B I O N O V A

NANO SKIN TECH™

EFFICACY DATA

INDEX

1.0. OVERVIEW

1.1. NANO TECH PLATFORM

As science pushes forward into the new millennium, skin care is benefiting greatly from new breakthroughs. Introducing BIONOVA NANO SKIN TECH™ – a unique skin care concept that boosts the application of Nano-technology in its formulas. With the recent and enormous growth of the skin care industry, BIONOVA takes on this huge market and breaks through the clutter by providing a safer, more effective and extremely natural skin care choice to consumers.

BIONOVA's technology is based on fundamental scientific research conducted by Michael Danielov, MD, PH.D., after years of study in his unique laboratory in the former Soviet Union. His 25 years of scientific research there led to the understanding of the human body's regulatory mechanisms. In United States, Dr. Danielov continued his research, creating biologically active complexes that actually repaired cells. Realizing that his ingredients were ideal to regenerate aging skin, Dr. Danielov decided to create his own line of skin care, and BIONOVA was born.

The basis of Dr. Danielov's theory is that everything that the body needs has already been placed within and that our cells know best how to fix themselves. BIONOVA's team of scientists have created methods to activate self-healing processes that naturally exist in the body, in essence jump-starting self-healing by supplying to the skin multiple biological active ingredients needed for repairing malfunction. The bio-active ingredients are delivered to the skin in 'Nano' sized (one billionth of a gram) molecules to effectively absorb into the skin, thus creating BIONOVA NANO SKIN TECH™, BIONOVA's trademarked effective skin care.

Skin care products are typically used as a palliative to temporarily ameliorate skin conditions caused by disease, aging or environmental conditions. However caused, the skin condition results from improperly functioning elements of the cellular metabolism of the skin.

BIONOVA's nanotechnological platform is based on cutting edge technology inventions, which can be grouped into four categories:

- **Opti-Path™** - natural Biologically Active Nano-Complexes™, which is an imitation of biological information transfer systems existing in a human organism. They are nanocomplexes, created by manipulation of nano-amounts and pico-amounts of multiple active substances with strong predictable physiological results.
- **NuCell-Direct™** - Delivery System for active substances, which is an imitation of a human cell membrane. NuCell-Direct™ provides benefits beyond its use as a delivery system and also as a powerful stabilizer of unstable substances, naturally present in living organisms. These powerful features of NuCell-Direct™ effectively make obsolete the Liposome delivery system currently used by pharmaceutical, nutritional, and skin care industries.
- **CDP™** - Custom Designed Process (modular production process), the fast and accurate manufacture of finished products depending on market necessity or even on individual customer profile. This modular production process is based on pre-existing nanomodules of Opti-Path™ biologically active nanocomplexes.
- **InterView Software™** - Automation Software, which translates personalized survey responses into a custom formulated product formula.

Opti-Path™ and NuCell-Direct™ technologies synergistically operate in tandem to re-activate the improperly functioning elements of the skin's cellular metabolism.

1.2. METHODOLOGY (MATERIALS & METHODS)

Fundamental scientific research for evaluation of the compositions containing various types of Bioactive Nano-Complexes (Opti-Path™**)** and Novel Delivery System (NuCell-Direct™) was performed extensively and reflected the functional condition of the main regulatory system of the organism and cell metabolism.

The major scientific research has been performed in the Institute of Experimental Morphology of Academy of Science in Georgia (former USSR). This research has been oriented to multiple pathologies, including Post-Aggressive Reactions of The Organism And Their Adaptation To The Critical Conditions.

For fundamental scientific research the effectiveness of various types of specific Biocomplexes (Nano-Complexes™) has been evaluated both in experimental (parenteral and topical applications) and clinical studies.

For skin dysfunctions and different skin diseases specific Biocomplexes (Nano-Complexes™) has been created and evaluated in topical applications. These studies have been focused on (a) Skincare Dysfunctions and on (b) Dermatological problems.

METHODS OF BIOLOGICAL ACTIVE SUBSTANCES STUDY

The concentration of hormones and biologically active substance (first and second degree messengers) has been evaluated by radioimmunoassay (RIA), which is characterized by high specificity, high sensitivity and highest possible precision. Radiometry of the samples was evaluated on eqipment for radiochemical analysis "Beta-1", "Beta-2", "Gamma-1", and "Gamma-12". These equipments represent one of the most sensitive tools to analyze biologically active substances in nano and pico quantities.

The names of hormones and biologically active substances are given in accordance with the nomenclature recommended by the International Biological Union.

A: FIRST DEGREE MESSENGERS

Adeno-Pituitary (Adenohypophysis) Function

- Adrenocorticotropic Hormone (ACTH, Corticotropin) – analyzed by ACTHK-PR (CIS International, France) and JNC-2400 (Immuno-Nuclear Corporation, USA) RIA systems.
- Lutropin (Luteinizing Hormone, LH) -- determined by LH-PR (CIS, France) and RS-4124 (Radioassay System Labor, USA) RIA systems.
- Follitropin (Follicle-stimulating Hormone, FSH) -- evaluated by FSHK-PR (CIS, France) and RS 4123 (Radioassay System Labor, USA) RIA systems.
- Somatotropin (Growth Hormone, STH) -- determined by HgHK (CIS, France) and CNR-722 (Cambridge Medical Diagnostics, USA) RIA systems.

Neuro-Pituitary (Neurohypophysis) Function

- Vasopressin (ADH) -- determined by Vasopressin RIA system (Buhlman Labor, Switzerland).

Cortico-Suprarenal Function

Glucocorticosteroids

- Hydrocortisone (11b,17a,21-trihydro-4-pregnene, 3,20-dion) -- evaluated by Cortk-125 (CIS, France) and ING-13170 (Immuno-Nuclear Corp., USA) RIA systems.
- Corticosteron -- determined by RIA system (Radioassay System Lab.USA).

Mineralocorticosteroids

- Aldosteron (11b,21-dihydroxy-3,20-dioxo-4 pregnene -18 al-18-11-hemiacetal) -- determined by SB-ALDO (CIS) and AS-888 (Wien Laboratories, USA) RIA systems.

Anabolic Steroids

Androgens

- Testosterone -- determined by RIA systems Amersham (England).
- Dehydroepiandrosrerone – evaluated by RIA systems Amersham (England).
- 5a-Dehydrotestosterone -- analyzed by RIA systems Amersham (England).

Estrogens

- 17a-Estradiol -- analyzed by ESTRK-RIA systems CIS (France).
- Estron -- determined by ES-RIA systems CIS (France).
- Estriol -- analyzed by RIA systems CIS (France).

Gestagens

- Progesterone -- analyzed by PG-RIA systems CIS (France).
- 17a-Hydroxyprogesterone – determined by RIA test systems from CIS (France).

Renin-Angiotensin System Function

- Plasma Renin Activity (PRA) -- determined by using the RENK RIA system (CIS, France).
- Serum Angiotensine Converting Enzyme (SACE) -- evaluated by means of IDL-200 system (Immuno-Diagnostic Laboratories, USA).

Medulla-Suprarenal Gland Function

Catecholamines

- Epinephrine
- Arterenol

  Both catecholamines were determined by enzymo-radioimmunoassay system via specific test system from Upjohn Diagnostics, USA.

B: SECOND DEGREE MESSENGERS

- Cyclic Adenosine Monophosphate (c-AMP; 3'5'-AMP) -- determined using TRK-425 RIA system (Amersham, England).
- Cyclic Guanosine Monophosphate (c-GMP; 3'5'-GMP) -- determined by means of TRK-500 RIA system (Amersham, England);
- Calmoduline (Calcium Binding Protein; Cyclic Nucleotide Phosphodiesterase Activator) -- evaluated by NEN test system (NEK-018), DuPont Co.

C: INTRACELLULAR TRANSMITTERS

- Prostaglandin A (PGA) -- determined using the CA-501 system (Clinical Assay, USA).
- Prostaglandin E (PGE) -- examined using the CA-501 system (Clinical Assay, USA).
- Prostaglandin E2 (PGE2) -- evaluated via test system SG-6001 from Seragen, USA.
- Prostaglandin E1 (PGE1) -- determined using the system SG-6013 (Seragen, USA).
- Prostaglandin F2a (PGF2a) -- determined by means of the CA-503 (Clinical Assay, USA) and SG-6002 (Seragen, USA) systems.
- PGF1a-6 keto -- determined by test system from Amersham, England.
- 13,14-dihydro-15-keto PGF2a -- determined by test system SG-6006 from Seragen
- 11-Deoxy-13,14-dihydro-15-keto-11b,16e-cyclo-PGE2 -- evaluated by test system TRK.800 (Amersham, England)

D: CELL MEMBRANE AND CYTOSOL RECEPTORS ACTIVITY

All membrane and cytosol receptors were evaluated using various types of proprietary radioisotope ligand techniques. Using corresponding isotope (ligand) the following receptors Activity and/or Amount have been determined:

Membrane Type of Receptors

- β1 and β2 - Adrenoreceptors
- α1 and α2 - Adrenoreceptors
- Angiotensin II receptors
- Prostaglandin E2 receptors (PGE_2)
- Prostaglandin F2α receptors ($PGF_{2\alpha}$)

Cytosol Type of Receptors

- Glucocorticosteroid receptors
- Mineralocorticosteroid receptors
- Estrogen receptors
- Androgen receptors.

METHODS OF BLOOD CIRCULATION (HEMODYNAMIC) EXAMINATION

Special algorithm and application package for automatic processing of over 80 parameters of blood circulation both on-line and off-line systems has been developed. Monitoring systems allowed controlling most of the homodynamic parameters.

In different part of body simultaneously with hormones and biologically active substances multiple parameters of the circulation has been monitored:

- Central (systemic) hemodynamic
- Contractile function of the myocardium
- Cerebral circulation
- Peripheral circulation
- Microcirculation

BIONOVA's products are one of the most effective skin care products on the market. It effectiveness is governed by its fundamental scientific research in area of Nano-technology of Nano-Complexes™ Modeling.

BIONOVA generated specific consumer and efficacy data for Bioactive Nano-Complexes™ and their use in the Finished Skin care products.

At the same time there are multiple substances in BIONOVA's products with well-known skin care benefits and their effectiveness is considered obvious from the formula and product presentation.

1.3. WHAT IS SO UNIQUE IN BIONOVA'S APPROACH

NANO SKIN TECH™ PRODUCT COMPOSITION

- The ingredients in NANO SKIN TECH™ products are replicas of bio-active ingredients. (Nano-Complexes™) that exists in young, healthy bodies. These ingredients are vital for reestablishing cellular communication.
- BIONOVA's Nano-Complexes™ and its cosmeceutical products are not simple blends of various active substances, or a mixture of various plants, vegetable and other extracts. They are based on a new technological approach to formulate skin care products with strong predictable results.
- BIONOVA's skin care products are composed of Bioactive Nano-Complexes™, which cab be characterized as a absolutely 'closed system'. It is impossible to add or to remove any component from this active system or to imitate the product without knowing the formula.
- Nano-Complexes™ are 100% indigenous to the human body and can therefore be easily absorbed and metabolized. They do not contain oils, animal, vegetable or fruit extracts since none of these is indigenous to the human body.
- BIONOVA is the only company with the technological capability to create precise bioactive ingredients (Nano-Complexes™) that target an individual's:
  - Personal profile (age, gender, ethnicity....)
  - Specific skin area (face, eyes, body....)
  - Skin problems (wrinkles, dark circles, acne scars, pregnant skin, Rosacea, Acne....)
- Each NANO SKIN TECH™ product is composed of 150 to 300 bioactive ingredients (Nano-Complexes™) that are specially formulated for each individual's skin profile.
- Quantities of the ingredients in NANO SKIN TECH™ products come in Nano (1 billionth of a gram) and Pico (1 trillionth of a gram) amounts, which are precisely within the natural range of comfort for our skin cells.
- BIONOVA uses active substances which are physiologically produced by the human body and can therefore be considered "truly natural" for the human organism.

