

Naturele Mega Brightening Serum supplements skin with antioxidant, healing and moisturizing bioactives while brightening sallow complexions and improving pigmentation disorders. With daisy flower extract to inhibit tyrosinase activity and reduce melanin formation, Naturele Mega Brightening Serum is a potent non-hydroquinone lightening agent. Containing increased levels of botanical brighteners such as azelaic acid, kojic acid, L-arbutin, and L-lactic acid, this product not only accelerates the brightening process, but supports cell turnover as well.

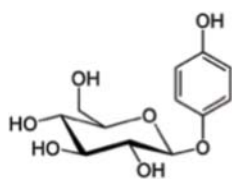
FOCUS INGREDIENTS

L-Arbutin – A naturally occurring form of hydroquinone derived from Bearberry extract with at least seven active ingredients in its leaves. L-Arbutin is split into glucose (a sugar) and hydroquinone with the sugar group attached to one of the alcohol groups of hydroquinone (HQ). Just like HQ, its shape resembles the amino acid tyrosine enough to fool tyrosinase, the enzyme that begins the first step in the transformation of tyrosine into melanin. Inhibition of an enzyme in this way is called “competitive” because the false compound, L-Arbutin, competes with the real one, tyrosine, for the active site on the enzyme.



Bearberry

L-Arbutin can inhibit melanin syntheses by inhibition of tyrosinase activity, and also appears to lighten existing pigment. While L-Arbutin and its metabolite hydroquinone are considered



the most important active ingredients, there are other compounds extracted from bearberry leaves that are thought to have antibacterial properties, as well as other beneficial chemicals including allantoin (anti-inflammatory), ellagic, gallic and ursolic acid.

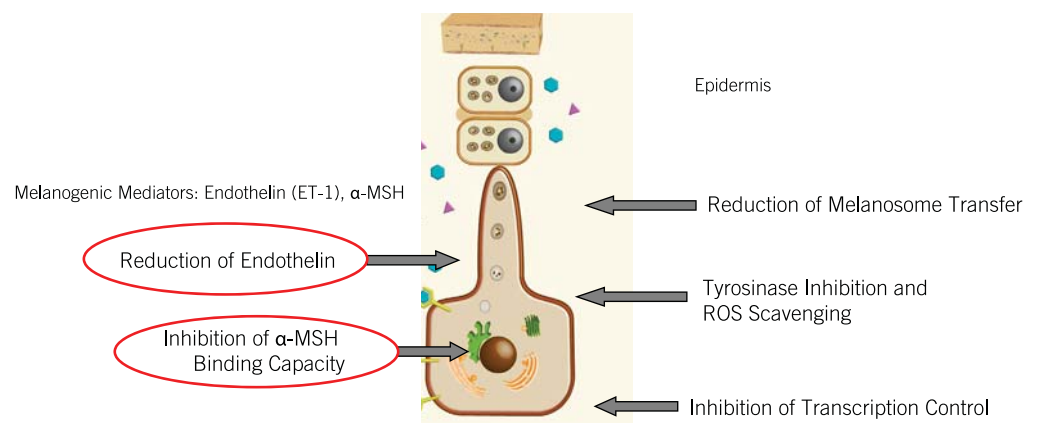
Bellis Perennis (Daisy) Flower Extract – Produced from blossoms of wild daisy flowers which are subjected to a unique production procedure, Bellis Perennis extract is a highly gentle, yet



efficient natural skin lightener that influences different pathways involved in melanin formation, counteracting age spots and balancing hyperpigmentation.

the number of melanosomes taken up by UV-stimulated keratinocytes. This unique mode of action exhibited by the preparation from BellisPerennis has been demonstrated both in vitro and in vivo.

