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NEW GENERATION OF NANO-COMPLEXES™ IN ENHANCEMENT OF
NON-SPECIFIC SKIN RESISTANCE IN CRITICAL CARE MEDICINE.
MD SCIENCE, INC. / BIONOVA, INC. USA**

Based on newly developed technological approach of Hyper-Natural Bioactive Complexes Modeling MD SCIENCE, Inc. in cooperation with BIONOVA, Inc. developed special NANO-COMPLEXES™ to enhance non-specific skin resistance toward multiple skin dysfunctions. Those NANO-COMPLEXES™ has been incorporated into customer friendly finished product in the form of 'serums'. It was formulated two form of finished product in form of 'Intensive Care Facial Serum' and 'Intensive Care Eye Serum'. Taking in consideration the fact the primary function of the skin is not the beauty and attractiveness, but the barrier function between surrounding environment and inner body system. Skin is one of the main systems which keep Homeostasis of Human Organism. In other word, skin as the biggest organ of a Human Body and needs to be addressed very precisely. Specially formulated Intensive Care Serums for topical application increases **skin non-specific adaptation mechanisms**, enhances skin homeostatic capability, improves cell metabolism, activates self-healing processes and skin barrier function. It is similar to treatment of critical condition, when the cause of terminal condition is becoming irrelevant and body activates all internal non-specific adaptation mechanism to survive. The same approach has been implemented in Bioactive NANOCOMPLEXES™ - increase the adaptation capacity of skin function. Overall it translates into better skin function and better performance of the 'major targeted product'. Intensive Care Serums are based on proprietary nanotechnological platform for creating products oriented toward enhancement of self-healing processes with specific curative effects to repair malfunctioning biological information transfer. This technological platform is based on the development of Bioactive Complexes Modeling (NANO-COMPLEXES™), which gives the ability to manipulate not only with nano (10⁻⁹), but also with pico (10⁻¹²) quantities of biologically active substances **1**, targeting the problem-specific biochemical pathway. The usage amounts of bioactive substances in NANOCOMPLEXES™ are precisely within the physiological concentration within the cells of the *Livi Eye Areas for there ability to **enhance skin's homeostatic system** reflecting in healthy looking skin, reduction of skin's fatigue and slowing down wrinkle formation.*

Key Words: Nano-complexs, Skion Resistance, Bioactive, adaptation, Intensive Care.

1.0. NATURE OF THE PROBLEM

It is well known fact that the skin is the largest organ of a human body. For many centuries, when medical tools were limited, the skin was the main indicator of disease. By looking at its color, texture, evenness, and other visual characteristic of the skin, doctors could tell what inner organ was affected. With the technological progress, when so many tools/tests became available, the importance of skin as a tool was forgotten and the skin became mostly a concern of a beauty business. Nevertheless, we always have to remember that the skin primary function is not its beauty and attractiveness, but the barrier function between surrounding environment (with its pollution and multiple unfriendly agents) and inner body system. Skin is one of the main systems which keep

Homeostasis of Human Organism. In other word, skin as the biggest organ of a Human Body and like other organs needs to be addressed very accurately, meaning the skin's beauty does not exist separately from its healthy function. We all support our inner organs with vitamins, care about heart, lungs brain, eat healthy remembering the digestive system... and what do we do specifically for the skin? not for aging, not for oiliness or dryness, not for acne ... , but for the skin's proper function and its adaptation to constant changes in the environment? In reference of skin function as part of homeostatic system, it requires a complex approach from inside [from the inner part of the body] as well as from outside [from topical application]. This dual approach targets non-specific [to the existing problem] activation of adaptation systems that allows skin functioning in its genetically determined physiological way. It is critically important what type of substances should be used to affect the inner [internal] and outer [topical] part of the body. Based on fundamental scientific research conducted by MD SCIENCE, Inc. in collaboration with BIONOVA, Inc. we can state that the best treatment approach is to use substances, which are 100% indigenous for the Human and which are bio-physiologically produced in a Human Organism **2**. This is true response oriented treatment approach.