NANO SKIN TECH™ PRODUCT PERFORMANCE

- NANO SKIN TECH™ does not act on the skin as traditional products do; rather they cause the skin to improve itself, working from its innermost layer (self-healing process).
- NANO SKIN TECH™ products restore cellular communication processes to their optimal state, which translates into younger-looking and healthier skin.
- NuCell Direct delivery ™ system (an imitation of the cell membrane) incorporates Nano-complexes™ and delivers them to the human cells. The cells recognize Nano-complexes™ and use them upon necessity.
- This is the only system actually able to reactivate dormant sebaceous glands typical for aging and dried up skin. It stimulates the production of sebum, a fatty natural lubricant that leaves skin moist and lustrous. This prevents premature aging; maintains the skin elasticity and firm; energizes and nourishes the skin cells; reduces capillary permeability; and increases oxygen utilization in the cells.

THE ONLY TRUE CUSTOMIZATION

- BIONOVA created NANO SKIN TECH™ lines, which offers multiple levels of customization – N1-CUSTOM™, IMPACT™, SPORT (TENNIS line), BN SCIENCE, etc.
- The NANO SKIN TECH™ lines offer each of our clients a product that is designed to address his/her personal skin needs.
- Unlike anything currently available on the market, NANO SKIN TECH™ is unique because it uses custom designed Nano-technology solutions, which target an individual's bio-physiological makeup:

Gender + Age + Personal Profile + Specific Skin Area + Skin Type + Skin Problem
=
NORMALIZATION OF SKIN CELL METABOLISM

1.4. PRODUCT BENEFITS COMPARISON

BIONOVA Products	*Competitors' Products*
• Do not act upon the skin, rather they cause the skin to improve its condition.	• All products act to improve conditions on the surface of the skin.
• Functional products with targeted skin-condition results.	• Broad variety of standard claims without any specifically targeted functional effects.
• Have therapeutic benefits with treatment effects for specific skin conditions.	• Minimum if any therapeutic benefits: unable to physiologically improve skin condition.
• Do not contain oils or any animal, vegetable or fruit extracts since none of those are indigenous to the human body.	• Contain vegetable or mineral oils. Usually they contain various botanical and vegetable extracts, vitamins, and moisturizing agents.
• One-of-a-kind and specifically formulated for each customer product.	• Product made for average consumer.

1.5. BIONOVA's PRODUCTS SAFETY

TOLERANCE

All BIONOVA's individually formulated products are based on the physiological substances that are equivalent to those, which are bio-physiologically produced, in the human organism. Namely, active ingredients in BIONOVA's products 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. BIONOVA's products are non-toxic and physiologically innocuous.

MSDS Forms available upon request

Safety & Irritation Test data available upon request

1.6. BIONOVA PRODUCTS EFFICACY TEST

BIONOVA's products are one of the most effective skin care products on the market. It effectiveness is governed by its fundamental scientific research in area of Nano-technology of Bioactive complexes Modeling Fundamental scientific research on 'The Concept of Biological Information Transfer' has been done in the Institute of Experimental Morphology Academy of Science (former USSR).

BIONOVA generated specific consumer and efficacy data for Bioactive Nano-Complexes™ and their use in the Finished Skin care products. All efficacy test data for skin care products has been generated in the U.S. in various independent laboratories.

At the same time there are multiple substances in BIONOVA's products with well-known skin care benefits and their effectiveness is considered obvious from the formula and product presentation.

For detailed Skin Care Test Data see appropriate chapters.

2.0. BIONOVA CREAM FOR OILY SKIN

EVALUATION OF CREAM FOR OILY SKIN FOR ITS ABILITY TO REDUCE SEBUM PRODUCTION

INTRODUCTION

Cream for Oily Skin (basic version) is a unique complex of active substances incorporated into the specially developed cream base and functioning on a cellular level.

This basic oily skin product has been especially created to reduce sebum production in oily skin (there are multiple variations of this product with targeted Nano-Complexes, to achive strong predictable physiological results). It consist of the following bioactive complexes which are indigenous to the human organism and contain ingredients (nanocomplexes) specifically formulated for oily skin:

- Opti-Path-OS™: bioactive complex for normalization of skin sebum production, which is incorporated into the NuCell-Direct™ delivery system
- Opti-Pro-IT™: bioactive complex of intracellular transmitters stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AX™: bioactive complex of antioxidants and anti-free radical scavengers stabilized in the CellDirect™ delivery system
- Opti-Pro-AOV™: complex of ascorbic acid and oil soluble vitamins stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AmA™: complex of essential amino acids incorporated into the NuCell-Direct™ delivery system
- Opti-Pro-ANF™: anti-inflammatory & anti-bacterial complex for prevention/reduction of skin inflammation incorporated into the NuCell-Direct™ delivery system
- Opti-Cor-VCB™: complex of water soluble vitamins with their specific coenzymes stabilized in the NuCell-Direct™ delivery system
- NuCell-Direct™ Delivery System is a unique novel delivery system especially formulated for stabilization and delivery of the bioactive complexes for oily skin. The composition and structure of the delivery system approximates the structure of a natural 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 SCM and acting synergistically in one "unit". The only NuCell-Direct™ technology has dual function: (1) stabilization of the non-stable active ingredients and (2) penetration enhansor with time release effects

PARTICIPANTS

Thirty (30) female subjects that had excessively oily skin and who could meet the study schedule were screened for the degree of oil production. Fifteen (15) panelists with the greatest oil production were selected for participation in the test phase of the study. Another fifteen (15) panelists were selected for participation in the placebo (control) phase of the study.

EFFICACY TEST

Test Sites

The chin, left and right sides of the forehead and cheeks (nasolobial fold).

Phases (Measurement Intervals)

- Baseline - evaluation of sebum production was made on Test Day 0
- Three weeks - post treatment
- Six weeks - post treatment

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 six weeks.

The test sites were wiped with 70% isopropyl alcohol and sebutape strips were applied to the left and right sides of the forehead and cheek (nasolobial fold) and to the chin. After thirty minutes of contact, the tapes were removed and sent for image analysis to quantify sebum production.

Sebutape Analysis

The sebutape analysis was evaluated by Image Analysis as follows:

- Prior to each analysis session and periodically during each session, the lighting conditions and system response was standardized to a reference gray target, ensuring reproducible illumination response at the video frame grabber.
- The patient data from each card was entered and through use of the same macro, each of the five sampled areas were measured by the analysis software. This assured identical manipulation of every analyzed area.
- The two (2) pieces of information gathered from the dark area on the sebutape patches representing trapped sebum were the number of spots and the total area of the spots detected in a given area (approximately 10mm * 8.2mm) of the patch. The area of spots was converted to nominal volumetric units from the known pore volume of the sebutape material (38%) and the thickness (0.0025cm).

Analyzed Parameters

- AG - the amount of Active Gland Count was expressed as counts/cm^2.
- SO (RSDR) - sebum output (Relative Sebum Delivery Rate) - volumetric sebum output was expressed as nanoliters/cm^2.
- IR - computed Inherent Rate = SO/AG.

Statistical Analysis

AG, SO and IR parameters were analyzed by repeated analysis of variance, as well as by linear regression by Least Square Method (LSM).

ADVERSE EFFECTS

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

TOLERANCE

BIONOVA's Cream for Oily Skin is based on the physiological substances, which are equivalent to those, which are bio-physiologically produced in the human organism. Namely, active ingredients in BIONOVA's Cream for Oily Skin 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. BIONOVA's Cream for Oily Skin is non-toxic and physiologically innocuous.

SUMMARY OF RESULTS

The results of the study show that 100% of the test panelist who received the formula containing BIONOVA bioactive complexes for Oily Skin experienced positive improvement ranging from moderate to superior.

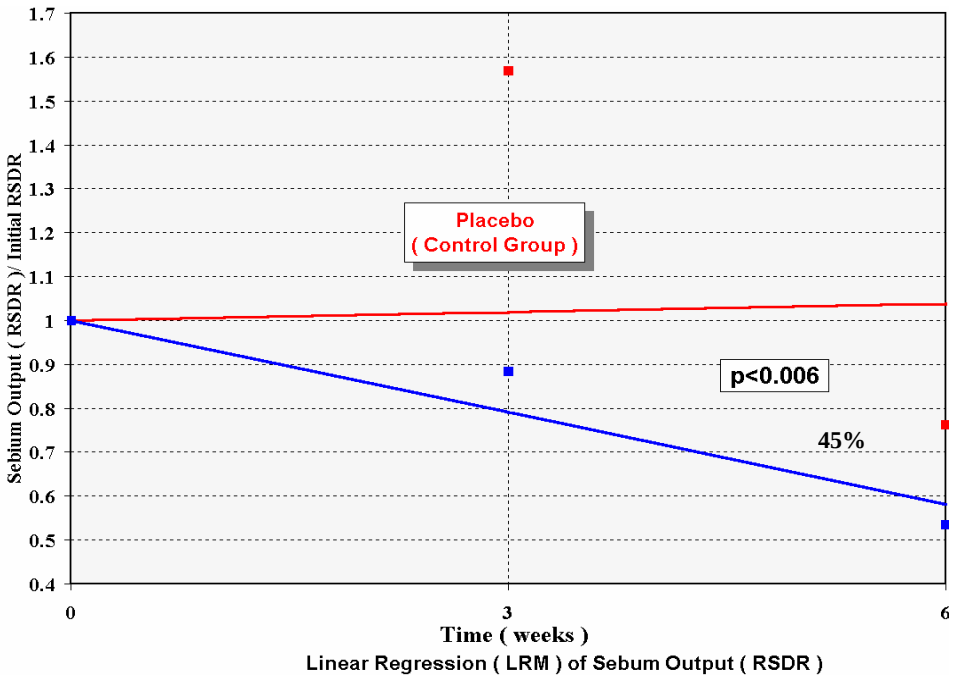
The results indicated that at week six (6), Sebum Output (RSDR) and the Inherent Rate (IR) parameters for the group treated with BIONOVA bioactive cream for Oily Skin were significantly lower than baseline ($p<0.006$ and $p<0.0176$ respectively), while there was no significant difference in either parameters for the control group.

On the following charts, we can observe that in the group treated with BIONOVA bioactive cream for Oily Skin, the RSDR (relative sebum delivery rate) in three weeks reduced by ~ 14 - 20%, and in six weeks RSDR reduced by ~ 42 - 45%. At the same time IR (Inherent Rate) in the group treated with BIONOVA bioactive cream in three weeks reduced by ~ 14 - 18%, and in six weeks IR reduced by ~ 35%.