Influence on Melanogenesis Pathways

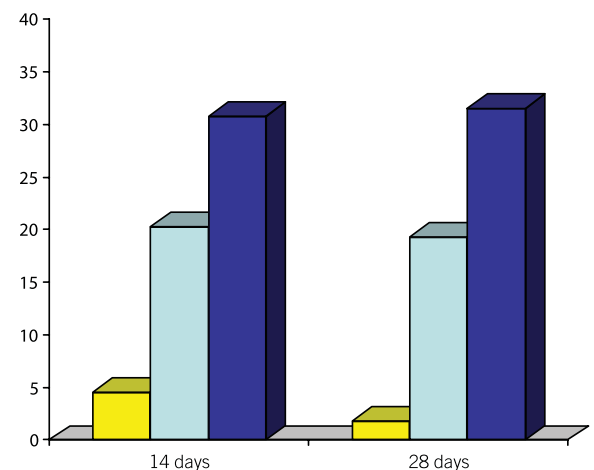


Lightening Activity

Increase in skin
Formulations were applied by 5 volunteers (pilot study) twice daily on the inner forearm.

Values are related to initial conditions.

- Placebo
- 2% Bellis Perennis Flower Extract
- 5% Bellis Perennis Flower Extract



Lightening Activity and Recovery after Stop of Application

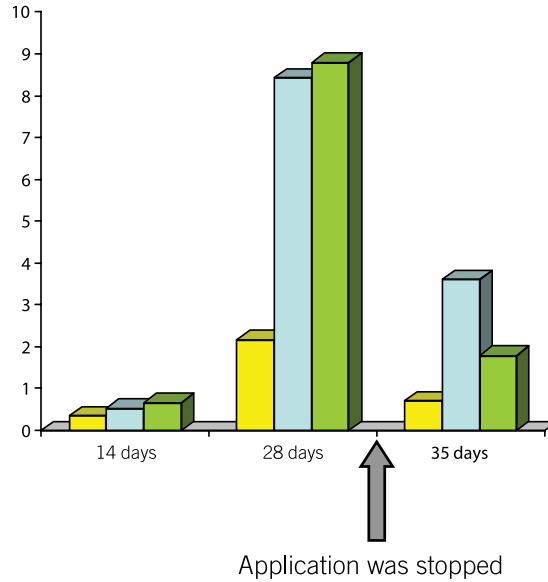
Increase in skin lightening (%)

Formulations were applied by 5 volunteers (pilot study) twice daily on the inner forearm.

After 28 days the application was stopped.

Values are related to initial conditions.

- Placebo
- 2% Bellis Perennis Flower Extract
- 2% Arbutin



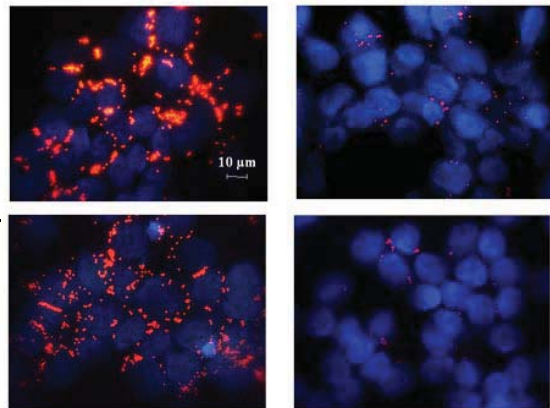
Phagocytotic Activity - Fluosphere Uptake

Fluosphere uptake (%)

Microscopic images showing the Fluosphere (red beads) uptake in control and in Bellis Perennis Flower Extract treated human keratinocytes.

For visualization of the phagocytosis cells were counterstained with DAPI (blue nuclei).

Phagocytosis was stimulated by UV light.