2.0. INTENSIVE CARE SERUMS COMPOSITION

Intensive Care Serums consist of indigenous for Human Organism Bioactive NANOCOMPLEXES™ stabilized in NuCell-Direct™ delivery system **3**. Intensive Care Serums is formulated from NANO-COMPLEXES™ specifically adjusted to the targeted area –Face and Eye. Bellow is the list of NANO-COMPLEXES™ used in formulations:

- IT NANO-COMPLEX™: Bioactive Transmitters NANO-COMPLEX™ for providing inter and intra-cellular signaling transmission;
- TB NANO-COMPLEX™: Age & Wrinkle Control NANO-COMPLEX™ for prevention of signs of premature aging of skin and containing short chain polypeptides and glycoproteins;
- AX NANO-COMPLEX™: Antioxidant & Anti-Free Radical Scavengers NANO-COMPLEX™ - complex of multiple potent antioxidants & anti-free radical scavengers stabilized in NuCell-Direct™ delivery system;
- VCB NANO-COMPLEX™: Vitamin-Coenzyme NANO-COMPLEX™ - complex of water soluble vitamins with their specific coenzymes and oil soluble vitamins stabilized in NuCell-Direct™ delivery system;
- SBRS NANO-COMPLEX™: Skin Barrier NANO-COMPLEX™ - complex of multiple bioactive lipids, bioactive carbohydrates, glycolipids and other bioactive substances for modeling natural Skin Barrier System to hydrate and protect the skin;
- IDL NANO-COMPLEX™: Intermediate Density Lipoproteins NANO-COMPLEX™ composed of bioactive substances modeling intermediate density lipoproteins to restore and protect skin lipids;
- NU-CELL DIRECT™ DELIVERY SYSTEM, a unique novel delivery system especially formulated for stabilization and delivery of bioactive substances formulated for Intensive Care Facial Serum. The composition and structure of the delivery system approximates the structure of a Human Cell membrane. NuCell-Direct™ composed of highly specialized proteins, carbohydrates, and lipids; the very same ones that comprise the human cell membrane. The NuCell-Direct™ is capable of delivering both, water soluble as well as oil soluble actives. The active ingredients are entrapped within the delivery system and acting synergistically in one "unit". NuCell-Direct™ technology has dual function: (1) stabilization of the non-stable active ingredients and (2) penetration enhancer with time release effects.

3.0. SONOGRAPHIC EVALUATION OF INTENSIVE CARE SERUM ON FACIAL SKIN PARTICIPANTS

28 women panelists in age 32 –57 who could meet the study criteria's were screened for the ultrasonic imaging of facial skin. Eighteen (18) panelists selected for participation in the test phase of the study had received Intensive Care Facial Serum. Another ten (10) panelists selected for participation in the placebo (control) study and received only pure serum base without NANO-COMPLEXES™.

TEST PHASES

- Phase 1 – Study Week 1 - Phase 6 – Study Week 6
- Phase 2 – Study Week 2 - Phase 7 – Study Week 7
- Phase 3 – Study Week 3 - Phase 8 – Study Week 8
- Phase 4 – Study Week 4 - Phase 9 – Study Week 9
- Phase 5 – Study Week 5 - Phase 10 – Study Week 10

ANALYZED PARAMETERS

According to the published scientific data ultrasonic imaging technique of the skin is a reliable noninvasive test to determine the skin thickness and dynamics of its changes during the treatment of skin care products. Ultrasonically on the images, the skin appears as two bands: a dark superficial one where the ultrasonic waves are propagated in a relatively homogenous or non-echogenic medium, and a deeper one, which is lighter in color, suggesting a heterogeneous medium.

The ultrasonic imaging technique we used provided cross-sectional images of facial skin in vivo with a resolution of about 80 microns axially (deep into the skin) and 250 microns lateral (parallel to the surface).