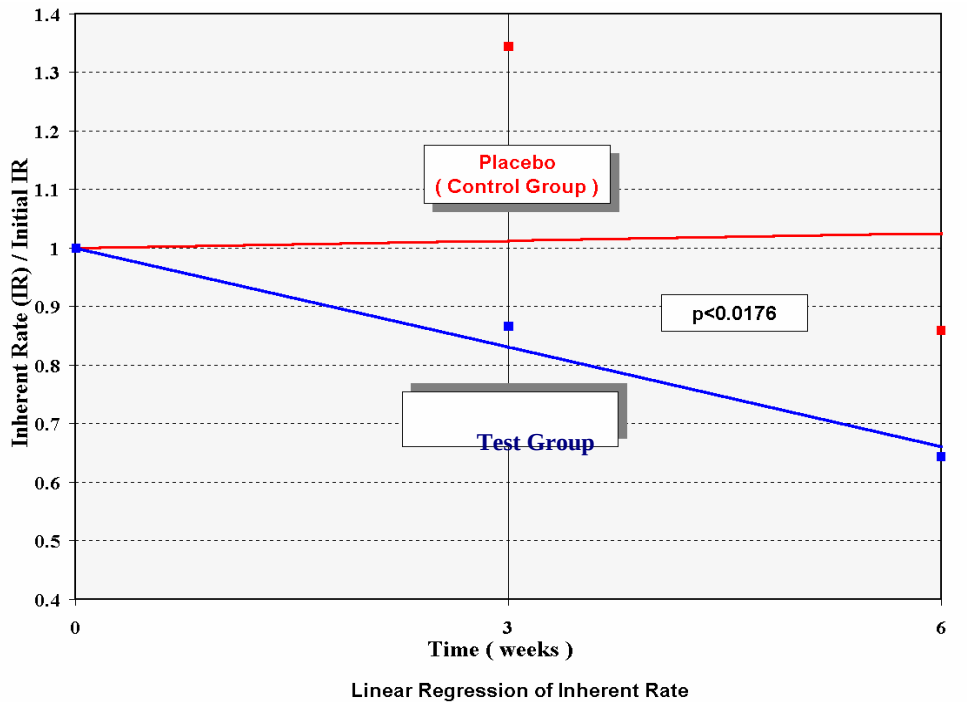
These data illustrate that using BIONOVA's Cream for Oily Skin it is possible to reduce endogenous sebum production by ~ 40 - 45% after six weeks as compared to the control. It is important to note that the actual number of active glands remained the same. Only the sebum output per gland decreased at each concentration tested.

Note: For additional targeted results provided by specific Nano-Complexes see appropriate data.

EFFECTS OF BIONOVA'S CREAM FOR OILY SKIN ON SEBUM PRODUCTION



EFFECTS OF BIONOVA'S CREAM FOR OILY SKIN ON SEBUM INHERENT RATE



BASIC EFFECTS OF BIONOVA'S CREAM FOR OILY SKIN

- Normalize endogenous oil production of the skin. Significant reduction in sebum production and normalization of the sebaceous gland function will be observed in 20 - 40 days and skin will remain normalized for an extended time period. The use of BIONOVA's Cream for Oily Skin results in full normalization of skin oil production. Other commercial products for oily skin only dry the superficial surface of the skin.
- Replenishes synthesis of skin natural collagen, elastin, and glycoprotein to minimize fine lines and wrinkle appearance.
- Prevents blemishes and blackheads for clear and shine-free skin appearance.
- Complex of natural inhibitors of inflammation prevents and reduces skin inflammation and exerts anti-bacterial effects.
- Stabilizes the skin cell membrane structure.
- Stabilizes extracellular matrix of the skin.
- Normalize lipid and protein metabolism in the skin cells.
- Provides time-release effects of the active ingredients.
- Complex of essential vitamins and their coenzymes increases skin cell healing ability, energizes and nourishes the skin, reduces capillary permeability, and increases oxygen utilization**.**

Note: For additional targeted benefits provided by specific Nano-Complexes see appropriate data.

3.0. BIONOVA CREAM FOR DRY SKIN

EVALUATION OF CREAM FOR DRY SKIN FOR ITS ABILITY TO INCREASE SEBUM PRODUCTION

INTRODUCTION

Cream for Dry Skin (basic version) is a unique complex of active substances incorporated into the specially developed cream base and functioning on a cellular level.

This basic dry skin product has been especially created to increase sebum production in oily skin (there are multiple variations of this product with targeted Nano-Complexes to achieve strong predictable physiological results). It consist of the following bioactive complexes which are indigenous to the human organism and contain ingredients (nanocomplexes) specifically formulated for dry skin:

- Opti-Path-DS™: bioactive complex for increasing endogenous skin sebum production is incorporated into the NuCell-Direct™ delivery system
- Opti-Pro-IT™: bioactive complex of intracellular transmitters stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AX™: bioactive complex of antioxidants and anti-free radical scavengers stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AOV™: complex of ascorbic acid and oil soluble vitamins stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AmA™: complex of essential amino acids incorporated into the NuCell-Direct™ delivery system
- Opti-Pro-ANF™: anti-inflammatory & anti-bacterial complex for prevention/reduction of skin inflammation incorporated into the NuCell-Direct™ delivery system
- Opti-Cor-VCB™: complex of water soluble vitamins with their specific coenzymes stabilized in the NuCell-Direct™ delivery system
- Opti-Cor-SBS™: complex modeling natural skin barrier system to hydrate and protect the skin;
- NuCell-Direct™ Delivery System is a unique novel delivery system especially formulated for stabilization and delivery of the bioactive complexes for dry skin. The composition and structure of the delivery system approximates the structure of a natural 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 SCM and acting synergistically in one "unit". The only NuCell-Direct™ technology has dual function: (1) stabilization of the non-stable active ingredients and (2) penetration enhansor with time release effects

PARTICIPANTS

Thirty (30) female subjects that had dry skin and who could meet the study schedule were screened for the degree of sebum production. Fifteen (15) panelists with dry skin were selected for participation in the test phase of the study. Another fifteen (15) panelists were selected for participation in the placebo (control) phase of the study.

EFFICACY TEST

Test Sites

The skin of the forehead, cheeks and chin.

Phases (Measurement Intervals)

- Visit I - Baseline - evaluation of sebum production 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.

The test sites were wiped with 70% isopropyl alcohol and sebutape strips were applied to the left and right sides of the forehead and cheek (nasolobial fold) and to the chin. After thirty minutes of contact, the tapes were removed and sent for image analysis to quantify sebum production**.**

Sebutape Analysis

The sebutape analysis was evaluated by Image Analysis as follows:

- Prior to each analysis session and periodically during each session, the lighting conditions and system response was standardized to a reference gray target, ensuring reproducible illumination response at the video frame grabber.
- The patient data from each card was entered and through use of the same macro, each of the five sampled areas were measured by the analysis software. This assured identical manipulation of every analyzed area.
- The two (2) pieces of information gathered from the dark area on the sebutape patches representing trapped sebum were the number of spots and the total area of the spots detected in a given area (approximately 10mm * 8.2mm) of the patch. The area of spots was converted to nominal volumetric units from the known pore volume of the sebutape material (38%) and the thickness (0.0025cm).

Analyzed Parameters

- AG - the amount of Active Gland Count was expressed as counts/cm^2.
- SO (RSDR) - sebum output (Relative Sebum Delivery Rate) - volumetric sebum output was expressed as nanoliters/cm^2.
- IR - computed Inherent Rate = SO/AG.

Statistical Analysis

AG, SO and IR parameters were analyzed by repeated analysis of variance, as well as by linear regression by Least Square Method (LSM).

ADVERSE EFFECTS

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

TOLERANCE

BIONOVA's Cream for Dry Skin is based on the physiological substances, which are equivalent to those, which are bio-physiologically produced in the human organism. Namely, active ingredients in BIONOVA's Cream for Dry Skin 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. BIONOVA's Cream for Dry Skin is non-toxic and physiologically innocuous.

SUMMARY OF RESULTS

The results of the study show that 100% of the test panelist who received the formula containing BIONOVA bioactive complexes for Dry Skin experienced positive improvement ranging from moderate to superior.

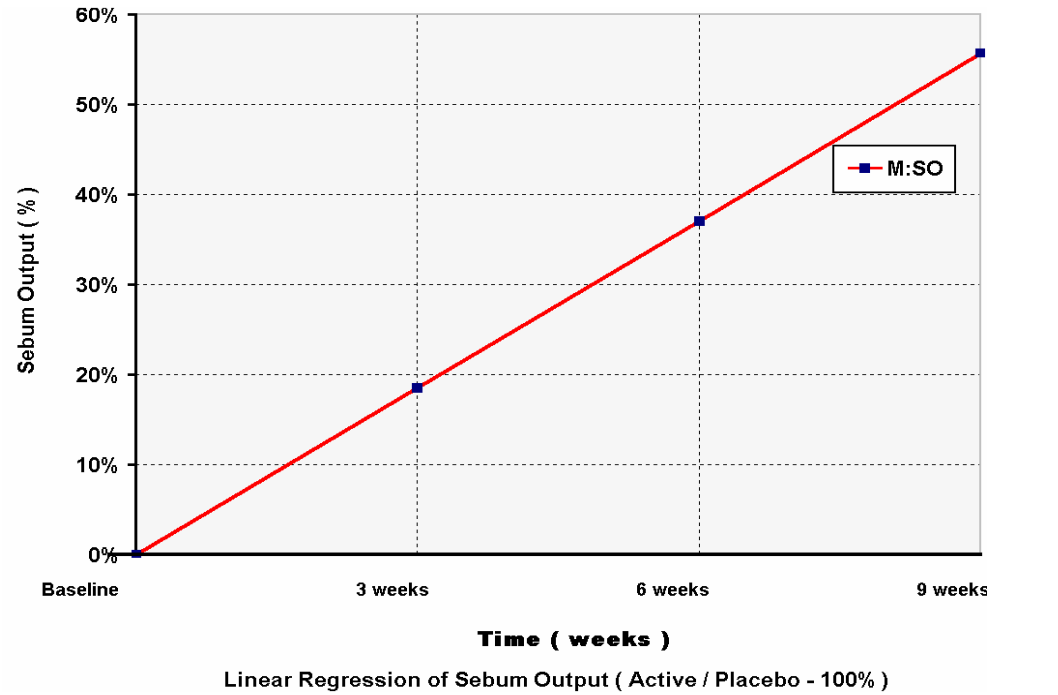
Test results indicated that at the beginning of week six, Sebum Output (RSDR), Active Gland Count (AG), and Inherent Rate (SO/GC) parameters for the group treated with BIONOVA Cream for Dry Skin were significantly higher than the baseline, while there was no significant difference for either parameters in the control group.

On the following charts, we can observe that in the group treated with BIONOVA bioactive cream for Dry Skin we can observe ~ 20% increase of Sebum Output (SO) relative to the baseline, after week three. Continued usage of tested product increases Sebum Output up to ~ 38% at week six, and 55% at week nine. At the same time Active Gland Count (AG) increases up to 20% at week six and ~ 32% at week nine. The test data also demonstrate an increase of the Inherent Rate, as a consequence of Sebum Output and Gland Count growth.

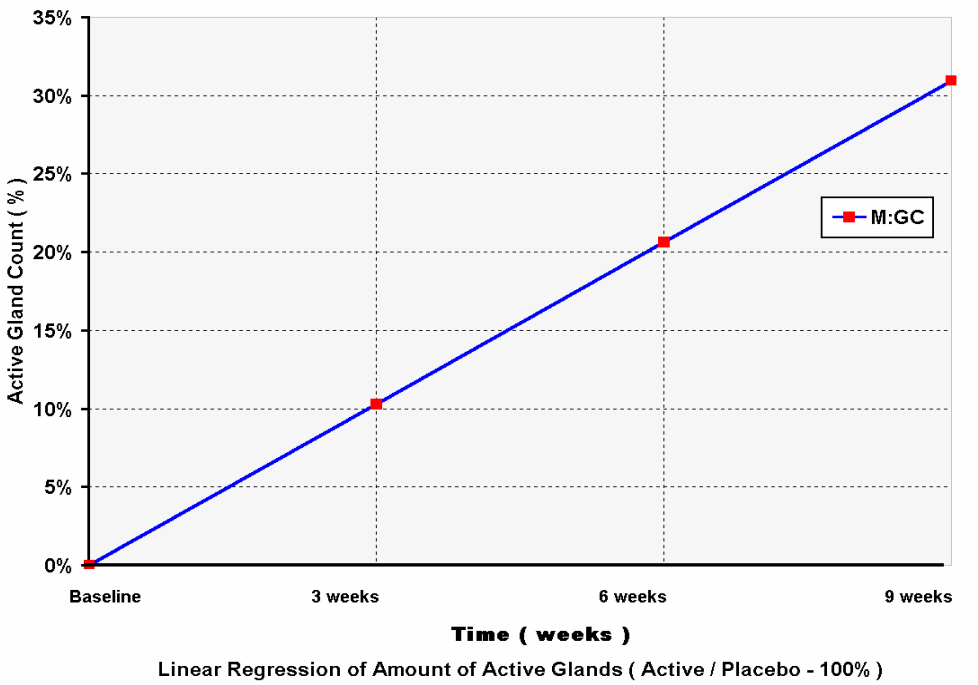
This data illustrate that using Cream for Dry Skin it is possible to increase endogenous sebum production by ~ 50% after nine weeks of use compared to the control. In addition, the amount of active glands producing sebum increased up to 32% after nine weeks of using BIONOVA's cream for Dry Skin.

