3 months.

Evaluation of the effectiveness of drinking collagen-vitamin complex "Beautisan drink" was performed in the dynamics of observation based on three visits: 1st day – before starting treatment (visit 1), control visit (6 weeks), final visit (12 weeks). Visits included evaluation of anamnesis and objective survey data. Also there was carried out a hardware diagnostics of functional and morphological parameters of the skin on SOFT PLUS hardware system, which included: corneometry, sebumetry, pH-metry, mecsametry.

During the diagnostics of functional and morphological parameters in dynamic monitoring, the measurements were performed in certain areas of the face, such as: corneometry in T-zone, U-zone of face, sebumetry, elastometry, mecsametry, pH-metry with automatic determination of the biological age of the skin (Fig. 3).



Areas of corneometry | Areas of sebumetry | Areas of elastometry | Areas of mecsametry | Areas of pH-metry

Fig. 3. *Areas of measurement of functional and morphological parameters of the skin*

In summarizing of the results of the study in the areas of the face, determined at visit 1, 2 and 3, the following average values of study results were received. Dynamic changes of the skin are provided (Fig. 4).

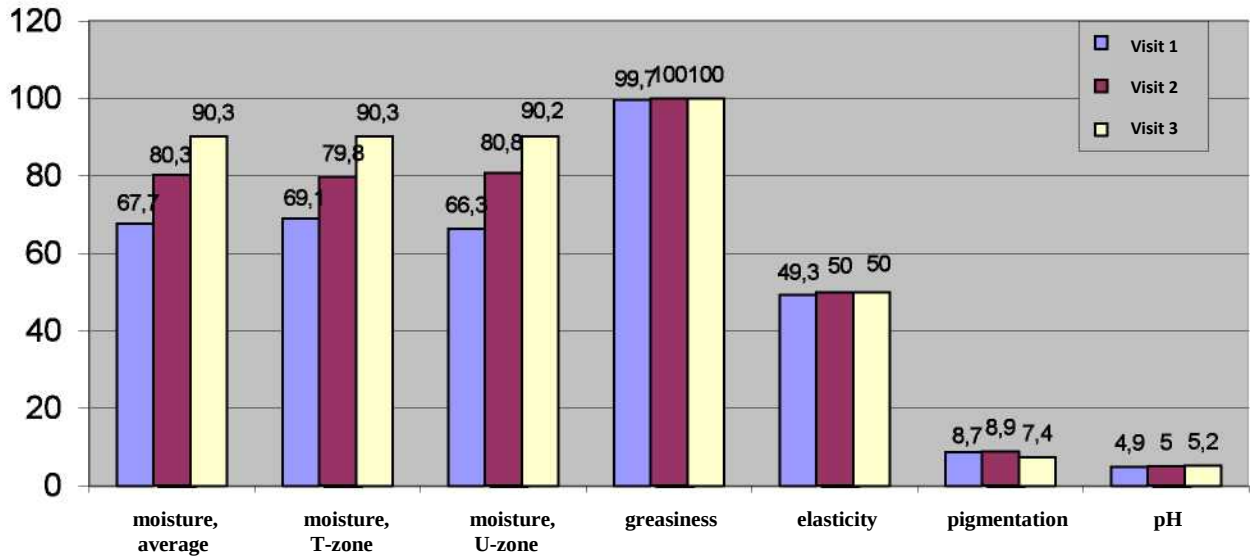


Fig. 4. *Dynamics of functional and morphological parameters of facial skin in patients (n = 30)*

In the analysis of the parameters of facial dynamic observation in patients there was found that skin moisture was increased by 22.6%, skin elasticity was increased by 0.7%, skin pigmentation was decreased by 1.3%, and the acidity of the skin was increased by 0.3%. Indicators of corneometry of definition of skin moisture in T-zone and U-zone testify to the balance in these areas, namely in the T-zone from 69.1% to 90.3%, and U-zone from 66.3% to 90.2%.