SUMMARY OF RESULTS

Table 1: Ultrasonic Imaging Data of Women in Test Group

Women on age 50 -55		Women on age 30 - 40	
Week of Observation	Facial Skin Thickness (mm)	Week of Observation	Facial Skin Thickness (mm)
Week 1	0.185	Week 1	0.325
Week 2	0.186	Week 2	0.329
Week 3	0.191	Week 3	0.332
Week 4	0.201	Week 4	0.336
Week 5	0.205	Week 5	0.339
Week 6	0.221	Week 6	0.343
Week 7	0.233	Week 7	0.345
Week 8	0.236	Week 8	0.348
Week 9	0.239	Week 9	0.35
Week 10	0.241	Week 10	0.353

Table 2: Ultrasonic Imaging Data of Women in Placebo Group

Women on age 50 -55		Women on age 30 - 40	
Week of Observation	Facial Skin Thickness (mm)	Week of Observation	Facial Skin Thickness (mm)
Week 1	0.186	Week 1	0.325
Week 2	0.186	Week 2	0.325
Week 3	0.186	Week 3	0.335
Week 4	0.187	Week 4	0.335
Week 5	0.187	Week 5	0.336
Week 6	0.187	Week 6	0.336
Week 7	0.187	Week 7	0.336
Week 8	0.189	Week 8	0.336
Week 9	0.189	Week 9	0.337
Week 10	0.189	Week 10	0.337

Diagram 1: Dynamics of Changes in Skin Thickness Changes of Woman in Test Group (Age 50-55)