Note: For additional targeted results provided by specific Nano-Complexes see appropriate data.

EFFECTS OF BIONOVA'S CREAM FOR DRY SKIN ON SEBUM PRODUCTION

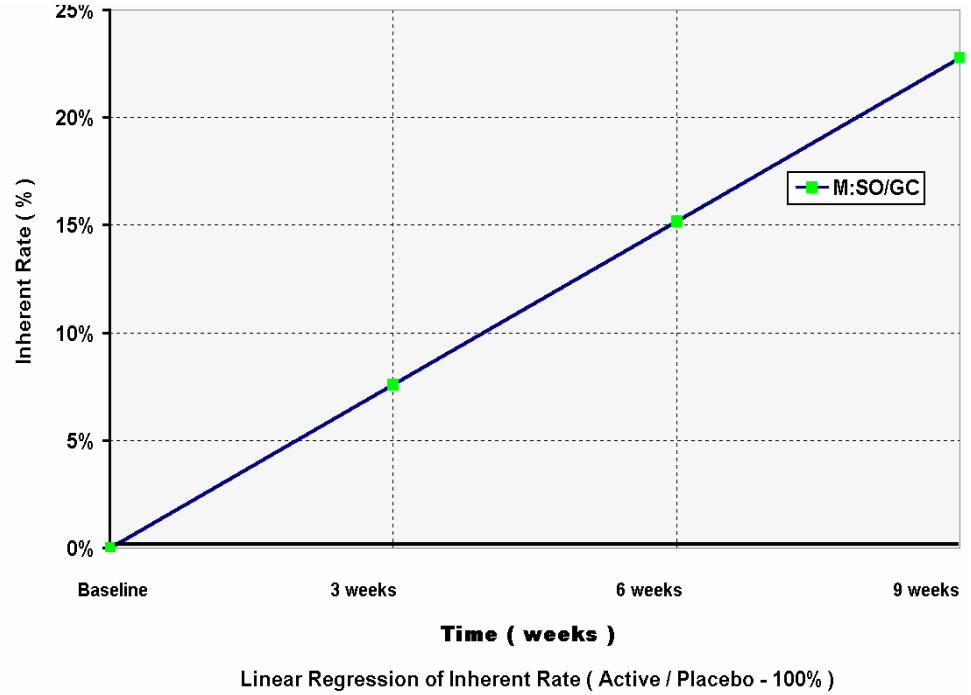


EFFECTS OF BIONOVA'S CREAM FOR DRY SKIN ON AMOUNT OF ACTIVE GLANDS



Linear Regression of Amount of Active Glands (Active / Placebo - 100%)

EFFECTS OF BIONOVA'S CREAM FOR DRY SKIN ON SEBUM INHERENT RATE



Linear Regression of Inherent Rate (Active / Placebo - 100%)

BASIC EFFECTS OF BIONOVA'S CREAM FOR DRY SKIN

- Stimulates production of endogenous skin oil by sebaceous glands. Significant increase of sebum production will be observed in 15 - 20 days. In an additional 20 - 30 days a complete normalization of sebaceous gland function will be noticed.
- Multifunctional skin barrier nanocomplex restores the skin natural hydration and refines skin texture.
- Increases the 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.
- Stabilize the skin cell membrane structure.
- Stabilize extracellular matrix of the skin.
- Provides time-release effects of the active ingredients.
- Nourishment and revitalization effects due to an improvement in the cell metabolism.

Note: For additional targeted benefits provided by specific Nano-Complexes see appropriate data.

4.0. BIONOVA CREAM FOR EYE WRINKLES & AGING

EVALUATION OF THE CREAM FOR EYE AREA FOR ITS ABILITY TO MINIMIZE FINE LINES AND INCREASE ELASTICITY OF SKIN

This study was conducted to evaluate the efficacy of the BIONOVA's bioactive complexes for Eye Area for its ability to minimize fine lines and increase elasticity of skin around the eyes.

INTRODUCTION

Cream for Eye Area Wrinkles & Aging (basic version) is a unique complex of active substances incorporated into the specially developed cream base and functioning on a cellular level.

This basic eye area product has been especially created to improve skin condition and its elasticity in the delicate skin area around eyes (there are multiple variations of this product with targeted Nano-Complexes to achieve strong predictable physiological results, such as Eye Puffiness, Dark Circles, etc.)). It consist of the following bioactive complexes which are indigenous to the human organism and contain ingredients (nanocomplexes) specifically formulated for eye area skin:

- Opti-Path-EA™: bioactive complex for skin cells metabolism normalization in eye area incorporated into the NuCell-Direct™ delivery system
- Opti-Path-TB™: bioactive complex for endogenous skin collagen, elastin, and glycoprotein syntheses stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-IT™: bioactive complex of intracellular transmitters stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AX™: bioactive complex of antioxidants and anti-free radical scavengers stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AOV™: complex of ascorbic acid and oil soluble vitamins stabilized in the NuCell-Direct™ delivery system
- Opti-Pro-AmA™: complex of essential amino acids incorporated into the NuCell-Direct™ delivery system
- OptiPro-NA™: complex of nucleic acids incorporated into the NuCell-Direct™ delivery system;
- Opti-Cor-VCB™: complex of water soluble vitamins with their specific coenzymes stabilized in the NuCell-Direct™ delivery system
- Opti-Cor-SBS™: complex modeling natural skin barrier system to hydrate and protect the skin;
- NuCell-Direct™ Delivery System is a unique novel delivery system especially formulated for stabilization and delivery of the bioactive complexes for eye wrinkles and aging. The composition and structure of the delivery system approximates the structure of a natural 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 SCM and acting synergistically in one "unit". The only NuCell-Direct™ technology has dual function: (1) stabilization of the non-stable active ingredients and (2) penetration enhansor with time release effects

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

BIONOVA's Cream for Eye Area Wrinkles & Aging is based on the physiological substances which are equivalent to those which are bio-physiologically produced in the human organism. Namely, active ingredients in BIONOVA's Cream for Eye Area Wrinkles & Aging 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. BIONOVA's Cream for Eye Area Wrinkles & Aging is non-toxic and physiologically innocuous.

SUMMARY OF RESULTS

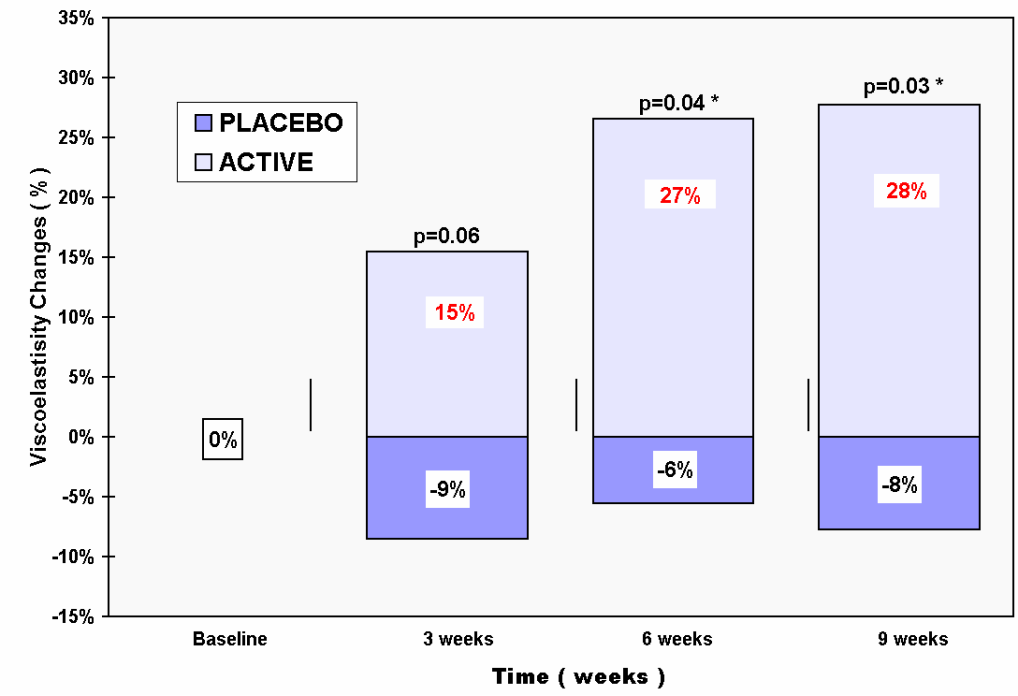
The results of the study show that 100% of the test panelist who received the formula containing BIONOVA bioactive complexes for Eye Area Wrinkles & Aging experienced positive improvement ranging from moderate to superior.

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'S CREAM 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

Note: For additional targeted benefits provided by specific Nano-Complexes see appropriate data.

5.0. BIONOVA VITAMIN & COENZYME NANO-COMPLEX EVALUATION

INTRODUCTION

VCBs (various compositions of Vitamin and Coenzyme Biocomplexes) are developed in BIONOVA, Inc. and produced in multiple varieties with different activities, depending on the purpose for which they are created. Basically they are unique biocomplexes containing seven to ten water soluble vitamins with their specific coenzymes, bioflavonoids, antioxidants, and three to four oil-soluble vitamins primarily encapsulated into a proprietary carbohydrate delivery system (CDS) and secondary into a more complex novel delivery system – NuCell-Direct™ Delivery System.

VCBs are biologically active complexes, supporting the natural defense mechanisms against the adverse effects of free radicals. They are useful additives in preventing lipid peroxidation in skin and as an active complex for skin care products. This new technology allows the water-soluble and oil-soluble vitamins to act synergistically in an integrated water-dispersible nanocomplex. This synergistic action noticeably increases the effectiveness of the vitamins multiple cellular effects while using a reduced concentration of vitamins.