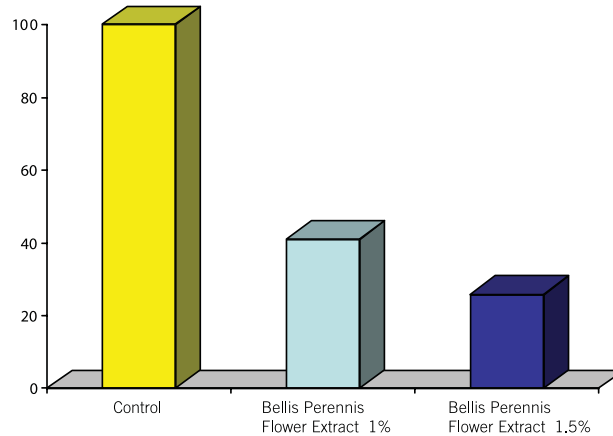
control

1% Bellis Perennis Flower Extract

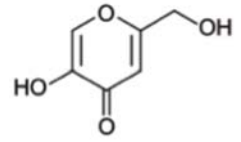
Reduction of Phagocytotic Activity

Phagocytotic activity
Fluosphere uptake (%)

Phagocytosis was induced with UV. The uptake of Fluospheres was detected with a fluorescence reader at 582 nm / 612 nm.



Kojic Acid – A chelation agent with antibacterial and antifungal properties produced by several species of fungi, especially



Kojic Acid

Aspergillus Oryzae, which has the Japanese common name “koji” and is a by-product in the fermentation process of malting rice, used in the manufacturing of sake, the Japanese rice wine. It is a mild inhibitor of the



formation of pigment in plant and animal tissues, and is used in food and cosmetics to preserve or change substance colors - lightening skin and treating skin diseases like melasma.

Azelaic Acid – Azelaic acid is a naturally occurring dicarboxylic acid derived from potato tuber that reversibly inhibits tyrosinase activity. Oxygenating oleic acid, an unsaturated fatty acid found in milk fats or potatoes, creates Azelaic Acid. Its growing role as a “pigment emulsifier” can be traced to its being a component of the great natural emulsifiers called “phospholipids”.

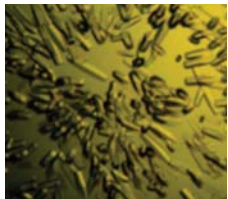
Azelaic Acid has been shown to be effective in the treatment of hyperpigmentation (including melasma). It is at least as effective as hydroquinone but it is less irritating and much better tolerated. It also has exfoliating and disinfecting properties. Azelaic acid is also effective in the treatment of comedonal and inflammatory acne, where it has been shown to be as effective as topical tretinoin, benzoyl peroxide, erythromycin and oral tetracycline. Azelaic acid



Red Potatoes

has been shown to be an anti-keratinizing agent, displaying anti-proliferative cytostatic effects on keratinocytes and modulating the early and terminal phases of epidermal differentiation. In addition, azelaic acid has been shown to be effective in the treatment of rosacea and has anti-tumorigenic power, and has synergy with AHAs and BHAs.

Thermus Thermophilus Ferment – A microorganism found off the deep sea Gulf of California. It is comprised of a cocktail of proteins including enzymes that are particularly effective at mopping up free radicals produced by UV exposure. The testing on this strain, via accelerated conditions, showed that 6 months of use prevented 5 years of aging! It worked to protect against age-spots, wrinkles and blemishes. It did so by protecting fibroblasts against the pro-oxidizing attack of free radicals.

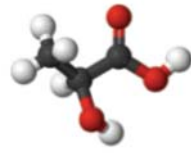


Thermus Thermophilus

This strain is a powerful anti-oxidant activated by heat and light and its activity is favorably comparable to Vitamin

E. *Thermus Thermophilus Ferment* also stimulates keratinocyte differentiation and maturation; it strengthens stratum corneum resistance against aggression – protecting against UV damage (lipoperoxidation, DNA and fibroblasts oxidation, and skin enzyme inactivation).