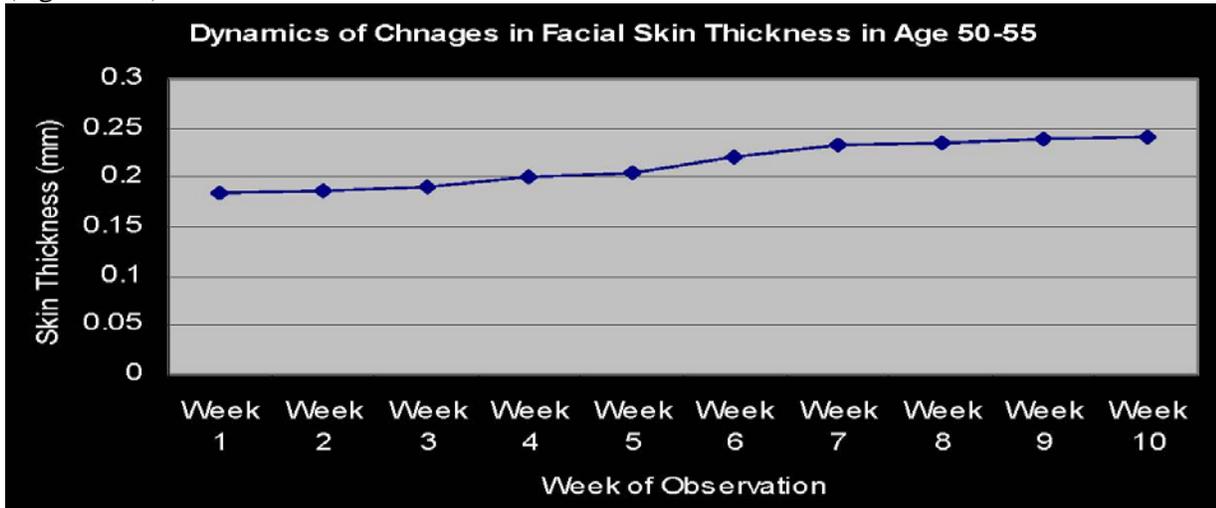
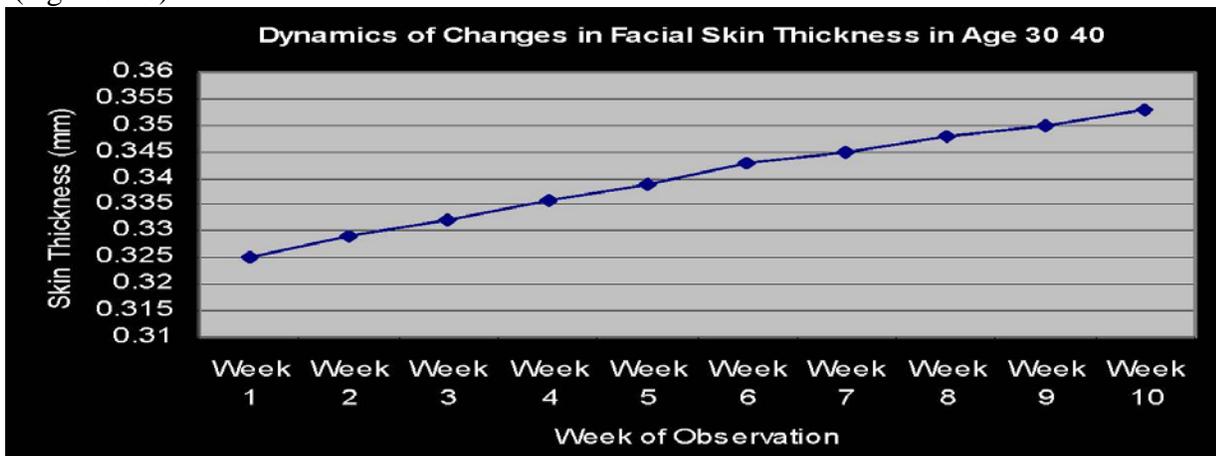
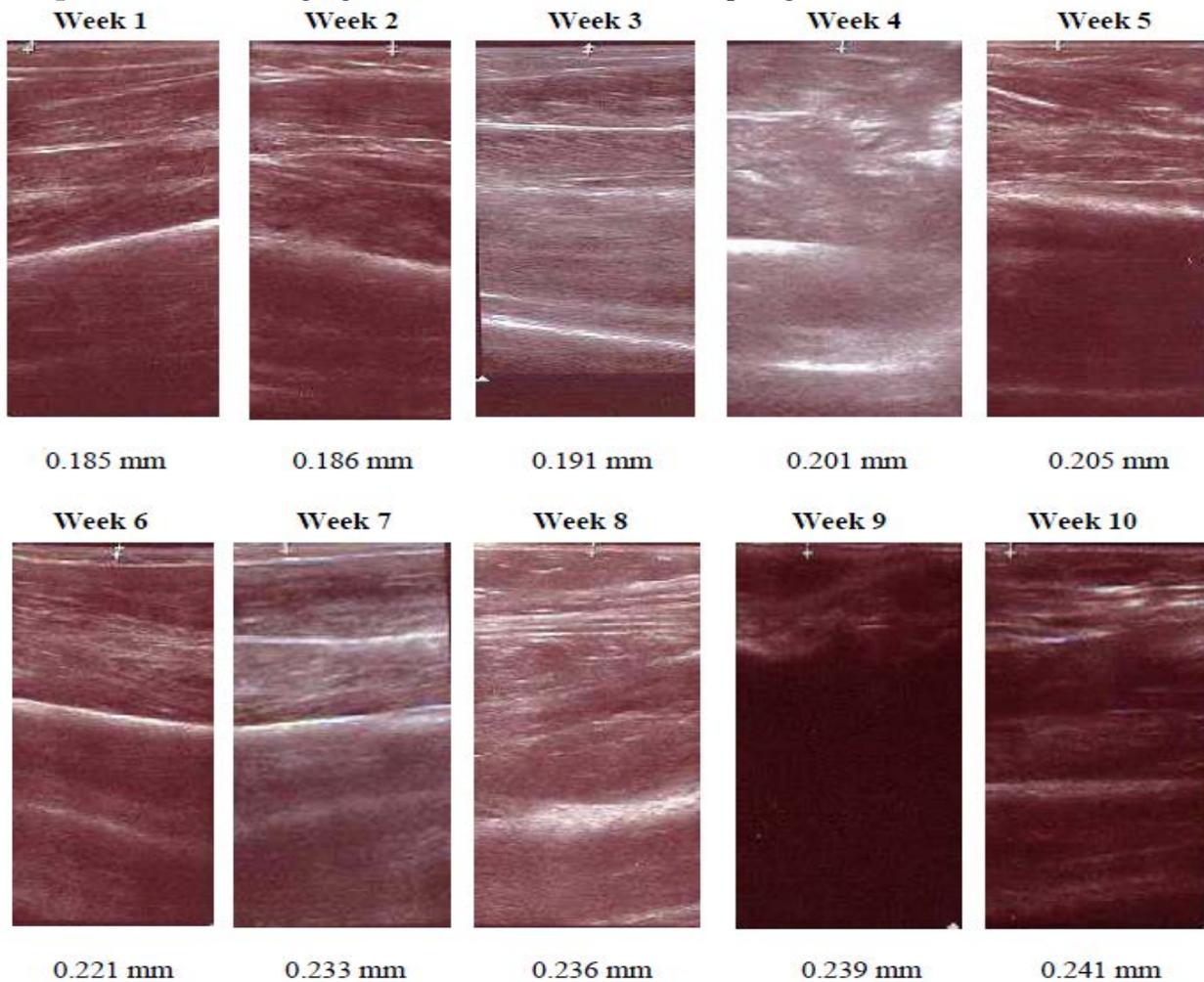