BIONOVA Vitamin & Coenzyme Biocomlpexes consists of the various combinations of following highly purified (95-99%) active ingredients:

Water Soluble Vitamins

* L-Ascorbic Acid (Vitamin C)
* Thiamin Hydrochloride (Vitamin B_1)
* Riboflavin (Vitamin B_2)
* Pantotenic Acid (Vitamin B_5)
* Pyridoxine Hydrochloride (Vitamin B_6)
* Nicotinamide (Niacinamide; Vitamin PP)
* Folic Acid (Pteroylglutamic Acid)
* Calcium Pangomat
* Choline Chloride

Oil Soluble Vitamins

* Retinyl Palmitate (Vitamin A)
* α-Tocopheryl Acetate (Vitamin E)
* Ergocalciferol
* Cholecalciferol Sulfate

Coenzymes

* Pyridoxal-5-Phosphate
* Coenzyme A (CoA)
* β-Nicotinamide Adenine Dinucleotide (NAD)
* β-Nicotinamide Adenine Dinucleotide Phosphate (NADP)
* Flavin Mononucleotide Sodium Salt (FMN)
* Flavin Adenine Dinucleotide (FAD)
* Tetrahydrofolic Acid
* Cocarboxylase
* Biotin (CoR)

Bioflavonoids

* Rutin Hydrate

* Quercetin
* Catechine
* Chrysin (5,7-dihydroxyflavone)

Antioxidants

* N-Acetyl-L-Cysteine
* Nordihydroguaretic Acid (NDGA)
* Selenium Oxide
* Ethylenediaminetetraacetic Acid
* Glutathion, Free Acid
* dl-Dithithreitol
* Aprotinin

BASIC EFFECTS OF VCBs

Depending on the composition of the particular VCB, they can participate in the following cell chemical reactions:

- Increased oxygen utilization in the tissue
- Increase decarboxylation and amino acid transamination
- Increase amino acids synthesis
- Increase nucleic acid synthesis
- Increase protein synthesis
- Ameliorate carbohydrate and lipid metabolism
- Antioxidant effects
- Anti-free radical effects
- Non-specific cell metabolism activation.
- Reducing effects

Many of the above mentioned benefits of VCBs are possible through new technology the basic idea of which is a synergistic action of the proper combination of water and oil soluble vitamins with their coenzymes in a single water soluble/dispersible biocomplex.

Using NuCell-Direct™ Delivery System it is possible to achieve the following additional benefits of Vitamins & Coenzyme Biocomplexes:

- Increase physical stability of the vitamins and coenzymes
- Time-release effects of the vitamins and coenzymes
- Stabilization of the extracellular matrix of the skin
- Increased viability of the skin cells
- Stabilization of the cell metabolism through non-specific effects of lipids, carbohydrates and proteins which are the major components of the SCM

TOLERANCE

VCBs are based on physiological substances, which have long been used in health care products. They are known to be non-toxic and physiologically innocuous. VCBs are very well tolerated by human skin and are based on the physiological substances, which are equivalent to those, which are biophysiologically produced in the human organism.

SUMMARY OF RESULTS

a) Anti-Irritation Effects Of Cream With Vitamin & Coenzyme Nanocomplex

The method described below evaluates the anti-irritant efficacy of Vitamin & Coenzyme Biocomplex (VCB) using biologically active human skin equivalents (MatTech EpiDermR). Irritation is generated in tissue using a solar simulator and irradiation with 1.5 MED/hr/cm2 (31.5mJ/cm^2) UVA/B. This dose is chosen for its ability to simulate human skin equivalents while causing minimum cytotoxicity.

Test material is exposed to UVA/B irradiated tissue for specified exposure times and cell viability is determined through the use of 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) dye. MTT, the indicator of cell viability used in this assay, is incorporated into the living cells via the mitochondria. This results in the formation of insoluble formazin crystals that remain internal to the cells until extracted with isopropanol. The intensity of the extracted purple color is directly proportional to the viability of the tissues.

The Mat-Teck Epi-Derm-R skin model consists of normal epidermal keratinocytes that have been cultured to form a multilayered, highly differentiated model of the human epidermis. Keratinocytes are cultured on specially prepared permeable cell culture inserts which allow attainment of differentiation on the cutting edge of in-vitro skin technology. Ultrastructurally, the EpiDermR skin model closely parallels human skin, thus providing a useful in vitro substrate to assess dermal toxicity.

OBJECTIVE

To evaluate the anti-irritation efficacy of the Vitamin and Coenzyme Biocomplex in Substitute Cell Membrane (VCB) using the MatTek EPI-100 assay.

TEST MATERIAL CONCENTRATION & CONTROL

- VCB tested in two concentrations: 0.5% and 1.0%.
- Source of cells: MatTeck Corporation; EpiDermR Skin Model (EPI-100).
- Negative control: negative control for this study was untreated EpiDermR.
- Positive control: positive control for this study was EpiDermR Skim Model irradiated with 1.52 MED UVA/B w/o adding VCB.

UVA/B EXPOSURE DOSE AND TIME

Irritation is generated in tissue using a solar simulator and irradiation with 1.52 MED/hr/cm2 (31.5 mJ/cm2) UVA/B.

MatTeck EpiDermR skin models were exposed to UVA/B irradiation during 1, 4, and 24 hours.

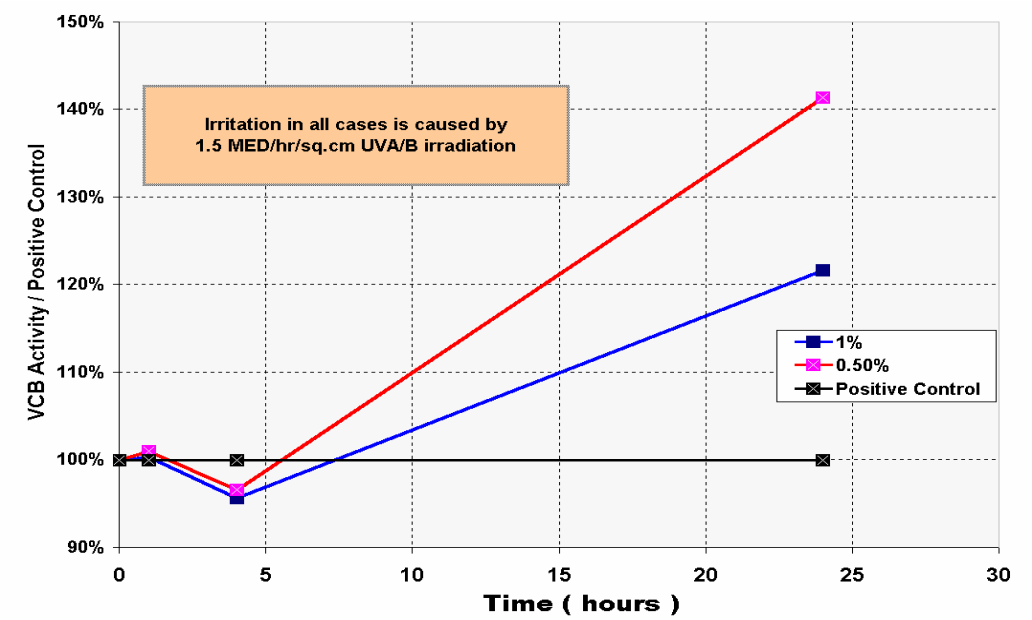
SUMMARY OF ANTI-IRRITATION RESULTS

At a concentration of 0.5%, the test material showed an enhancement of cell viability of 42% compared to the positive control at 24 hours.

The enhancement of viability at a concentration of 1% was less, approximately 22%. This may be due to the sensitivity of the tissue to the preservatives.

The positive test results of the VCB show an increase in cellular activity in the area of cell metabolism and its proliferation

ANTI-IRRITATION EFFECTS OF EFFECTS OF BIONOVA'S VITAMIN & COENZYME NANOCOMPLEX



b) CYTOSTIMULATION POTENTIAL OF CREAM WITH VITAMIN & COENZYME NANOCOMPLEX

This cytostimulation assay measures the Vitamin & Coenzyme Biocomplex's (VCB) ability to stimulate an increase in the metabolic activity of the fibroblasts in culture. Fibroblasts are seeded into individual wells of a tissue culture plate that contains a nutrient-poor media. Test material is then containing nutrient-poor media so that the final specified test material concentration is reached. Cultures are incubated for approximately 48 hours. A cytostimulant will stimulate cellular metabolic activity despite the nutrient-poor media. After approximately 48 hours, the metabolic activity of the culture is measured using 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium (MTT).

The MTT assay is a calorimetric analysis of the metabolic activity of the cell. Reduction of MTT by mitochondria results in the formation of insoluble blue formazin crystals, which are extracted from the cells with isopropanol and quantitative spectrophotometrically. The intensity of the blue color is directly proportional to the metabolic activity of the cells and inversely proportional to the toxicity of the test material. Test material which increases the metabolic activity of the culture compared to the control is considered a cytostimulant.

OBJECTIVE

To evaluate the cytostimulation potential of the Vitamin and Coenzyme Biocomplex in Substitute Cell Membrane (VCB).

TEST MATERIAL CONCENTRATION & CONTROL

VCB tested in the following concentrations: 0.5% and 1%.

The negative control for this study was culture media, while the positive control was culture media supplemented with 10% albumin.

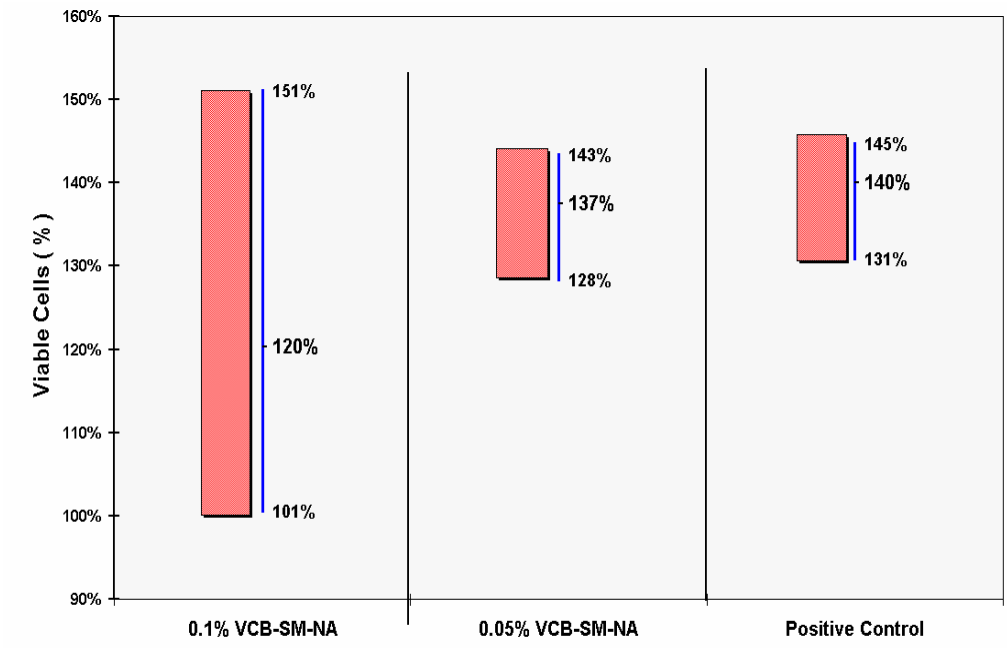
SUMMARY OF CYTOSTIMULATION RESULTS

The results show a significant increase in cellular metabolism at each concentration tested

Compared to the negative control, the test material, at a concentration of 0.05%, showed an average enhancement of cell viability of 37.5%, nearly equal to the cells grown in complete nutrient media. The average viability at a concentration of 0.1% was less, approximately 20.5%, than the results at 0.05%. Cells grown in tissue culture show enhanced sensitivity to preservatives; therefore, the apparent decline in efficiency with increasing VCB concentration may be due to the level of preservatives present in the VCB complex.

The data indicates reduction of stress factors on cell viability.

ANTI-IRRITATION EFFECTS OF EFFECTS OF BIONOVA'S VITAMIN & COENZYME NANOCOMPLEX



Metabolic Activity of Fibroblasts

48 Hours Exposure MTT Test; upper, mean and lower values

6.0. BIONOVA's ASCORBIC ACID STABILIZED IN NuCell-Direct™ DELIVERY SYSTEM

INTRODUCTION

Stabilized Ascorbic Acid (SAA) is a unique complex of ascorbic acid antioxidants, and oil soluble vitamins primarily encapsulated into a proprietary carbohydrate delivery system (CDS), and secondary into a more complex delivery system - CellDirect™.

SAA is a technology, which allows the combination of water-soluble vitamins, antioxidants and oil-soluble vitamins to act synergistically in a single water dispersible complex. It represents a new technology that markedly increases efficiency of the functional ingredients on a cellular level because all the ingredients act simultaneously.