L-Lactic Acid – Lactic acid, a gentle AHA exfoliant also known as milk acid, is noted for its rich moisturizing attributes and its ability to exfoliate dead skin cells without provoking skin irritation. Increasing desquamation and evenly thinning the stratum



L-Lactic Acid

corneum, lactic acid is well known for its skin hydrating and rejuvenating properties. A gentle, yet very effective anti-aging treatment, lactic acid also presents the added benefit as a skin softening agent which makes it an excellent option for sensitive skin types.

- Diminishes fine lines and wrinkles
- Reduces the appearance of age spots
- Reduces hyperpigmentation
- Improves skin texture
- Stimulates collagen production

Glycyrrhiza Glabra (Licorice) Root Extract

– The English name licorice is derived from “liquiritia,” itself a corruption of the ancient name *Glycyrrhiza*, which now serves as the scientific generic name for the plant group. Licorice is a member of the legume (Fabaceae) family whose roots and stems are very rich in monoammonium glycyrrhizinate.

Licorice extract contains a multitude of fractions that play distinctly different roles.

Dipotassium Glycyrrhizinate is water soluble, and a natural anti-inflammatory, used in sensitive skin components. Testing has shown that it also has anti-hyaluronidase activity (fights the breakdown of Hyaluronic acid), UV erythema reduction and inhibits histamine release. *G. glabra* Glabridin has antioxidant properties, UV absorbing action, in addition to comparatively higher tyrosinase-inhibition activity than either Kojic Acid or Ascorbic Acid, and is a very safe



Licorice Plant

ingredient. Stearyl Glycyrrhinate is oil soluble and has natural anti-inflammatory properties, according to extensive testing. Other fractions have antimicrobial activity and Super-Oxide Dismutase-like activity.

Gamma-Aminobutyric Acid (GABA)

– GABA is a non-essential amino acid found naturally in beans, brewer's yeast, dairy products, eggs, fish, legumes, meat, nuts, seafood, seeds, soy, whey, and whole grains.



This amino acid contains skin lightening properties because of its activity as a tyrosinase inhibitor. Also, when the cutaneous barrier is disrupted, application of GABA, which binds to a specific receptor, can help repair it and prevent the hyperplasia that can follow barrier disruption. Topically, GABA acts as an antioxidant that has inhibitory effects on the deeper pigmentation caused by aging and free radical damage. It is worth noting that, in the brain, GABA has neurotransmitter activity, but this is not true for the skin.

Sodium Ascorbyl Phosphate – Derived from citrus fruits, sodium ascorbyl phosphate is a hydrophilic derivative of ascorbic acid, which has improved stability arising from its chemical structure; a stable salt-form of vitamin C that is able to sustain its presence in the skin longer and enhance its reactivity with the skin.

Sodium ascorbyl phosphate has been shown to be stable in both types of o/w and w/o microemul-



sions composed of the same ingredients for topical delivery. It is used in cosmetic and pharmaceutical preparations since it has many favorable effects in the skin, the most important being antioxidant action. In order to achieve this, it has to be converted into free ascorbic acid by enzymatic degradation in the skin. Several forms of topical Vitamin C have been shown to reduce melanin formation, encouraging skin brightening. These include L-ascorbic acid, magnesium ascorbyl phosphate and sodium ascorbyl phosphate; these play an antioxidant role as well.

Epigallocatechin Gallate (EGCG) – The active constituents in green tea are the catechin polyphenols called Epigallocatechin Gallate (EGCG). Green tea catechins are commonly derived from the plant *Camellia Sinensis*. The polyphenols in green tea are responsible for its medicinal properties. These include catechin (C), gallic acid (GC), epicatechin (EC), epigallocatechin (EGC) and epigallocatechin gallate (EGCG).

Green tea catechins are potent antioxidants that provide health benefits beyond their ability to neutralize free radicals. The polyphenolic catechins in the *Camellia Sinensis* have antibacterial effects on *Streptococcus*, in addition to inhibiting viral infections. It is also anti-inflammatory, but can be sensitizing to certain individuals.