Diagram 2: Dynamics of Changes in Skin Thickness Changes of Woman in Test Group (Age 30-40)



Example: Ultrasonic Imaging Data of Woman in Test Group (Age 50-55)

Data generated on panelist shows that in age 50 and more (postmenopausal women w/o hormone replacement therapy) use of Intensive Care Serum promoted the average increase of skin thickness from 0.185 – 0.188 mm to 0.241 – 0.250 mm which equals to **30.3 – 33.0%** average increase in skin thickness. In age 30 to 40 (active reproductive period) use of Intensive Care Serum promoted the average increase of skin thickness from 0.321 – 0.325 mm to 0.353 – 0.358 mm which equals to **8.6 - 11.3%** average increase in skin thickness. At the same time panelists used placebo (serum base without Bioactive NANO-COMPLEXES™) shows no changes in skin sonogram images and its thickness.

CONCLUSION

Skin thickness is a direct and proportional indicator of its elasticity and youthfulness. The data presented above clearly indicates that the tested Intensive Care Serum **increases skin thickness, elasticity up to 33.0 percent in 10 weeks of usage.**

4.0. CONTACT THERMOMETRIC ASSESSMENT OF INTENSIVE CARE SERUM ON FACIAL SKIN

A linear relationship between skin blood flow and temperature was confirmed by numerous of scientific works. The purpose of this study was to observe dynamics of changes in facial skin temperature during the treatment with BIONOVA's Intensive Care Facial Serum.

PARTICIPANTS

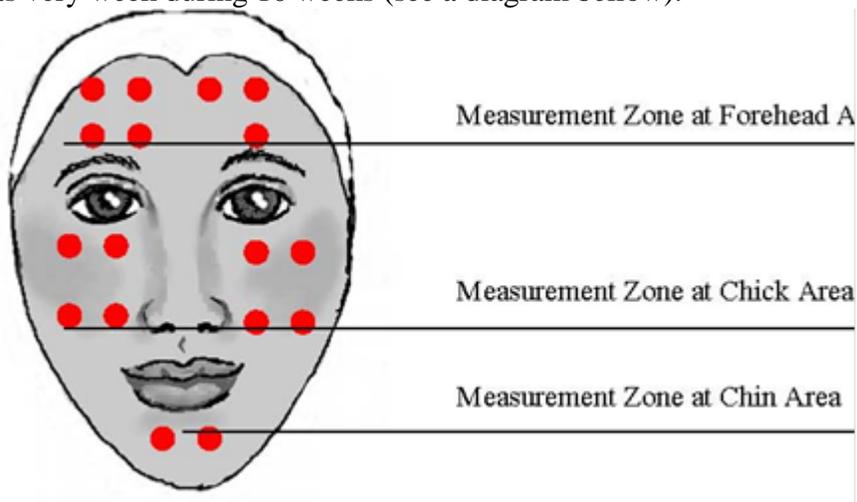
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TEST PHASES