Stabilized Ascorbic Acid composed from active substances, which are essential for normal cell metabolism and functioning both on the skin surface, as well as on the epidermal levels.

COMPOSITION

Stabilized Ascorbic Acid consists of the following highly purified (95-99%) active ingredients:

Water Soluble Vitamins

* L-Ascorbic Acid (Vitamin C)

Oil Soluble Vitamins

* Tocopherol (Vitamin E)
* Retinyl Palmitate (Vitamin A)

Antioxidants

* Antioxidants
* N-Acetyl-L-Cysteine
* Glutathion
* dl-Dithithreitol
* Glucose Oxidase
* Selenium Dioxide
* Catalase

Carbohydrate Delivery System

* All active ingredients are primarily incorporated into a special carbohydrate delivery system.

Novel Delivery System - Substitute Cell Membrane

* NuCell-Direct™ is a unique novel delivery system especially formulated for stabilization of Vitamin C in water containing vehicles. The composition and structure of the NuCell-Direct™ approximates the structure of a Natural Cell Membrane. The NuCell-Direct™ is 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 Ascorbic Acid, Oil Soluble Vitamins, and Antioxidants are entrapped within the NuCell-Direct™ and acting synergistically in one "unit".

EFFICACY TEST

Test Material

Ascorbic Acid (Vitamin C) was incorporated into BIONOVA's CellDirect™ Delivery System (SAA). The freeze-dry powder of SAA was dissolved in aqua distillate. SAA concentration in water equal 10%. pH of solution = 3.7.

Measurement Conditions

Stability of Ascorbic Acid stabilized in CellDirect™ Delivery System was measured under the different conditions:

- At room temperature, under the ultraviolet radiation
- In refrigerator, at 4^0C
- At room temperature (RT)
- Acceleration test, at 37^0C

Measurement Intervals

Stability of Ascorbic Acid stabilized in CellDirect™ Delivery System was measured at day 3, 5, 7, and than once in a week for 33 days.

SUMMARY OF RESULTS

Stability test result of SAA demonstrates supperior stability of Ascorbic Acid under all the tested conditions (UV, 4^OC, RT), even under the accelerated temperature (37^OC).

In the control group the significant reduction of Ascorbic Acid started on day 3 and reduced to minimum detected concentartion in a one week.

STABILITY OF ASCORBIC ACID IN CELLDIRECT™ DELIVERY SYSTEM

(10% H_2O Solution, pH 3.7)

Test	UV		4°C		R.T.		37°C	
	Asc. Ac.	[%]	Asc. Ac.	[%]	Asc. Ac.	[%]	Asc. Ac.	[%]
Original	10.94	**100**	10.94	**100**	10.94	**100**	10.94	**100**
3 days	11.42	**104.4**	10.96	**100.2**	11.74	**107.3**	11.54	**105.5**
5 days	12.17	**111.2**	11.96	**109.3**	11.63	**106.3**	10.14	**92.7**
7 days	12.12	**110.8**	12.58	**115.0**	11.95	**109.2**	9.62	**87.9**
12 days	11.74	**107.3**	12.58	**115.0**	12.49	**114.2**	10.19	**93.1**
19 days	11.01	**100.6**	12.71	**116.2**	11.95	**109.2**	9.21	**84.2**
26 days	11.17	**102.1**	12.21	**111.6**	11.92	**109.0**	-	-
33 days	10.55	**96.4**	12.42	**113.5**	10.64	**97.3**	-	-

7.0. BIONOVA's ANTIOXIDANTS NANO-COMPLEX

NATURE OF THE PROBLEM

FREE RADICALS: Atoms usually complete their outer shells by sharing electrons with other atoms. By sharing electrons, the atoms are bound together and satisfy the conditions of maximum stability for the molecule. Normally, bonds don't split in a way that leaves a molecule with an odd, unpaired electron. But when weak bonds split, free radicals are formed. Free radicals are very unstable and react quickly with other compounds, trying to capture the needed electron to gain stability. Generally, free radicals attack the nearest stable molecule, "stealing" its electron. When the "attacked" molecule loses its electron, it becomes a free radical itself, beginning a chain reaction. Once the process is started, it can cascade, finally resulting in the disruption of a living cell.

Free radicals arise normally during metabolism. The body's immune system purposefully creates them to neutralize viruses bacteria, and other foreign substances. However, environmental factors such as pollution, radiation, cigarette smoke and herbicides spawn excessive unnecessary amount of free radicals that is damaging for human health.

Normally, the body can handle free radicals, but if antioxidants are unavailable, or if the free-radical production becomes excessive, damage can occur. Unwanted free radicals accumulate with age.

ANTIOXIDANTS: An antioxidant refers to a substance that prevents or retards the oxidation of sensitive molecules found in the body or in foods. Antioxidants occur in many foods as nutrients or non-nutrients, or as synthetic additives. Antioxidants help prevent widespread cellular deterioration by willingly donating components to stabilize free radicals.

NANOTECHNOLOGICAL APPROACH IN NEW GENERATION OF ANTIOXIDANTS

Antioxidant Biocomplex (AXB) is a unique proprietary complex of antioxidants and anti-free radical scavengers developed and produced in BIONOVA for its custom designed skin care products. The usage of AXB in each particular skin care product depends on multiple factors, for which BIONOVA developed its own unique algorithm.

AXB composed from active substances which are absolutely indigenous to the human organism and are essential for normal cell metabolism to support natural defense mechanisms against the adverse effects of free radicals. AXB is a complex of biologically active substances functioning both on the skin surface as well as on the epidermal levels and was especially created to prevent oxidation under the sun exposure. They are useful additives in preventing lipid peroxidation in skin and as an active complex for skin care products.

AXB represents a new technology that markedly increases efficiency of the functional ingredients on a cellular level because all the ingredients act simultaneously. This technology allows the combination of various types of pure water-soluble and oil-soluble antioxidants to act synergistically in a single water-dispersible complex. AXB composed from active substances, which are absolutely indigenous to the human organism and are essential for normal cell metabolism. All antioxidants incorporated into a BIONOVA's proprietary novel delivery system – NuCell-Direct™ Delivery System.

COMPOSITION

Antioxidant Biocomplex is a complex system comprised of the following nanocomplexes:

a) NANO-COMPLEX™ OF ANTI-FREE RADICAL SCAVENGERS PERFORMING ON:

- Extra-Cellular Level - first level of defense
- Cellular Level - second line of defense

b) NANO-COMPLEX™ OF ANTIOXIDANTS:

- Specific Bioflavonoids
- Peptide Antioxidants
- Caratenoids

d) DELIVERY SYSTEM:

- NuCell Direct™ Delivery System

Antioxidant Biocomplex consists of the following highly purified (95-99%) active ingredients:

Basic Antioxidants

* Acetyl - L-Carnitine Hydrochloride (Vitamin B7)
* Dithiothreitol
* Nordihydrguaiaretic Acid
* N-Acetyl-L-Cysteine
* Glutathione, Reduced Form
* Glutathione ReductasePeptide Antioxidants
* Carcinine
* L-Carnosine
* a-Lipoic Acid
* L-Carnosine
* Genistein
* Coenzyme Q10

Extracellular Defence – Anti-Free Radicals Scavenger

* apo-Transferrine, Iron Poor
* Xanthine

Cellular Defence – Anti-Free Radicals Scavenger

* Superoxide Dismutase
* Catalase
* Glucose Oxidase

Bioflavonoid Antioxidants

* Astaxantin
* Morin
* Biotin (Vitamin H)
* Quercetin
* Rutin

Novel Delivery System - Substitute Cell Membrane

* NuCell-Direct™ is a unique novel delivery system especially formulated for stabilization of Antioxidant Biocomplex. The composition and structure of the NuCell-Direct™ approximates the structure of a Natural Cell Membrane. The CellDirect™ is 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 multiple individual antioxidants are entrapped within the NuCell-Direct™ and acting synergistically in one “unit”.

SHORT DESCRIPTION OF MAJOR ANTIOXIDANTS

Acetyl-L-Carnitine acts as an antioxidant, has protective effects in the brain, and stimulates hormone (including testosterone) release.

N-Acetyl-L-Cysteine (NAC) is a powerful antioxidant and a premier antitoxin and immune support substance. NAC has been shown to provide protection against free radicals as well as a broad range of toxic hazards. The key to this protection is the sulfur and sulfhydryl groups contained in NAC and its derivative, glutathione. Supplemental NAC may have an anti-aging effect by increasing glutathione levels in the liver, lungs, kidneys and bone marrow.

Glutathione (GL) is a small molecule, which exists in almost every cell of the body. However, GL must be generated within the cell from its precursors before it can work effectively in the body. The presence of GL is required to maintain the normal function of the immune system. Furthermore, the cells of the immune system produce many oxiradicals resulting in a need for higher concentrations of antioxidants than most cells.

a-Lipoic acid (aLA)is a potent antioxidant in both fat- and water-soluble mediums. Furthermore, its antioxidant activity extends to both the oxidized form and its reduced form. aLA capable of chelating certain metals. It forms stable complexes with copper, manganese and zinc.

L-Carnosine (CN) functions primarily as a buffer in muscle tissue. High carnosine levels are associated with an increase in physical performance especially anaerobic performance. CN is best known for its ability to buffer lactic acid in muscle tissue and for its multiple antioxidant capabilities.

Quercetin (QT), which is primarily found in apples, onions, and black tea, is a type of flavonoid that serves as a building block for other members of the flavonoid family. QT appears to help fight a host of disorders, from asthma to cancer to heart disease. Among people with high dietary intakes of quercetin and other major flavonoids, studies show lower rates of stomach, lung, pancreatic, and breast cancers.

Genistein (GN), an isoflavone phytonutrient derived from soybeans. GN can bind to the same receptor sites as estrogen. Soybeans are the only significant dietary source of genistein; however, the amount of soy foods necessary to meet the body's needs can be difficult to incorporate into today's diet. In Asia, where soy is a staple, the daily intake can be up to 20 times that of a Western diet. GN is a scavenger of reactive oxygen species and inhibits lipid peroxidation.

Biotin (BT) is a water-soluble vitamin, generally classified as a B-complex vitamin. After the initial discovery of BT, nearly forty years of research were required to establish it as a vitamin. BT is required by all organisms but can only be synthesized by bacteria, yeasts, molds, algae, and some plant species.

Catechin (CT) is a bioflavonoid that is found in Green Tea. It works both alone and in conjunction with other flavonoids found in tea, and has both antiviral and antioxidant qualities. CT has been shown helpful in the treatment of viral hepatitis. It also appears to prevent oxidative damage to the heart, kidney, lungs, and spleen.

Rutin (RT) have antioxidant, anti-inflammatory, anticarcinogenic, antithrombotic, cytoprotective and vasoprotective activities. Many, if not most, of rutin's possible activities can be accounted for, in part, by rutin's antioxidant activity. Rutin can chelate metal ions, such as ferrous cations.