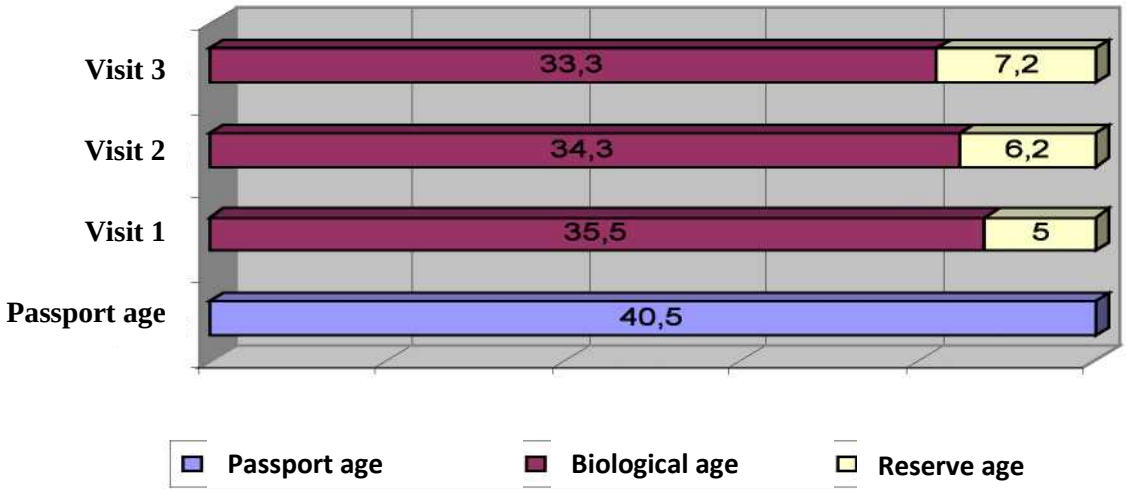


Fig. 5. *Dynamics of the age reserve of facial skin in patients (years) (n = 30)*

In the analysis of the age aspect of the patients there was found that the average age of patients was 40.5 years (Fig. 5). In determination of the skin condition of the patients, by using the standard "biological age" of SOFT PLUS hardware system there was revealed that at the first visit the average age index of the skin was 35.5 years, i.e. the reserve potential of facial skin was 5 years. After 6 weeks the average age index of the skin was decreased to 34.3 years and a reserve potential of facial skin respectively increased by 1.2 years. After 12 weeks the average age index of the skin is decreased to 33.3 years and the reserve potential of facial skin is respectively increased by 1 year that in general the increase of age potential of the skin was 2.2 years, approximately.
Fig. 6 shows data of comparative analysis of the skin in female and male patients.