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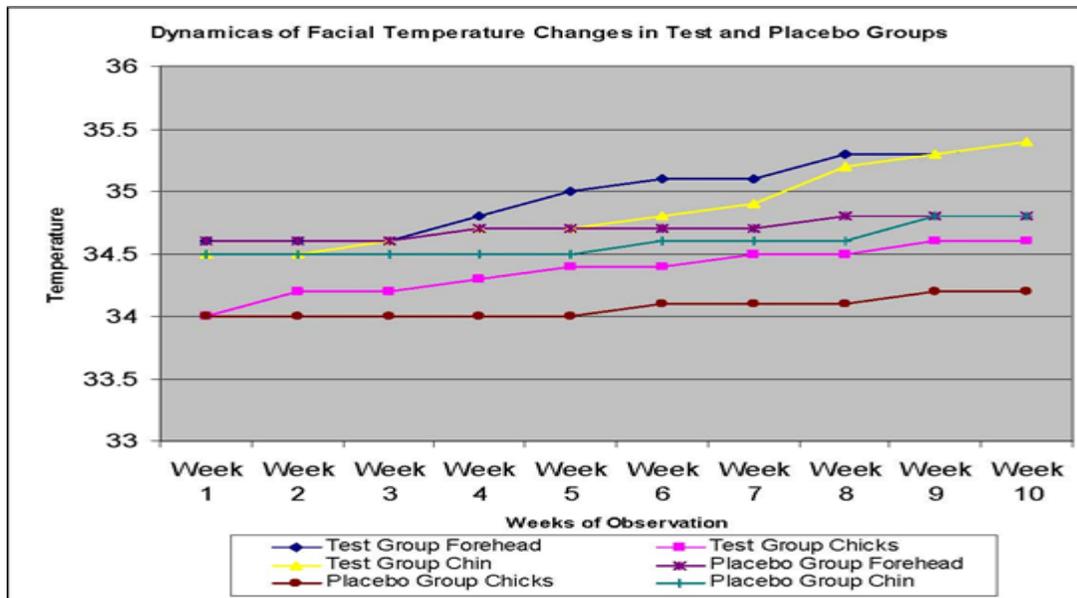
ANALYZED PARAMETERS

Temperature measurements were taken after 20-minute accommodation of panelists to the room temperature 22oC. The contact thermometric technique we used provided dynamics of facial skin temperature changes with a resolution of 0.1oC. Contact thermometric measurements were taken in 18 onstant dots on the following regions of facial skin: Forehead – 8 dots, Chicks – 8 dots, Chin – 2 dots very week during 10 weeks (see a diagram bellow):



SUMMARY OF RESULTS: Results of the study are shown bellow:
Dynamics of Temperature changes in Test and Placebo Group.

	Test Group			Placebo Group		
	Forehead	Chicks	Chin	Forehead	Chicks	Chin
Week 1	34.6	34.0	34.5	34.6	34.0	34.5
Week 2	34.6	34.2	34.5	34.6	34.0	34.5
Week 3	34.6	34.2	34.6	34.6	34.0	34.5
Week 4	34.8	34.3	34.7	34.7	34.0	34.5
Week 5	35.0	34.4	34.7	34.7	34	34.5
Week 6	35.1	34.4	34.8	34.7	34.1	34.6
Week 7	35.1	34.5	34.9	34.7	34.1	34.6
Week 8	35.3	34.5	35.2	34.8	34.1	34.6
Week 9	35.3	34.6	35.3	34.8	34.2	34.8
Week 10	35.4	34.6	35.4	34.8	34.2	34.8
ΔT	0.8	0.6	0.9	0.2	0.2	0.3



The test data showed a steadily increase of the facial temperature up to 0.80°C in test group. That correlates to increase of skin blood circulation up to 2.5%. In placebo group temperature dynamics fluctuated in range 0.20°C that indicates at the absence of blood circulation increase.

CONCLUSION

There is a linear relationship between skin blood flow and local skin temperature. The data presented above indicates that the tested Intensive Care Facial serum **promotes steady increase of facial skin blood flow up to 2.5 percent in 10 weeks of usage.**

5.0. IN-VIVO EVALUATION OF EYE AREA INTENSIVE CARE SERUM FOR ITS ABILITY TO INCREASE VISCOELASTICITY OF THE SKIN IN EYE AREA

This study was conducted to evaluate the efficacy of the Eye Area Intensive Care Serum for its ability to increase viscoelasticity of the skin around eyes.

PARTICIPANTS

Fifteen (15) panelists were selected for participation in the test phase of the study. All panelists have Moderate and Advanced fine lines near the eye, as determined by the modified Glogau classification.

EFFICACY TEST

Test Sites: The skin around the crow's feet area of the eyes.

Phases (Measurement Intervals):

- Visit I - Baseline - ballistometer measurements was taken on Test Day 0
- Visit II - After three weeks of product use
- Visit III - After six weeks of product use
- Visit IV - After nine weeks of product use

Panelists were randomly assigned either the test material or a placebo control. They were given sufficient test material to use two times a day for nine weeks.