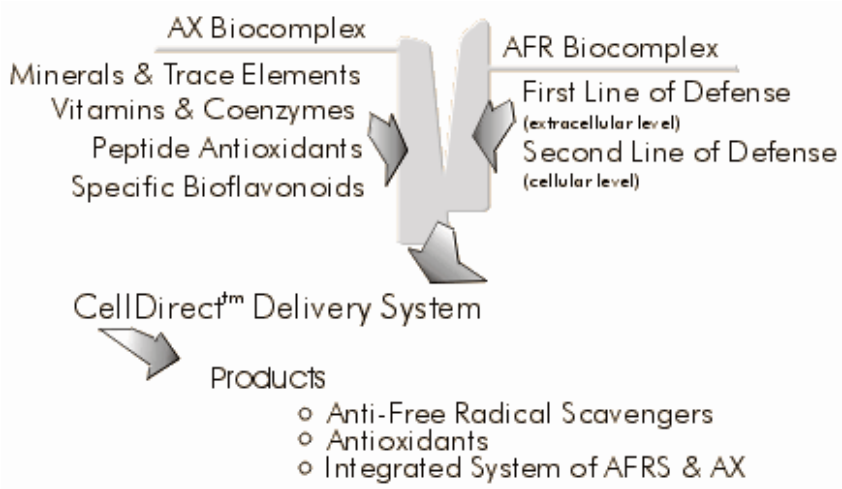
Astaxanthin (AX), a naturally occurring carotenoid pigment, is a powerful biological antioxidant. Astaxanthin exhibits strong free radical scavenging activity and protects against lipid peroxidation and oxidative damage of LDL-cholesterol, cell membranes, cells, and tissues.

Superoxide Dismutase (SOD) catalyzes the destruction of the O_2-free radical. It protects oxygen-metabolizing cells against harmful effects of superoxide free-radicals. The O_2-ion, which has been considered important in aging, lipid peroxidation and the peroxidative hemolysis of red blood cells is formed by the univalent reduction of O_2 during various enzymatic reactions or by ionizing radiation.

Coenzyme Q10 (also known as **CoQ10**, **Q10**, vitamin Q10, ubiquinone, or ubidecarenone) is a compound that is made naturally in the body. Q10 is used by cells to produce energy needed for cell growth and maintenance. It is

also used by the body as an antioxidant. The highest amounts of Q10 are found in the heart, liver, kidneys, and pancreas. The lowest amounts are found in the lungs. Tissue levels of coenzyme Q10 decrease as people get older.

STRUCTURE OF BIONOVA'S ANTIOXIDANTS & ANTI-FREE RADICAL SCAVENGERS BIOCOMPLEX



BENEFITS OF ANTIOXIDANT BIOCOMPLEX

Numerous scientific studies have concluded that by consuming foods and supplements, which are rich in antioxidant properties, the incidence of diseases associated with the consequences of Free Radical oxidization can be reduced. This does not mean that these diseases can be cured, treated or prevented. Rather, it means that in scientific studies, people who consumed significant levels of antioxidants had lower incidences of these diseases including:

- skin cancer
- fights against oxidative stress
- alleviates symptoms of chronic dysfunctions
- boost immune system
- enhances self-healing

8.0. BIONOVA's LIPOPROTEIN NANO-COMPLEXES

INTRODUCTION

Lipoprotein Bioactive Complexes (LBCs) represent a new generation of active ingredients and a new technology that remarkably increases efficiency of the functional ingredients on the cellular membrane and extracellular levels. The body responds to the administration of LBCs by restoring intercellular biological information transfer and stabilizing the internal information bonds between the cells.

LIPOPROTEIN BIOACTIVE COMPLEXES TECHNOLOGY

LBCs are members of the group of raw materials, which can be used in a health care industry as a well balanced food supplement (dietary product) and in skin care industry.

LBCs for cosmetics are completely unique combination of raw materials for the skin care formulations. Each type of LBC is a complex of substances especially balanced to improve skin cell membrane and extracellular matrix metabolism in a specific type of skin. The usage of type of LBC in each particular skin care product depends on multiple factors, for which BIONOVA developed its own unique algorithm.

LBCs technology allows the combination of various types of pure lipids and proteins to act synergistically in a single complex.

LBCs are produced from active substances which are absolutely indigenous to the human organism and are essential for normal cell metabolism. To increase the benefits of the LBCs and to obtain multiple skin care effects, LCBs are typically used in custom designed skin care products simultaneously with one of the BIONOVA's VCBs (Vitamin and Coenzyme Biocomplex).

TYPES OF LIPOPROTEIN BIOACTIVE COMPLEXES

- OptiCor-LDL™ - Low Density Lipoproteins
- OptiCor-VLDL - Very Low Density Lipoproteins
- OptiCor-IDL™ - Intermediate Density Lipoproteins
- OptiCor-HDL™ - High Density Lipoproteins
- OptiCor-SBS™ - Skin Barrier System

EFFECTS OF LIPOPROTEIN BIOACTIVE COMPLEXES

- Stabilize cell membrane structure
- Stabilize extracellular matrix of the skin
- Hydration effects on the skin surface
- Ameliorate lipids and protein metabolism in specific type of skin
- Increase elasticity and firmness of the skin
- Protect against moisture loss
- Made from ingredients natural to the human body
- Protects and restores normal cell metabolism in the specific type of skin for a long period of time
- Time release effects of the active ingredients

GENERAL STRUCTURE OF BIONOVA'S LIPOPROTEIN BIOCOMPLEXES

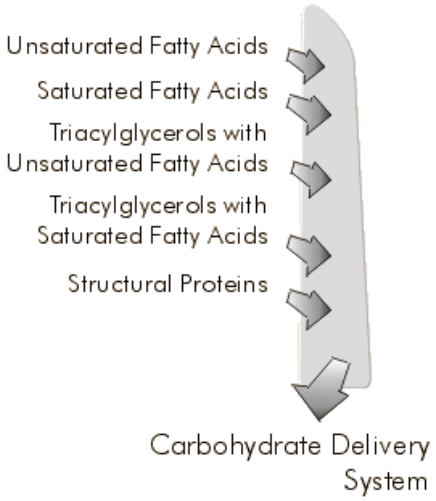
LBCs consists of the six various group of active ingredients. Each group represented by combination of 4-6 highly purified (95-99%) active substances, which are primarily encapsulated into a proprietary carbohydrate delivery system:

* Saturated Fatty Acids
* Unsaturated Fatty Acids
* Triacylglycerols with Saturated Fatty Acids
* Triacylglycerols with Unsaturated Fatty Acids
* Cholesterols
* Biologically Active Carbohydrates
* Structural Proteins
* Carbohydrate Delivery System

All the above-mentioned groups of bioactive ingredients are incorporated into a special carbohydrate delivery system.

The exact composition of any specific LBCs depends on the purpose for which it is created.

To increase the benefits of the Lipoprotein Biocomplexes and to obtain multiple skincare effects in the finished cosmetic product simultaneously with LBCs we used BIONOVA's Vitamin & Coenzyme Biocomplex and/or Antioxidant Biocomplexes.

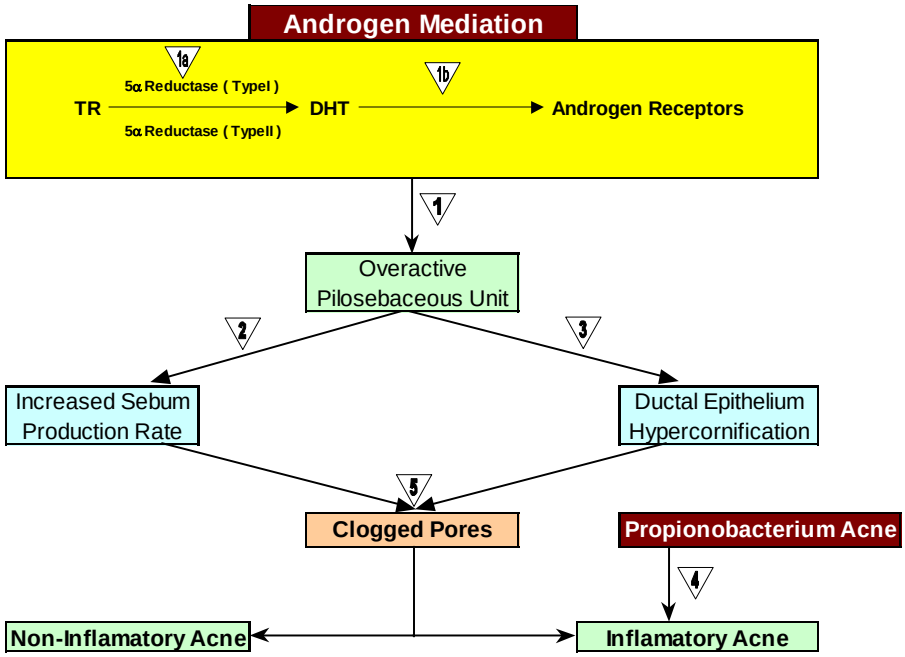


TOLERANCE

LBCs are based on physiological active substances, which have long been used in health care products. They are known to be non-toxic and physiologically innocuous. LBCs are very well tolerated by human skin.

9.0. BIONOVA's ACNE NANO-COMPLEX

PATHOGENESES OF ACNE



PRODUCT COMPOSITION

Acne Biocomplex consists of the following Bioactive Complexes indigenous to the human organism and especially stabilized in Delivery System:

NANO-COMPLEXES

- Complex for local skin cells anti-androgen effects: suppression of 5a-reductase (for blockage of testosterone transformation into dihydrotestosterone) and competitive blockage of androgen receptors
- Complex of transmembrane & intracellular transmitters, which includes phosphorylate precursors, second degree messengers and nucleotide coenzymes especially balanced for acne skin
- Complex for reduction of oil production and normalization of the sebaceous gland function
- Complex of enzymes for triacylglecerols cleavage and for fatty acids transport into the mitochondrias
- Complex for reduction of the follicles hyperkeratinization
- Complex for inhibition of epithelium hyperkornification
- Complex of anti-inflammatory agents for inhibition of propionobacterium acne activity
- Complex of structural proteins & polypeptides especially balanced for acne skin
- Specially balanced complex of unsaturated fatty acids for skin lipids metabolism normalization

DELIVERY SYSTEMS & ACTIVE INGREDIENTS STABILIZER

- Carbohydrate Delivery System - active ingredients are primarily incorporated into a special CDS.
- Novel Delivery System – NuCell-Direct™ Delivery System. All above-mentioned bioactive complexes are entrapped within the NuCell-Direct™ and acting synergistically in one 'unit;. The NuCell-Direct™ technology allows to stabilize non-stable active ingredients and enhance its penetration ability, with time release effects.

10.0. EFFECTIVENESS OF VARIOUS BIONOVA's NANO-COMPLEXES TO MODULATE DESIRABLE RESULTS

Effectiveness of the topical application of the specifically composed Nano-Complexes™ incorporated into the NuCell-Direct™ Delivery System was evaluated in several types of experiments. Each Nano-Complex™ was created for very specific end result:

(a) increase and/or reduce membrane or cytosol receptors;

(b) increase/reduce/stabilize specific intracellular transmitters.

Using specific composition of Nano-Complexes™ for topical application the individualized reaction of cellular metabolism can be observed. Below we will demonstrate only some data of various Nano-Complexes™ for topical applications:

MBAC-AR-5 Topical Application

MBAC-AR-5 was created especially to depress cell membrane β2-adrenoreceptors and to stabilize α2-adrenoreceptors.

After application of the MBAC-AR-5, in the second phase of experiments, substantial depression of the β2-adrenoreceptors is observed (~ 10 - 15% from basic level), while activity of the α2-adrenoreceptors remains the same. All this changes in the adrenergic receptors activity results in increasing of local microcirculation (Chart # 17).

MBAC-ERA Topical Application

MBAC-ERA has been created for stimulation of the Estrogen receptors activity (cytosol type of receptors). After topical application of the MBAC-ERA the activity of the Estrogen receptors increased up to 160% from the basal level (Chart # 18).

MBAC-GFR-8 Topical Application

MBAC-GFR-8 has been created for selective activation of the Growth Hormone receptors located in the cell membrane.

MBAC-GFR-8 application results in the stimulation of the Growth Hormone receptors activity up to ~150% at the end of the first phase and continues at the same level on the second phase of the experiment (~ 165 minutes after application). In the third phase Growth Hormone receptors activity reaches ~ 300% from the primary level (Chart # 19).