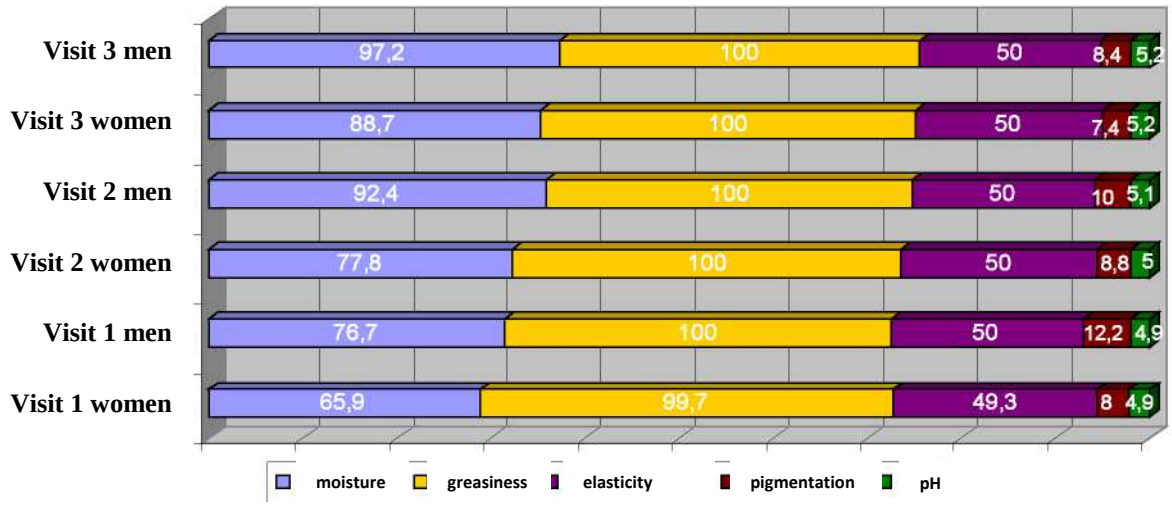


Fig. 6. *Comparative analysis of functional and morphological parameters of facial skin in male and female patients (n = 30)*

Comparative analysis of the indexes shows that the skin of female patients at the first visit was slightly worse compared to male patients. Namely, in women the skin moisture was 10.8% less than in men (76.7% men vs. 65.9% women). The skin elasticity of women was also reduced by 0.7% (50% men vs. 49.3% women). The acidity of the skin was equivalently increased by 0.2% in patients of both genders. It testifies to the recovery of acid-lipid mantle of physiological indicators. The women had lower level of skin pigmentation than men by 4.2% (12.2% men vs. 8% women), due to the use of cosmetics for skin care that contain sunscreen ingredients by the majority of the women. The data of slightly worse facial skin condition in women are adjusted according to the age structure of patients, namely, the average age of women was 40.9 years compared with men whose average age was 38.4 years, i.e. 2.5 years less than in women. After 6 weeks of using “Beautisan drink” there was observed that the facial skin moisture was increased by 11.9% in women and by 15.7% in men. Over the next 6 weeks the increase of facial skin moisture made 10.9% in women and only 4.8% in men. In general, the increase of facial skin moisture was 22.8% in women and 21.1% in men. It testifies to equivalent efficacy of “Beautisan drink” in patients of both genders, regardless of age characteristics.

During dermatoscopy, there was noted that patients with problem skin had positive dynamics of the normalization of the skin. For instance: in a patient N. aged 41 years old, during the first examination according to functional and morphological parameters, there was revealed a quite unusual skin condition, namely, the skin was greasy but dehydrated. In dermatoscopy the signs of pronounced dry skin were observed. After 6 weeks of oral administration of "Beautisan drink" improvement was observed, and after 12 weeks the functional and morphological parameters showed the normal skin type parameters, as confirmed by micrographs (Fig.7).

Visit 1 Visit 2 (after 6 week) Visit 3 (after 12 week)

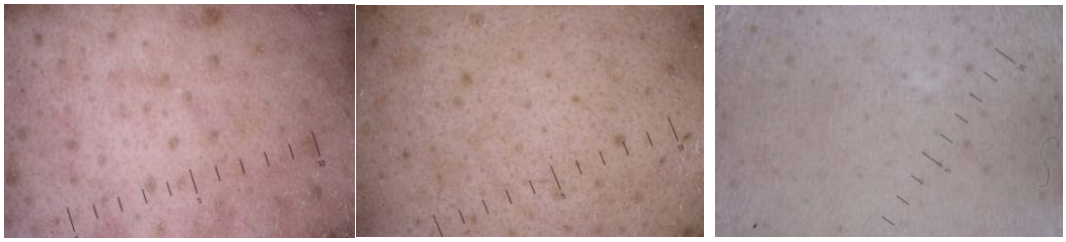
Fig.7. *Patient N., 41 years old.*
Facial skin is greasy and dehydrated

Patient O. is 34 years old. She had dry skin at the first visit. After 12 weeks of observation a significant improvement in skin condition was reported. No peeling and irritated skin were observed (Fig.8).