Retinol – Retinols/Retinoids are the precursors to Vitamin A. Remember that retinoids (all-trans retinoic acid or tretinoin) are the prescription ingredient in Retin-A® or Renova®

and retinols are the less irritating ingredients available in a wide variety of products, accelerating cellular renewal and assisting in collagen synthesis. All of the natural and synthetic derivatives of Vitamin A (also called all-trans retinol) are included in a group known as retinoids.

Retinoids have many important biologic effects: they regulate growth and differentiation of epithelial cells, diminish malignant cell growth, decrease inflammation, and enhance the immune system. The discovery that Vitamin A derivatives or molecules that interact with retinoids receptors have beneficial effects in many skin diseases, particularly acne, has been one of the major therapeutic advances in dermatological therapy.

Retinol is a pro-drug that can be converted to retinoic acid by the skin (it will be changed to all-trans retinoic acid within the keratinocytes and become active). Topical retinoids promote the normalization of follicular epithelial desquamation and reduce cellular cohesion, promoting drainage of existing comedones and preventing the development of microcomedones (the precursor of all acne lesions). Retinoid products are better used at night, when degradation by light is minimal. It is important for patients on retinoids of any kind to apply sunscreen daily, as retinoid use is associated with increased photosensitivity.

Ursolic Acid – Ursolic acid is present in many plants, especially in extracts of rosemary, Greek sage (*Salvia Triloba*), oleander, periwinkle and spike



Retinol Molecule

lavender and contains anti-inflammatory, antitumor, and antimicrobial properties. Through the inhibition of human leukocyte elastase, an enzyme that catalyzes rupture of the cell membranes in inflamed tissues, ursolic acid inhibits inflammation and maintains structural integrity of cells and the intercellular matrix. It also inhibits 5-lipoxygenase and cyclooxygenase activity. Ursolic acid also increases ceramide and collagen and preserves the structure of collagen fibers. These properties, together with its inhibition of elastase activity, make it a good anti-aging and anti-wrinkle ingredient. Other activities reported for ursolic acid include: antihistaminic, antiviral, cancer preventive.



Salvia Triloba

Nymphaea Coerulea (Blue Lotus) Seed Extract – Extremely rich in phytosterols and flavonoids (rutin and quercetin), which provide potent antioxidant and immune-enhancing effects; promotes microcirculation, antibacterial support, and anti-inflammatory benefits to calm the skin.



Blue Lotus Flower

Epilobium Angustifolium (Willow Herb) Extract – A member of the evening-primrose family, willow herb provides



Willow Herb Flower

a good natural alternative to hydrocortisone and is a naturally soothing, anti-inflammatory botanical. The main

bioactive molecule found in Canadian willow herb extract is oenothein-B. This molecule has been patented for its wide ranging bioactivity including anti-viral, antitumor, and anti-hyperandrogenic applications and also has demonstrated free radical scavenging ability. It has been shown that the extract kills *Propionibacterium acne*, the bacterium associated with acne.

COMPOSITION

Aqua (Water), Alcohol Denatured, Witch Hazel (*Hamamelis Virginiana*) Water, Glycerin, Arbutin, *Bellis Perennis* (Daisy) Flower Extract, Kojic Acid, Polysorbate 20, Azelaic Acid, *Thermus Thermophilus* Ferment, L-Lactic Acid, *Glycyrrhiza Glabra* (Licorice) Root Extract, Gamma-Aminobutyric Acid (GABA), Sodium Ascorbyl Phosphate, Epigallocatechin Gallate (EGCG), Retinol, Xanthan Gum, Ursolic Acid, *Nymphaea Coerulea* (Blue Lotus) Seed Extract, *Epilobium Angustifolium* (Willow Herb) Extract, *Lavandula Angustifolia* (Lavender) Oil, *Jasminum Officinale* (Jasmine) Flower Oil, *Pogostemon Cablin* (Patchouli) Oil, *Citrus Sinensis* (Sweet Orange) Oil, Methylcellulose