Ballistometer Measurement

The Ballistometer was used to measure the firmness of the skin around the crow's feet area of the eyes. The Ballistometer scores increased where the skin become more firm.

Statistical Analysis

All Ballistometer parameters were analyzed by repeated Analyzes of Variance measures.

ADVERSE EFFECTS

No adverse effects were noted during the course of the study.

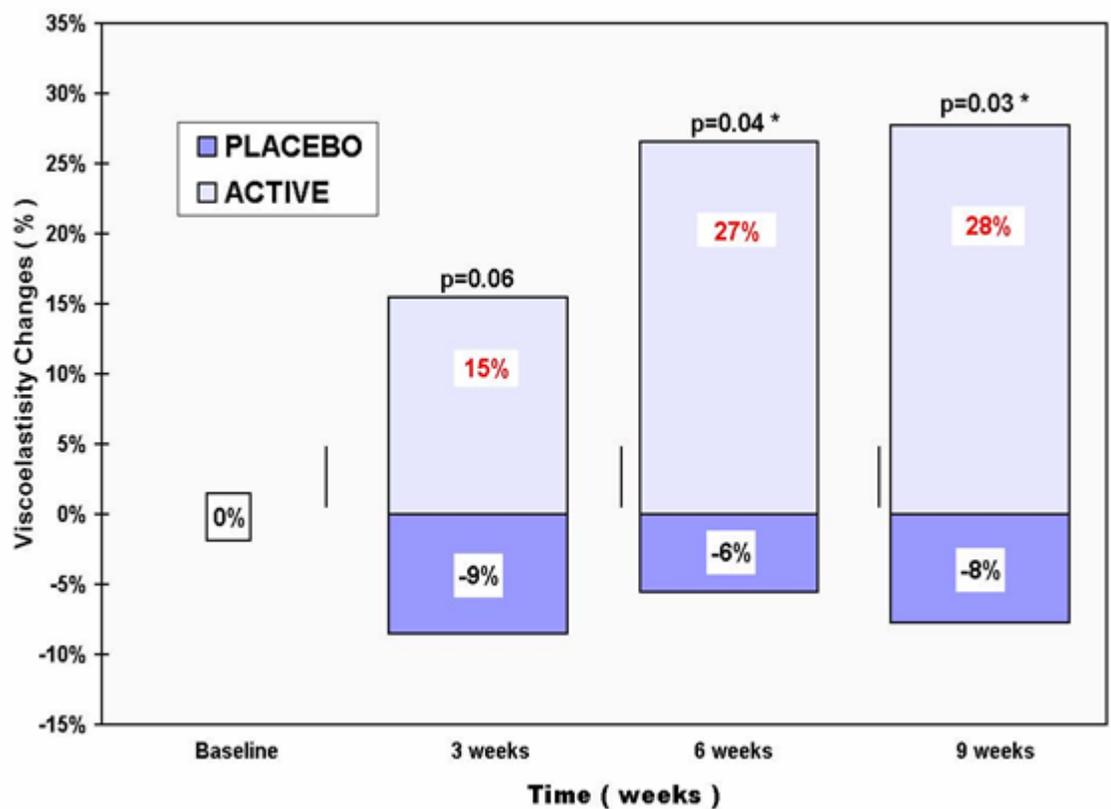
TOLERANCE

Eye Area Intensive Care Serum is based on the physiological substances which are equivalent to those which are bio-physiologically produced in the human organism. Namely, active ingredients in Eye Area Intensive Care Serum are 100% physiological to the human organism. They contain only what the human body has already produced, but for different reasons cannot accept at the cellular level.

SUMMARY OF RESULTS

The results of the study show that 100% of the test panelist who received the formula containing BIONOVA bioactive complexes for Eye Area Wrinkles & Aging experienced positive improvement ranging from moderate to superior. The results indicated that at week six (6), Ballistometer parameters for the treated group were significantly higher than in the control group ($p < 0.04$). On the chart, we can observe ~ 18% increase of Ballistometer test scores in three weeks in the treated group. Continued usage of product increases Ballistometer test scores up to ~ 27% at week six and stabilized these scores at week nine. During the same time period viscoelasticity of the eye area in the control group decreased by ~ 8%. All the above Ballistometer test results illustrate that in using BIONOVA's Cream for Eye Area it is possible to increase viscoelasticity of the skin and reduce the puffiness in the delicate eye area by ~ 28-35% after six weeks of use of the test formula when compared to the control.