Visit 1 Visit 2 (after 6 week) Visit 3 (after 12 week)

Fig.8. *Patient O., 34 years old. Dry facial skin*

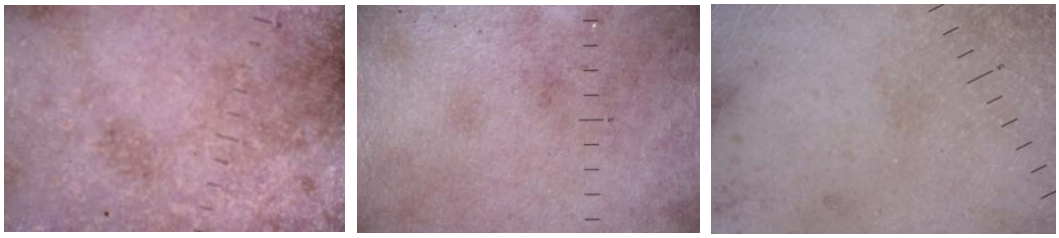
Patient O. is 50 years old. She had greasy skin type. On dermatoscopic images it is showed in the form of extended pores of sebaceous glands. Dynamic visualization has shown the reduction of the number and significant constriction of the orifice of sebaceous glands (Fig.9).



Visit 1 Visit 2 (after 6 week) Visit 3 (after 12 week)

Fig.9. *Patient O., 50 years old. Greasy facial skin*

Patient V. is 30 years old. At initial examination she had pronounced facial skin pigmentation that was marked as the highest index of the average pigment distribution among the studied women. After 6 weeks pigment desaturation in the cells was observed, and after 12 weeks a significant decrease of pigmentation with its uniform distribution was observed (Fig.10).



Visit 1 Visit 2 (after 6 week) Visit 3 (after 12 week)

Fig.10. *Patient V., 30 years old. Pigmented facial skin*

Patient Yu. is 39 years old. He had the dry and irritated skin. After 12 weeks of using "Beautisan drink" the patient has noticed a significant improvement of the skin condition. This improvement, such as the elimination of redness and peeling, reduction of the amount of extended capillaries, was recorded on micrographs in dynamic observation (Fig.11).

Visit 1 Visit 2 (after 6 week) Visit 3 (after 12 week)

Fig.11. *Patient Yu., 39 years old. The facial skin is dry and irritated.*

On macrographs the patients demonstrate an improvement of overall condition of the facial skin, a normalization of the skin color, a reduction of the number and depth of facial wrinkles on different areas of face both in women and in men.

Patient O. is 38 years old. In spite of usual skin care (cleansing lotion, day cream, night cream) at the first visit the patient's skin looked "tired". The skin had moderate signs of photo-aging without visible signs of keratosis. signs of age-related pigmented disorders (early stages of lentiginosis). At rest, static superficial and medium deep wrinkles that present in outer corners of the eyes, on the forehead and in brow and perioral areas

became visible. In dynamics the expression wrinkles became visible at the corners of the eyes and around the mouth. According to hardware diagnostics data of the skin (corneometry, sebumetry, elastometry, mecsametry) there was determined that the skin was greasy with the reduced level of moisture. After 12 weeks of using “Beautisan drink” on the background of usual care, there was observed a significant improvement of the skin, such as a skin lightening with the uniform distribution of pigmentation, a reduction of the depth and the number of static and dynamic wrinkles, and an increase of skin moisture from 54.2 to 85% % (Fig.12).

Visit 1 **Visit 3 (after 12 weeks)**

Fig.12. *Patent O., 38 years old.*

Patient N. is 47 years old. The static superficial and medium deep wrinkles at the outer corners of the eyes were visible. After 12 weeks there was observed a significant reduction of the wrinkles and normalization of the skin color (Fig.13).

Visit 1 **Visit 3 (after 12 weeks)**

Fig.13. *Patient N., 47 years old.*

Patient B. is 32 years old. On a background of the absence of skin care, in addition to regular washing with soap after using "Beautisan drink" the smoothing of wrinkles around the eyes and improvement of skin condition were observed (Fig.14).

Visit 1 **Visit 3 (after 12 weeks)**

Fig.14. *Patient V., 32 years old.*

Patient K. is 50 years old. She noticed a significant improvement of the skin condition, a significant decrease of the depth and the number of static and dynamic wrinkles, and pigment desaturation that are well showed on macrographs of forehead skin (Fig.15).