MBAC-ARA Topical Application

MBAC-ARA has been created to increase mineralocorticosteroid Aldosterons receptors activity located in the cytosol. Result of the topical application of the MBAC-ARA illustrates that at the end of the second phase (~ 165 minutes after application) Aldosteron's receptors activity increased up to 400% and stabilized on this level on the third phase of experiments (Chart # 20).

MBAC-GRA Topical Application

MBAC-GRA was created to increase glucocorticoid Cortizol receptors activity located in the cytosol. Experimental data demonstrates that after application of the MBAC-GRA Cortizol's receptors activity increased at the end of the

first phase (one hour after application) up to 400% from the basic level and remains the same during the second and third phases of experiments (Chart # 21).

MBAC-CA-16 Topical Application

MBAC-CA-16 has been created to affect on the Calmoduline (Phoshodiestarase 3'5'-Cyclic Nucleotide Activity).

After topical application of the MBAC-CA-16 the activity of the calcium binding protein was increased up to ~ 380% in a half hour and remain on the same level up to end of the observation (four hours after application of the MBAC-CA-16); (Chart # 22).

MBAC-CN-4 Topical Application

MBAC-CN-4 was created to influence on the activity of the major intracellular second-degree messengers.

Experimental data illustrates that after application of the MBAC-CN-4 the concentration of the 3'5'-AMP at the end of the first phase increase up to 140% (30' after application). On the second and third phase concentration of the 3'5'-AMP remain at the average of 130% level (Chart # 23).

In the same application concentration of 3'5'-GMP practically remain the same as on the basic level (Chart # 24).

Most important parameter of the Cyclic Nucleotides activity is not individual concentration of the 3'5'-AMP and 3'5'-GMP, but their ratio - K=3'5'-AMP/3'5'-GMP. The result of the topical application of the MBAC-CN-4 is demonstrates, that activity of 3'5'-AMP is much higher than 3'5'-GMP activity, which has direct reflection in the increased level of K=3'5'-AMP/3'5'-GMP (Chart # 25).

PRESENTED DATA SHOWS THAT USING TARGETED BIONOVA'S NANO-COMPLEXES™ IT IS POSSIBLE TO INCREASE/DECREASE, OR STABILIZE SPECIFIC CELLULAR FUNCTIONS WHICH ARE NECESSARY TO ACHIEVE THE DESIRED THERAPEUTIC OR SKIN CARE RESULTS.

11.0. BIONOVA NuCell-DIRECT™ NOVEL DELIVERY SYSTEM

INTRODUCTION

The most important aspect of any therapeutical method is the delivery of the active ingredient to the target receptors or cell of the organism. The delivery system utilized must provide stability for the incorporated active ingredient, while allowing its absorption and delivery. Especially in the areas of topical administration, it is critical to efficacy to provide a delivery system which crosses the cell membrane and allows the active agent or agents to exert their effects.

Stratum corneum, the outer layer of skin, is a multicellular membrane of flattened, metabolically active cells. In living organisms, the cell membrane is dynamic, and the transfer or non-transfer of various agents across this membrane is an important basis of cosmetic therapy. In order to provide useful therapeutic and cosmetic formulations, it is necessary to utilize a delivery system which is both compatible with the skin, i.e., non-irritating, and which will allow and preferably facilitate the transfer of the active agent, whether cosmetic or therapeutic, across the skin membrane. It is additionally necessary to utilize a delivery system in which the bioactive components are physically and chemically stable, yet still available for absorption in bioavailable form.

BIONOVA, Inc. has developed a new generation of proprietary delivery systems, specifically designed for the stabilization and proper delivery of very unstable active ingredients. Each specially designed delivery system, called the NuCell-Direct™ Delivery System, imitates the cell's own design, and provides a unique and effective system for the delivery active ingredients across the skin membrane. The NuCell-Direct™ Delivery System technology provides maximum flexibility in choice and quantity of active ingredient delivered.

BIONOVA's proprietary NuCell-Direct™ Delivery System is thus not only useful as a topical vehicle for the bioactive substances/complexes, but also can be used as a penetration enhancer for topical application of other skin treating agents. Bioactive agents/complexes are incorporated into the NuCell-Direct™ Delivery System, which enhances the absorption of the bioactive substances into the cell, thereby providing a useful therapeutic tool for both cosmetic and medical applications.

FUNCTIONALITY AND MECHANISM OF CELLDIRECT™ DELIVERY SYSTEM

The composition and structure of the NuCell-Direct™ Delivery System approximates the structure of a natural cell membrane. The NuCell-Direct™ Delivery System is composed of highly specialized proteins, lipids, and carbohydrates; the very same ones that comprise the human cell membrane. The NuCell-Direct™ Delivery System is capable of delivering both water-soluble as well as oil-soluble active substances.

The NuCell-Direct™ Delivery System has a more sophisticated composition and integrated structure than liposomes (the most advance delivery system currently available). In terms of physical stability, the choice of liposomes is often limited. In the NuCell-Direct™ Delivery System architecture of the multiple long chain lipids and saturated alkyl acids, simultaneously with carbohydrates, proteins, and attachment matrix factors provide rigid bilayers with low permeability for small, non-bilayer interacting compounds. The actives are actually entrapped within the NuCell-Direct™ Delivery System and are an intricate part of the NuCell-Direct™ Delivery System as opposed to being encapsulated in the liposomes and other delivery systems. In other words, active substances become an integrated part of the NuCell-Direct™ Delivery System. That is why, even if the entire structure of the NuCell-Direct™ Delivery System for some extreme reasons is collapsed, crumpled or partially destroyed, active substances will continue to be protected.

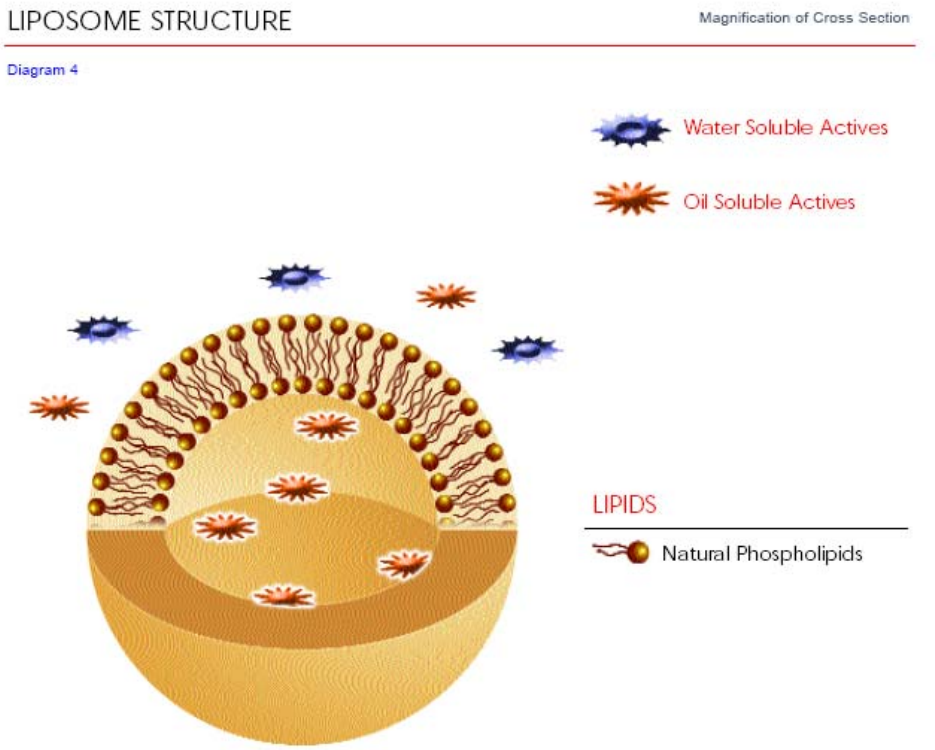
Using NuCell-Direct™ Delivery System technology it is possible to incorporate or attach many different active substances, which in other delivery systems are very unstable. NuCell-Direct™ Delivery System technology is highly capable of providing modulated time-release effects.

Each specific NuCell-Direct™ Delivery System is specially designed to maximize the effectiveness of the specific bioactive complex which is being stabilized and delivered. Using proprietary algorithms, BIONOVA efficiently creates specific NuCell-Direct™ Delivery Systems matched to the active substance.

GENERAL STRUCTURE OF CELLDIRECT™ DELIVERY SYSTEM

The NuCell-Direct™ Delivery System has an integrated structure, close to that of a human cell membrane and consists of the substances vital for a human body:

- Lipids
- Carbohydrates
- Proteins
- Attachment Matrix Factors

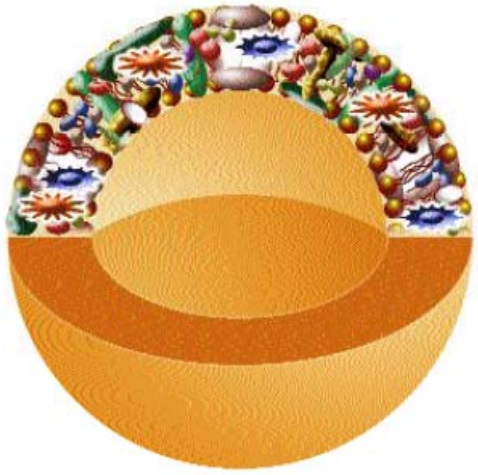


	Stabilizing Ability	Penetration Ability	Targeted delivery of active ingredients	Technology
LIPOSOMES	Active ingredients are stabilized (encapsulated) inside the liposome globule. If the globule ruptures, than the active ingredients are discharged out of the globule and loose their stability.	Moderate, because of low affinity (association) between the liposome structure and the composition of the human cell membrane.	Minimal, because liposome itself has no tissue specific features. Also, the liposome composition cannot be substantially adjusted to the structure of active substances.	Conventional technology is used in pharmaceutical and skin care industries.
NUCELL-DIRECT™	Active ingredients are incorporated and reliably stabilized inside the NuCell-Direct™ membrane wall. If the membrane ruptures it does not affect the stability of active ingredients, because they are still inside the membrane wall.	Excellent, because the composition of NuCell-Direct™ is an imitation of the integral parts of a human cell membrane.	Strong ability to deliver particular active ingredients to targeted biological tissues or groups of cells. The composition of NuCell-Direct™ can be adjusted to the structure of active substances and can target specific cells.	A unique sophisticated Nano-Technology. Modeling on the basis of a human cell membrane, and imitating living biological systems.

NUCELL-DIRECT™ DELIVERY SYSTEM

Magnification of Cross Section

Diagram 5



PROTEINS
- Peripheral Proteins
- Structural Proteins

CARBOHDRATES
- Glycoproteins
- Glycosoaminoglycans

LIPIDS
- Sphingolipids
- Fatty Acids
- Natural Phospholipids
- Modified Phospholipids
- Glycosphingolipids
- Unsaturated Fatty Acids
- Esterified Nonpolar Lipids
- Triacylglycerols

Loading capacity	Production limitations	Formulating limitations	Shelf Life	
Limited due to the size and loading capacity of the liposome's globule, and other physical and chemical factors.	Can be produced only in liquid form.	Use of liposome is limited by adverse effects of such factors as temperature, pH, shear mixing, surfactants, alcohol, etc.	Limited depending on the type of Liposome. In general the shelf life does not exceed three months.	LIPOSOMES
Large. Can hold and stabilize water-soluble and oil-soluble molecules simultaneously Also can incorporate proteins, carbohydrates lipids, and their mixtures.	Can be produced in any form including fine freeze-dried powder	Practically unlimited formulating abilities.	Practically unlimited shelf life.	NUCELL-DIRECT™

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