Note: For additional targeted results provided by specific NANO-COMPLEXES™ see appropriate data.



EFFECTS OF BIONOVA'S CREAM FOR EYE WRINKLES AND AGING BASIC EFFECTS OF BIONOVA SERUMS FOR EYE AREA WRINKLES & AGING

- Revives skin cell metabolism and reduces the signs of aging around eyes
- Increases elasticity and firmness of the Eye Area Skin
- Replenishes synthesis of skin natural collagen, elastin, and glycoprotein to minimize fine lines and wrinkle appearance
- Natural antioxidants and bioflavonoids protect the skin against damaging free radicals and oxidative stress
- Potentiate anti-aging effects and preserve skin's youthful appearance
- Complex of essential vitamins and their coenzymes increases skin cell healing ability, energizes and nourishes the skin, reduces capillary permeability and increases oxygen utilization.

CONCLUSION

Intensive Care Serums for topical application with non-specific activation of skin homeostatic system are products that targets the skin regardless any specific concern. They improves skin cell metabolism, enhances skin self-healing processes and skin barrier function through activation of nonspecific adaptation mechanisms. They functioning similar way as to treatment of critical condition, when the cause of terminal condition is becoming irrelevant and body activates all

internal non-specific adaptation mechanism to survive. The same concept utilized in treatment of skin - activate general cellular metabolism, increase the adaptation capacity of skin function. Overall it translates into better skin function and better performance of the 'major targeted product'.

Enhancement of non-specific skin resistance improves skin function as a vital organ of the body and:

- Provides non-specific (general) activation of skin homeodynamic ability, reflecting in healthy looking skin and reduction of skin fatigue after internal & external stress factors.
- Enhances the skin's ability to respond to environmental and internal aggressions, stimulating energetic level of the skin, causing skin to reinforce its tone brightness and elasticity.
- NANO-COMPLEX™ of Hyper-Natural™ ingredients indigenously presented in the healthy body in of skin sagginess and increasing its tightening.
- Intensive Care Serums is not one more filler and do not act on the skin as a temporary "masking" agent to change the skin appearance. It works from inside using Hyper-Natural™ ingredients biophysiologicaly produced in a Human Organism.
- Billed-in proprietary Hyper-Natural™ Biological Systems helps to inhibit/slow down wrinkle formation, restoring skin youthful appearance.
- Specially developed NANO-COMPLEXES™ protect skin against harmful factors and from amaging UV photo-aging factors.
- Intensive Care Serum reduces the appearance of skin sagginess, noticeably helps lifts the skin, firms its matrix and provides instant skin radiance.
- This multi-functional product that has both an immediate and a long-term effect resulting in a heathy skin appearance.

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მ. დანიელოვი, ა. სეპპერი.

ახალი გენერაციის ნანო-კომპლექსები კანის არასპეციფიკური დაზიანების სამკურნალოდ კრიტიკულ მედიცინაში.

MD SCIENCE, INC. / BIONOVA, INC. აშშ

შემუშავებულია ახალი ტექნოლოგიური მიდგომა ჰიპერ-ნატურალური ბიოაქტიური კომპლექსის სახით, რომელიც მოდელირდა MD Science, inc- და BIONOVA, inc მიერ. ამგვარი ტექნოლოგიით მომზადებული ნანო-კომპლექსები ამაღლებენ კანის რეზისტენტობას და შესაძლებელია მათი გამოყენება კრიტიკულ მდგომარეობათა დროს. ისინი გამოიყენება კანის ფუნქციის გასაუმჯობესებლად. ამ ნანო კომპლექსებს აქვთ შრატის ფორმა. ეს უკანასკნელი ამაღლებს კანის დამცველობით ბარიერს, აუმჯობესებს უჯრედების მეტაბოლურ ფუნქციას და თვითრეგენერაციის პროცესს. ის ხელს უწყობს კანის უკეთეს “ფორმაში შენახვას” კრიტიკული მდგომარეობის დროს.