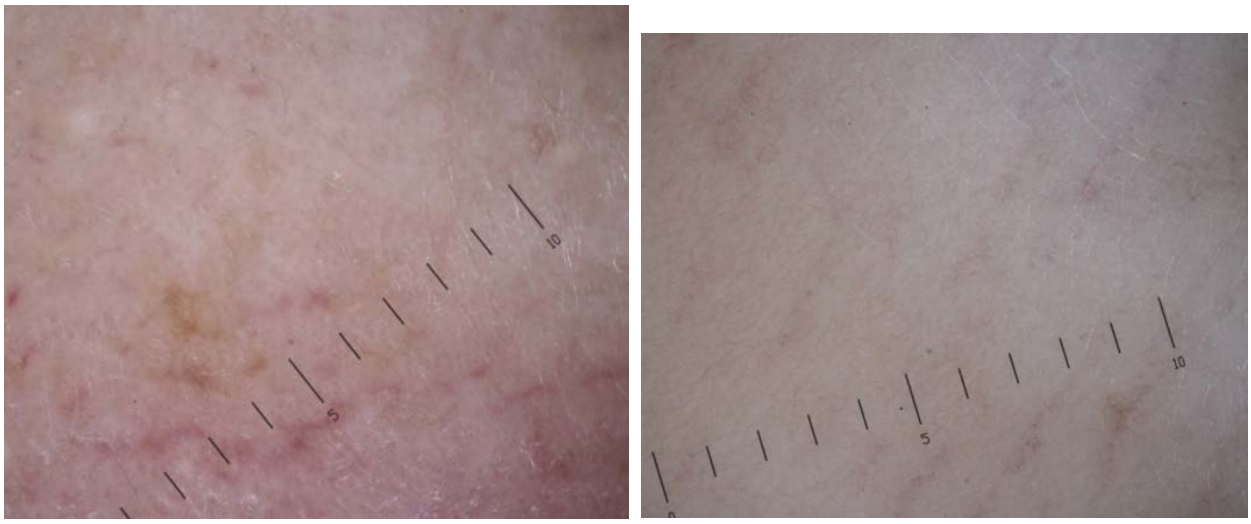
Visit 1 **Visit 3 (after 12 weeks)**

Fig.15. *Patient K., 50 years old.*

In addition to the positive effect on the facial skin condition, both female and male patients have noticed an improvement of the overall skin condition, such as a good moisture and a pleasant elasticity of the body skin (56.7%), accelerating growth of hair and nails with the improvement and strengthening of their condition (53.3%), reduction of the skin pigmentation, namely normalization of skin color (30%), uniformity of suntan in insolation (20%), accelerating skin regenerative properties (23.3%), reduction of cellulite signs have noticed 23.3% of women.

Patient O. is 34 years old. She had pronounced striae that had appeared during pregnancy. After 12 weeks of using the vitamin and collagen preparation "Beautisan drink" the patient has noticed a significant improvement of the skin, visual reduction of the width and length of striae. The striae became small and short. By the defragmentation of pigment clusters and constriction and reduction of vascular network, the normalization of skin color is dermatoscopically observed (Fig.16).

Macrograph of the abdominal skin.



Visit 1 **Visit 3 (after 12 weeks)**

Fig.16. *Patient O., 34 years old. Macrograph of the abdominal skin*

Therefore, the main focus to preserve the youth and health of our body is maintenance of the balance of synthesis and utilization of collagen, elastin and hyaluronic acid. It is necessary not only to lead a healthy lifestyle, but also to "rejuvenate" the main development "factories" of these proteins, and to provide the body with vitamins and provitamins for catalytic function and humoral regulation of active centers and metabolism in the body. Today, one of the leading cosmetic trends of recent years is a combined use of external care products and the products of "beauty from within" category. These are nutraceutical products including biostimulatory vitamin-collagen anti-aging complex drink "Beautisan drink", which corresponds to advanced scientific opinion regarding the anti-aging effect of the skin and it is recommended for:

- men and women over 25 - 30 years old, and especially during the age involution. From this age the body starts to produce less collagen and hyaluronic acid and therefore you can safely begin to rejuvenate and restore the skin from the inside;
- women and men who are interested not only in skin rejuvenation but in a complex correction of the general health: the restoration and protection of cells from aggressive environmental factors, improvement of the immune system, promotion for the growth, development and restoration of connective tissue in the skin, joints, cartilage, tendons , muscle and blood vessels;
- office workers. The product improves the moisture level of the skin which was dehydrated because of air conditioning and heating equipment, removes dark circles and reduces puffiness. It contributes to a psycho-emotional stability due to the vitamin B complex;
- those who suffer from excessive dryness of the skin;
- those who tan in solariums or lie in the sun under ultraviolet rays;
- women and men to reduce and eliminate striae.

Thus, according to the study results, the recommended vitamin-collagen complex improves skin moisture; eliminates hyperemia and peeling skin; reduces the number and depth of static and expression wrinkles; improves elasticity and flexibility of the skin; reduces striae and vascular network; normalizes the skin color, reduces dark spots; increases reserve capacity of the skin up to 7 years.

References:

1. Атлас по дерматологии Мартин Рёкен, Мартин Шаллер, Эльке Заттлер, Вальтер Бургдорф; пер. с нем. М.: МЕДпресс информ, 2012. 408с.: ил.
2. Ахмятов С.Н.. Бутон Ю.С. Пракгическая дерматокосметология. – М.: Медицина, 2003, – 395с.
3. Дерматология Фицпатрика в клинической практике: в 3т. / Клаус Вольф, Лоуэлл А. Голдсмит. Стивен И. Кац и др.; пер с англ.; общ. Ред.. акад А.А.Кубановой. – М.: Издательство Панфилова. БИНОМ Лаборатория знаний. 2012. Том 2. – 2012. – с.: ил.
4. Кожа как объект косметологического воздействия / Под общ, ред. Эрнандес Е.И. Издательский дом "Косметика & Медицина", 2013. – 208с.
5. Кошевенко Ю.Н. Кожа человека. Том 1: Структура, физиология и предназначение функциональных элементов каждого органа чедовека. – М.: Медицина, 2012. – 360с.
6. Новая косметология. Основы современной косметологи / Эрнандес Е.И., Марголина А.А, – Издательский дом "Косметика & Медицина", 2014. – 600с.
7. Elizabeth C. Naylor Molecular aspects of skin ageing / Elizabeth C. Naylor, Rachel E.B. Watson, Michael J. Sherratt // Maturitas: Volume 69, Issue 3, July 2011, Pages 249-256.
8. Fibrillar collagen: the key to vertebrate evolution? A tale of molecular incest. Boot-Handford RP, Tuckwell DS. Bioessays. 2003 Feb;25(2): 142-51.
9. Franzke CW, Bruckner P, Bruckner-Tuderman L. Collagenous transmembrane proteins: recent insights into biology and pathology. J Biol Chem. 2005 Feb 11;280(6):4005-8.
10. Gary J. Fibroblast Collapse and Therapeutic Implications / Gary J. Fisher, PhD; James Varani, PhD; John J. Voorhees, MD // Arch Dermatol. 2008;144(5):666-672. doi:10.1001/archderm.144.5.666
11. Grant ME. Prockop DJ. The biosynthesis of collagen. N Engl J Med 1972; 286: 194-9.
12. Helary C, Abed A. Mosser G. Louedec L. Meddahi-Pelle A. Giraud-Guille MM. Synthesis and in vivo integration of improved concentrated collagen hydrogels. J Tissue Eng Regen Med. 2011; 5:248-52.
13. Lapierre LA. The molecular structure of the tight junction. Adv Drug Deliv Rev 2000; 41: 225-64.
14. West MD. The cellular and molecular biology of skin aging. Arch Dermatol 1994; 130: 87-95.